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## INVESTIGATION OF THE THORACIC ELECTRICAL IMPEDANCE DURING ENDOTOXEMIA IN DOGS

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The purpose of our study was to examine the effect of sustained low-dose endotoxin infusion on changes in thoracic electrical impedances ( $Z_0$  at end-expiratory apnoea,  $Z_{\max}$  at end-inspiration),  $Z_{\max}-Z_0$ , hematocrit (H) values, and extravascular lung water (EVLW) estimated with gravimetric analysis (WW/DW) and the impedance method ( $dEVLW_{\text{imp}}$ ) in anesthetized dogs. To define the role of H in changes in the  $Z_0$  and  $Z_{\max}$ , we applied splenectomy. To determine whether changes in respiration might be involved in changes in  $Z_0$  and  $Z_{\max}$ , mechanically ventilated dogs were examined. During the infusion of endotoxin there was an increase in  $Z_0$ ,  $Z_{\max}$ , H and the respiratory rate in the spontaneously breathing dogs. In splenectomized dogs both impedances slightly increased without any significant change in H. In the ventilated dogs  $Z_0$  and  $Z_{\max}$  increased similarly, and H increased to a slightly lower level than in the spontaneously breathing dogs. In the ventilated-splenectomized dogs no changes were found in the impedances and in H. The EVLW values showed no serious edema in the endotoxemic groups. The results suggest that  $Z_0$  increased mainly in association with the increase in H. The  $Z_{\max}-Z_0$  parameter proved to be a suitable parameter for demonstrating the changes in respiration.

### Introduction

The constant (thoracic tissues) and changing (resistivity of blood, gas and fluid volume) factors in the thorax may contribute to the basal thoracic electrical impedance ( $Z_0$ ). Any change in these parameters would be expected to cause change in  $Z_0$ . As  $Z_0$  is determined, in part, by blood resistivity, it seems likely that changes in H may have effect on  $Z_0$ . An earlier report demonstrated a linear relationship between changes in lung volume and in  $Z_0$  during breathing [1]. As  $Z_0$  increases during inspiration, measurements of this parameter at end-inspiration ( $Z_{\max}$ ) can be used to monitor the respiratory changes. Another study [4] showed that there was an altered ratio of air to fluid volume and lung resistivity in serious sepsis and this can be attributed to pulmonary edema, atelectasis and the altered hemodynamics in the lung. Therefore we designed a series of experiments to investigate the effect of endotoxemia induced by prolonged, slow infusion of a low dose of endotoxin on the thoracic impedances. Our purpose was to study 1. the change in  $Z_0$ ,  $Z_{\max}$ , H and respiration, 2. the role of H in  $Z_0$  changes, 3. the effect of respiration on changes in  $Z_0$  and  $Z_{\max}$ , 4. the extravascular lung water (EVLW).



## Methods

Mongrel dogs of both sexes were anesthetized with sodium pentobarbital (30 mg/kg iv). Impedance cardiography system was used to measure the thoracic impedances ( $Z_0$ ,  $Z_{\max}$ ), and cardiac output was calculated according to an empirical equation [2]. Hemodynamic parameters (arterial blood pressure, central venous pressure, pulmonary arterial pressure, systemic vascular resistance), arterial blood gas parameters ( $pO_2$ ,  $pCO_2$ , pH), hematocrit (H), respiratory rate ( $R_f$ ) and white blood cell counts were measured or estimated. At the end of experiments  $Z_0$  values were used to estimate EVLW ( $dEVLW_{imp}$ ) [3], and lungs were removed for the gravimetric analysis (WW/DW). Four protocols were performed in this study: I.1. control group (*CONT*, n=8): saline infusion. 2. endotoxin group (*ETX*, n=9): endotoxin infusion (120 minutes): 7.25  $\mu$ g/kg during 45 minutes, 6.25  $\mu$ g/kg during 75 minutes. II.1. splenectomized control group (*SPL CONT*, n=5): saline infusion after splenectomy. 2. splenectomized endotoxin group (*SPL ETX*, n=6): endotoxin infusion at the same rate as the *ETX* group. III.1. ventilated control group (*RESP CONT*, n=6): saline infusion. 2. ventilated endotoxin group (*RESP ETX*, n=9): endotoxin infusion at the same rate as the *ETX* group. IV.1. ventilated-splenectomized control group (*RESPL CONT*, n=5): saline infusion. 2. ventilated-splenectomized endotoxin group (*RESPL ETX*, n=6): endotoxin infusion at the same rate as the *ETX* group. Nonparametric tests were used for the statistical analysis, and a value of  $P < 0.05$  was considered significant.

## Results

Hemodynamic data showed no serious septic responses in our model of endotoxemia. In the *ETX* group  $Z_0$ ,  $Z_{\max}$  and  $Z_{\max}-Z_0$  significantly increased up to the end of endotoxin infusion. Then  $Z_0$  decreased toward the baseline value more than  $Z_{\max}$ .  $Z_{\max}-Z_0$  remained elevated up to the end of experiments. In the *SPL ETX* group there was only a moderate increase in  $Z_0$  and  $Z_{\max}$ , and there was a rise in  $Z_{\max}-Z_0$  at the beginning of the infusion. In the *RESP ETX* group thoracic impedances increased more slowly and to a lower value than in the *ETX* group. There were no significant changes in the impedances in the *RESPL ETX* group. In addition, no changes in  $Z_{\max}-Z_0$  were observed in the two *RESP ETX* and *RESPL ETX* groups. There was a significant increase in H only in the *ETX* and *RESP ETX* groups in response to endotoxin infusion.  $R_f$  increased significantly in *ETX* and *SPL ETX* groups.  $pO_2$  increased initially, then decreased in the *ETX* and *SPL ETX* groups. Serious pulmonary edema did not occur in the endotoxemic groups as shown by both types of EVLW measurements.

## Discussion

We investigated the effect of a prolonged low-dose endotoxin infusion on the changes of  $Z_0$ ,  $Z_{\max}$  and  $H$ , and the role of changes in  $H$  and respiration in the impedances. Our results indicated that endotoxemia increased thoracic impedances,  $H$  and changed respiration. There was a significant effect of  $H$  on  $Z_0$  changes as shown by the splenectomized dogs. Changes in respiration can be estimated with measuring the  $Z_{\max}-Z_0$  parameter. Our findings showed that serious pulmonary edema did not occur in the endotoxemic groups as indicated by the  $dEVLW_{\text{imp}}$  and the  $WW/DW$  measurements. We conclude that the thoracic impedance method can be used successfully to detect changes in respiration and to estimate EVLW changes in the thorax.

## Summary

The noninvasive measurements of the changes in thoracic impedances can be used continuously to monitor the fluid and gas shifts in the thorax.

## Acknowledgements

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## **TECHNIQUE AND RESULTS OF DUODENUM-PRESERVING RESECTION OF THE HEAD OF THE PANCREAS IN THE TREATMENT OF CHRONIC PANCREATITIS**

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Surgical treatment of chronic pancreatitis is either by ductal decompression or resection of the pancreas. Among various resection operations the duodenum preserving resection of the head of the pancreas is the newest surgical technique. At the 2nd Dept. of Surgery of Debrecen Medical University duodenum preserving resection of the head of the pancreas with simple modified reconstruction was performed in 22 patients with chronic pancreatitis. The authors evaluate the early and late results: there was no mortality. The rate of complication was 27,2%. Considering late results complete relief of pain was found in about 80% of patients. The authors suggest that this type of resection can be well applied in the treatment of chronic pancreatitis with low risk and relatively good late results.

### **Introduction**

Surgical management of patients with chronic pancreatitis is either by ductal decompression [3] or resection of the pancreas [4]. The duodenum and stomach preserving resection of the head of the pancreas is a newer method, which was introduced with the aim to save the highest possible endocrine and exocrine pancreatic function [2].

### **Patients and Methods**

At the 2nd Dept. of Surgery of Debrecen Medical University 22 duodenum preserving resection of the head of the pancreas were performed for chronic pancreatitis between 1991 and 1996. All the patients were male and the average age of them was 42,2 years, ranging between 29 and 56 years.

Considering the aethiological factors alcohol abuse was found in 21 patients and unknown aethiology was in one patient. The main symptom was the abdominal pain (in all patients).

Insulin dependent diabetes mellitus was present in 3 patients, non-insulin dependent diabetes mellitus in one patient.



Preoperative diagnosis was performed by ultrasound, computerised tomography and endoscopic retrograd cholangio-pancreatography showing enlargement of the head of the pancreas and duct deformities.

During resection of the head of the pancreas the mesoduodenal vessels were preserved by leaving a little pancreatic tissue at the duodenal rim. The resection line of the remnant pancreatic head was sutured. Then one layer anastomosis was performed between the cut surface of the distal pancreas and the posterior wall of the stomach.

## Results

From the 22 operated patients 16 recovered without complications. We reoperated one patient because of bleeding from the retroperitoneum on the 4th postoperative day. Pancreatic juice have been drained for 8 and 15 days respectively in two patients. Bile leakage has been observed through the drain in one case for 10 days. Two patients had required gastric suction for 6 and 10 days respectively. The hospitalisation period varied between 14 and 38 days, 17,5 days on average. There was no hospital mortality. Considering the late results 1 patient was excluded from the evaluation because he disappeared 1 year after the operation. No patient has died during the follow-up time (average 2 years). Abdominal pain was stopped after the operation in 80,9% of the patients and only one patient (4,8%) had recurrent strong pain. In 47,6% of patients the body weight has not changed, in 8 cases (38,1%) has increased (average 4,2 kg) and in 3 patients (14,3%) has decreased (average 3,3 kg). Two patients had frequent diarrhoea despite pancreas exocrine substitution. Oral glucose tolerance test was performed in 18 patients. Cases IDDM were not tested. As compared with the preoperative condition it can be found that in one IDDM has been developed (one diabetic patient was excluded from the evaluation). Glucose tolerance was normal in 12 patients (against the preoperative 11). Number of patients with NIDDM has increased (from 1 to 3).

## Discussion

Beger et al. described first the duodenum preserving resection of the pancreatic head [1]. We have performed duodenum preserving pancreatic head resection when the chronic inflammatory head of the pancreas had not caused icterus and dilatation of the common bile duct and serious duodenum stenosis. In these cases with the preservation of the duodenum the common bile duct has remained intact so the operative risk has been lower without biliodigestive anastomosis. We applied pancreatogastrostomy in reconstruction of the duodenum preserving resection of the head of the pancreas. The pancreatogastrostomy was technically easier to perform than pancreatojejunostomy and with regard to pain relief Pain and Knight suggested that pancreatogastrostomy gave better results than pancreatojejunostomy [5]. There was no early and late mortality and only one patient needed reoperation because of bleeding. The rate of the complication

was 27,2%. Seventeen (80,9%) out of 21 patients were free of pain and only one (4,8%) had strong abdominal pain. These data are similar to other's late results [4]. Changes of body weight are different in the literature in our cases the unchanged weight was characteristic (47,6%). According to these data we think that duodenum preserving resection of the head of the pancreas is an effective operative method in the treatment of chronic pancreatitis. Without intrapancreatic stricture of the common bile duct and serious duodenum stenosis our method following resection of the pancreas can be applied with safety.

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## **OPERATIVE HYSTEROSCOPY: MINIMALLY INVASIVE SURGERY TO CONTROL OF MENORRHAGIA**

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Diagnostic hysteroscopy is a valuable method for evaluation of intrauterine disorders. After diagnosing, the endoscopic treatment of these pathologies is the major question of past decade. Possibility of solving cause of infertility or abnormal uterine bleeding without laparotomy or hysterotomy/hysterectomy is the great advantage of operative hysteroscopic methods. In Department of Obstetrics and Gynaecology of University Medical School of Debrecen more than 1400 hysteroscopic interventions were performed from 1 September 1989 to 31 December 1996. In treatment of intractable uterine bleeding 347 operative hysteroscopy (targeted biopsy, polypectomy, transcervical endometrial ablation, fibroid resection etc.) were performed. The rate of complications was low, only 2% (4 perforations and 2 bleedings). The high success rate and low rate of complications offers a modern, safe, minimally invasive method for treatment of menorrhagia.

### **Introduction**

Abnormal uterine bleeding is a common complaint in gynaecology. The precise diagnosis is essential for correct therapy. D&C (dilatation and curettage) has been used for diagnosing causes of bleeding, but this blind method misses focal pathologies in 30–50% of cases. Hysteroscopy gives the possibility of accurate diagnosis and operative hysteroscopy offers the possibility to remove focal lesions, i.e. submucous myoma, polyps etc. The new high frequency (HF) surgical instrument, the resectoscope is the ideal tool for intrauterine surgery [1]. Transcervical resection of myoma (TCRM) and transcervical resection of endometrium (TCRE) is the only method to conserve the uterus in case of intractable uterine bleeding with minimal risk of complications [2].

### **Methods**

From 1. September 1989 to 31. December 1996 347 operative hysteroscopic interventions were performed for treatment of menorrhagia in the Department of Ob./Gyn. of University Medical School of Debrecen. The indications were abnormal uterine bleeding, unsuccessful conservative treatment or suspicious transvaginal ultrasonographic findings (e.g. pathologic thickness of endometrium, foreign body, fibroid, polyp etc.). The mean age of patients was 44,8 years (range 28–84 years). Diagnostic hysteroscopic examinations were performed with an 8 mm continuous-flow



diagnostic hysteroscope and operative interventions were carried out using a continuous flow resectoscope fitted with a 90° wire loop (Karl Storz GmbH, Tutlingen). Uterus distension was achieved with 1,5% sterile glycine solution delivered by gravity pressure or Hamou Hysteromat pump (Karl Storz GmbH, Tutlingen).

## Results

During the examined period 128 targeted biopsies, 71 polypectomies, 60 transcervical endometrial ablations, 40 fibroid resections, 39 foreign body removals and 9 transcervical endometrial resections combined with fibroid resections were performed. During these 347 hysteroscopic procedures 6 complications (2%) emerged: 4 perforations and 2 cases of bleeding. In only 2 of these above cases was hysterectomy necessary to solve the problem. The follow up shows the success rate of TCRE to have been 89% and of TCRM: 95%, and of polypectomy: 98% .

## Discussion

Our results are closely to other published figures [3,4]. Operative hysteroscopy offers women with menorrhagia safe, minimally invasive surgery method with minimal risk, and savings cost (one day surgery) and the expensive time for doctors and patients.

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## **FREQUENCY OF LOCOREGIONAL AND AXILLARY RECURRENCES AMONG PATIENTS FOLLOWING BREAST CANCER OPERATIONS**

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Our department performed 554 operations for breast cancer between 01. 01. 1986 and 31. 12. 1995. When following up these 554 patients, we recognized local recurrences, axillary and neck-region lymphonode recurrences in 32 cases (5.8%). Breast conserving procedure was introduced at our department within the period above. What our experience proves is, that the raise in the frequency of breast conserving procedures did not make the rate of locoregional recurrences grow. Together with applying breast conserving procedures we extended the application of axillary block dissections, in terms of indications, and also of numbers of lymphonodes removed. The past five years axillary recurrences did not appear among our patients.

### **Introduction**

Our department performed 554 operations for breast cancer between 01.01.1986 and 31.12.1995. Regarding their age, general condition, histology, lymphonode status, our patients went through chemo- and radiotherapy, which was performed at the Department of Oncoradiology of the county Hospital. When following up these 554 patients, we recognized local recurrences, axillary and neck-region lymphonode recurrences in 32 cases (5.8%).

### **Methods and Results**

We classified the same 554 patients respecting the Springer Hungarica TNM Atlas:

- St. T<sub>1</sub>: 166 patients (30%)
- St. T<sub>2</sub>: 241 patients (43.5%)
- St. T<sub>3</sub>: 31 patients (5.6%)
- St. T<sub>4</sub>: 108 patients (19.5%)
- St. T<sub>x</sub>: 8 patients (1.4%).

As a tendency, the number of early breast cancer (T<sub>1</sub>N<sub>0</sub>) showed growing, but the number of other stadiums did not decrease to the same degree. This is not the case at departments applying a wide range of screening methods [1]. The lymphonode status of 76 patients (13.7%) was unknown. The past five years this rate was reduced under 8%. 55.3% of T<sub>1</sub> and T<sub>2</sub> together did not have axillary recurrences,

while this rate is 26.9% among T<sub>3</sub> and T<sub>4</sub>. We started to introduce breast conserving procedures published by Fisher and Veronesi in 1989, being a bit late with it compared to Hungarian publications. [5] Together with applying breast conserving procedures we extended the application of axillary block dissections. [3]

32 patients (5.8%) went through operation for local recurrences, axillary and neck-region lymphonode recurrences. The past five years axillary recurrences were not recognized. Axillary recurrences are rarely referred in publications either. [5, 4] As treatment, we performed breast ablation in 2 cases, while excision in all other cases. 18 patients underwent chemo- and radio-therapy as adjuvant therapy. The histo-pathological classification of the 32 patients is as follows: in 29 cases cc duct. infiltr., in 2 cases cc. duct. infiltr. Paget-disease type, in 1 case cc. medull. anaplast type.

15 patients went through operation for local recurrences, 2 more patients for local and axillary recurrences in coincidence. Bilateral breast cancer was found in cases of 2 patients of the 17. The appearance of recurrences dispersed in time between 3 months and 10 years. 2 patients had local recurrences after breast conserving procedure, the final surgical treatment being breast ablation. [2] The lymphonode status of the 17 patients mentioned above was as follows: 5N<sub>x</sub>, 5N<sub>1-2</sub> 2 patients of this group have already died.

### Summary

Within the 10 years' period the raise in the frequency of breast conserving procedures did not make the rate of locoregional recurrences grow. Together with applying breast conserving procedures we extended the application of axillary block dissections. The past five years axillary recurrences did not appear among our patients.

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## PENETRATING KERATOPLASTY FOR PSEUDOPHAKIC BULLOUS KERATOPATHY

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Corneal decompensation after cataract surgery and intraocular lens (IOL) implantation has become the leading indication for penetrating keratoplasty during the past decade. We reviewed the clinical course and the surgical management of 212 patients with penetrating keratoplasty for pseudophakic bullous keratopathy treated at our Department during the last 15 years. Corneal transplantation for pseudophakic bullous keratopathy was successful in 76%. One third of the patients achieved a long-term visual acuity of 0.5 and more. At keratoplasty the original IOL was left in place in 129 eyes. We removed from and not replaced the IOL in 37 eyes and we performed IOL exchange in 46 eyes. The secondary IOL was an angle-supported flexible anterior chamber lens in 40 cases, and a suture fixated posterior chamber lens in 8 cases. During the penetrating keratoplasty for pseudophakic bullous keratopathy the most important question is how to manage the previously implanted intraocular lens. We have to decide whether the intraocular lens should be removed or replaced at the time of surgery. The choice of removing, retaining or replacing the intraocular lens at keratoplasty depends on the variable intraocular pathological conditions and each case requires individual evaluation.

**Keywords:** Corneal transplantation, intraocular lens implantation

### Introduction

Corneal decompensation after cataract surgery and intraocular lens implantation has become the leading indication for penetrating keratoplasty during the past decade in the United States. The reasons for this are numerous. The number of cataract extractions was increasing and the average age of the patients with whom surgery is done also became higher. Cataract surgical technique was changed. Intracapsular cataract extraction has been almost completely replaced by extracapsular cataract surgery with intraocular lens implantation. This combined procedure may cause increased intraocular trauma to the corneal endothelium. Late corneal endothelial cell loss may develop postoperatively related to the toxic effect and the inaccurate positioning of the implant [1].

### Methods

We evaluated a series of 1590 cases with keratoplasty (1534 penetrating and 56 lamellar cases) performed at our Department during the last 15 years and analyzed the clinical indications for penetrating keratoplasty. We reviewed the clinical course and

the surgical management of 212 patients with penetrating keratoplasty for pseudophakic bullous keratopathy treated during this period. We focused on the management of the intraocular lenses at the time of surgery.

## Results

While 10–15 years ago pseudophakic bullous keratopathy was a rare indication for penetrating keratoplasty at our Department, in the past 4 years it became one of the first 3 most common reasons for corneal transplantation. Penetrating keratoplasty for pseudophakic bullous keratopathy was successful in 76%. One third of the patients achieved a long-term visual acuity of 0.5 and more.

The previously implanted intraocular lens was an anterior chamber IOL in 141 eyes, iris claw lens in 2 eyes, and a posterior chamber IOL in 69 eyes. The original IOL was left in place in 129 eyes. We removed from and did not replace the IOL in 37 eyes and we performed IOL exchange in 46 eyes. The secondary IOL was an angle-supported flexible anterior chamber lens in 40 cases, and a suture fixated posterior chamber lens in 8 cases (6 sulcus fixated, 2 iris fixated).

## Discussion

Pseudophakic bullous keratopathy has become an important complication of cataract surgery and the leading indication for penetrating keratoplasty [1]. During penetrating keratoplasty for pseudophakic bullous keratopathy the most important question is how to manage the previously implanted intraocular lens [3]. The management is depending on lens-related factors and on the nature and the degree of anterior segment abnormalities. A pseudophakos can be retained, if the lens is in good position and appears stable, the eyeball is quiet and the pupil is mobil. The lens should be removed and not replaced in patients with recurrent hemorrhages, uncontrolled glaucoma or chronic iritis resistant to medical treatment, after other causes are ruled out. IOL exchange is recommended in cases of all closed loop, semiflexible anterior chamber lenses, iris-supported or unstable lenses, as such lenses have been increasingly associated with corneal decompensation and with poor macular function post-operatively. Due to the presence of synechiae around the haptics in the angle and strong adhesions to the iris, vitreous and capsular bag, such lenses may be difficult to remove at the time of corneal transplantation. To avoid complications during removal of the lens implant the loops must be cut through, the lens has to be separated carefully and rotated gently to free it from the fibrous tissue. If the anterior and posterior chambers are filled with dense fibrous material a complete anterior segment reconstruction is indicated. In the absence of a possibility for capsular support we may implant sutured-in posterior chamber lenses or angle - supported flexible anterior chamber lenses. Currently the first possibility has become more popular [2].

## Summary

During the penetrating keratoplasty for pseudophakic bullous keratopathy we have to decide whether the intraocular lens should be removed or replaced at the time of surgery. The choice of removing, retaining or replacing the intraocular lens during keratoplasty depends on the variable intraocular pathological conditions and each case requires individual evaluation.

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## **SCLERAL REINFORCEMENT IN PROGRESSIVE MYOPIA AND INTRAOPERATIVE ULTRASOUND CONTROL OF THE CADAVER FASCIA LATA STRIP**

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Scleral reinforcement (sustentaculum sclerae) is one of the operations against myopia. During the progression of myopia the eye grows. The chorioretinal layer can only moderately follow the expansion of the sclera, and mostly this is the cause of the complications that can cause permanent visual acuity decrease. The aim of the operation is to strengthen the posterior part of the sclera by implantation of a cadaver fascia lata strip, that slows down or stops the expansion of the eyeball, and this way prevents the development of complications. At our Department we perform the Snyder-Thompson technique. Between 1984 and 1994 343 operations were performed at our Department. We followed up the changes of the axial lengths by ultrasound (A-mode) examinations. The axial length decreased in 43,7% remained unchanged in 22,2% and increased in 34,1% of the cases. We controlled the location of the strip intra- and postoperatively with B-mode ultrasound. Nowadays scleral reinforcement is still the only possibility to stop or slow down the expansion of the eyeball in cases of progressive high myopia.

**Keywords:** scleral reinforcement, progressive myopia, intraoperative ultrasound control

### **Introduction**

The main pathological change in progressive myopia is the expansion of the eye-ball [2]. This can cause many complications, such as early degenerative changes of the vitreous body, subretinal haemorrhage in the macular region, peripheral degeneration of the retina, and retinal detachment [1]. These complications can be responsible for the visual impairment of the patients. At present the only surgical procedure that may prevent or stop the increase of the axial length of the globe is scleral reinforcement [5]. At our Department we use the Snyder-Thompson technique [4].

### **Method**

The process of surgery is as follows: After the mobilization of the conjunctiva around the limbus we put a thread underneath the rectus muscles (except the inferior one) and the inferior oblique muscle. Then we put the cadaver fascia lata strip under the muscles and push it back with the help of a curved forceps. The fascia lata strip previously had been sterilized by  $\gamma$  radiation and soaked in antibiotic solution preoperatively. After the strip had been carefully positioned at the posterior pole of the globe right by the temporal side of the optic nerve we fix both ends of it onto the sclera by stitches at the nasal side of the insertions of the superior and inferior rectus muscles [3]. At the end of surgery we check the position of the fascia lata strip by B mode ultrasound. If on examination the strip is

not situated in the right position (right at the temporal side of the optic nerve), we perform the reposition of the strip during the same operation.

## Results

Between 1984 and 1994 343 operations were performed at our Department. We followed up the changes of the axial lengths by ultrasound (A-mode) examinations. The axial length decreased in 43,7% remained unchanged in 22,2% and increased in 34,1% of the cases. We controlled the location of the strip intra- and postoperatively with B-mode ultrasound. The fascia lata strip was in the proper position in 211 eyes (61.6%), was temporally displaced in 33 eyes (9.5 %), could not be detected on B scan in 99 eyes (28.9%). The refraction (best correction) of the eyes became higher in 55 eyes (16.1%), lower in 166 eyes (48.5%), did not change in 122 eyes (35.4%).

## Discussion

During the progression of myopia the eye grows, the axial length of the bulb becomes longer. The chorioretinal layer can only moderately follow the expansion of the sclera, and mostly this is the cause of the complications: subretinal haemorrhage in the macular region, peripheral degenerations of the retina that sometimes results in retinal detachment, early degenerative changes of the vitreous body [1, 2].

The aim of the operation is to strengthen the posterior part of the sclera by implantation of a cadaver fascia lata strip. During the operation we put a cadaver fascia lata strip under the superior, inferior, external rectus, and the inferior oblique muscles and push it back so that the implant supports the posterior pole of the eyeball at the temporal side of the optic nerve. We fix the two ends of the strip onto the sclera by stitches at the temporal side of insertions of the superior and inferior rectus muscles [4].

It is essential to control the location of the strip intra- and postoperatively with B-mode ultrasound and make corrections if necessary. Failures can be avoided this way.

Nowadays scleral support by the implantation of a fascia lata strip is the only way to stop or slow down the expansion of the eyeball in cases of progressive high myopia, any modification that makes this surgical procedure more safe and more effective is very important.

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## **PANCREATIC PSEUDOCYST PROPAGATING INTO RETROPERITONEUM AND MEDIASTINUM**

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The extrahepatic pseudocysts of pancreatic origin sometimes propagate into mediastinum and retroperitoneum. A large pseudocyst of pancreatic origin propagating into the mediastinum up to the aortic arch is published. The surgical intervention has been urged by the dislocation of the heart, by the danger of autodigestion of the mediastinal aorta and by the danger of rupture. Attention is directed to the external drainage operation which is suitable for emptying of the pseudocyst not independently from the ripeness of pseudocyst wall and the characteristics of the pseudocyst content. Should the time short after the exacerbation and should the amylase content high in the cyst, the immediate result of external drainage better and reliable safe.

### **Introduction**

The occurrence of pseudocysts in the pancreatic disease is about 17–25% [1,2,3,4]. The extrapancreatic pseudocysts are most frequently found in the peripancreatic region. The pseudocyst very rarely propagates into retrocardium.

The danger of rupture exists. Due to the danger of rupture, autodigestion of aorta, so the elective operation of pseudocyst over 20 cm diameter is absolute indicated [5,6,7,8].

### **Materials and Methods**

In our high circulation patient material the number of patients treated and operated because of pancreatic pseudocyst is important and gradually growing. In 1996 we observed a patient because of in retroperitoneum respectively sand-glass-like in retrocardium a multilocular extensive pseudocyst.

### **Result**

We applicated two psychrophore external drainages into the retroperitoneum and mediastinum. The content of pseudocyst emptied. The patient was emitted after two weeks of operation. Complications were not observed.



## Discussion

Our patient is a 36 years old man. In December 1996 he arrived our department from the medical ward. He had got more and more serious epigastric pain. The abdominal ultrasound and computer tomography detected a hydrocyst in diameter 165x77x120 mm. Hydrocyst propagated into retroperitoneum and respectively sand-glass-like in retrocardium. At the first sight we thought aortic aneurysm, because it located beside the abdominal aorta. The ultrasound described turbulence in the multilocular extensive hydrocyst. Finally the colour duplex scan verified the pancreatic pseudocyst. By means of aspiration we gained fluid of high amylase content. The pancreatic pseudocyst gradually expanded. Due to increasing pressure inside the chest, the heart became dislocated, and severe tachycardia appeared. Two psychophore external drainages into the retroperitoneum and mediastinum by Willenegger has been applied at operation.

The postoperativ treatment were rinsing, and wound toilette. We could the drainages eliminate ten days later and emitted on the end of the second weeks. The external drainages most frequent complications is the fistula. But in our case hadn't got any complication.

On basis of our case we direct attention that external drainage operations are suitable for emptying most diversified sized exsudates not independently from the ripeness of pseudocyst wall and the characteristics of pseudocyst content. We analyse the reliable security of diverse preoperative diagnostic possibilities.

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## TRANSABDOMINAL PREPERITONEAL HERNIORRAPHY: TECHNIQUE AND RESULTS

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As enthusiasm for laparoscopic surgery has grown, laparoscopic approaches to the groin hernia have evolved. The most widely accepted laparoscopic repair employs the placement of a large sheet of mesh in a preperitoneal position to cover potential hernia spaces. Between March 1994 and February 1997 160 inguinal and 3 femoral hernia were operated of an transabdominal preperitoneal (TAPP) polypropylen mesh. 131 patients were operated (128 males and 3 females, ranging in age from 19 to 82 years), 31 (23%) of them had bilateral hernias. Recurrent hernia was the indication in 52 (32%) cases. Average operating time for unilateral repair was 80 minutes and for bilateral repairs was 108 minutes. Postoperative complications included 7 (4,3%) cases of transient neuralgias, 20 (12%) cord/scrotal transient seromas-hematomas and 2 (1,2%) hydrocele. The 5 (3,1%) early recurrences were considered to be caused by technical unexperience and/or too small prosthetic patch. The laparoscopic hernioplasty has definitive advantage: minimal postoperativ pain, short hospital stay (average postoperativ time of hospitalization 3,1 days) and early restoration of full physical activity (in 1 to 2 weeks). The method should be considered as a potential "best option" in patients with recurrences and bilateral inguinofemoral hernias.

### Patients and Methods

From March 1994 until February 1997 we have employed the transabdominal preperitoneal (TAPP) repair for groin hernias at the 3rd Surgical Department Semmelweis University Medical School, Budapest and at the General Surgical Department, Nagykanizsa City Hospital. During this time fram, 163 laparoscopic repair were carried out in 131 patients. The age range of this group of patients was 19 to 82 years and there were 128 men (98%) and 3 women (2%). There were 101 (77%) unilateral and 31 (23%) bilateral repairs. Of the 163 hernias repaired 111 (69%) were primary and 52 (32%) recurrent. General anesthesia used for oll patients. Polypropylene mesh was used routinely, to cover all potential hernia spaces in the groin region (Table 1.).

Table 1.  
Data of patients and types of hernias (163 TAPP)

|                              |                                                                       |
|------------------------------|-----------------------------------------------------------------------|
| Number of patients: 131      | 101 (77%) with monolateral hernias<br>31 (23%) with bilateral hernias |
| Distribution by sex, M/F     | 128/3                                                                 |
| Ages of patients in years    | 19-82 (average: 52)                                                   |
| Hernias primary<br>recurrent | 111 (68%, included 3 femorale)<br>52 (32%)                            |



## Operative technique

Three trocars are used. One 10 mm trocar inserted in the umbilical region, and the 30 degree telescope is introduced. Both groin region are inspected. The operative port (12 mm) is placed lateral to the umbilicus on the edge of the rectus abdominis on the opposite side from the hernia. A third 5 mm additional trocar is inserted on the other side of the umbilicus. If bilateral hernias are present, the dissection is initiated on the more symptomatic side first. In essence, a long curvilinear incision is made in the peritoneum above the hernia spaces to develop a large flap of peritoneum which is pulled downward to expose Cooper's ligament, and the lateral iliopubic tract. A large enough space must be created to accommodate the mesh which measures 10x14 cm. All hernia sacs are dissected free from surrounding structures. Occasionally a large indirect hernia cannot be reduced and the sac is amputated. It is important not to excise the reduced sac otherwise subsequent peritoneal closure will be difficult. The polypropylene mesh is carefully positioned and stapled to Cooper's ligament and the lateral abdominal wall. Care must be taken not to staple the inferior epigastric vessels nor the region of the triangle of doom described by Spaw. Which we feel includes the entire area below the iliopubic tract, lateral to the vas deferens where not only the iliac artery and vein, vas deferens and testicular vessels reside, but also the femoral, genitofemoral and femoral cutaneous nerve. Once the mesh is properly placed, extraperitonealization is carried out.

## Results

### *Intraoperative complications*

- ◆ One case of epigastric pedicle injury was immediately electrocoagulated to stop the hemorrhage.
- ◆ There was no lesion of the bowel, of the vesical nor of the spermatic vessels.
- ◆ There were two cases of conversion due to impossible correct peritoneal dissection in voluminous hernias "par glissement" (Table 2).

**Table 2.**  
**Intraoperative complications (163 TAPP)**

|                               |                                  |
|-------------------------------|----------------------------------|
| Section of epigastric pedicle | 1 (0,6%)                         |
| Conversion                    | 2 (1,2%, hernias par glissement) |
| Vesical, bowel puncture       | 0                                |
| Cord injury                   | 0                                |

The average operating time was 80 minutes for unilateral hernia repairs (range 52 to 130 minutes) and 115 minutes for bilateral repairs (range 85 to 195 minutes). As the experience grew in the technique and the teamwork improved the operative time shortened significantly.



### *Postoperative complications and recurrences*

- ◆ In 20 (12%) cases fluid collections (seroma, hematoma) of the spermatic cord and/or the scrotum were noticed and followed up by sonogram on the following day. In 18 cases spontaneously disappeared in 2–4 weeks. In two patients hydrocele was diagnosed and later reoperated.
- ◆ We had no infection nor ejection of the mesh.
- ◆ Residual postoperative pain was observed in 7 cases. This complaint was caused by irritation of the nerves in the region (nerve femoral cutaneous lateral, genitofemoral). These symptoms disappeared without sequel 1–3 weeks spontaneously or after being treated with vitamin B<sub>1</sub>.
- ◆ 5 (3,1%) recurrences should be mentioned. All five recidives was observed in the early postoperative period (1–12 weeks), and caused by technical inexperience: to small mesh, the mesh was not installed/fixed correctly (Table 3.).

**Table 3.**  
**Postoperative complications and recurrence (163 TAPP)**

|                                 |                        |
|---------------------------------|------------------------|
| Seroma-hematoma                 | 20 (12%)               |
| Hydrocele                       | 2 (1,2%, reoperations) |
| Neuralgia                       | 7 (4,3%)               |
| Infection, ejection of the mesh | 0                      |
| Bowel obstruction               | 0                      |
| Recurrence                      | 5 (3,1%)               |

In the postoperative period our patients was discharged only on oral analgesics and there was no dietary restrictions. The mean postoperative hospital stay was 3,1 days (range 1 to 7 days). Usually professional activity was resumed after 1–2 weeks.

### **Discussion**

Laparoscopic tension-free hiernioplasty is rapidly processing from a procedure in evolution to an acceptable surgical option for inguinofemoral hernia repair. To date there have been several reported techniques of laparoscopic hernia repair. In 1982 Ger [7] scribed the management of indirect inguinal hernia by stapling the opening of the hernia sac. Schultz [8] described a laparoscopic repair that used mesh plugs to occlude and obliterate the inguinal canal. Fitzgibbons [6] has repaired defects by placing large mesh directly over the defect in an intraperitoneal position. Corbitt [3] has reported success through a technique in a preperitoneal fashion. According to the literature, only the TAPP and TEP approaches are regularly used in the laparoscopic treatment of inguinal hernia: the optimal placement of mesh in a preperitoneal fashion is the best approach to these inguinal defects [2]. A large sheet of mesh properly placed in the groin region which widely obliterates all three hernia spaces should be associated with a very low recurrence rate, irrespective of the mode of access for placement [1,5].

Laparoscopic herniorraphy has the following advantages:

- ◆ less postoperative discomfort and pain
- ◆ reduced recovery time, allowing an earlier return to full activity
- ◆ easier repair of a recurrent hernia, because the repair is performed in tissue that has not been dissected previously
- ◆ the ability to treat bilateral hernias
- ◆ the performance of a simultaneous diagnostic laparoscopy.

When of the surgeon and were often due to the use of a small prosthesis or inadequate fixation of the mesh.

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## INTRAOPERATIVE ULTRASONOGRAPHY FOR COMMON BILE DUCT EXPLORATION DURING LAPAROSCOPIC CHOLECYSTECTOMY

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The "Endomedix Laparoscans Diagnostic Ultrasound" from the Medilas Ltd. and the "Leopard" and "Panther" type intraoperative ultrasound instruments from the Green Sound Ltd. have been used with success in sixty cases during laparoscopic cholecystectomy (LC) by the authors. Of these patients in four cases common bile duct (CBD) stones and in one case only sludge have been found. Of those with CBD stones, in one case four little stones have been observed despite of negative intraoperative cholangiography (IC) and in one case calculus in the retropancreatic CBD part was detected. On the basis of preoperative findings the CBD stones have not been expected. According to the authors the intraoperative ultrasound (IOUS) can be used with no exception in all cases eligible for LC, and also it can be used for the examination of neighboring organs (liver, pancreas, hepatoduodenal ligament). The method is extremely useful, performance quick, simple and informative as well as it can replace IC during LC.

### Introduction

One of the crucial points of biliary operations is the requirement to detect possible stones of the biliary duct. Out of the different diagnostic procedures IC is used in almost every surgical department. The same can not be said of the process of LC. Though Reddick and Olsen [4] has already developed the method and it is becoming more and more a routine intervention with such operations as well however, it may undoubtedly extend the duration of operations, increase the number of conversions and – last but not least – radiation hazard can not be entirely eliminated. The demand has justifiably emerged for the development of such a process which, when used with LC may substitute IC. A suitable method for this process seems to be the laparoscopic ultrasonic inspection [1,2,3,4]. In 1993 and 1994 we were given a medical instrument called "Endomedix Laparoscans Diagnostic Ultrasound" by Medilas Ltd. (Manufacturer: Endomedix Corporation, 2162 Michelson Drive, Irvine, CA, USA, 92715), later we got two other instruments namely "Leopard Ultrasound Scanner Type 2001" and "Panther Colour Ultrasound Scanner Type 2002" from GreenSound Ltd. and they have been used by us in sixty cases eligible for LC.



angle of 45°. At present we applied the latter solution. The "Leopard" and "Panther" models (Manufacturer: B and K Medical A/S Sandtoften 9,2820, Gentofte, Denmark) have a flexible transducer Type 8555 and can be steered from the handle. The convex array sector has a broad field of view from the surface and helps the user to get a good orientation. All transducers can be introduced through the 10 mm diameter trocar into the abdominal cavity.

The CO<sub>2</sub> pneumoperitoneum was performed in the normal way followed by the introduction of the trocar and optics and then patients were put into Trendelenburg position and turn a bit right. Through the trocar tube of 10 mm size located, in the median line, we injected saline of into the subhepatic region through the Aqua purator, in a quantity quite enough to cover the choledochus and the ligamentum hepatoduodenale. The position of the transducer introduced through the same trocar can be continuously monitored through the laparoscopic optics. By positioning the transducer above the choledochus and following its contours, the cross section of the choledochus could be checked step by step, then turning the head away by 90°, we could see also the longitudinal sections of the choledochus. With the same method also the surrounding organs such as the liver, pancreas, duodenum and the hepatoduodenal ligament can be examined [3].

## Results and Discussion

Sixty examinations were performed by us. Dilated common bile duct with calculi in it was detected in four cases. Only sludge of the CBD was diagnosed in one case. In one case four little stones could be seen in the CBD despite of negative intraoperative cholangiography. In one case one stone was detected in the retropancreatic part of the CBD at the level of papilla of Vater. On the basis of results of preoperative work-up in these cases CBD stones might have not been expected.

During the preoperative medical tests, on the basis of anamnesis, physical and laboratory tests as well as on the basis of abdominal ultrasonic testing – a very accurate and effective testing method today, we can predict with great certainty cholelithotomy of the bile duct. With the abdominal ultrasonic test made prior to operation, the widening of the bile duct can be detected with a certainty of 90% but the reason of widening can not be evidently testified. It is evident however, that the result of preoperative ultrasonic test can serve as a basis for the selection of the mode of operation best suited, though we know that in certain cases, even with bile ducts of normal widening unexpected and undetected cholelithiasis can be found. The intravenous cholangiography, the HIDA passage and computer tomography is not sufficiently informative in the detection of cholelithiasis in the bile duct so any accurate preoperative result can be expected only from endoscopic retrograde cholangiography (ERC). Opinions on routine-like ERC are different. The process is invasive, can cause complications and can not be equally carried out everywhere.

In case of the cholelithiasis of the bile duct it can be reasonable to use for curative reasons as well, since endoscopic sphincterotomy and the successful preoperative removal of the bilestone enables a laparoscopic gallbladder removal at a later time. The unexpected and undetected cholelithiasis of the bile duct increases the possibility of reoperations, though by the postoperative EST and stone removal this can be avoided. The surgeon – even if he has an excellent endoscopic background – strives for definitive solutions, so he does not leave solution for a later time especially, if though in small percentage he reckons with some factor of uncertainty.

We think that if there is no proper and exact preoperative diagnosis (ERC) we must consider using some kind of intraoperative diagnostic process like cholangiography or the ultrasonic test described above in detail.

The intraoperative diagnostic ultrasonic instruments are simple to use, and specially designed for laparoscopic surgery and have a number of advantages. They enable during the laparoscopic cholecystectomy the inspection of ductus cysticus, the choledochus, the intraoperative inspection of the gallbladder. As opposed to intra-operative cholangiography it is less time-demanding, the execution of the inspection is easier and no radiation hazard occurs. Despite the unquestionable advantages of the minimal invasive surgery – namely less pain and less exposure, shorter treatment time – it does not make possible the careful scanning of the organs in the abdominal cavity. The instruments can be used to perform some scanning as well. They can be used for scanning of the liver, the intrahepatic bile ducts and hepatic parenchyma, for the direct inspection of the pancreas, for the detection of cysts and tumors [1,2,3,5]. The instruments, in the majority of cases, can be used as a substitute of intraoperative cholangiography, though it is unlikely to reach the specificity of the latter (e.g. it is not suitable for functional inspection). With a practice gained from their use for a prolonged period of time and by refining its technique of application, the intraoperative ultrasound plays a considerable role in detecting unexpected CBD stones and can reduce considerably the number of possible reoperations.

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## **A CASE OF FIBRIN SEALANT APPLICATION FOR CLOSING BENIGN TRACHEA-ESOPHAGEAL FISTULA (TEF)**

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Surgical treatment of upper airway-esophageal communications are frequently lead to failure. Having previous experience of thoracic administration of Tissucol fibrin glue authors attempted the local application in a case of TEF. A young lady suffering from myasthenia gravis required longstanding artificial ventilation. Not surprisingly a TEP developed in the area of the tracheostomy. There was no room for surgical repair of the TEF. Two administrations of rapid acting form of Tissucol was needed following local adstringent therapy and enzymatic debridement to achieve a complete and permanent closure of a tracheobronchial sinus in a diameter of 5 mm. In addition of meticulous technique and of general supporting therapy special attention was paid to the followings: 1/ healthy wound edges 2/ local infection control 3/ dry environment 4/ patient building up strategy.

### **Introduction**

Upper airway – esophageal tract communication are serious challenge to thoracic surgeons frequently leading to failure [1]. Experiencing efficacy of intrapleural [2] and peribronchial administration of Tissucol fibrin glue authors facing a problem of solving TEF attempted the local application [3].

### **Case presentation**

A 38 year old lady underwent emergency thymectomy for life threatening myasthenia crisis. Impending respiratory failure required ventilatory support. Endotracheal intubation was maintained for 3 weeks. A permanent tracheostomy was mandatory as moderate improvement made the patient's limited mobilisation possible in one month time. Two weeks following the discharge from our department, an urgent readmission was undertaken as the patient developed alarming symptoms of TEF. A central necrosis of an ulcer developing on the posterior wall of the trachea just below the level of the tracheostomy resulted in a tracheo-esophageal sinus.

The general condition of the patient did not allow further surgical intervention. Therefore a locally administered, conservative treatment was decided as limited aggressive approach.

Following one week of daily enzymatic debridement and local adstringent therapy the edges of the sinus became clear and healthy. Securing a dry environment the central hole



in the bottom of the tracheal ulcer of a diameter of 5 mm was attempted to cover using the rapidly acting components of Tissucol. Narrowing of the permanent sinus was noted but a second application was needed in three days time to achieve a complete and permanent closure.

## Result

The TEF symptom free patient was discharged from our department in three weeks after the second admission. At an outpatient control in one month time no recurrence was detected.

## Discussion

The described time, energy consuming and highly expensive process has its limited role in decision making where no alternatives to the conservative therapeutical modalities exists. In this case of a seriously compromised patient being an obvious candidate for conservative treatment modality, a limited agressivity approach was choosen. A step-by step building up process requires reliable biologically viable pillars [4] in the form of the newly constructed membrane. A strong matrix of Tissucol must be created as a continuation of the remainder elements of the posterior wall of the trachea.

In addition to meticulous technique and wide range of general supporting therapy special attention was paid to the minor technicals hints.

Clues of success were seen to be:

1. Fresh and statically reliable wound edges
2. Local infection control
3. Dry environment
4. Patient building up strategy.

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## EFFECT OF THE DNA PLOIDITY ON SURVIVAL IN PATIENTS WITH CARCINOMA OF PAPILLA OF VATER

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The authors investigated the possible prognostic factors for survival after pancreaticoduodenectomy for carcinoma of papilla of Vater. From 1984 to 1995, 8 patients underwent radical surgical intervention for tumor of papilla of Vater. The mean age of the patients was 58 years. Three of them were over 60 years. In one case Whipple procedure was performed, and pylorus-preserving pancreaticoduodenectomy was carried out in 7 patients. Using flow cytometry, the authors measured the nuclear DNA content of tumor cells. DNA ploidy status was evaluated from paraffin-embedded tumor tissues. Perioperative mortality occurred in one patient. Reoperation was performed on 2 patients, because of presence of anastomotic leakage. Survival was 50% at 1 year, 37,5% at 3 years, and 25% at 5 years. Tumor size ( $> 2$  cm) was not negative prognostic factors for survival. The mean survival of patients with diploid cancer (n:6) was 17 months, and the mean survival of patients with aneuploid carcinoma (n:2) was 56 months. The proliferative index of the diploid carcinomas ranged from 3% to 11%. The proliferative index of the aneuploid tumors ranged from 17% to 28%. In conclusion, tumor size ( $> 2$  cm), DNA ploidy status and proliferative index were not significantly negative prognostic factors for survival in patients with tumor of papilla of Vater.

### Introduction

Improved detection of ampullary carcinomas by US, CT and ERCP should result treatment in earlier stage. Whipple procedure or pylorus-preserving pancreaticoduodenectomy (PD) is recommended for curative treatment of patients with tumors of papilla of Vater. The modalities of treatment, however, have been the object of a long series of controversies

The nuclear DNA content of cells from various malignant tumors has been measured by many investigators as flow cytometer has come into wide use, but there have been only a few reports of the DNA content of carcinomas of pancreatic head region [2, 4, 5].

The aim of this study was to determine the prognostic factors for survival in patients with carcinoma of the papilla of Vater.

### Materials and Methods

Between 1984 and 1995, 8 patients underwent radical surgery for cancer of the papilla of Vater. The mean age of the patients was 58 years. Three patients were over 60 years. There were 6 men and 2 women. Jaundice was the most frequent symptom occurring in 8

patients. Abdominal pain was present in 5 cases. Weight loss occurred in 4 patients. US was performed in 8 patients and it was positive in 6 cases. ERCP was carried out in 8 patients and was positive in all of them. CT was performed in 3 of the 8 patients and was positive in 2 cases.

After surgery detailed histological examination (pTNM) and determination of heterogeneity in the nuclear DNA content of tumor cells were performed.

Preparation and staining of tumor tissue fixed in formaldehyde solution and embedded in paraffin for flow cytometric analysis were performed to the modified procedure described by Lapis [3]. Tissue pieces were digested with the following solution: 0,25% trypsin in 0,01 M TRIS-HCl, pH 7,5, containing 0,025% ribonuclease, 0,03% EDTA, 0,1% Triton X-100, 0,05% sodium azide, at room temperature, overnight. DNA analysis was carried out without previous knowledge of the pathologic or survival data.

## Result

One patient underwent Whipple procedure and pylorus-preserving PD was performed in 7 patients. Following PD end-to-end pancreaticojejunostomy (n:3) or end-to-side pancreaticogastrostomy (n:5) was performed. Reoperation was carried out in 2 patients. Cause of reoperation was anastomotic leakage after pancreaticogastrostomy. Perioperative mortality occurred in one patient.

Survival was 50% at 1 year, 37,5% at 3 years, and 25% at 5 years.

Six tumors were more than 2 cm in diameter, and lymph node involvement was not present in our cases.

The survival for women was significantly better, then for men. The patients age had no effect on survival in our series. A tumor size of more than 2 cm was not significant influence for survival.

Of the 8 carcinomas 6 were diploid and 2 were aneuploid. A tumor with a single G0/G1 peak was regarded as being diploid. The median survival of patients with diploid cancers was 17 months in comparison to 56 months for patients with aneuploid tumors. The DNA indicis ranged from 1,3 to 1,7 in the aneuploid tumors. The DNA index of aneuploid carcinomas was calculated as the ratio of the DNA content of the abnormal DNA stremline to that of the diploid peak. The average of the proliferative index (PI) was 7,5% (ranged from 3,5% to 11%) in diploid cancers, and it was 22,5% (ranged from 17% to 28%) in aneuploid tumors. The PI is the proportion of tumor cells in the S and G2/M phases of the cell cycle.

## Discussion

In 1935, Whipple introduced the PD to common clinical use for treatment of neoplasms of pancreatic head region. Pylorus-preserving pancreaticoduodenectomy was reported by Traverso-Longmire in 1978. The choise between performing a Whipple procedure and



pylorus-preserving operation for carcinoma of the pancreatic head region a subject of controversy.

Allema investigated the prognostic factors for survival after PD for patients with carcinoma of the pancreatic head region. He reported that tumor size ( $>2$  cm) and lymph node involvement were negative prognostic factors, apart from the group of patients with ampullary cancer [1]. These factors had not significant effect for survival in our series.

Several studies reported that DNA content of tumor cells may provide prognostic information. The few published studies have reported discordant results with regard to the prognostic information. An increased proportion of aneuploid carcinomas in advanced tumor stages was described by different authors. Reviewing the literature we found that DNA ploidity had a significant effect on survival in pancreatic cancer.

In conclusion, tumor size ( $>2$  cm), DNA ploidity and PI were not identified as a negative prognostic factors in cancer of papilla of Vater in our series. However, because DNA ploidity and PI were identified as an independent prognostic factor, it should be used as an additional factor in future randomised trials of this carcinoma.

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## KERATOPROSTHESIS. IMPLANTATION OF ARTIFICIAL CORNEAS

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Keratoprosthesis (implantation of artificial, plastic cornea) is indicated in severe cases with corneal leucoma (non-transparent, cicatrized cornea) in which keratoplasty (corneal transplantation) is not possible or has repeatedly failed. In the past 40 years we implanted 37 artificial corneas (7 Cardona type, 29 Konstantinov type, 1 Fjodorov type). The visual acuity increase was temporary (lasting from a few weeks to a few months) in 25 patients. The visual acuity was at least 0.2 three years following the implantation of keratoprosthesis in 12 patients. One patient had 1.0 vision 10 years after surgery. Our results indicate that the implantation of artificial corneal is still an "ultimum refugium", an operation that can be justified only in monocular patients, in eyes that cannot be and/or had unsuccessfully been operated on with repeated keratoplasties. The visual improvement is temporary, but in some cases may last for several years. Still this is the only procedure by which useful vision can be provided, for shorter or longer time intervals, for patients suffering from corneal blindness (nontransparent cornea in otherwise functioning eye) whose only eye cannot be treated with corneal transplantation. Keratoprosthesis with better biocompatibility, better fixation techniques, and wider visual fields have to be developed before the implantation of artificial cornea can be looked upon as a surgical procedure with which full optical rehabilitation can be achieved.

**Keywords:** keratoprosthesis, artificial cornea.

### Indications

Trachoma, corneal infections, malnutrition leading to vascularized corneal leucoma, corneal staphyloma, total symblepharon and ankyloblepharon are still the leading cause of blindness in developing countries, threatening the vision of at least 200 million people all over the world. In industrial countries corneal injuries, severe dry eyes, Sjögren's syndrome, ocular pemphigoid, Stevens-Johnson's syndrome and Lyell's syndrome often cause similar corneal complications. Keratoprosthesis (implantation of artificial, plastic cornea) is indicated in severe cases with corneal leucoma (non-transparent, cicatrized cornea) in which keratoplasty (corneal transplantation) is not possible or has repeatedly failed [5].

### Various types of artificial corneas

Contact lenses and intraocular lenses are ophthalmological examples of exo- and endoprosthesis. Keratoprosthesis can be characterized as mesoprosthesis being partly embedded in living tissues and partly exposed to the open air. Artificial corneas consist



of a transparent cylinder shaped optical part, that is inserted into a central circular opening of the opacified cornea, and of a haptical part buried under and fixed to the neighbouring tissues, usually the surrounding cornea, the limbus, sclera or in case of total ankyloblepharon to the eyelid. Different artificial corneas bearing the name of their inventor (Cardona, Castroviejo, Fjodorov, Konstantinov, Strampelli, Worth) vary in their haptical part, while the optic is basically similar, differing in case of some models only in their refractive power (40 Diopters for phakic and 65 Diopters for aphakic eyes). [2]

### **Surgical techniques**

Various surgical techniques have been developed: 1. corneal keratoprosthesis (artificial cornea is implanted into and fixed to the cornea of the recipient), 2. sclerokeratoprosthesis (implantation into and fixation to the periferial sclera, heterotopic keratoprosthesis), 3. osteo-/odonto-/chondro-keratoprosthesis (fixation to autologous connective tissue, simultaneously or priorly transplanted into the cornea) 4. blepharokeratoprosthesis (in case of total syn- and ankyloblepharon the implantation is performed in between the margins of the apposed upper and lower lids, or through the upper lid that is covering the cornea) 5. prosthokeratoplasty (implantation is combined with penetrating or lamaller keratoplasty) 6. prosthokeratosclero-plasty (plastic cornea is implanted into the cornea, fixation is solved with simultaneous implantation of cadaver sclera) [3].

### **Clinical results**

The first keratoprosthesis implantation at our Department was performed by Alberth in 1954. The patient had useful vision for two weeks that was lost due to the formation of a retrocorneal membrane. The first implanted artificial cornea was rejected after 5 months from the eye that showed signs of intense inflammation. After ten years interval a new type of artificial cornea (Cardona "through and through" keratoprosthesis) was introduced into our clinical practice. Seven such artificial corneas were implated in 10 years. In the late seventies a two piece keratoprosthesis was developed by Konstantinov the use of which significantly increased the tolerability and the visual results of keratoprosthesis implantations [1]. In the past 40 years we implanted 37 artificial corneas (7 Cardona type, 29 Konstantinov type, 1 Fjodorov type). The visual acuity increase was temporary (lasting from a few weeks to a few months) in 25 patients. The visual acuity was at least 0.2 three years following the implantation of keratoprosthesis in 12 patients. One patient had 1.0 vision 10 years after surgery. Our results indicate that the implantation of arteficial corneal is still an "ultimum refugium", an operation that can be justified only in monocular patients, in eyes that cannot be and/or had unsuccessfully been operated on with repeated keratoplasties. The visual improvement is temporary, but in some cases may last for several years. Still this is the only procedure by which useful vision can be provided, for shorter or longer time intervals, for patients suffering from



corneal blindness (nontransparent cornea in otherwise functioning eye) whose only eye cannot be treated with corneal transplantation.

### Future perspectives

The basic problem of keratoprosthesis lies in the fact that it is partly exposed partly embedded in the tissues, by other words the plug like keratoprosthesis is situated in a hole, in a never closing wound in the cornea. This situation results in a continuous possibility of infection, and could be solved only if the optical part of the prosthesis could be covered by a transparent corneal layer. Presently this is impossible because we perform keratoprosthesis implantation only in cases with nontransparent corneas. Theoretical possibility, however, exists to develop artificial corneas the surface of which can be populated by human corneal epithelial cells, therefore a continuous epithelial layer (covering both the prosthesis and the recipient cornea) can be reformed. Such a biocompatible keratoprosthesis would help to minimize the inflammatory reaction caused by the mechanical irritation and the toxic effect of the presently used plastic materials. The second problem is the proper fixation of the implanted artificial cornea. The cicatrized, sometimes thin corneal tissue does not offer a proper site for fixation, and continuous movements of the prosthesis will result in usuration of the recipient bed and cause the falling out of the artificial cornea even in the absence of significant inflammatory reaction. New models with stainless steel haptical parts (metal plate, metal meshwork, steel sutures), either implated interlamellarly into the recipient cornea or fixed to the periferial sclera, offer somewhat better possibilities [4], but ideal, permanent fixation is presently far from reality. The third problem is associated with the non-physiological optical properties of the optical part of the keratoprosthesis. The presently used artificial corneas, inspite of the relatively good central vision, give very small visual fields to the patients. Keratoprosthesis with much wider visual fields have to be developed before the implantation of artificial cornea can be looked upon as a surgical procedure with which full optical rehabilitation can be achieved.

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## ROLE OF ENDOTOXINS AND BILE ACIDS IN THE PATHOGENESIS OF SEPTIC CIRCULATORY SHOCK

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It has long been known that the toxic effects of endotoxins under experimental conditions can be induced only when they are administered parenterally. However, in naturally occurring enteroendotoxemic diseases (e. g. septic and intestinal ischemic shocks) the endotoxins – which are produced by gram negative members of intestinal flora –, absorb from the intestinal tract to the blood circulation and can elicit pathological processes. It is an important distinction between natural and experimental endotoxin shock. If the common bile duct of rats were chronically cannulated a significant amount of perorally administered endotoxin was absorbed into the blood. This endotoxin shock can be prevented by bile acids. The physiological surfactants, the bile acids, are important facts in the defense of macroorganisms against endotoxins (physico-chemical defense). The production and passage of bile acids depend from the function of liver and the cholecystokinin (CCK) synthesis of small intestine wall. If the bile (bile acid) content of the intestinal canal decreases the endotoxin can translocate to the body and elicits toxic symptoms. So most important parts of defense against endotoxins in natural conditions are the CCK and bile acids. The consequence of damage of liver (place of bile acid synthesis) or small intestine (place of CCK synthesis) is the absorption of endotoxins.

It is well known that the bacterial endotoxins play an important role in the pathogenesis of irreversible septic (surgical) shock. The endotoxins can initiate the production of noxious mediators (e.g. cytokines, prostaglandins etc.) and these factors are the elicitors of the endotoxic shock.

It has long been also known that the toxic effects of endotoxic lipopolysaccharides (LPS) under experimental conditions can be induced only when they are administered parenterally. However, in naturally occurring enteroendotoxemic diseases (e.g. various shocks, etc.), the LPS absorb from the intestinal tract. The parenterally (intraperitoneal or intravenous) administered LPS induces prostration, diarrhea, and circulatory disturbances indistinguishable from those observed in natural diseases. At autopsy, animals killed by parentally administered LPS show changes that are similar to the natural diseases of species sensitive to LPS (intestinal edema, hemorrhages, etc.). The generally used experimental models differ from natural diseases only in the mode by which LPS enters into the blood circulation [2, 7]. Given orally, LPS has no effect, even on sensitive species, when given in doses from 500 to 3.000 times the minimal parenterally lethal dosage. It is also ineffective when the intestinal mucosa of the experimental animal has been damaged by various interventions. There is no in vitro



evidence of the existence of some intestinal enzyme which could specifically decompose the LPS and thus produce resistance to the orally administered material. As a matter of fact, orally administered LPS can be recovered essentially unaltered from the gastrointestinal tract by means of the phenol-water extraction procedure. Even in a lead acetate sensitizing procedure, orally administered LPS has not been found to be toxic. The way in which LPS reaches the circulation from the intestinal tract in natural endotoxic diseases remains a mystery.

The first clue to the explanation for resistance to orally administered LPS was the demonstration that its treatment *in vitro* with sodium deoxycholate resulted in detoxification due to fragmentation of the LPS molecules. This process is completely reversible when the sodium deoxycholate is removed by dialysis [8]. These studies suggested to us that bile acids *in vivo* might be significant in the inactivation of LPS.

On the basis of the above-mentioned results, we wanted to demonstrate the *in vivo* role of bile in the absorption and detoxification of LPS. For this purpose the common bile ducts of rats were chronically cannulated. In the bile-deprived rats a significant amount of perorally administered LPS was absorbed from the intestinal canal into the blood. Absorption was demonstrated by the lethal effect of LPS previously hypersensitized by lead acetate and by radioactivities found in blood samples. In addition, the presence of active LPS was also demonstrated biologically by the administration of the sera to other rats made hypersensitive to LPS with lead acetate. The intestinal absorption of LPS in rats deprived of bile can be prevented by sodium deoxycholate or bile protected the majority of animals against the lethal effect of LPS. These *in vivo* experiments demonstrated that the physiological surfactants, the bile acids, play an important role in the gastrointestinal tract in relation to the toxic properties of bacterial LPS. Provided that the rats were made bile deficient by the chronic cannulation of their common bile duct, the absorption of perorally administered LPS from the intestinal tract into the blood could be provoked in a quantity that was sufficient to elicit a typical endotoxin shock experimental enteroendotoxemia. However, these experiments demonstrated the protective effect of bile acids against the experimental enteroendotoxemia [7].

These findings were confirmed by other methods. It was demonstrated in rats (with lead acetate hypersensitization) that the absence of bile salts in the intestinal tract in obstructive jaundice (induced by ligation of bile duct) allows perorally given LPS to be absorbed and that this absorption can be prevented by the oral administration of bile salts [1, 6]. Endotoxemia was also demonstrated with the Limulus test in human patients with renal failure in obstructive jaundice [1]. These findings suggest that bile acids play an important role in the defense mechanism of the macroorganism against bacterial LPS [2, 3]. However, the mechanism of LPS absorption from the gastrointestinal tract of bile-deficient rats requires further elucidation.

In another experiment the "antiendotoxic" effect of various detergents (sodium lauryl sulfate, acetylammonium bromide, benzalkonium chloride, Tween 20, polyoxyethylene sorbitan monolaurate) were tested, but only one of them (sodium lauryl sulfate) showed a



sufficient effect [3]. Probably the antiendotoxic effect of polymixin B sulfate is also based on its detergent property [4].

All studies indicate that the intestinal detoxification of LPS is primarily due to the detergent effect of bile acids.

The role of bile in detoxification of LPS was also demonstrated in the experimental intestinal ischemia induced by the superior mesenteric arterial occlusion (SMAO). The SMAO is also an enteroendotoxemia [9]. If the rats were deprived of bile by the chronic cannulation of the common bile duct, the lethality of SMAO increased, because the detoxification of LPS in the intestinal tract was insufficient. Namely, the SMAO produces some significant decrease in bile acid production of rats [5].

On the other hand, with bile preparation pretreatment the lethality of SMAO could be prevented in the majority (70%) of dogs. This finding may be a good possibility for prevention of the development of fatal intestinal ischemic shock of humans after the revascularization of SMAO [3]. It is worth mentioning that the administration of bile acids into the loop terminal ileum in the strangulated ileus of rats resulted about a 50% longer survival time as compared to the control group. This result is explained by the antiendotoxin (detergent) effect of bile acids [3].

Moreover, it is reasonable to suggest that this phenomenon may have a more general application because the detergent effect of bile acids was shown not to be confined to protection against bacterial LPS. A similar destructive detergent action might well be a significant factor in the natural resistance against potential toxins or infectious agents with a lipoprotein or lipid outer structure. Thus, certain viruses (e. g. the herpes group) which have a lipoprotein envelope are sensitive to the detergent action of bile acids. This defense mechanism of macroorganisms based on the detergent activity of bile acids is called the physico-chemical defence [2, 3].

On the basis of a few preliminary experiments, it is supposed that the sensitivity and resistance of different species to endotoxin may be correlated with the bile acid composition of their bile [3].

It may also be that bile acids are significant factors in bacterial LPS detoxification in the liver as well as the intestines. It is quite likely that the endotoxin hypersensitivity induced by lead acetate is due to some alteration of the detergent effect of the bile acids. Namely, the liver homogenate of lead acetate treated rats cannot detoxify the LPS. This hypothesis may serve as an explanation of lead acetate-induced hypersensitivity.

Finally, it is also worthy of note that in the natural disorders an insufficient production of cholecystokinin (CCK) could be the cause of bile deficiency and consequence for LPS absorption/translocation. It is well known that the CCK is produced in the wall of small intestine and via blood circulation can bound to the special receptors on the gall bladder and can produce the contraction of it. If the CCK production is insufficient the bile can not evacuate into intestinal canal. So the detergent effect of bile acids can not act on the LPS molecule. In this case the LPS can translocate – in toxic form from the intestinal tract to the blood circulation.

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## THE CURRENT SURGICAL TREATMENT OF PRIMARY MALIGNANT MELANOMA OF THE SKIN

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In our Department, between 1991 and 1996, 132 patients, there of 87 male-45 female, average age of 48,2 years underwent surgery because of stage 1 (T2) to stage 3 melanoma that was located on the skin. None of patients suffered from early or in situ melanoma. Our retrospective study was based on those 94 patients who had been followed up by Department or dermatology-oncology in our medical centre. Surgery is still the primary treatment for cutaneous malignant melanoma. Thin melanomas (up to 2mm in thickness) can be excised with 2 cm margins. Whether this is also true for thicker melanomas is not known and the only way to obtain more knowledge is to participate in prospective randomised studies. Elective lymph node dissection is associated with significant morbidity which includes lymphedema, wound complications and paresthesias of the extremity. For this reason we use an alternative operative approach uses selective lymphadenectomy with identification of the sentinel node.

### Introduction

It is important to understand the management of patients with melanoma because of constantly rising incidence of this cancer in Europe. The most importance prognostic factors are the tumour thickness (Breslow-thickness) and the level of invasion (Clark level) [1, 4]. Patients with early melanoma (thickness less then 1mm) have an excellent prognosis and are effectively treated with narrow local excision (1 cm radius) [1, 2, 5, 6].

Those with locally advanced melanomas (tumour thickness more than 4 mm) have a high risk of metastases and are treated with wider local excision (2-3 cm radius). Controversies surrounding the management of patients with intermediate-thickness melanoma (1-4 mm) centre on the issues of local excision and management of regional lymph nodes [3]. Randomised trials have shown that a 2-cm radius of excision will minimise the risk for local recurrence, and they have not shown a benefit for the early elective regional lymph node dissection. Techniques are now available to identify the sentinel lymph node (SLN). SLN the first node draining the primary tumour site. Detection of a SLN metastasis is a strong argument for local lymphadenectomy [1, 3].

### Materials and Methods

In our Department, between 1991 and 1996, 132 patients, there of 87 male-45 female, average age of 48,2 years underwent surgery because of stage 1 (T2) to stage 3



melanoma that was located on the skin. None of patients suffered from early or in situ melanoma. Our retrospective study was based on those 94 patients who had been followed up by Department of dermatology-oncology in our medical centre. We want to discuss our results and try to determine the effect of oncological adjuvant therapy. We report 4 cases of locally advanced primary skin melanoma, treated by surgical wide excision combined therapeutic regional lymph node dissection and extirpation of in-transit metastases.

## Discussion

Surgery is still the primary treatment for cutaneous malignant melanoma. During the last 15 years randomised studies have given information on how to excise and we know now that in situ and early melanoma can be treated with narrow excision. Thin melanomas (up to 2mm in thickness) can be excised with 2 cm margins. Whether this is also true for thicker melanomas is not known and the only way to obtain more knowledge is to participate in prospective randomised studies.

## Summary

In our practice, approximately 20% of melanomas greater than 0.76 mm in thickness metastasise to the regional lymph nodes if treated with wide local excision alone. Elective lymph node dissection is associated with significant morbidity which includes lymphedema, wound complications and paresthesias of the extremity. For this reason we use an alternative operative approach uses selective lymphadenectomy with identification of the sentinel node.

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## LAPAROSCOPIC FENESTRATION OF SYMPTOMATIC SOLID SPLEEN CYST WITH HARMONIC SCALPEL INSTRUMENT

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The treatment of two operated solid splenic cysts has been reported by authors. Laparoscopic cyst fenestration has been demonstrated to be a useful alternative method to open surgery. The aim of the authors was to analyse the use of Ultracision Harmonic Scalpel in two spleen preserving procedures. Cysts were located in the superior and the anterior-inferior pole of the spleen. Cyst wall not covered by spleen tissues was removed, drain was left in the abdomen. In the demonstrating spleencyst operation the advantages of HS instrument was the clean operating field, correct coagulation of cyst wall, short hospital stay. Authors believe that this new technology will make it easier and more desirable for surgeons to fenestrate symptomatic spleen cysts.

### Introduction

Several issues is available in the relevant literature about the laparoscopic fenestration of solid liver and retroperitoneal cysts [1, 3].

Some authors have published about their cyst fenestration procedure in the cases of the posttraumatic spleen cysts [2, 4].

We initiated a new procedure by means of our brand new Harmonic Scalpel Instrument in the second half of 1996 in our department.

We supplied this scalpel in spleen cyst fenestration after laparoscopic cholecystectomy and operations of cardiac region (achalasia gastroesophageal reflux, hiatal hernia), which are common procedures in our department. Till 1994 in many articles Amaral has dealt with the application of this instrument.

### Methods

In 1996 two patients underwent laparoscopic spleen cyst fenestration with HS instrument. Two young female patients had mild left hypochondrial pain, ultrasonic and CT study was performed which revealed a splenic cyst of 5x6x8 cm. One was located in the lower, the other one was in the superior position of spleen. There was no calcium in the cyst capsule, hydatid serology was negative. Four ports were placed as is usual for laparoscopic splenectomy [5]. Cyst were not punctured preoperatively.

By means of this Harmonic Scalpel we removed that part of cyst wall which wasn't covered of spleen tissue, coagulated the rest and took a drain in the residual place.

## Results and Discussion

There was no intraoperative and postoperative complications. Both patients were discharged from the hospital on the 4th postoperative day, the control CT was negative.

Well known fact that asymptomatic solid spleen cysts don't require surgical intervention, otherwise the symptomatic solid cysts indicates the laparoscopic cyst fenestration.

This Ultracision Instrument gave us possibility for this new bloodless operation technique.

## Summary

The perfect cosmetic outcome and the short hospital period is also a great benefit in favour for the patient.

Based on the obtain results it could be concluded that laparoscopic spleen cyst fenestration is an effective method in treating benign solid spleen disorders.

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## LAPAROSCOPIC HIATAL RECONSTRUCTION AND USE OF HARMONIC SCALPEL INSTRUMENT

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The method of laparoscopic repair of hiatal hernia is accepted in surgery. Usually associated with Nissen fundoplication which is the most commonly performed antireflux operation. Within a ten-year period authors have done 90 antireflux operations, 52 was laparoscopic procedures. (30 operations for GERD, 10 for hiatal hernia, 12 for the combination of both.) A patient was submitted to operation with large hiatal hernia. He was treated laparoscopic way with success and good results. The Ultracision Harmonic Scalpel instrument helped their operation in many ways, and provided correct bloodless preparation of cardiac region. The authors demonstrate our procedure and the use of the Harmonic Scalper. Their patient were completely pleased with the results after discharge, they are still under regular control.

### Introduction

Laparoscopic hiatal reconstruction and fundoplication is a generally accepted method in minimal invasive surgery [3]. The long term results of the laparoscopic operations similar to the open procedure. Compared to the formerly used "open technique" we tried to use the advantages of laparoscopic technique.

These are: shorter recovery time and hospital stay, similar functional results. Recent publications accept the fact that apart from laparoscopic cholecystectomy, laparoscopic operation of the cardiac region (hiatal hernia, gastroesophageal reflux, achalasia,) give the similar results as the open procedure.

Our aim was to analyse the results of our operation, to get acquainted with the Ultracision instrument in these operations follow up our patient [1, 2].

### Methods

After our learning course and experiences at laparoscopic operation in the cardiac region – between December 1993 and December 1996 we have performed 30 operations in cases of GERD, 10 operations to solve hiatal hernia and 12 procedures treating the combinations of both. One patient of ours after an adequate preoperative assessments was submitted to operation with large hiatal hernia.

We would like to demonstrate our most difficult laparoscopic operation, where we have solved a large hiatal hernia – the four fifth of the stomach was in the thoracic cavity partly through the two typical crus and partly herniated through the right ruptured crus

itself. We applied Ultracision Harmonic Scalpel for division of the tissues and coagulation of the vessels especially short gastric vessels [4, 5].

### Result and Discussion

During our operation we didn't have any secondary injury. There was no need for conversion. The blood loss was minimal, there was no need for transfusion.

In the demonstrated rolling-hernia operation the advantages of the HS were:

- ◆ clean and bloodless operating field,
- ◆ easy and safe transection of vessels and tissues [3, 4]
- ◆ a shorter operation time.

Our patient are regularly controlled, he is free of any complaints, he is all pleased with the results of the operation [5].

### Summary

Based on our experiences and on the data of the literature the laparoscopic technique is a feasible method in the treatment of hiatal hernia and to perform an antireflux procedure. In this operation we have solved during laparoscopic way a large hiatal hernia with success and good results applying Harmonic Scalper for dissection and coagulation.

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## HAEMARTHROS INDUCED ARTICULAR CARTILAGE DEGRADATION

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The statement that blood in the articular cavity is cause of cartilage degradation is widely accepted as an axiom. Although the causes of the different articular diseases were explained in numerous studies, none of them has clarified the pathomechanism of haemarthrosis. Our aims were: 1/ to give a morphological description of the blood induced changes in the cartilage, 2/ to verify that the haemarthrosis is the cause of the cartilage degradation. 10 white rabbits were used in our experimental model. Artificial haemarthrosis was produced in their left hind knees by intraarticular injection of their own blood. The right hind served as control. The rabbits were divided into to five groups based on the time of the haemarthrosis (22–50 days). Samples of the condylar cartilage were taken for light, polarization, transmission and scanning electron microscopy examinations. Signs of the desorganisation of the matrix structure were showed by polarisation microscope and serious lesions were detected in the perichondrium by scanning electron microscope. Similarity have been suggested amongst the pathomechanism of haemarthrosis and other degenerative cartilage diseases (e. g.: osteoarthritis, rheumatoid arthritis), so we made the same comparison. In many cases similar morphological changes were observed, as described by other authors in case of degenerative diseases.

### Introduction

The causes of different articular diseases have been explained in numerous studies, but none of them have clarified the pathomechanism of haemarthrosis [2]. There are many factors (biomechanical, nutritional, immunological, etc.) which can take part in the development of haemarthrosis (HA) induced cartilage damage. These can play a role in other well known articular diseases (e.g. rheumatoid arthritis, osteoarthritis). We assumed that there is lot of similar features between the pathomechanism of the mentioned diseases and haemarthrosis.

In our experimental model, we tried to verify our assumption and to show the pathogenic effect of blood alone in the articular cavity, so as to clarify the role of the HA in articular cartilage degradation.

### Methods

10 white rabbits were used in our experimental model. Artificial HA was induced in their left hind knees by injecting 1.5 ml of own blood in the articular cavity. The injections were controlled by the palpation of the joint. The rabbits left knees were kept intact as



controls. The rabbits were divided into five groups based on the time of HA (22, 29, 36, 43, 50 days). Samples of the condylar cartilage were prepared for light and polarisation microscopic investigations (Zeis Docuval microscope) as well as for ultrastructural examinations using transmission and scanning electron microscopic techniques (JEOL 1200, JEOL 6300).

## Results and discussion

### *Light microscopy*

At 50 days, the periodic acid Schiff (PAS) reagent stained samples were showed that the amount of glycogen had increased slightly in the cells as compared to the controls. This is similar to the results shown by others in cases of the ischaemic cartilage models [1]. The cells from the other groups as compared to the control cells appeared without significant alterations.

### *Polarisation microscopy*

The toluidin blue staining shows changes of the regular matrix structure and the amount of sulfated glycosaminoglicans (GAG) and proteoglycans (PG). On the control samples the color of extracellular matrix was pink and white, but the damaged cartilage had turned greenish yellow, due to decrease in metachromatic effect and the birefringence. When the hyaluronic acid molecules were stained by aldehyde-bisulfite-toluidin blue reaction, the above mentioned changes were appeared more pronounced [5]. The changes in colour were most express in the 50 days group and decreased accordingly in the other groups. These facts suggested that the amount and/or the order of the GAG- and PG-molecules had been changed significantly.

### *Scanning electron microscopy*

On the samples treated less than 29 days, abrasion-like injuries appeared in some places on the surface. 50 days after initiating treatment spots on the matrix had decreased and the fibers seemed clear, and the cartilage surface seemed to be porous. Similar changes were found by other authors in case of condromalacia patellae, osteoarthritis and subchondral ischaemia [1, 4]. These results showed that the lesions of perichondrium can play a key role in HA induced cartilage degradation.

### *Transmission electron microscopy*

The cells from the upper zones of the normal cartilage were elongated and their outlines were almost smooth. They had uniformly short cytoplasmic footlets. The chondrocytes from the treated condyles had expressively elongated cytoplasmatic footlets and contained many vacuoles and glycogen. The nuclei were deformed. Similar results were found in case of rheumatoid arthritis [3].

## Summary

In these present experiments artificial HA was produced in left hind knees of rabbits. Our model allowed us to define the role of HA in cartilage degradation and proved that blood by itself can create articular cartilage damage. These facts direct attention to the importance of early diagnosis and treatment of HA. The changes we have described are similar in several aspects to those found in osteoarthritis, rheumatoid arthritis, chondromalacia patellae, ischaemic cartilage degradation. So we think that there is lot of same features between these diseases and haemarthrosis. These results have encouraged us to further continue this investigation.

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## **IN VITRO AMYLASE RELEASE OF PRESERVED PANCREAS: A SIMPLE TEST TO ASSESS THE VIABILITY OF PANCREATIC ALLOGRAFT DURING PRESERVATION IN THE PIGS**

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To determine an *in vitro* marker of viability during pancreatic preservation, 12 pigs underwent total pancreas harvesting, and grafts were stored in Euro-Collins or Belzer perfusion solution for up to 24 hours. Amylase concentration of the storage solution was analyzed in regular periods and tissue samples were taken for acridine-orange histochemical evaluation of viability in the same time. *In vitro* pancreatic amylase release (IU/g pancreas tissue) was calculated from the volume of solution and the weight of graft. A significant increase of amylase release was found in the course of preservation in both media. Comparing amylase release in different solutions we found significant difference between Euro-Collins and Belzer media (4 hours: 6.45 IU/g vs. 2.2 IU/g, 8 hours: 11.5 vs. 3.58, 24 hours: 8.7 vs. 42.8, respectively). Comparison of amylase release with histochemical evaluation of viability showed strict correlation. We concluded that amylase release is a good marker for exocrine tissue destruction as well as viability of preserved pancreas. Our data confirms that Belzer solution is superior in pancreatic preservation. It is suggested that after adaptation into human model *in vitro* pancreatic amylase release could be a time- and cost-saving, useful method in predicting pancreatic transplant function *prior* graft implantation.

### **Introduction**

The role of pancreatic transplantation in treatment of type 1 diabetes mellitus complicated with renal failure has won greater importance as survival rates are continuously increasing. Pancreas is very sensitive to intraoperative handling and preservation, so the condition of the harvested organ remains questionable in some cases and the graft should be discarded [2]. A time- and cost-saving but reliable method to determine the viability of the removed pancreatic graft and to predict the transplant function *prior* implantation could decrease the number of discarded organs. For this reason we monitored *in vitro* amylase release of pancreatic graft during preservation and compared results with histochemical findings of formerly developed test based on acridine-orange uptake [1].

### **Materials and Methods**

Half-year-old normal pigs weighting about 30 kg were applied for the experiments. The feeding of the animals was stopped a day before the operation but they had free access to water. In intratracheal isoflurane narcosis we explored the abdominal cavity from total



midline laparotomy. The gastrocolic ligament was divided. Left gastric artery and a. diverticuli were ligated and dissected. The splenic artery and vein were ligated and dissected distal from the pancreas. The left lobe and the body of pancreas were freed. Hepatic artery was dissected after originating the gastroduodenal artery. Superior mesenteric artery and portal vein was identified and ligated distal from the pancreas. Coeliac artery at its origin, portal vein proximal from the pancreas and mesenteric artery at its origin were dissected without ligation. After removal and flush-out of body and tail of pancreas a/ 10 to 60 minutes of warm ischaemia in 25°C, 250 ml Ringer solution (n=4) (as control ) or 2 to 24 hours of cold ischaemia in either b/ 250 ml Euro-Collins (EC) (Fresenius AG, Germany) (n=4) or c/ 250 ml Belzer (Du Pont Ltd, UK) perfusion solution (n=4) was applied. 1 ml of preservation solution was taken after 10-20-30-40-50-60 minutes of warm ischaemia or 2-3-4-5-6-8-20-21-22-23-24 hours of cold storage. Amylase concentration was determined by Wohlgelmuth-method. *In vitro* pancreatic amylase release (IU/g pancreas tissue) was calculated from the volume of solution and the weight of graft. At the same time a small piece of graft was dissected and placed in 0.02% acridine-orange solution for 5 minutes. Thick sections (10 µm) made by rapid frozen technique were examined by fluorescence microscope. The extent of membrane lesions was estimated by 1/ intensity of fluorescence, 2/ rate of the fluorescence area and 3/ morphology of the cells [1]. (The time of ischaemia when solution and tissue samples were taken had been determined by preliminary rat experiments.)

## Results

No significant difference in weight or perfusate flow of pancreas were identified between the 3 groups of animals. No significant changes were observed in electrolyte concentration of cold storage solutions all along the preservation period. The following averages of four values of amylase release were calculated in case of cold storage solutions:

### *Average amylase release (IU/gr pancreas tissue)*

| Storage (hours)       | 0   | 2   | 3   | 4   | 5   | 6   | 8   | 20  | 21  | 22  | 23  | 24  |
|-----------------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Euro-Collins solution | 0.6 | 2.3 | 4.6 | 6.5 | 8.0 | 9.2 | 11  | 35  | 38  | 39  | 42  | 43  |
| UW-Belzer solution    | 0.6 | 1.4 | 1.8 | 2.2 | 2.7 | 3.0 | 3.6 | 6.2 | 6.8 | 7.5 | 7.9 | 8.7 |

The next averages of four values of amylase release were calculated in case of warm storage:

### *Average amylase release (IU/gr pancreas tissue)*

| Storage (minutes) | 0   | 10  | 20  | 30  | 40  | 50  | 60 |
|-------------------|-----|-----|-----|-----|-----|-----|----|
| Warm ischaemia    | 0.5 | 1.7 | 3.9 | 6.1 | 7.8 | 9.4 | 11 |

Histochemical results of viability were made by evaluating microscopic findings from multiple sections of every specimen in the whole series. We compared histochemical results to respective amylase release values and the following correlation was found: total cellular disintegration could be observed above 8.4 IU/gr amylase release; serious lesions

(orange discoloration with intact cellular structure) were found above 6.3 IU/gr amylase release and slight damage of exocrine pancreas (yellow discoloration with uninjured cellular structure) was observed above 2.8 IU/gr amylase release.

## Discussion

Today pancreatic transplantation is the only treatment of type I. diabetes that establishes an exogenous insulin-independent, constant normoglycemic state. The penalty for this benefit is the need for immunosuppression in the recipients. Thus, most pancreas transplantations are performed in patients with advanced diabetic nephropathy who receive kidney transplant to treat uremia and who are obligated to immunosuppression for this reason [3].

However, pancreas – primarily the exocrine part of the gland [2] – is very sensitive to intraoperative handling and preservation. So the condition of the harvested organ remains questionable in some cases and the graft should be discarded to avoid preservation injury which results in graft failure from progressive parenchymal damage secondary to graft pancreatitis [4]. For this reason a careful search is going on by pancreas transplantation research for a parameter predicting the transplant function. If a reliable index of viability can be found, then a great part of graft failures would be prevented and number of transplantation would be increased. In this work we measured *in vitro* pancreatic amylase release during preservation.

According to our results *in vitro* amylase release is a good marker for progressive exocrine tissue destruction during pancreatic preservation. Comparing to formerly standardized viability test – acridine-orange uptake [1] – *in vitro* amylase release seems to be a reliable index of pancreas graft viability in pig. Our data confirms that Belzer solution is superior in pancreatic preservation [4].

It is suggested that after adaptation into human model *in vitro* pancreatic amylase release could be a time- and cost-saving, useful method in determining pancreas viability and predicting pancreatic transplant function *prior* graft implantation. Pancreas is very sensitive to intraoperative handling and preservation, so the condition of the harvested organ remains questionable in some cases and the graft should be discarded.

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## INDICATIONS, NEW SURGICAL TECHNIQUE AND RESULTS OF COLON INTERPOSITION OR BYPASS IN ESOPHAGEAL SURGERY

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Over a 5-year period, 29 patients with esophageal disease underwent colon interposition or bypass. The indication was cure of cancer in 11 patients, who underwent earlier a gastric resection. Other indications was benign stricture in 7 patients, bypass for unrespectable cancer in 6, having a caustic injury in 3 and after an esophageal perforation in 2. In 14 patients the left colon, in 15 the right colon was used. The colon was transected without dividing the mesentery other than just along its mesenteric border. This preserves additional blood supply from the marginal artery, also improves the function of the graft in transporting food. Anastomosis leakage occurred in 4 cases (13,7%). Graft necrosis occurred in 2 of 29 patients, one of whom later underwent a successful second reconstruction. The 30 day operative mortality rate was 13.7%. A colon interposition provides good quality of deglutition, and is the organ of choice for patients who require an esophageal substitute and are potential candidates for long survival, or when the stomach is unsuited for replacement or bypass.

### Introduction

The use of long colonic segments either for replacement or bypass was introduced by Kelling [1] in 1911. Since then, the colon has emerged as a well-functioning and durable esophageal substitute. Two critical factors in the success of using colon as an esophageal substitute are the adequacy of the blood supply to the colon graft used and its ability to transport food effectively from pharynx to stomach. Consequently, seemingly minor judgemental or technical errors can have disastrous consequences on the initial viability or long-term function of the graft.

### Patients and Methods

Over a 5 year period 29 patients with esophageal disease underwent colon interposition or bypass in the 1<sup>st</sup> Surgical Clinic of the University Medical School of Pécs.

The indications was cure of cancer in 11 patients, who underwent earlier a gastric resection. Other indications:

|                                  |   |
|----------------------------------|---|
| ◆ acute caustic injury           | 3 |
| ◆ benign stricture               | 7 |
| ◆ esophageal perforation         | 2 |
| ◆ bypass for inresectable cancer | 6 |



There were 8 two stage operations. Out of 8 cases 3 were reverse two stage operations (first bypass and second esophagus resection).

## Results

In 14 patients the left colon based on the inferior mesenteric artery was used, and in 15, the right colon was used.

The 30 day operative mortality rate was 13,7%. Graft necrosis occurred in 2 of 29 patients, one of whom later underwent a successful second reconstruction.

The route of reconstruction was as follows intramediastinal 6, substernal 22, antesternal 1.

The esophago-colic anastomosis was performed with a single-layer 3/0 PDS running suture. Anastomosis leakage occurred in 4 cases (13,7%).

## Discussion

We introduced a new technique in the preparation of the distal end of the colon graft. At the site of division, the colon is freed from its mesentery for a longitudinal distance of 2 cm along its mesenteric border by dividing the small end vessels. Care is taken not to injure the marginal artery. The colon is transected without dividing the mesentery other than just along its mesenteric border. This preserves additional blood supply from the marginal artery via Riolan arcade in case of right colon replacement, and via sigmoid arteries and venous drainage through the haemorrhoidal and sigmoid veins [3] in case of left colon replacement.

## Conclusion

A colon interposition provides good quality of deglutition, is very durable, and is the organ of choice for patients who require an esophageal substitute and are potential candidates for long survival [2].

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## EXPERIMENTAL STUDIES FOR THE SURGICAL CORRECTION AND FIXATION OF DORSAL SPINE DEFORMITIES

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One of the specific features of the scoliosis operations with a posterior approach is that both the correction of the deformity and then the maintaining of the corrected situation are carried out with the help of the implants. With the currently applied systems based on the CD principle it is still difficult to control the rotational component of the scoliotic curve. To complement the systems based on the CD principle, we have developed an implant family whose application makes the correction of the dorsal deformity generally simpler and derotation more effective. Our method is based on the application of such hooks which, linked to the longitudinal rods and hooked on both transverse processes of the instrumented vertebrae, transmit the concerted forces exerting their influence in the direction of the correction. Depending on their symmetrical relations, the hooks are capable of tilting in the frontal plane and derotating in the horizontal plane simultaneously, in the direction of our choice. The stability and applicability of the hooks were tested in implants into cadavers, and then the intimate relations of the implants were examined by means of radiological tests and dissection on instrumented specimens. On the basis of our results, the implants can already be used in clinical practice.

### Introduction

One of the specific features of the scoliosis operations with a posterior approach is that both the correction of the deformity and then the maintaining of the corrected situation are carried out with the help of implants. Therefore these implants are expected not only to have a good stabilising effect but also to be able to control the correction manoeuvres. The surgical correction of scoliosis with a posterior approach has become a routine operation ever since the CD system of Cotrel and Dubousset [1] was introduced in 1984. The original implants have been modified by numerous manufacturers, and today they are available in a great variety with different technical features. Operational techniques have also changed a lot during the past decade, and, as a result, more and more effective corrections can be achieved with these systems. In spite of this fact, one of the components of scoliosis, namely the rotation of the vertebrae, is still difficult to control with the help of these basically identical methods during operation.

### Methods

Over a six-year period, to complement the systems based on the CD principle, we have developed an implant family whose application makes the correction of the dorsal deformity generally simpler and derotation more effective. Our method is based on the



appliation of such hooks which, fixed to the longitudinal rods and hooked on both transverse processes of the instrumented vertebrae, transmit the concerted forces exerting their influence in the direction of the correction.

Hooks are basically made in two forms, one symmetrical, the other asymmetrical, in various sizes. They turn around behind the vertebra, and both of their hooked ends are prepared in such a way that they circle around the bases of the transverse processes and are fixed in the costo-transverse space.

The asymmetrical hooks, which are available in both right-hand and left-hand versions, are capable of tilting in the frontal plane and derotating in the horizontal plane simultaneously. The symmetrical hooks are used for fixing the end vertebrae and reducing the dorsal kyphosis. The hooks are fixed to the two longitudinal rods forming the bases of the CD systems.

## Results

The prototypes of the hooks were tried in cadaver experiments in 23 cases. The experimental implantation in each case was carried out on the middle dorsal portion. Since cadavers with scoliosis are very rare, we could not rely on experiments with such cadavers. Therefore during operations performed on cadavers we tried to create deformities corresponding to the components of scoliotic deformities on originally normal spines. This is how we examined the correcting ability of the hooks on the vertebrae. As far as the arthrosis of the spine allowed us, we always managed to create deformities characteristic of scoliosis.

During these experiments we worked out the surgical strategy and the necessary steps to be followed during the application of the hooks.

At the same time, the implantations also made it possible for us to roughly assess the stability of the montages. In the case of correct placement, breaking of the transverse processes was found only in 5 cases but even then we could explain it with the highly advanced osteoporosis of the cadavers or with some technical error of implantation.

Then, with the permission of the Research Ethics Committee of the University Medical School of Debrecen, we removed the instrumented part of the spine in about 15 cases. A-p, lateral and half oblique x ray pictures were taken of the removed part of the spine. On the basis of these pictures we could clearly see the good ergonomic form of the hooks and the deformity created during experiments, and we found them adequate.

In order to make a more refined analysis of the vertebra-implant relationship, we performed CT-examination both on the usual transverse and sagittal planes. Here we could see how closely the hooks were linked to the transverse process, which we found acceptable, and their fitting the costo-transverse space, found ideal.

Finally, to clarify the close anatomical relationships we performed an autopsy of the vessel-nerve structures at the fixation points of the hooks on the instrumented part of the spine. In no case did we notice fixations endangering the spinal roots or the ramus spinalis.



## Discussion

The complementary dorsal implant developed by us breaks with the current practice which reduces the deformity of the spine by fixing the hooks separately to the two longitudinal rods and hooking them on various points of the vertebrae, and then – by connecting the two rods to one another – they make the montage capable of holding the spine. By means of these hooks each instrumented vertebra can be shifted in the direction of the correction with greater lever arms and by forming a couple on the same vertebra. In our experiments they have proved very promising in making scoliosis operations simpler and more effective, primarily because of their derotating effect. We find that we managed to develop such a new implant which, on the basis of the results, seems to be applicable in clinical practice.

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## POSTERIOR LUMBAR INTERBODY FUSION (PLIF) USING THE BONY ELEMENTS OF THE DORSAL SPINAL SEGMENT

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Many different types of surgical technics for treating unstable degenerative spondylolisthesis of the lumbar spine has been reported. The most important part of the different procedures is to achieve a solid bony fusion between the two vertebrae. Authors report a new simple method of posterior lumbar interbody fusion in spondylolisthesis. The whole posterior segment of the mobile neural arch is removed and used for fusion. Corticospinosus dowels and small bone chips are impacted into the disc space emptied totally before. Monosegmental transpedicular fixateur is required for stability. 33 patients with an average follow up of 20 months showed a clinical improvement of 88%. The radiologically proved fusion rate was 90%. Authors achieved good clinical outcome and high bony fusion rate with the one stage operation from posterior approach for treating lumbar spondylolisthesis.

### Introduction

Interbody fusion represents an important step of any surgical treatment for lumbar spondylolisthesis. Successful fusion is the most important condition of good late clinical results [1]. To achieve successful fusion the whole intervertebral disc should be removed and the two neighboring bodies should be connected by bone. Rigid implants of foreign material (titanium, ceramic, carbon etc.) may increase intervertebral stability by the time of ossification. Interbody fusion can be performed from anterior (anterior lumbar interbody fusion, ALIF) or posterior (PLIF) approaches. Autologous, heterologous or allogenic bone is usually used as disc replacement. Any kinds of bony substitutes may be resorbed instead of forming new bone. That's why the origin of the bone and the method of insertion is very important for the later ossification.

According to the majority of authors (1-4) we also prefer autologous bone. In order to achieve a proper fusion we tried to develop a method of implantation from posterior approach with immediate mechanical stability and without using foreign materials between the vertebrae. Posterior approach is important because each step of the operation (decompression, reposition, plate/rod fixation) can be performed during the same session. No supplementary operation for taking autologous bone is necessary using this method.

### Operative procedure

In prone position from posterior approach the dorsal part of the slipped vertebra and the neighbouring segments are skeletonized and the mobile posterior neural arch is removed in one piece. The upper and lower articular processes are also removed. Complete

discectomy follows, the annulus fibrosus must be cut out as far lateral as possible on both sides. An attempt is made for reposition with spreading disc space. The removed posterior arch is thoroughly cleaned off any soft tissues and 3–4 corticospinosus dowels are cut from the bone. The dowels are wedged anteriorly into the disc space. The remaining bone is morselled and also impacted into the intervertebral space. Bilateral transpedicular screws are introduced and connected with rods under compression.

## **Patients**

33 patients has been operated on during the last 4 years using the surgical procedure described above. Progressive low back pain, sciatic pain and radiologically proved segmental instability due to lumbar spondylolisthesis were the main indications for operation. X-ray and clinical neurological investigations were performed 1 weeks, 6 weeks, 3 months, 6 months, 1 year and every further years after the operation. The assessment of clinical outcome was categorised according to the criteria described by Wetzel et al. [4] into the following categories: 1. excellent (free of symptoms, no pain even if loaded), 2. good (marked improvement, occasionally pain under load, occasional use of analgesics), 3. fair (limited improvement only, continuous need for analgesics), 4. poor (no improvement or worsening, regular analgesic use).

## **Results**

### *Clinical evaluation:*

29 of the 33 patients operated on showed unambiguous improvement over preoperative status (88%), 4 patients remained unchanged (12%). No significant worsening was observed. The average score of clinical outcome resulted in 1.7 for the whole group of patients with an average follow up period of 20 months.

### *Radiological evaluation:*

21 of the 33 patients had longer than 1 year follow up. Only these 21 were taken into consideration. Radiological signs of fusion were assessed according to the criteria of Lin [3]. In 19 of the 21 patients signs of good ossification could be observed. Twelve months postoperatively X-ray detected that the screws had broken with other signs of failed fusion in two patients. Thus, 90% was the fusion rate after one year using the method detailed above.

## **Discussion**

The most frequent complication of surgical procedures with the aim of fusion and fixation of degenerative lumbar spondylolisthesis is the failure of interbody fusion. The ration of successful and deficient ossification is the most important factor in qualification



of any surgical methods. The clinical results strongly correlate with the success of interbody fusion [1, 3]. Failure of fusion may be depended on general (age, osteoporosis, metabolic disturbances, space smoking etc.) and local (inadequate removal of the disc, wrong quality of the implanted bone, few amount of bone, infection, unstable fixation etc.) factors. In order to achieve good ossification, the disc space must be filled out with as much bone as possible [2]. It is well known, that the spinous process and the lamina are excellent implants for bony fusion. The amount of bone removed during posterior decompression is entirely enough to fill out a single disc space.

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## **DIFFERENT TECHNIQUES FOR CREATING OESOPHAGEAL ANASTOMOSES. A HISTORICAL REVIEW AND PERSONAL EXPERIENCE**

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Among the surgical techniques used to create a reliable oesophageal anastomosis, mention should be made of the handmade (in one or two layers, wire or Vicryl) and the different stapler anastomoses. 41 oesophageal anastomoses were performed by stapler technique between 4 March 1985 and 4 March 1991. The EEA stapler was used in 15, and the SPTU stapler in 26 patients. The average age was 56,8 years overall, 53,6 in the female (7 patients) and 57,4 years in the 34 male patients. Tumours in the middle and lower third of the oesophagus and on the cardia were the indications for resection in 30 instances. Total gastrectomy was performed in 9 patients and oesophageal resection for peptic stricture in 2 cases. Replacement with stomach was carried out after oesophageal resection (17 patients), and with Roux-loop in 24 cases. The EEA anastomoses were not covered by a hand-made layer of interrupted sutures as is compulsory in the case of the SPTU gun. The intraoperative complication rate was 12,2% – two severe complications with the SPTU and 3 mild ones with the EEA (2 cases) and SPTU (1 case) machines. The postoperative complication rate was 17% – the severe ones with the SPTU gun. The only fatal anastomosis insufficiency was observed in this group. 3 of the 41 patients died – a mortality rate of 7,3% – but only one of them was due to technical failure in the SPTU group: 2,4%. Consequences: Both the intra- and postoperative complications were more severe with the SPTU technique. The early postoperative complications are closely related to the intraoperative ones. Mortality due to technical failure was only observed in the SPTU group. The EEA stapler gun is superior in every respect to the SPTU sewing-machine. The future belongs to the even more sophisticated bent and modifiable devices. These were used in our Department Between 1992 and 1997, with practically no morbidity and no mortality. Although they are the most expensive of all the possibilities, the low morbidity and mortality rates pay off from the aspects of the short hospital stay and the savings in human life.

### **Introduction**

Several operative-technical methods have been devised, and different suture materials have been used for creating reliable oesophageal anastomoses and to prevent anastomosis insufficiency, which is one of the most difficult tasks in surgery. Belsey introduced atraumatic, monofilament wire stitches in one layer to perform oesophageal anastomosis [1]. Imre and his co-workers and Kiss and his team subsequently achieved good results with this technique in Hungary [5]. An alternative was the development of staplers in oesophageal surgery. From 1950, Russian PKSZ-25 and SPTU staplers were invented in Moscow for this purpose. In the early 1960-s, the U.S. Surgical Corporation started to produce the EEA stapler on the functional basis of the Russian SPTU device, but with significant alterations.

## Methods

41 oesophageal anastomoses were performed by stapler technique between 4 March 1985 and 4 March 1991. The EEA stapler was used in 15, and the SPTU stapler in 26 patients. The average age was 56,8 years overall, 53,6 in the female (7 patients) and 57,4 years in the 34 male patients. Tumours in the middle and lower third of the oesophagus and on the cardia were the indications for resection in 30 instances. Total gastrectomy was performed in 9 patients and oesophageal resection for peptic stricture in 2 cases. Replacement with stomach was carried out after oesophageal resection (17 patients), and with Roux 100 in 24 cases. The EEA anastomoses were not covered by a hand-made layer or interrupted sutures as is compulsory in the case of the SPTU gun.

## Results and Discussion

The intraoperative complication rate was 12,2% – two severe complications with the SPTU and 3 mild ones with the EEA (2 cases) and SPTU (1 cases) machines. The postoperative complication rate was 17% – the severe ones with the SPTU gun. The only fatal anastomosis insufficiency was observed in this group. 3 of the 41 patients died – a mortality rate of 7,3% – but only one of them was due to technical failure, in the SPTU group: 2,4%. Herczeg and his co-workers reported an 8,4% mortality arising from anastomosis insufficiency after the use of the PKSZ-25 stapler in 1985 [4]. Giuli [3] found 13–17% mortality in collected material after oesophageal resections from left and right side thoracotomies after anastomoses made with the stapler technique. These results were compared with that of the hand-made anastomoses and there was no significant difference in either morbidity or mortality. Chasseray [2] published significant differences in insufficiency rate and mortality between oesophageal anastomoses on the neck and in the thorax. The mortality rate was relatively low, derived from a high insufficiency rate on the neck, while a low rate of anastomosis insufficiency in the thorax resulted in a higher mortality. 10–14% mortality was reported by other European and Japanese authors although small series were published with no mortality at all after oesophageal resection with stapler anastomosis.

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## **PRIMARY RESECTION WITH ANTEGRADE COLONIC IRRIGATION AND PERITONEAL LAVAGE VERSUS SUBTOTAL COLECTOMY IN THE MANAGEMENT OF OBSTRUCTED LEFT COLON CANCER**

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Between 1980 and 1996 122 patients with acutely obstructed resectable carcinomas of the colon and rectum were treated in our hospital. Ninety-four has undergone one stage operation of immediate resection and primary anastomosis without proximal colostomy. Intraoperative colonic irrigation was performed in 34 patients, subtotal/total colectomy in 30 patients, right hemicolectomy in 30 patients. There were 2,3 and 1 operative deaths, respectively. The average hospital stay for the survivors was 19.8 days in the primary resection and anastomosis group, and 41.0 days in staged operation group. Concerning the possibility of multiple lesions the authors recommend subtotal/total colectomy except for tumours localized in the sigma where they apply total colectomy only when the proximal part of the colon is necrotized or filled with solid stool.

### **Introduction**

In one fifth of all cases of colonic cancer develops complete obstruction [4].

The question is whether the presence of obstruction indicates the primary resection and anastomosis by use of intraoperative colonic irrigation (IACI) with peritoneal lavage or subtotal/total colectomy?

The aim of this paper is to present our results with these two procedures.

### **Materials and Methods**

During the 17 year period (1980–1996) we performed the following procedures in the treatment of resectable obstructive colon carcinoma: multistage operation, right hemicolectomy, IACI and subtotal/total colectomy. Our technique of IACI is published previously [2].

### **Results**

During the 17 year period (1980–1996) we operated on 817 patients for colorectal cancer. There were 443 men and 374 women ranging in age from 15 to 92 years (average 65.1 years).

Of the 195 patients with urgent operation 30 were treated by right hemicolectomy, 22 patients by multi-stage procedure, 6 patients by Hartmann's procedure, 34 by IACI and primary anastomosis and 30 patients by subtotal/total colectomy. In the group of IACI

and subtotal/total colectomy there were 2 and 3 operative deaths respectively. The average hospital stay for the survivors was 19.8 days in the primary resection and anastomosis group.

Early and late complications: in the group of IACI there were 3/1 anastomosis leakage/death, at the subtotal/total colectomy group 3/1 leak of anastomosis/death was observed. In the group of IACI 4 recurrences was detected within 24 months.

## Discussion and Conclusion

The modified IACI and peritoneal lavage [2,3] creates circumstances similar to those of classical method in elective surgery for performance of the anastomosis and its healing. By its decompressing and detoxicating effect it increases the endurance of the patient in the perioperative period. Each patient with IACI and peritoneal lavage left the operating table in better condition than at the start of the operation.

Some authors [5] advocate treating obstructing carcinomas of the colon by more extensive resection to avoid multiple lesions. Bat [1] has demonstrated that synchronous neoplasm occurs significantly more often in patients with occluding cancer. Most of the synchronous lesions are undetectable by palpation.

Our answers concerning the questions put in the title are the following:

1. We recommend extended right hemicolectomy for resectable obstructing tumours localized in the splenic flexure, without any further procedure.
2. In cases of obstructing tumours of the sigmoid colon we perform IACI.
  - ◆ If the tumour of the sigmoid colon is associated with cecal necrosis we suggest subtotal colectomy.
  - ◆ When in addition to the stenosing tumour of the sigmoid colon the whole colon is filled with solid stool, the total colectomy should be taken into account, too.
3. In case of detected synchronous tumour total colectomy should be chosen, if the patients general condition permits.
4. In Dukes' B<sub>2</sub> stage, especially in case of patients under 50 years of age we recommend to apply IACI, too.

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## **TREND FROM LAPAROTOMY TO LAPAROSCOPY IN THE CASE OF TREATMENT OF ECTOPIC PREGNANCY**

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Ectopic pregnancy is a very hazardous, life threatening complication of the women. Diagnosis and treatment previously were very conservative. When not typical symptoms were found, only waiting or observing was the main task of hospitalisation and only the beginning of typical signs came laparotomy. Nowadays, with the introduction of vaginal ultrasound, color doppler or power imaging techniques and sensitive blood HCG analysis greatly reduced hospitalisation period. The need for the change from laparotomy to laparoscopic treatment in surgical operations became everyday practice. We analysed the data in our department for the operation procedures of ectopic pregnancies from 1990.

### **Introduction**

Increasing number of ectopic pregnancies can be detected within the past few decades. One of the reasons can be the enormously greater number of IUD insertions, the change of sexual behavior, introduction of assisted reproductive techniques (AIH, AID, different methods of IVF) etc. [1].

Nowadays the diagnosis is based on observing the typical symptoms, the change of HCG or beta HCG in blood samples and sensitive transvaginal ultrasound examination [2, 3]. When diagnostic signs are found in ultrasonographic pictures or elevated HCG levels are detected with or without typical symptoms the advanced method of treatment is laparoscopic surgery.

### **Methods**

We begun laparoscopic treatment of the ectopic pregnancies from 1990. In the beginning the rate between laparotomy and laparoscopy was not too good. All the patients who underwent laparoscopy had general intratracheal anaesthesia and deep Trendelenburg position is required. The instrumentation we use is made by Karl Storz GmbH, Tuttingen. The type of operations were salpingotomy, salpingectomy, adnexectomy, and partial salpingectomy [4]. The optical instrument is inserted 1 cm under the umbilicus. Two or three suprapubic ports were inserted. The average CO<sub>2</sub> intraabdominal pressure was 12–15 mmHg.



## Results

The laparoscopic operative treatment varied from 20% in the beginning to 192% nowadays in the case of ectopic pregnancies. The hospitalisation after the operations changed from the average 5,2 day to 2,4 day. The type of operations goes from the so called radical techniques to the organ saving methods. Transfusion of blood was necessary in only very few cases. The cosmetic result is much more acceptable for the women. Conversion from laparoscopy to laparotomy was 30% in the beginning but now it clown to a minimal 4% as the experience of surgeons increased.

## Discussion

Laparoscopic treatement of the ectopic pregnancy is a modern and acceptable way of todays gynecologic surgery. From the beginnings the diagnostic tool has changed to operative possibilities as the skill and knowledge of the operativ team enhanced. The unforgettable benefit of laparoscopic treatment of ectopic pregnancies is the strong decision to widen the territory of the minimally invasive endoscopic operation techniques. The social and individual benefits are also impressive [5].

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## MINIMALLY INVASIVE LAPAROSCOPIC SURGERY ON EXPERIMENTAL ANIMAL MODELS

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Our goal was to find a very good model for gynecological laparoscopic operations. The main purpose of the operations was to perform the same types of laparoscopic operations as we use daily in our clinical practice at the Department of Obstetrics and Gynecology. UMSD. The uterus of female dogs seemed to be ideal for this work. In every experiment we carried out 10 different interventions on identical part of different dog uteruses. The operations were performed at identical time period of day (a.m.). The weight of the female dogs were similar. The anaesthesia was also performed the same way in every case. The main purpose of the operations was to find some significant changes or differences between the 10 different surgical techniques. The histological investigation were carried out with normal microscope and electronmicroscope.

### Introduction

10 female dogs were the "patients" for laparoscopic interventions. The uterus of the dogs were the target point and both ovaries. In every uterus ten different operations were performed, similar types to those used in human female [2, 3]. The different surgical techniques were the following:

- ◆ unipolar coagulation on the uterus
- ◆ bipolar coagulation and cut
- ◆ sterilisation with Yoon ring
- ◆ sterilisation with Filshie clip
- ◆ ovarian biopsy on the right side
- ◆ surgical knot with absorbable material (cat-gut)
- ◆ surgical knot with another absorbable material (Dexon)
- ◆ surgical knot with non absorbable material (Prolen)
- ◆ excision of uterine tissue
- ◆ unipolar cautery of the left ovary

### Methods

10 animals were chosen for the laparoscopic operations. Previously the ethical committee gave license for the animal experiments. The average weight of the dogs was 22 kg. The analgesia was identical in every case – intramuscular analgetics were used [1]. Blood

samples were collected before the operations for future blood analysis of qualitative and quantitative changes of different blood cells and enzymes. Blood sampling was continued for two days postoperatively in every case. During the laparoscopic operations we performed pneumoperitoneum with CO<sub>2</sub> to a maximum pressure of 12 mmHg. One optical instrument was inserted under the umbilical area and three small operation ports were inserted ten cm under the umbilicus for manipulators. After performing the above mentioned ten surgical techniques pneumoperitoneum was discontinued, the instruments were removed and the skin was closed with sutures.

Three groups were set up from the dogs. In the first group we performed the tissue sampling one week after laparoscopy, after two weeks in the second group, and after six weeks followed the original procedure.

## Results

All of the experimental animals survived the operation. All were in good postoperative condition. The removal of the uterus and ovaries for further examination performed easily under a second intervention.

## Discussion

The dog seems to be an ideal experimental animal for modelling gynecological laparoscopic operations [4]. The procedures can be performed easily. The relative cost of the dogs was much smaller compared to pigs as animal model.

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## THE VALUES OF DETECTION OF FREE RADICAL MEDIATED REACTIONS IN PATIENTS

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The peroxidative processes and individual antioxidant protection were measured in patients with different cardiovascular diseases. We concluded that monitoring of this system we were able to detect not only the actual changes of lipid peroxidation and antioxidant defence mechanisms, but additionally the therapeutic efficacy of the treatment.

### Introduction

There is a great interest in oxygen free radicals (OFR) and the peroxidative damage associated with their possible role in diseases such as atherosclerosis, reperfusion injury, septic shock, heart disease, cancer, as well as in the degenerative processes associated with aging [2, 4, 5]. Although considerable progress has been made in identifying and understanding the mode of action of OFR and biological antioxidants, there have been few attempts to determine their actual changes during different stages of disease [1, 3]. The aim of present study was: i./to estimate the value of our laboratory protocol for monitoring of OFR mediated reactions and ii./to follow up the changes of biochemical parameters regarding the therapeutic intervention.

### Material and Methods

Patients with different cardiovascular diseases were involved in our study. Group I.: patients (n=38) with acute myocardial infarction (AMI) treated by systemic thrombolysis; Group II: patients (n=47) with essential hypertension treated by beta-blockers, and ACE inhibitors; Group III.: patients (n=28) with ischemic heart disease, before and after administration of nitrates and lipid lowering drugs. The protocol for biochemical monitoring were the following: peripheral venous blood samples were taken from patients before the administration of any drugs and one or two weeks after starting the treatment. We measured the parameters which could reflect the increased activity of free radicals or decreased endogenous scavenger capacity. The marker of lipid peroxidation (MDA) in whole blood and plasma, the activity of antioxidant enzymes (SOD, catalase, GPX) in washed erythrocytes, the amount and ratio of reduced (GSH) to oxidised glutathione (GSSG) in the whole blood and in plasma and the superoxide radical generating capacity of isolated neutrophils (PMN) were determined.

## Results and Discussion

We are the first to demonstrate that patients with AMI following thrombolysis could be divided into groups on the basis of the changes of measured biochemical parameters [4]. In every patient marked MDA elevation was present during the first day following AMI, but in the patients who survived the acute period of AMI the value of MDA decreased consecutively. In contrast, patients who had persistent high MDA level died during the first week of acute heart attack. The serious oxidative stress was shown by decrease of endogenous scavenger capacity, especially by decrease of GSH/GSSG ratio in the plasma. In the group of survivors the signs of oxidative stress almost disappeared on the end of the first week, while in patients who died in the first period of AMI there was no improvement. Based on these results it can be suggested that measurement of free radical activity and endogenous scavenger content could give some indication as to the prognosis in early stage of acute heart disease.

Essential hypertension is one of the most popular diseases in our country. The investigation of such patients, prior to serious complications is very important. Our measurements clarify that at the time of the first laboratory investigation an altered balance was present between OFR caused lipid peroxidation and endogenous scavenger capacity. Some of the patients showed a marked decrease in scavenger enzyme activity and GSH content and in the other patients significantly elevated GSH levels was found without any signs of increased MDA. It was surprising that following antihypertensive treatment the measured biochemical parameters normalised in more than half the patients, however in the other patients the above mentioned parameters were unchanged or worsened. These results suggest that determination of antioxidant potential in such patients could give an early information about therapeutic efficacy of the administered drugs. It seems to be that amongst the measured parameters glutathione system was the first which changed significantly, while changes of antioxidant enzymes (SOD, catalase) could be detected later.

Our results were the same in patients with ischemic heart disease regarding the initial value of biochemical parameters. If we compared these values to other groups of patients it was characteristic that increased superoxide radical production of isolated PMN was present almost in every case, showing their *in vivo* activation. Administration of nitrates beneficially influenced the stimulated state of PMNs and activity of antioxidant enzymes just after one week of treatment, together with elevation of reduced glutathione.

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## RESULTS OF CONTACT $\beta$ – IRRADIATION OF CHOROIDAL MELANOMAS

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Between the end of 1986 and the end of October 1996 81 patients suffering from choroidal melanoma were irradiated at the Department of Ophthalmology University Medical School of Debrecen. The irradiations were performed with Ruthenium-106  $\beta$  ray emitting scleral plaques (ophthalmic applicators). The radioactive plaques were implanted surgically, fixed by episcleral sutures onto the sclera covering the base of the tumour, and removed by another operation when sufficient time for irradiation had elapsed. For the treatment of tumours in the vicinity of the optic nerve special plaques were used with a notch for the nerve. Precise localisation of the tumours was established by intraoperative ultrasonography and transillumination. The mean follow up period was 3.5 years after the irradiation. Tumour regression was recorded by fluorescein angiography, ultrasonography and fundus photography. In 75 cases (92.5%) the treatment was successful. Additional laser photocoagulation was performed after irradiation in 26 cases. The irradiation by Ruthenium-106 scleral plaques of choroidal melanomas proved to be an effective treatment in cases of small and medium sized choroidal melanomas in our practice and the results are similar to those of the largest radiotherapy centers of Europe.

**Keywords:** intraocular melanoma, ophthalmic applicators, Ruthenium-106

### Introduction

Melanomas are the most challenging cases for any conservative treatment. The malignant tumour must be completely destroyed, but the treatment is only valuable if the macula and the optic disc can be saved from the destructive effect of irradiation. Various ocular oncologists have advocated individualized medical and surgical approaches for the treatment of choroidal melanoma [1]. These include periodic observation with photographic documentation for small lesions, photocoagulation in selected cases, and enucleation for large tumours that occupy large part of the globe. Radiation may be performed in the form of external beam irradiation therapy [2, 5].

### Patients and methods

Between the end of 1986 and the end of October 1996 81 patients (41 male and 40 female) suffering from choroidal melanoma were treated at our Department. The suspected diagnoses had been confirmed by ultrasonography and fluorescein angiography, as well. The irradiation of the tumours were performed with special scleral plaques (radioactive ophthalmic applicators). The radioactive material is evenly distributed in the shell shaped plaques that are covered by a thin radioprotective layer on



the outer surface. The ophthalmic applicators have two ears by means of which they can be sutured onto the sclera [3]. Different types of Ruthenium applicators are available. For the treatment of tumours in the vicinity of the optic nerve head the plaques have a notch for the nerve. The necessary irradiation dose were calculated to reach 100 Gy at the apex of the tumours.

Under local or general anesthesia the conjunctiva, the subconjunctiva were incised and the plaque was sutured onto the sclera, covering the base of the tumour. Precise localisation of the tumours was established during the operation by ultrasonography and transillumination, as well. The regression of the tumours was recorded by fluorescein angiography, ultrasonography and fundus photography [4].

## Results

In 75 cases (92.5%) the treatment was successful, these patients are all alive without any sign of metastases. In five cases the affected eye had to be enucleated. Three patients died due to generalized metastases, and one patient had liver metastases that was successfully treated cytostatic treatment within the follow up period. Repeated plaque therapy was necessary in nine cases.

Those patients whose tumours had either changed to a flat scar or the choroidal melanoma had shrunk to cicatrised greyish or black mass, which had remained unchanged for more than one year, were considered to be successful.

Additional laser photocoagulation with Krypton red laser was performed after irradiation in twenty six cases.

Of the successfully treated 75 patients 65 developed flat scars. The retained visual acuity varied between 1.0 and light perception determined by the localisation of the tumour (tumours reaching the optic nerve head an/or the macula had worse visual outcome).

## Discussion

The irradiation by Ruthenium – 106  $\beta$ -ray scleral plaques of choroidal melanomas proved to be an effective treatment in cases of small and medium sized choroidal melanomas in our practice and the results are similar to those of the largest ophthalmic radiotherapy centers of Europe.

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## INTEGRIN EXPRESSION ON NORMAL AND NEOPLASTIC HUMAN BREAST EPITHELIUM

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Integrin adhesion receptor expression of different benign and malignant breast tumours was examined by means of immunohistochemical techniques. A panel of seven different anti- $\alpha$  and two different anti- $\beta$  subunit antibodies was used. Normal breast epithelium displayed a well characterized and constant pattern of integrin expression consisting of strong  $\alpha$  1,2,3,6 and  $\alpha$ v, and a relatively weaker  $\beta$ 1 and  $\beta$ 3 staining. No staining for  $\alpha$ 4 or  $\alpha$ 5 could be detected on the epithelial cells. Benign fibroadenomas did not show changes in their receptor expression compared to normal tissues. In the cases of different types of breast cancer, there was a significant downregulation of all subunits. The staining pattern was distinct if there could a basement membrane like structure be detected around the invading tumour nodules. When laminin and collagen type IV surrounded the tumour cells, those cells in contact with the extracellular matrix components still displayed strong positivity for the integrin subunits. Other cells inside the tumour cell nests or not surrounded by basement membrane did not express integrins. The positively staining cells might be more differentiated owing to the effect the basement membrane. Myoepithelial labeling of the integrin expressing cells gave negative results. The observed integrin expression heterogeneity renders the histologic picture difficult to interpret with regard to clinical behavior of the tumour.

### Introduction

Integrins are a family of heterodimeric transmembrane receptors of cell adhesion molecules [1]. They are known to play primary roles in cell-extracellular matrix interactions but several integrins are shown to mediate intercellular interactions as well. Each cell in the organism is expressing multiple adhesion receptors and the differential expression of integrins is characteristic of the specific cell type. The changes of receptor expression following malignant transformation may have significant roles in defining the invasive behavior of a tumour. Both upregulation of receptors, normally not expressed on the cell surface, and loss of integrins may occur after malignant transformation even in the same tumour type.

Malignant melanoma cells consistently upregulate the  $\beta$ 3 subunit expression when they enter the vertical growth phase, which is coupled with collagenase type IV expression and thus with the appearance of the invasive phenotype [2]. In case of lung cancers no consistent integrin expression pattern could be established, although an overall downregulation of receptors was observed. Downregulation of integrin expression have been observed on human breast cancer cells as well, although, conflicting data exist on the presence or absence, and clinical significance of some of the subunits.



We have undertaken this study to examine the integrin repertoire of different benign and malignant breast tumours with special regard to heterogeneity of integrin expression in malignant tumours.

## Methods

Breast tissue samples were obtained in the 1st Dept. of Surgery, Medical School of Debrecen, during therapeutic interventions where intraoperative frozen section diagnosis was necessary. Cryostat sections of five cases of normal breast, five fibroadenoma and six intraductal, fortysix infiltrating ductal carcinoma and twelve lobular carcinoma were placed on poly-L-lysine coated slides and fixed with  $-20^{\circ}\text{C}$  acetone for 10 min. The following anti-integrin monoclonal antibodies were used, either commercially purchased or generously provided by the following investigators: P1H5, P1B5 and P1D6 ( $\alpha 2$ ,  $\alpha 3$  and  $\alpha 5$ ) Drs. Elizabeth Wayner and William Carter; TS2/7 and B-5H10 ( $\alpha 1$  and  $\alpha 4$ ) Dr. Martin Hemler; GoH3 ( $\alpha 6$ ) Dr. Arnoud Sonneberg; SSA6 ( $\beta 3$ ) Drs. Joel Bennett and James Hoxie; anti- $\beta 3$  Dr. József Tímár. The primary antibodies were detected with the Vectastain Elite ABC system (Vector Laboratories, Burlingame, CA). Light counterstain was added when necessary to identify specific structures. Fluorescent second antibody systems were also used. Anti-laminin and anti-collagen type IV antibodies were purchased commercially. Slides were evaluated by two independent pathologists on Opton Axioplan and Zeiss fluorescent microscopes.

## Results and Discussion

Normal breast epithelium displayed a stable pattern of integrin expression consisting of strong  $\alpha 1$ -3, 6 and  $\beta 1$  and a weaker  $\alpha v$  and  $\beta 3$  staining. Integrin distribution was mostly pericellular with basolateral intensification. A small portion of the cells showed intracellular reactivity as well. Benign tumours (fibroadenomas) did not change their integrin expression compared to normal epithelium. However, breast cancers displayed a significant reduction in reactivity for all types of integrin subunits. This loss of staining was not uniform. Even in the same field of view, when laminin and collagen type IV surrounded the tumour cell nests, the cells on the periphery of the tumour cell foci and in contact with these extracellular matrix components still displayed strong positivity for the integrin subunits. This repertoire resembled normal expression of integrins. In the case of the  $\alpha v \beta 3$  "classic vitronectin receptor" the staining was even stronger. Other groups of cells not bordered by basement membrane did not express integrins in this manner. The cells, staining positively for integrins, could theoretically be the remnants of normal excretory ducts in the cases of infiltrating ductal carcinomas. Labeling for myoepithelium failed to identify these cells, thus we considered them malignant epithelial cells. Several authors noted previously the loss of specific integrin subunits in different breast cancers [3]. Conflicting data exist on the expression of  $\alpha 2$  and  $\alpha 6$  (3,4) on tumour cells and its



relation to axillary nodal status [5]. Our results suggest a more complex and probably a more unpredictable biology of breast cancers.

### Summary

Seven different anti- $\alpha$  and two different anti- $\beta$  subunit antibodies were used to examine the integrin repertoire of different benign and malignant breast tumours. Normal breast epithelium displayed a well characterized and constant pattern of integrin expression consisting of strong  $\alpha$  1,2,3,6  $\beta$  1 and a relatively weaker  $\alpha$  v and  $\beta$  3 staining. Benign fibroadenomas did not show changes in their receptor expression compared to normal breast epithelium. In the cases of different types of breast cancer, however, there was a significant downregulation of all subunits. The pattern was distinct if there could a basement membrane like structure be detected around the invading tumour nodules. The cells in close contact with the basement membrane expressed integrins in a manner resembling normal epithelium. These findings reflect the well known phenomena of tumour cell heterogeneity, and implicate the potential differentiating effect of basement membrane components. Clinical relevance is that even in histologically and immunologically well defined tumours the clinical behavior might be difficult to predict owing to heterogeneous biology of breast tumours.

### Acknowledgements

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## ANAESTHESIOLOGICAL INDICATIONS AND CONTRAINDICATIONS OF MINIMALLY INVASIVE SURGERY

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Spreading of laparoscopic techniques caused changes in anaesthesiological contraindications. In the first period laparoscopy was contraindicated in ischemic heart disease (IHD). Early mobilisation and short postoperative period are positive goals, IHD was taken out of contraindications. Present study compares changes in circulatory, blood gas and acid-base balance values during laparoscopic cholecystectomy (LC) in groups of patients ASA I-II. and ASA III. with IHD. There were 30 patients in group ASA I-II, 30 patients with IHD in category of ASA III. investigated during LC. Fifteen patients of both groups went under Propofol-Fentanyl (TIVA) anaesthesia, others were on Propofol-Fentanyl-N<sub>2</sub>O (IVA) protocol. All of them got also Atracurium. Pulse rate, mean arterial pressure, O<sub>2</sub> saturation and end tidal CO<sub>2</sub>, blood gases and acid-base state were recorded before induction, after CO<sub>2</sub> insufflation, after desufflation, 1 and 3 hours postoperatively. After CO<sub>2</sub> insufflation there was a moderate tachycardia in both ASA III. groups (74/min->88/min). In all groups pCO<sub>2</sub> increased (40->48 mmHg) but normalised till the 3<sup>rd</sup> postoperative hours (42 mmHg). Ventricular extrasystoles appeared in 3 ASA III. patients in IVA group. Three high risk patients had serious metabolic acidosis postoperatively. Present time the ischaemic heart disease does not contraindicates laparoscopic interventions. TIVA with Propofol is better choice because of its favourable effects on circulation and acid-base balance. Using N<sub>2</sub>O caused higher grade of intestinal distension. The cardio-respiratory, blood gas parameters and acid-base balance have to be monitorised in perioperative period of laparoscopic surgery.

### Introduction

Wide spreading of minimal invasive laparoscopic techniques in general surgery caused changes in points of anaesthesiological contraindications. During laparoscopic intervention we have to pay attention to the circulatory and respiratory influences of this method. They mean the mechanical disadvantages of pneumoperitoneum and also the effects of peritoneal CO<sub>2</sub> absorption [3,4]. Noticing these problems, at the introduction of laparoscopy the ischemic heart disease (IHD) was one of the most important anaesthetic contraindications. Later the advantages of laparoscopic technique came to light: early mobilisation, minimised intraoperative stress and postoperative pain, short hospital period, which are the positive goals [5]. During last two years IHD was taken out of absolute contraindications.

Present study compares the changes in circulatory, blood gas and acid-base balance values during laparoscopic cholecystectomy in groups of patients ASA (American Society of Anaesthesiologists Physical Status Classification) I-II. and ASA III. class with IHD to evaluate benefits and cardio-respiratory effects of minimal invasive surgery.



## Patients and Methods

During laparoscopic cholecystectomy 60 were investigated. There were 30 patients in group ASA I-II. and 30 patients with IHD in category of ASA III. Fifteen patients of both groups went under total intravenous anaesthesia (TIVA) with Propofol-Fentanyl, other 15-15 were on intravenous anaesthesia (IVA) protocol (Propofol-Fentanyl-N<sub>2</sub>O). All of them got Atracurium as long acting muscle relaxant.

Circulatory parameters (pulse rate-P, mean arterial pressure-MAP), O<sub>2</sub> saturation (by pulse oximetry), and end tidal CO<sub>2</sub> (by capnography) were monitored, acid-base balance and blood gases were analysed (by micro Astrup method) before induction, after CO<sub>2</sub> insufflation, after desufflation, 1 and 3 hours after the operation. Student t-test was used to examine the changes of parameters and significance between risk groups (ASA I-II. and III.) and the anaesthesia types (TIVA, IVA).

## Results

After CO<sub>2</sub> insufflation there was a moderate increase in average pulse rate in both ASA III. groups (78/min->88/min). There were no significant changes in mean arterial pressure. (Table 1.) Arrhythmia (ventricular extrasystoles) appeared during the narcosis in 3 cases in ASA III. patients in IVA group.

**Table 1.**  
**Pulse rate (P) and mean arterial pressure (MAP)**

|                   | BO<br>P | BO<br>MAP | CO <sub>2</sub> in<br>P | CO <sub>2</sub> in<br>MAP | CO <sub>2</sub> ex<br>P | CO <sub>2</sub> ex<br>MAP | AO1<br>P | AO1<br>MAP | AO3<br>P | AO3<br>MAP |
|-------------------|---------|-----------|-------------------------|---------------------------|-------------------------|---------------------------|----------|------------|----------|------------|
| TIVA<br>ASA I-II. | 78      | 98        | 80                      | 94                        | 80                      | 93                        | 82       | 94         | 80       | 96         |
| TIVA<br>ASA III.  | 80      | 98        | 82                      | 93                        | 86                      | 92                        | 87       | 93         | 85       | 95         |
| IVA<br>ASA I-II.  | 76      | 96        | 82                      | 94                        | 83                      | 93                        | 84       | 95         | 82       | 95         |
| IVA<br>ASA III.   | 78      | 98        | 83                      | 92                        | 88                      | 93                        | 85       | 94         | 83       | 95         |

In all groups pCO<sub>2</sub> increased (40->48 mmHg) after the operation but normalised till the end of the 3<sup>rd</sup> postoperative hours (42 mmHg). Only 4 patients had long lasting hypercapnia (pCO<sub>2</sub>> 50 mmHg after the 3<sup>rd</sup> hour), three of them suffered from ischemic heart disease. (Table 2.)

In the acid-base state there were no significant changes. (Table 3.) Three of ASA III. patients had metabolic acidosis which needed correction postoperatively, 2 were from IVA and 1 was from TIVA group.

In case of Propofol-Fentanyl anaesthesia combined with N<sub>2</sub>O intestinal distension appeared markedly during the operation.



**Table 2.**  
**Partial oxygen (pO<sub>2</sub>) and carbon dioxide (pCO<sub>2</sub>) tension**

|                   | BO<br>pO <sub>2</sub> | BO<br>pCO <sub>2</sub> | CO <sub>2</sub> in<br>pO <sub>2</sub> | CO <sub>2</sub> in<br>pCO <sub>2</sub> | CO <sub>2</sub> ex<br>pO <sub>2</sub> | CO <sub>2</sub> ex<br>pCO <sub>2</sub> | AO1<br>pO <sub>2</sub> | AO1<br>pCO <sub>2</sub> | AO3<br>pO <sub>2</sub> | AO3<br>pCO <sub>2</sub> |
|-------------------|-----------------------|------------------------|---------------------------------------|----------------------------------------|---------------------------------------|----------------------------------------|------------------------|-------------------------|------------------------|-------------------------|
| TIVA<br>ASA I-II. | 80                    | 40                     | 136                                   | 34                                     | 134                                   | 39                                     | 82                     | 45                      | 80                     | 41                      |
| TIVA<br>ASA III.  | 76                    | 42                     | 110                                   | 39                                     | 101                                   | 42                                     | 75                     | 48                      | 75                     | 46                      |
| IVA<br>ASA I-II.  | 81                    | 39                     | 138                                   | 36                                     | 130                                   | 40                                     | 80                     | 45                      | 80                     | 40                      |
| IVA<br>ASA III.   | 75                    | 41                     | 98                                    | 40                                     | 96                                    | 42                                     | 70                     | 49                      | 72                     | 47                      |

**Table 3.**  
**Actual pH (apH) and base excess (BE)**

|                   | BO<br>apH | BO<br>BE | CO <sub>2</sub> in<br>apH | CO <sub>2</sub> in<br>BE | CO <sub>2</sub> ex<br>apH | CO <sub>2</sub> ex<br>BE | AO1<br>apH | AO1<br>BE | AO3<br>apH | AO3<br>BE |
|-------------------|-----------|----------|---------------------------|--------------------------|---------------------------|--------------------------|------------|-----------|------------|-----------|
| TIVA<br>ASA I-II. | 7,40      | 1,26     | 7,42                      | 1,05                     | 7,40                      | 0,28                     | 7,38       | 0,30      | 7,40       | 0,50      |
| TIVA<br>ASA III.  | 7,41      | 2,05     | 7,42                      | 0,80                     | 7,40                      | 0,21                     | 7,37       | 0,16      | 7,39       | 0,39      |
| IVA<br>ASA I-II.  | 7,39      | 1,38     | 7,40                      | 1,20                     | 7,41                      | 0,12                     | 7,39       | 1,3       | 7,38       | 1,30      |
| IVA<br>ASA III.   | 7,42      | 1,26     | 7,41                      | 0,50                     | 7,41                      | -0,10                    | 7,37       | -0,10     | 7,38       | 0,25      |

## Discussion

Laparoscopic technique has special characteristic cardio-respiratory effects. Higher intraabdominal pressure due to pneumoperitoneum causes lower preload, smaller stroke volume. On the other hand, CO<sub>2</sub> absorption mobilises catecholamines, that could compensate the negative circulatory changes.

In ASA III. group there was an increase in pulse rate probably because they have smaller compensatory reserve capacity.

Pneumoperitoneum mechanically decreases vital capacity and compliance, peak inspiratory pressure, dead space ventilation and central venous pressure increase. These mechanical disadvantages can be eliminated by using lower abdominal filling pressure (up to 14–15 mmHg) or special abdominal retractor and suitable mechanical ventilation.

Peritoneal CO<sub>2</sub> absorption raises pCO<sub>2</sub> and et CO<sub>2</sub> which appeared postoperatively but solved relatively rapidly in 3 hours. In patients with cardiac disease hypercapnia can be prolonged.

## Conclusion

Present time the ischemic heart disease does not contraindicate laparoscopic interventions because of the favourable postoperative conditions for recovery but we have to monitorise the cardio-respiratory and acid-base balance during the perioperative period [2]. TIVA with Propofol is better choice for these patients because of its advantageous effects on circulation and intestinal distension [1].

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## LATE COMPLICATIONS AFTER PHARYNGOGASTROSTOMY

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A case of severe stricture and a case of tracheogastric fistula after laryngopharyngo-esophagectomy and pharyngogastrostomy for cervical esophageal cancer are described. Stricture is often seen but tracheogastric fistula is a rare complication, however, both are devastating conditions. According to the literature, the survival rate is poor in both cases. The surgical management demands several principles. Recurrent or metastatic cancer must be ruled out. The patients' general condition and nutritional status must be optimized. Pulmonary infection must be cleared. The surgical management of the stricture was a free jejunal transfer after failed attempts of several dilation procedures. The treatment of tracheogastric fistula was suturing the stomach and covering the trachea with a pedicled left sternocleidomastoideus flap. The survival of the patient treated with free jejunal interposition exceeds 24 month. Unfortunately, the patient with tracheogastric fistula, treated with interpositioned sternocleidomastoideus muscular flap, lived two weeks after this operation. The surgical managements described in this report may provide palliation or definitive treatment for these devastating complications.

### Introduction

Dysphagia due to stricture of the anastomosis or tracheogastric fistula with respiratory infection after esophageal replacement for malignant esophageal lesions is a challenging problem. The former is quite common and most lesions are located at the cephalic end of the esophageal substitute [2]. If the anastomotic stricture is not correctable by dilation or anastomotic leakage or necrosis of the substitute occurs, surgical revision has to be performed [2]. The development of an esophagorespiratory fistula is a rare and devastating complication. The percentage of patients with primary or recurrent malignant esophagorespiratory fistula, alive after 12 months, varies between 0-7% [1].

Tracheogastric fistula developing after surgical treatment of cervical esophageal cancer is scarcely seen [4]. We present a case of strictura developed after pharyngogastrostomy treated with free jejunal transplant and a case of tracheogastric fistula and its treatment.

### *Case report 1:*

A 52-year-old man presented with carcinoma planocellulare of the pharyngoesophageal junction. There was no evidence of metastatic disease. The patient had hypertension and hepatitis in his previous history but was otherwise in good health, with only minimal weight loss. Pharyngo-laryngoesophagectomy, suprasternal tracheostomy,



pharyngogastrostomy and pyloromyotomy were performed. Owing to some extraluminal parenteral nutrition was continued to the 16th postoperative day when intact anastomosis was shown by the x-ray swallowing examination. Two weeks after his discharge, anastomotic leakage and subcutaneous inflammation developed. Endoscopic control showed slightly narrowed anastomosis. A nasojejunal feeding tube was inserted and open drainage was introduced in the subcutaneous region. With this conservative care, the leakage was managed and adequate swallowing was achieved after 17 days. Four weeks later, severe anastomotic strictura developed with dysphagia. Endoscopic balloon dilation was unsuccessful. All endoscopic samples were free of recidiv tumor. The strictured anastomosis was resected and a free jejunum transplantation was performed. Large skin defect forced us to cover the region with a pedicled pectoral musculocutan flap. The wound healing was without incident. Two weeks after free jejunal transplant, the patient resumed oral intake. 30. months after his original cervical exenteration, and 24 months after free jejunal transplantation, the patient has a good swallowing function, is on a regular diet and his quality of life is excellent.

### ***Case report 2:***

A 63-year-old man presented with carcinoma planocellulare of the cervical esophagus. The CT scan showed partial involvement of the left thyroid gland. There was no evidence of any further metastatic disease. The patient was in good health but had 11 kg of weight loss. The tumor was resected by pharyngo-laryngo-esophagectomy and total thyroidectomy. Pharyngogastrostomy, and parathyreoid placement in the left sternocleidomastoideus muscle was performed. There was no leakage in the cervical region at the time of his discharge but a minimal dehistentia developed in his median laparotomy which required resuture. A year later having had regular checkups he developed swallowing difficulty and severe coughing. The examinations revealed a tracheogastric fistula of between 6–7 mm in diameter and 60 mm below the suprasternal tracheostomy on the pars membranacea of the trachea probably caused by a metal tracheostomy tube. Tissue adhesive and suture was applied with an unsuccessful result. Nasojejunal hyperalimentation was applied for three weeks with no oral intake. After readmission in better general health, mediastinotomia anterior was performed and the tracheogastric fistula was explored in full length. The gastric leak was closed with knotted suture. At the level of the lesion, the trachea had no pars membranacea. It was covered with a left sternocleidomastoideus muscle flap. Until the 9th postoperative day, the patient showed normal recovery than a severe right bronchopneumonia developed and on the 15th postoperative day he deceased.

## **Discussion**

Persistent or recurrent dysphagia after esophageal replacement for benign or malignant esophageal lesions is a challenging problem. These strictures are most often caused by leaky anastomosis, progressive scarring of the hypopharynx, or partial ischemic necrosis

of the esophageal substitute. When surgical revision has to be performed, free jejunal transplant is scarcely used [2] although good functional outcome is reported by others [3]. Despite the poor prognosis of the primary disease and the high complication rate after free jejunal transplant [3], this method seems to be a reliable procedure to manage strictures after pharyngogastric anastomosis. Tracheogastric fistula after esophagectomy is a rare and devastating complication. In our case the fistula was due to a metal tracheostomy tube which was used permanently and for an unnecessary long time. The management demands the following strict principles: the patient should be free of tumor recurrence or metastatic disease, be free of pulmonary infection and have an adequate nutritional status. These patients have an extremely poor prognosis and therapy is aimed at palliation of respiratory tract contamination although report of successful management can be found [4] which encourage us to perform such procedures.

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## CHANGING TECHNIQUES AND INDICATIONS FOR LAMELLAR KERATOPLASTY

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In recent decades, the number of lamellar keratoplasties (LKs) being performed worldwide has been gradually decreasing. However, new technical procedures have been developed and microsurgions must consider modified indications for lamellar grafting. In the period 1946–1995, in the Department of Ophthalmology University Medical School of Debrecen, Hungary 3889 consecutive keratoplasties were performed of which 608 were LKs. In the period 1946–1960 special surgical material (biosutures) was used without operating microscopes and the leading indication for LK was corneal scar (leukomas). Between 1961 and 1979 with the development of microsurgical procedures (10/0 nylon sutures, operating microscope), the LK technique became more advanced. In the period 1979–1995 precision lamellar grafting could be performed with the widely available improved modern techniques. Changing indications for LK were noted in the second period and this tendency has subsequently continued. Currently the main indications for LK are "immediate" keratoplasty after chemical burns, and sclerokeratoplasty against recurrent pterygia. Their observations lead the authors to conclude that the possible reasons for the changing indications of LK are the new technical procedures, the increasing knowledge, the better immunological tests and the improved postoperative therapy.

**Keywords:** corneal transplantation, lamellar keratoplasty, indication for lamellar grafting

### Introduction

The use of lamellar keratoplasty (LK) at present is limited by a number of conditions. In recent decades, the number of LK interventions being performed has been decreasing. Lamellar grafting is currently indicated as a microsurgical method for some special groups of corneal diseases [1]. At least four fields of indication have been created for lamellar grafting:

1. **Therapeutic** (chemical injury, recurrent pterygium, recurrent focal epithelial defect): therapeutic grafts may be necessary after a deep lamellar keratectomy, when excess tissue has been removed.

2. **Tectonic** (Moorens ulcer, keratoglobus): this type of LK is used to restore the normal surface of the anterior segment by replacing localized or generalized areas of corneoscleral thinning. In many situations it is used to strengthen the cornea or sclera and to prevent rupture of the globe [2].

3. **Optical** (keratoconus, corneal scar): rarely used today, since the penetrating keratoplasty has a better visual prognosis [3, 4].

4. **Cosmetic** (rare indication): only in eyes with no visual potential.

Essential differences may be detected in the technical procedures as well. In view of the fundamental developments, the relevant cases over a long period of time in our Department have been surveyed in order to follow the changes in the indications for LK and to assess the introduction of new operative techniques.



## Method

We retrospectively evaluated all cases of lamellar grafting at the Department in the interval 1946–1995. Three periods were set up: 1946–1960, 1961–1979, and 1979–1995. Within these periods, the indications, the suture materials and the surgical techniques were evaluated.

## Results

In the period 1946–1995, 3889 consecutive keratoplasty cases were treated, of which 608 involved LK. In the period 1946–1960 only 19 LK interventions were carried out. This time was the learning era for this type of operations and the technical conditions were not adequate enough. The postoperative therapy was not appropriate. The lack of local antibiotics and steroid eyedrops meant that the surgeons faced difficult problems when dealing with keratoplasty plans. The leading indications for LK were deep corneal scar (leukoma, 73%) and chemical injuries (5.2%). In the period 1961–1979, 251 cases underwent lamellar grafting. During this period, new instruments, 10-0 nylon sutures and modern microsurgical techniques were introduced at the Department. Lamellar grafts were performed in cases of corneal scars (48.4%) and chemical injuries (22.5%). In the period 1979–1995, 64 LKs were carried out using the widely available advances in the latest microsurgical procedures. The main indications for LK were "immediate" keratoplasty following severe chemical injuries (68%) and partial lamellar sclerokeratoplasty against recurrent pterygia (15%). In this period the surgical method was supported by preoperative pachymetry, the use of viscoelastic material, micrometer corneal knives and the appropriate sutures, which were of interrupted or running types.

## Discussion

The data showed that therapeutic LK was the most common indication group at our Department. The surgical approach has changed since 1946. The number of LKs has dramatically reduced due to the more predictable visual results of penetrating keratoplasty. The possible reasons for changing and narrowing the fields of indication could be the extensive technical development in microsurgery, wide possibilities in preoperative therapy, and new management of the immunological background. Other factors include a form of decrease in the number of cases with severe chemical injuries, and adequate primary therapy against corneal chemical combustion. Accordingly, LK may be considered a good procedure for special corneal diseases. Lamellar grafting has recently become popular to solve other problems, e.g. refractive errors. This tendency may influence the indications for LK in the near future.

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## EXPERIENCE ACQUIRED BY APPLYING GENTAMICIN-SPONGE

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Chronic suppuration is a reverting problem in surgical practice. The concerned region either has insufficient circulation due to basic disease, or systemic antibiotics takes no effect due to inflammatory barrier developed meanwhile. For this reason Authors initiated systematic use of gentamicin sponge (Garamycin, Schering-Plough, USA) two years ago. During this period we implanted gentamicin sponge in 40 cases. After primary intervention in 85% of treated patients we observed complete recovery, or in case of ulcerus cruris we reached proper condition for skin-transplantation. Three patients needed further incision and in two cases amputation of diabetic foot could not be avoided. Our results support the effectivity of gentamicin sponge in treating local inflammatory processes supplementing and increasing efficiency of surgical procedures.

### Introduction

Chronic suppuration is a reverting problem in surgical practice. The concerned region either has insufficient circulation due to basic disease, or systemic antibiotics take no effect due to inflammatory barrier developed meanwhile. These problems has drawn our attention to local antibiotic treatment. Demand is high antibiotic level in the local and surrounding tissue; and successive continuous dissolution from proper carrier material. Local antibiotic treatment undoubtedly gained significance in this narrow area of indications.

### Material and Methods

Authors initiated systematic use of gentamicin sponge (Garamycin, Schering-Plough, USA) two years ago. During this period we implanted gentamicin sponge in 40 cases.

Indications consisted of contaminated ulcerus cruris, cyst of sacral dermoid, infected vascular graft, inflammatory processes of the limbs, inflammation of soft tissue.

### Results

Mean hospital stay was 12 days with a dominance of treatment time of infected vascular graft and diabetic foot. Two patients died due to other diseases, there was no connection between the treatment and the cause of death. After primary intervention in 85% of

treated patients we observed complete recovery, or in case of ulcer cruris we reached proper condition for skin-transplantation. Three patients needed further incision and in two cases amputation of diabetic foot could not be avoided.

Our results support the effectivity of gentamicin sponge in treating local inflammatory processes supplementing and increasing efficiency of surgical procedures.

### **Discussion**

Nowadays the expense of treatment is very important beside physiological factors. Long lasting systemic antibiotic treatment can be replaced by a proper local product. Its effective substance is gentamicin. This broad spectrum antibiotic takes effect on both Gram negative and Gram positive bacterial strains. The carrier collagen has considerable haemostatic and proliferative effect. As a control group authors examined 40 patients treated previously, they had similar distribution of diseases. Long lasting diseases with chronic suppuration could mean severe difficulties of organisation, cost and treating in hospitals with high turnover. In case of proper indication expensive systemic antibiotic treatment could be replaced by the effective and successful local treatment.

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## THE PATHOLOGICAL PLICA IN THE KNEE

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Fourteen patients were evaluated who had an arthroscopic removal of the symptomatic mediopatellar plica of the knee in this retrospective study. The main complaint of the patients was the pain at the medial side of the knee. Before the operation only in 3 cases was the diagnosis the pathological plica. The arthroscopy was performed in a routine way. The plica was considered pathological, and removed, when it was thickened. There was grade I or II chondropathy in the knee on the medial femoral condyle and the patella respectively, caused by the plica. Good to excellent results were obtained in 93% of the knee with or without chondromalacia.

### Introduction

The plica synovialis mediopatellaris, which is also known as the medial patellar plica or medial shelf, is existed, but the recognition of its pathologic form prior to the advent of arthroscopy was difficult. The first anatomic description of the plica was made by Fullerton [2] and the first arthroscopic description was made by Iino [3]. It was Pipkin who mentioned first the plica in the literature as a cause of the knee pain [5].

Different authors estimated between 20–60% the incidence of mediopatellar plica in the knee, in an average population [4].

Our purpose was in this study to determine factors in the patients' clinical presentation and arthroscopic findings that may be prognostic of a good or bad result.

### Materials and Methods

A retrospective review has been performed with those patients who had a postoperative diagnosis of plica at the Department of Orthopaedic Surgery Medical School University of Debrecen, from 01 April 1990 to 30 September 1994. In this period 646 arthroscopies were performed in our department. Only those 31 patients were included in the study, in which no other abnormality was noted at the time of the arthroscopy. The arthroscopy was performed in a routine way. The plica was considered to be pathologic when it was thickened, similar to a "bowstring". It was cut by arthroscopic scissors and removed.

Preoperatively the clinical symptoms as pain, swelling, lock of the knee, patello-femoral crepitus, history of the trauma, meniscus tests were recorded.

Follow-up data were obtained by interview and physical examination from 14 patients. The follow-up time was 18,07 months (7–35). The average age at the time of operation was 23,6 years (15–43). There were 7 males and 7 females. At eleven patients on the left knee, at three patients on the right knee were involved. The average time between the beginning of the complaint and the operation was 15,53 months (0,5–72).

The preoperative diagnosis and the operative finding was compared. The pain was registered from 0–5 on a scale at the follow up. Clinical result was evaluated and graded using a scale as excellent (no symptoms return to unlimited activity), good (occasional mild symptoms, return to most or all activity), poor (no change in symptoms, persistent limitation of activity), bad (worse in the symptoms, no activity).

## Results

The main complaint before the operation was the pain in all patients. It was able to provoke by a pressure for the medial femoral condyle or for the medial joint line. In one patient a thickened band was palpable over the medial femoral condyle extending from superior to medial aspect of the patella medially and inferior. There were swelling in two patients, patello-femoral crepitus in 9 cases and in 7 cases the meniscus tests were positive. In 9 cases there was lock of the knee before the operation. In 9 cases there was trauma in the case history. In all patients there were a full of range of motions.

Preoperatively, our diagnosis was meniscus rupture in seven cases and in only 3 cases the diagnosis was pathological plica. There was no pathological deterioration on the routine X-ray pictures. At the operation the pathological plica has been removed. There was I grade chondropathy in 3 cases, II grade chondropathy in 1 case, and III grade chondropathy in one case on the patella, and there was I grade chondropathy in 9 cases, and II grade chondropathy in one case on the medial femoral condyle.

At the follow up there was no swelling of the joint, and in 4 cases there was pain in the medial joint line. The average was 2,35 on the scale from 0–5. There was no crepitus and no lock of the knee. All patients had full range of motions and there were no positive meniscus tests. The X-ray pictures did not show any deterioration. The overall results were 27% excellent, 66% good and 7% poor. There was no correlation between the duration of the symptoms and the evaluation of the patients. There was no recurrence or complication.

## Discussion

Plicae are very wide in both form and size. It can be distinguished after the localisation suprapatellar, medial suprapatellar, mediopatellar, infrapatellar, and lateral. Only the mediopatellar plica is the cause of the pain. After trauma, direct or indirect, an effusion or intermittent synovitis would appear and the plica could become fibrosed, thickened, hyalinized and rarely calcified thus losing flexibility. In our study this hypothesis is

seems to be supposed. 9 patients had a trauma in the case history. This trauma was not so hard to effect meniscus rupture, ACL rupture or hyaline cartilage deterioration. The false positive meniscus test can be explained with the same anatomy position. The plica could result a chondropathy on the medial femoral condyle and on the medial facet of the patella as an impingement sign. Among the preoperative diagnosis the plica was found only three times. It is the result of the false positive diagnosis of the meniscus rupture and the overestimation of the symptoms of chondropathy. The main complaint was that every patient had pain. During the arthroscopy beside the plica we found a chondropathy in different grade on the medial femoral condyle and on the medial facet of the patella. All the other cases except one belonged to the I and II grade chondropathy so the resection of the plica was satisfactory. The patients' subjective opinion after the operation was favourable. That patient who had bad result the age was over 30 at the time of the operation. This data is supported by literature [1].

### Summary

It is always necessary to think of the plica as a cause of the pain in region of the medial side of the knee.

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## RELEVANCE OF CYTOKINE PRODUCTION TO INFECTED PANCREATIC NECROSIS

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The purpose of this study was to evaluate the role of cytokines in septic conditions following acute pancreatitis and to elaborate a new strategy in the treatment. Increased TNF and IL-6 serum levels were found in 30% of the patients (n=40), while the IL-6 level was elevated in all of them. There was a positive correlation between the serum IL-6 and sICAM-1 levels. The *in vitro* TNF and IL-6 producing capacities were initially higher in the study group, but decreased on subsequent days, especially in fatal cases (n=3). Administration of pentoxifylline [PTX] (400 mg/day) to septic patients following necrotizing pancreatitis resulted in TNF and IL-6 production similar to that observed in control donors. The level of sICAM-1 also decreased following PTX therapy. These results suggest that cytokines produced by activated leucocytes are important in the pathogenesis of infected pancreatic necrosis, and their inhibition might be of therapeutic advantage.

### Introduction

Sepsis and septic shock are the most frequent complications of extended necrosis following acute pancreatitis. The purpose of this study was to evaluate the role of cytokines in these conditions and to elaborate a new strategy in the treatment. Tumor necrosis factor (TNF) plays a pivotal role in the initiation of septic syndrome [1]. TNF is produced mainly by monocytes, macrophages and granulocytes in response to various stimuli, of which endotoxins derived from Gram negative bacteria, are the most potent. Serum TNF, IL-1 $\beta$ , IL-6, ICAM levels and the TNF-producing capacity of the leucocytes has been checked in patients with presumed sepsis following necrotizing pancreatitis. Recently, hemorrheologic agent pentoxifylline [PTX] has been shown to inhibit TNF production [2]. We therefore investigated the effects of PTX not only on TNF and IL-6 synthesis *in vitro* and in septic patients in clinical practice but also on the serum level of soluble ICAM-1 (sICAM-1) [3].

### Patients and Methods

Forty patients with infected pancreatic necrosis were studied. All patients had positive cultures from the abdominal fluid and abscess discharge with Gram negative rods. 25 of the forty patients had positive blood cultures as well. In all patients the surgical

treatment consisted of wide-ranging necrosectomy combined with continuous widespread washing and suction drainage. PTX has been administered in an open unblinded study in a dose of 400 mg/day as a complement to conventional antibiotic therapy. The results were compared with those of earlier conventional intensive therapy without PTX (n=20). The severity of the illness was evaluated in accordance with the APACHE II score system. *Titration of TNF and IL-1 $\beta$*  in the sera was measure by TNF ELISA and IL-1 $\beta$  ELISA (Medgenix<sup>®</sup>) respectively. TNF content in cell supernatants was checked in bio-assay based on cell line WEHI 164 clone 13. TNF activities were calibrated against recombinant human TNF (Genentech<sup>®</sup>). *IL-6 assay* was performed using the IL-6 dependent B-9 cell line proliferation test. *Determination of sICAM-1* was performed by sICAM-1 ELISA (Bender Med. System, Vienna), according to the instruction of the manufacturer. *Stimulation of leucocytes*: whole blood was incubated for 24 hr at 37 °C with heat killed *Staphylococcus aureus* or with *E. coli* LPS (Sigma<sup>®</sup>) respectively. The supernatants were tested for the presence of TNF.

## Results

Initial serum samples for TNF, IL-1 $\beta$  and IL-6 determination were obtained between 12 and 20 hr after onset of sepsis, following by daily sampling. Of the serum samples taken, only 30% of patients contained detectable TNF. All serum samples positive for TNF were obtained within 48 hr of onset of the clinical signs of sepsis. The similar tendency in the kinetic of appearance of IL-1 $\beta$  in the serum could be observed (50% of the patients vs. 30% of patients on day 1 and day 2). In contrast to IL-1 $\beta$  and TNF, IL-6 serum levels were almost always above normal value in septic patients. The mean peak value of TNF in septic patients was 110 pg/ml and there was no significant difference between survivors and nonsurvivors. The peak value of IL-1 $\beta$  did not differ between survivors and nonsurvivors as well. The serum levels of IL-6 seemed to be correlated with the severity of illness (250 U/ml vs. 400 U/ml peak value). The level of sICAM-1 was the highest among nonsurvivors in average 2000 ng/ml. There was a positive correlation between serum IL-6 and sICAM-1 levels ( $r=0.6837$ ,  $p < 0.001$ ). Stimulation of whole blood cultures with *Staphylococcus aureus* led to higher TNF production than it was measured in the control group. The follow-up study of septic patients revealed that in vitro TNF production decreased in later phase of disease, on correlation of severity of illness. PTX significantly decreased the TNF production of mononuclear cells in a dose-dependent manner when either LPS or *Staphylococcus aureus* was the inducer. In contrast, there was only a moderate decrease in IL-6 production. Beneficial effect of PTX in septic syndrome was observed following necrotizing pancreatitis. As a consequence of PTX therapy, the TNF production dropped to the normal level on day 2. There was a moderate decrease in the level of IL-6 production. The circulating sICAM-1 level was significantly higher in septic patients then in normal controls and it remained elevated for the subsequent days. PTX administration resulted in a rapid decrease in sICAM-1 level. The severity of illness was evaluated in accordance with the APACHE II



score system, PTX therapy resulted in a decreasing tendency in the scores, which tended to change inversely with the improvement in the clinical status, and the laboratory parameters.

## Discussion

Using a bio-assay or ELISA a revealed circulating TNF in 30% of patients with infected pancreatic necrosis. There was no clear association of TNF level and the development of septic shock or fatal outcome of the disease. The *in vitro* TNF-producing capacity was high in the patients in the study group. The decrease in inducibility before the fatal outcome of the disease might be due to the exhaustion of the leukocytes. This decrease of responsiveness might be of prognostic value. Our results suggest that determination of the TNF producing capacity of the leucocytes might be more informative than measurement of the serum TNF level in evaluation of the severity or prognosis of sepsis. In our studies, the production of TNF was inhibited by PTX not only after LPS stimuli, but also after stimulation of effector cells by heat-killed *Staphylococcus aureus*. The circulating or soluble intercellular adhesion molecule (sICAM-1) reflects a state of general cell activation, or can be regarded as a marker of the presence of inflammatory mediators and cytokines. A decrease in sICAM-1 was observed in parallel with decrease in APACHE II score of our patients treated with PTX. PTX may therefore improve therapeutic strategies in septic complications following necrotizing pancreatitis.

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## **TGF- $\beta$ 1 AND IL-6-NEW ASPECTS IN PANCREAS REGENERATION?**

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Plasma levels of interleukin-6 (IL-6) and transforming growth factor-beta1 (TGF- $\beta$ 1) were studied during cholecystokinin octapeptide (CCK-8)-induced regeneration after pancreas resection in rats. The weight of the pancreas and the DNA and protein contents increased significantly. The serum levels of TGF- $\beta$ 1 and IL-6 were increased significantly on days 7 and 14. There was no significant change in serum amylase levels. These findings indicate that cytokines such as TGF- $\beta$ 1 and IL-6 may play a role in the pathomechanism of pancreas regeneration.

### **Introduction**

IL-6 is a multi-functional cytokine that is produced by numerous types of cells. It is involved in the cytokine network and in immunological mechanisms. High levels of IL-6 have been found in trauma and sepsis. IL-6 acts on a wide range of tissues, exerting growth-inducing, growth-inhibitory and differentiation-inducing effects, depending on the nature of the target cell. TGF- $\beta$ 1 demonstrates regulatory effects on many different cell types. It induces a mitogenic or antiproliferative effect depending on the cell line and cell type. It participates part in embryogenic differentiation in the immune system and also in tumor development. TGF- $\beta$ 1 has been found to take part in liver regeneration. The aim of this study was to investigate whether changes occur in the serum TGF- $\beta$ 1 and IL-6 levels during pancreas regeneration, and whether there is a connection between their levels and the rate of the regeneration in rats.

### **Materials and Methods**

Male Whistar rats (n=5/group), weighing 350–450 g were used. Distal pancreas resection (75%) was performed after ether anaesthesia. The resected part of the pancreas was cleaned and weighed. CCK-8 was administered subcutaneously in a 300 ng/kg dose 3 times per day to the investigated group, while the control animals received the same amount of saline. The rats were examined 3, 7, 14 and 28 days after the first injection. Blood samples were taken from the aorta for IL-6, TGF- $\beta$ 1 and amylase determinations. Serum TGF- $\beta$ 1 levels were determined by ELISA, and IL-6 levels by bioassay on the

B-9 IL-6-dependent cell line. DNA contents were determined by the procedure of Giles & Meyers, protein contents by the Goa method; assayed with colorimetric method. For measurement of the amylase levels the Phadebas method was used. The residual pancreas was weighed, and the changes were calculated in each case to the formerly resected weights respectively, by mathematical methods.

## Results

The wet weights of the residual pancreas increased in both groups up to day 3. Subsequently, the weights decreased in the controls, but increased continuously in the CCK-8-treated group. There was a significant difference on day 14, and on day 28 the pancreas weight was almost doubled in the CCK-8-group, whereas in the controls it has decreased to normal level. The DNA content of the pancreas was continuously higher in the treated than in the control group. It reached the maximum level on day 28, with a significant difference ( $1850 \pm 350$  vs.  $780 \pm 240$   $\mu$ /pancreas). The protein content reached its highest level on day 28 in the CCK-8-treated group ( $32.435 \pm 7.88$  mg/pancreas). A significantly higher level of IL-6 was measured on days 7 vs. the control ( $250 \pm 70$  vs.  $50 \pm 30$  pg/ml). It later decreased, but remained above the control level. Significantly different TGF- $\beta$ 1 levels were measured on days 7 and 14 ( $290 \pm 40$  vs.  $155 \pm 60$  and  $295 \pm 8$  vs.  $155 \pm 55$  ng/ml, respectively). There was no difference between the TGF- $\beta$ 1 and IL-6 levels in the two groups on day 28. No significant changes were observed in the amylase levels; they remained at a normal level ( $5.3 \pm 0.5$  U/ml). This indicates that the increase in pancreas weight was not caused by pancreatitis.

## Conclusions

Earlier reports suggested that TGF-beta isoforms may act by both autocrine and paracrine mechanisms in the pancreas [6]. In chronic pancreatitis and in pancreatic cancer [1], TGF- $\beta$ 1 involvement has been found. Our study revealed a transient increase in TGF- $\beta$ 1 level in the treated group. The significant changes in the pancreas weight and the protein and DNA contents indicated pancreas regeneration. In a previous study, TGF- $\beta$ 1 was thought to be an autocrine growth inhibitor of the pancreas [3]. However significant differences in the pancreas parameters were found only after the TGF- $\beta$ 1 peak. Further in the control group the TGF- $\beta$ 1 level remained at the basal level. There was only a slight increase in pancreas weight, but no significant difference in the protein, or DNA contents. The TGF- $\beta$ 1 level remained high until day 14, and then decreased. Additionally the pancreas trophism induced by CCK-8 could be detected in increasing level up to the end of the first month [4]. After cerulein-induced pancreatitis, TGF- $\beta$ 1 was found to be involved in the regulation of extracellular matrix regeneration [2]. No earlier data were found on the role of IL-6 in pancreas regeneration. It seemed that, if IL-6 is implicated in hepatic regeneration, this cytokine is not produced by the



regenerating liver and must be delivered to the liver exogenously to modulate hepatic cancer [5]. The IL-6 level was significantly higher than the control level on day 7. Although on day 3 we found high serum levels of IL-6, it seemed to be a late effect of trauma, after the pancreas resection. IL-6 may support TGF- $\beta$ 1 in pancreas regeneration, or it may be inhibited by TGF- $\beta$ 1, as the TGF- $\beta$ 1 level was still high while the IL-6 level decreased. Our findings reveal that regular low-dose CCK-8 injections resulted in pancreas regeneration following 75% distal resection. This was indicated by increases in pancreas weight, and in the DNA and protein contents of the pancreas. Significantly elevated serum TGF- $\beta$ 1 and IL-6 levels were also detected up to day 14. These data show that cytokines can modulate the development of the pancreas and suggest roles for TGF- $\beta$ 1 and IL-6 in regulating the *in vivo* regeneration of the pancreas.

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## **WHY THE INTERNAL MAMMARY ARTERY IS AN IDEAL GRAFT FOR MYOCARDIAL REVASCULARISATION? (AN EXPERIMENTAL MODEL WITH OMENTOPLASTY)**

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Ten dogs underwent coronary artery bypass grafting through a right thoracotomy. Free internal mammary artery grafts (IMA) was used for aortocoronary bypass to right coronary artery (RCA) without temporary cardiopulmonary bypass. In upper median laparotomy approach, mobilization and lengthening of the omentum was performed through the retrosternal part of the diaphragm. An epiploic muff was effectuated surrounding the IMA graft. After three months the animals were sacrificed and the grafts folded by omentum were used for microscopical study. The histological evaluation has shown that the omentum has formed a new adventitia around the graft. In the new-formed adventitia, newly formed vessels can be found and these are grouped around the adventitia-media border zone, very rarely penetrating into the external layer of the media. This graft-omentoplasty offer a good experimental model which facilitates to investigate in vivo the blood supply needed by free IMA grafts through the adventitia in experimental conditions. The biological mechanism of angiogenesis in graft wall can be investigate as well.

### **Introduction**

Graft patency is an important determinant of late clinical results after coronary artery bypass and the IMA is superior to the other arterial conduits because: low vasospastic characteristics, resistance to atherosclerosis and the particularity of the intima and internal elastic lamina [4].

Arteries require oxygenation and nutrition to survive, which they receive from two sources: the flowing blood in their lumens and small adventitial blood vessels, the vasa vasora [1].

Previous investigators have shown that experimental interruption of blood supply from adventitial vasa vasora results in necrosis in the media [5]. It seems that stripped, free IMA graft had a higher incidence of thrombosis, intimal thickening and medial injury than the pedicled. This difference may be due to early vascular wall ischemia as a result of poor early perfusion of the vasa vasorum.

The aims of the present study were to investigate in vivo the blood supply needed by free IMA grafts through the adventitia and to determine the histological border-line between intimal and adventitial sources of free IMA graft wall in experimental conditions.

## Methods

10 mongrel dogs weighing 10 to 16 kg were anesthetized with pentobarbital sodium (2,5 mg/kg intravenously), intubated and ventilated with a volume ventilator.

A right fourth interspace thoracotomy was performed and a fragment from the IMA was mobilised from the chest wall, without electrocautery, stripped gently from surrounding tissues with fine scissor and the collaterals were ligated with 6-0 Prolene sutures.

The pericardium was incised parallel to the right phrenic nerve and RCA was isolated in the atrioventricular sulcus, following systemic heparinization. The proximal end of the graft was anastomosed with a partial occlusion clamp to the ascending aorta, using a 7-0 Prolene running suture. The distal anastomose to the proximal segment of the RCA was effectuated with the same 7-0 Prolene running suture on beating heart, without temporary cardiopulmonary bypass [3].

In upper median laparotomy approach, mobilization and lenghtening of the omentum was directed to the origin of the right gastroepiploic artery (RGEA) and brought up in the chest through the retrosternal part of the diaphragm. An epiploic muff was effectuated surrounding the graft and fixed with interrupted 6-0 Prolene sutures to the epicardium in such a manner that the graft wouldn't be distorsed.

After three months, under general anesthesia, the animals were sacrificed with intravenous concentrate potassium chloride solution. Cutting through the distal end of the grafts, patency of the grafts was checked.

Histological examination was made from the proximal, middle and distal segments of the grafts on serial sections. Specimens embedded in paraffin were stained with hematoxilin - eosin and Goldner's methods.

## Results

All grafts were patent after three months. Histological results: no intimal thickening or media fibrosis were seen. The contact zone of omentum with IMA wall has a lamellar structure. It has loose connections to the external connective tissue layer of the graft and it can be well defined from the omental structures. The contact zone is free from any fibroid reactions. In this area some little and larger vessels can be found as well. Thin vegetative fibre fascicles appear also on the circumference of the IMA. This structure is valid for the 2/3 contour of the graft. The rest 1/3 correspond to that territory where the surrounding omentum forms a pedicle for the graft. On this zone the newly-formed adventitia is a homogenous, loose connective texture containing numerous vessels. Here the capillary density is 3-4 times higher than anywhere else around the graft. New-formed permeable capillaries, solid vascular buds and variously shaped sinuous vessels can be found in this area. This fact supports the hypothesis that the tight symbiosis between omentum and graft goes together with intensive angiogenesis, but the new-formed vessels are never penetrating through the external elastic lamina.



## Discussion

The use of omentoplasty for revascularisation is an old practice in surgery. Due to its exceptional adhesive and angiogenic properties, the great omentum was wide-ranging employed by revascularisation of different organs.

Our work can not demonstrate if the omentoplasty will be able to prolongate the patency of the graft, but it's a fact that the omentum assures a rich vascular source for the stripped IMA. The new-formed capillaries disposed in the graft-omental adhesion zone very rarely penetrate into IMA wall, respecting mostly the external border of the media. *It seems that the laminated layers of elastic tissue in the media and nutrition of graft wall in part from the lumen*, represents a biological barrier for the penetrating new-formed vessels, versus other experimental omentum-muffled muscular tubular organs where this reaction is more intensive. For example, according to our own earlier research, in the wall of the ureter covered with omentum numerous newly-formed vessels penetrate deep under the urothelium [2].

The needs of the IMA free graft is low in comparison with the omentum vessels «offer» in the above mentioned circumstances, probably because of the thin vascular wall and structural particularities of the IMA. Our researches support the premise that the free grafts folded by omentum is an adequate experimental model for angiogenesis study in free arterial grafts and to determine the «need» for adventitial revascularisation.

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## LATE EPIGASTRIC INCISIONAL HERNIAS FOLLOWING LAPAROSCOPIC CHOLECYSTECTOMY

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By the introduction of laparoscopic cholecystectomy a new "gold standard" procedure became a routinely performed operation in the field of biliary tract surgery. Thus, the incision related early and late complications are thought to diminish, especially the formation of incisional hernias. Five patients had been referred to our department suffering from chronic incisional hernias following laparoscopic cholecystectomy. All of the hernias were located to the site of the epigastric trocar. The contents of the hernias proved to be omentum. The documentation's of the laparoscopic cholecystectomies revealed the extraction of thick walled gallbladders that contain large stones, and the wounds through which the extraction was performed had not been closed. Taking into consideration the fact of the "Chimney Effect" caused by the desufflation of the pneumoperitoneum at the end of the laparoscopic operation, bowel or omentum can easily escape through the relatively large wound formed during the extraction of the gallbladder, resulting in the formation of incisional hernias. This can be avoided by the complete desufflation and the prompt closure of the wound.

**Keywords:** Laparoscopic cholecystectomy, incisional hernia, epigastric trocar site, pneumoperitoneum, desufflation.

### Introduction

By the introduction of laparoscopic cholecystectomy it had been stated that it abolishes so many early and late postoperative complications. Freedom from incisional hernia formation is one of the benefits of laparoscopic cholecystectomy which remain to be documented by prospective studies [1]. Since that time just few papers had been reported in relation to post-laparoscopic hernia formation, or Richter's hernia [2,3,4]. These reports deal with early post-laparoscopic hernia formation with bowel obstruction, but none of them report about late post-laparoscopic cholecystectomy incisional hernia formation [5].

### Material and Methods

5 patients (4 women and one man) had been referred to our department because of epigastric hernias. The mean age was 51 (range, 36–73 years). All these patients had undergone laparoscopic cholecystectomy for symptomatic cholelithiasis. History revealed chronic cholecystitis with thickened gallbladder wall, and all of them had large stones. Laparoscopic cholecystectomy had been achieved successfully, and the extraction of the gallbladder with the stones was performed with the aid of an extractor, through the epigastric trocar site, and only the skin was closed with sutures. All these patients suffered from shoulder pain in the postoperative period. 2–6 months following the operation they observed the formation of a hernia in the epigastric region under the scar of the site of the epigastric port.

## Results

All the five patients were operated on for the incisional hernias. At the operation in all of the cases the hernia sac contained omentum. No sutures had been found in the operation area, and it must be stated that no adhesions has been observed between the abdominal wall and the subhepatic region.

## Discussion

Incisional hernias following laparoscopic procedures seem to be very rare, and they relatively occur in the early postoperative period in the form of Richter's hernia [4] associated with bowel obstruction [3]. For this reason Williams [4] recommended the promotion of specific fascial closure after laparoscopy at trocar sites sized 10 mm or larger. Only one report had described the phenomena of the late post-laparoscopic cholecystectomy incisional hernia formation [5], and also related it to the insufficient closure of the 10 mm or larger trocar sites. Reviewing the clinical history and the documentation's of our five patients it seems that the three following important facts should be mentioned:

1. The postoperative shoulder pain indicates that the desufflation of the abdominal cavity from the pneumoperitoneum was insufficient,
2. The gallbladders extraction was managed with the aid of an abdominal wall retractor, leading to the enlargement of the trocar site,
3. No fascial closure was promoted.

The insufficient desufflation of the abdominal cavity from the pneumoperitoneum through the trocars leads to the retention of the gas that escapes through the wound, making a "Chimney effect", and enhancing the omentum to move towards the wound continuously, and to pass the fascial border through the enlarged wound until it reaches the subcutaneous region. When the skin is closed, the omentum remains under the skin to form the first step towards the late incisional hernia formation.

To avoid post-laparoscopic hernia formation we suggest that the desufflation of the abdominal cavity should be managed correctly, the fascial defects at 10 mm or more should be closed specifically, and when possible, only trocars at 5 mm or less should be used.

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## **INFLAMMATORY MEDIATORS AND SURGICAL TRAUMA REGARDING LAPAROSCOPIC ACCESS: FREE RADICAL MEDIATED REACTIONS**

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In this prospective study the free radical mediated reactions, the changes of endogenous antioxidant defense mechanism and activation of leukocytes were measured from the blood of patients undergoing elective cholecystectomy because of symptomatic cholelithiasis. The patients were randomised into two groups. Group one contained 21 patients treated by open cholecystectomy (OC). Group two consisted of 21 patients treated by laparoscopic cholecystectomy (LC). Both groups had similar patient characteristics. Patients with acute cholecystitis, pancreatitis, choledocholithiasis or other disease were excluded. Values from patients in both groups were compared. The measured biochemical parameters are the following: malondialdehyde (MDA) as a marker of the free radical induced lipidperoxidations, reduced and oxidised glutathione (GSH-GSSG), as endogenous scavengers as well as markers of oxidative stress and myeloperoxidase activity (MPO) of leukocytes. The results showed significantly lower values of postoperatively measured MDA, GSH-GSSG, and MPO activity of leukocytes in patients with laparoscopic cholecystectomy, indicating a lesser stress response and tissue trauma in this group of patients. The results correspond to the favourable results of most other trials evaluating clinical aspect of LC.

### **Introduction**

In many retrospective and prospective studies, LC compares favourably with respect to length of hospital stay, postoperative and pulmonary function to OC, a diminished operative trauma [3]. Whereas significant hormonal and inflammatory responses following OC are documented [2], the response to LC have only been investigated in a few studies [3], especially the free radical mediated reactions have hardly ever been investigated. However, investigation of these pathological factors may be useful for better understanding of laparoscopic surgery. The aim of this study was, to compare the free radical mediated mechanism and activation of leukocytes after OC and LC in a randomised group of patients.

### **Methods**

Forty-two patients were randomised for elective cholecystectomy. Of these 21 underwent OC and 21 LC. Criteria for exclusion from the study included acute cholecystitis, choledocholithiasis, pancreatitis, malignant disease or any concurrent illness. Both group had similar patients characteristics. The study was approved by the ethics committee and



informed consent was obtained from each patient. Anaesthetic techniques were similar in the two groups. Ceftriaxon 2 g was administrated as antibiotic prophylaxis 2 h before surgery. OC was performed via a standard subcostal incision, LC was performed by a four-cannula technique. All patients made an uneventful postoperative recovery. Peripheral venous blood samples were taken 3 h before the operation from an indwelling venous cannula and every day for 5 days following the operation, at the same hour. MDA concentration was determined by spectrophotometric method at 532 nm according to Placer in the whole blood, while for measurement of plasma MDA we used Okahowa method at 535 nm. The contents of reduced glutathion (GSH) and oxidised glutathion (GSSG) in the plasma as well as whole blood were determined as described by Tietze and slightly modified according to Guarnieri using an enzymatic method for spectrophotometric evaluation at 412 nm. The amount of serum MPO was determined in sera with colorimetric reaction at 560 nm. To evaluate the results, mean and standard errors (SE) were calculated. The statistical significance of change was determined by Student's paired *t* test and the preoperative values served as control.

## Results and Discussion

According to our results the level of MDA in the whole blood in the OC group continuously increased during the observation period from  $393.1 \pm 19.8$  nmol/ml to  $462.3 \pm 22.0$  nmol/ml by the 4th postoperative day. This elevation was significant ( $p < 0.01$ ), as compared to only a small rise seen in the LC group. The plasma level of MDA in the OC group increased only on the first postoperative day ( $0.92 \pm 0.10$  to  $1.10 \pm 0.15$ ), while the level of MDA in plasma decreased significantly during the same time in the LC group ( $1.03 \pm 0.11$  nmol/ml to  $0.87 \pm 0.11$  nmol/ml). There was a marked fall ( $p < 0.01$ ) in values of GSH in the OC group measured in plasma fraction during the first 3 postoperative days ( $0.89 \pm 0.05$  nmol/ml to  $0.70 \pm 0.04$  nmol/ml). In contrast the laparoscopic intervention caused only a temporary depletion of GSH ( $0.90 \pm 0.04$  to  $0.77 \pm 0.04$  nmol/ml). The level of GSH in the whole blood decreased significantly ( $p < 0.05$ ) on the 3th postoperative day in the OC group  $1357 \pm 107$  nmol/ml to  $1190 \pm 87$  nmol/ml, while it remained practically unchanged in the laparoscopic cases. MPO activity of leukocytes significantly ( $p < 0.001$ ) differed in the two groups. Increased MPO activity showed stimulation of leukocytes in the OC group from  $1.25 \pm 0.18$  OD/ml reaching a peak of  $1.98 \pm 0.20$  OD/ml on the 4th day, while MPO activity remained basically unchanged in the LC group. This study has demonstrated characteristic metabolic responses to both OC and LC on the basis of measured parameters with significant differences between the two types of procedure. It has been recently acknowledge that laparoscopic intervention results in less postoperative pain, a smaller decline in pulmonary function after operation, better postoperative oxygen saturation and a speedier return to normal activity than open cholecystectomy [4]. However, some aspect of the free radical mediated reactions after laparoscopic procedure have not yet been reported. Reactive radicals can abstract H atoms from allelic sites in lipid

membranes and in the presence of oxygen this leads to chain reactions propagating to involve lipid peroxy radicals and hydroperoxides. This process leads to lipid breakdown and the production of highly reactive aldehydes [5]. The MDA level measured in whole blood and/or in plasma fraction is an indirect marker of such a process. The level of this marker differed significantly between the two groups in our series. The GSH peroxidase/GSSG-reductase system is critical as a cellular defense mechanism against oxidizing molecules such as hydroperoxides. During oxidative stress GSH is oxidised to GSSG [5]. The surgical trauma induced stress affects this process. Our data reflect the different changes in GSH values between the two groups, which can be taken as a good indicator of oxidative stress, which in itself is a good demonstrator of patients postoperative recovery. MPO activity of leukocytes differed significantly in the two groups. It seems to be, that LC is less disruptive to neutrophil function than conventional open procedures. This observation is supported by others [1].

### Summary

The present trial was designed to examine stress response to open and laparoscopic cholecystectomy characterised by free radical mediated reactions. Significantly lower values of MDA, GSH-GSSG and MPO activity of leukocytes were observed after laparoscopic operation. The results support the favourable results of other trials evaluating clinical aspect of LC.

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## ACUTE ARTHROSCOPY

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The role and significance of acute arthroscopy have been evaluated in the treatment of knee joint injuries on the basis of findings during 59 arthroscopic operations which were conducted within two weeks after the accident. The injuries developed isolated in more than half of the cases (65%) whereas they appeared in a combination of two or more in 26% and in 9%, respectively. Injuries requiring operation were found in 91.5%, most of which were ruptures of the ACL (33 cases) and menisci (23 cases). In the case of ACL rupture, in the acute phase on sportsmen and physical workers primary arthroscopically assisted transligamentary replacement was performed with patellar graft while in the case of proximal rupture of the ACL reinsertion and augmentation were carried out with semitendinosus tendon. The ruptures of dislocated eminence were refixed in each case. In the case of the rupture of meniscus the refixation of the meniscus or resection of the ruptured part was attempted. By means of acute arthroscopy the lesion of the intraarticular structures or that of their combinations can be exactly diagnosed. Depending on the findings of arthroscopy the injuries can be treated immediately or operated on at a later time, thus preventing the joint from further deterioration.

### Introduction

In the acute phase right after knee injury, because of the pain and muscle spasm, the lesion of the intraarticular structures cannot always be exactly diagnosed by physical examination. The lack of adequate treatment may, in the long run, result in the further deterioration of the joint.

### Materials and Methods

Between 1 April 1990 and 1 September 1995 there were 845 arthroscopic operations performed at the Orthopaedic Department of the Medical School, University of Debrecen, 59 of which were acute arthroscopies (operations carried out within 14 days after the accident). None of the patients operated on during the acute phase had had knee injuries before.

40 of the patients were men and 19 women, their average age was 27.3 years (13–60 years old).

We examined the cause, mechanism and type of the injury, the most common combinations of injuries as well as the frequency of haemarthrosis. Our tactics during the primary operations will be discussed below.



## Results

The frequency of the injury of the right and left knee was the same (29:30). The injuries were caused by sports in 33 cases (football: 19, ski: 8, basketball: 2, handball: 2, other sports 2), by falling in 17, by accidents at home in 5 and by road traffic accidents in 4 cases. The most serious accidents (the rupture of both the ACL and the PCL) were caused by road traffic accidents.

The injuries in most cases were caused by direct (20), flexion-external rotational-valgus (17) or flexion-external rotational (11) stresses. Flexion-internal rotational-varus stress (6) and hyperextension (5) were less common.

Our patients were admitted to hospital on an average of 7.1 days (4–10) after the injury.

Out of the 47 haemarthroses puncture took place in 25 cases during which an average of 43 ml blood was aspirated. 6 of the 25 patients had an osteochondral fracture while 19 had a rupture of the ACL or the capsule.

Arthroscopic findings: Ruptures of the anterior cruciate ligament (ACL) were found in 30 cases (21 total, 6 partial, 3 elongation), posterior cruciate ligament (PCL) in 5 cases (3 total, 2 partial), medial meniscus (MM) in 13 cases (4 bucket handle, 4 pediculated, 3 longitudinal, 2 radial), lateral meniscus (LM) in 10 cases (5 pediculated, 4 longitudinal, 1 radial), medial collateral ligament (MCL) in 8 cases, lateral collateral ligament (LCL) in 1 case, capsule in 7 cases. There were 8 patients with osteochondral fractures (3 eminentia, 2 lateral femoral condyle, 2 patella, 1 medial tibial condyle).

The injuries appeared isolated in 35 cases (12 ACL, 7 capsule, 6 osteochondral fracture, 4 MM, 4 LM, 2 MCL) whereas in 14 cases in a combination of two (6 ACL+MCL, 5 ACL+LM, 2 ACL+MCL, 1 MM+fracture) and in 5 cases in a combination of more (2 ACL+PCL+MM+MCL, 2 ACL+MCL+LM+MCL, 1 ACL+MCL+LCL). In 5 cases only haemarthrosis was found in the knee joint without any other abnormalities.

In the case of ACL rupture, in 11 patients primary arthroscopically assisted transligamental replacement was performed with a free middle-third patellar bone-tendon-bone graft. In 9 cases with proximal rupture of the ACL reinsertion and augmentation were carried out with semitendinosus tendon. In 10 cases primary reconstruction of the ACL was not performed. In two of these cases resection of the bulky ends of the ruptured ACL was performed.

In all three cases of total PCL rupture, in addition to the reconstruction of the ACL, the ruptured PCL was sutured.

Because of medial meniscus rupture the ruptured part was resected in 9 cases and arthroscopic suture was performed in 4 cases. Because of lateral meniscus rupture 7 resections and 1 suture were performed. 2 stable ruptures were not operated on.

The 3 dislocated eminentia fractures were refixed and in 5 cases the small osteochondral fragments were removed.

The isolated medial collateral ligament rupture was not operated on.

## **Discussion**

During the studied five-year period only 59 of our 845 arthroscopic operations (7%) were performed in the acute phase. In our opinion this rather low proportion can be explained by the fact that neither the injured patients nor the doctor responsible for their treatment have realised the seriousness of the injury.

In compliance with the data in the literature [5], in acute arthroscopy we have also found that in a high proportion of the cases – 54 of 59 (91.5%) – the intraarticular lesion, most frequently ACL and meniscus rupture, required operation [1].

56% of our patients had ACL rupture.

The injuries developed isolated in more than half of the cases (65%) whereas they appeared in a combination of two or more in 26% and in 9%, respectively. The most serious combined injuries in our cases were also caused by road traffic accidents [4].

On the basis of our findings in acute arthroscopies the injuries frequently cause isolated ACL rupture which leads to one-plane or simple rotational instability.

If the ACL rupture is not recognised and not treated properly and the patient continues to do strenuous sports or other strenuous activities, because of the overstretching of the active and passive secondary stabilizers of the knee, a serious and combined rotational instability may develop with time. The pathological changes caused by the instability in the knee may result in meniscus rupture, the injury of the joint cartilage and later osteoarthritis.

## **Our tactics in acute treatment**

ACL injury: the rupture of dislocated eminentia was refixed with a screw or wire loop.

In the case of proximal rupture, reinsertion used to be quite frequent but more recently it is applied only in those rare cases where the ACL is ruptured directly at the insertion and the substance of the ligament is good. Reinsertion has always been augmented with a distally pediculated semitendinosus tendon.

In the case of the rupture of the midal part of the ACL, in sportsmen and active persons primary operation or, after the cessation of post-traumatic symptoms, reconstructive much overweight or low activity conservative treatment is recommended for isolated ACL rupture [2].

In the case of combined ruptures of both the cruciate ligaments and the collateral ligaments or menisci primary reconstructive operation is to be performed.



In the case of the partial rupture of the ACL extending to more than 50% of its diameter re-rupture is frequent.

In the case of the rupture of the red part of the meniscus in acute case suture is indicated. In any other cases, the ruptured part of the meniscus must be resected. Small stabile ruptures do not require operation.

Isolated medial collateral ligament rupture can generally be treated conservatively [3].

Small osteochondral fragments have to be removed while bigger ones may be refixed.

If during primary arthroscopy nothing but haemarthrosis is found, after joint lavage weigh-bearing of the knee is allowed at once.

As a matter of course, operations will produce good results only if the patients undergo adequate postoperative rehabilitation programme.

### Summary

Acute arthroscopy performed right after knee injury can exactly diagnose the lesion of the intraarticular structures or that of their combinations. Depending on the findings of arthroscopy the injuries can be treated immediately or operated on at a later time, thus preventing the joint from further deterioration.

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## **THERAPEUTIC VALUE OF CONTINUOUS PASSIVE MOTION AFTER ANTERIOR CRUCIATE REPLACEMENT**

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The aim of this study is the evaluation of the therapeutic value of continuous passive motion after ACL replacement. After 41 ACL reconstruction in 13 cases only active motion, in 28 cases active motion and CPM were used postoperatively. Stability, the range of motion and complications were evaluated at the time of discharge, 3 and 6 months after the operation. The flexion-extension in the CPM group was significantly greater at the time of discharge, but this difference was practically eliminated in 6 months after the operation. There were not any other significant difference between the two groups. The CPM gives only a little advantage in the rehabilitation after the ACL replacement.

### **Introduction**

The continuous passive motion (CPM) is a useful method in the postoperative treatment of total knee arthroplasty [2] and the articular cartilage defect [5]. Using CPM the haemarthrosis is absorbed twice as fast from a joint subjected to CPM as from one is immobilized [4]. Noyes [3] strongly recommended early motion program to decrease the morbidity of major intraarticular ligamentous procedure. The purpose of this study: to evaluate of the therapeutic value of CPM after ACL replacement.

### **Materials and Methods**

Arthroscopically-assisted reconstruction of chronic ACL rupture with middle third patellar bone-tendon-bone graft was performed with interference screw fixation on 41 patients. There was not any other concomitant injury in 30 cases, meniscus rupture was treated by partial arthroscopic meniscectomy in 11 cases. There was no patient with chondropathy of more than stage II.

Postoperatively 13 patients (8 male, 5 female, with the average age of 29,7 years) underwent a rehabilitation program, whereas 28 patients (19 male, 9 female, with an average of age of 27,7 years) were treated similarly in addition to continuous passive motion. CPM was used 6 hours daily for 5 days from full extension up to the painful flexion position of the knee (70-80° on an average). The patients in both groups spent the same period after the operation in the hospital (an average of 6,2 days). The evaluation of the result was based on the IKDC knee ligament evaluation standard. The range of motion was measured with a goniometer at the time of discharge of the patients as well as 3 and 6 months following the operation.

Knee stability, subjective results and complications were evaluated 6 months after the surgery. The acute pain was measured by assessing the amount of total intake of pain medication during the stay in hospital.

## Results

The flexion-extension in the CPM group was significantly greater at the time of discharge (7,7–87,6° vs 15,8–73,8°), but this difference gradually decreased (2,8–107,7° vs 8,1–94,2°) 3 months after the operation and it was practically eliminated in other 3 months (1,1–123,7° vs 2,7–116,9°).

The evaluation of the knee stability by IKDC standards gave the similar results in the two groups six months after the surgery [CPM: group A:22 (78,6%), group B:5 (17,8%), group C:1 (3,6%); non-CPM: A:9 (69,2%), B:3(23,1%), C:1 (7,7%)].

At the same time there were no significant difference in the patients' subjective assessment either [CPM: A:20 (71,4%), B:5 (17,9%), C:3 (10,7%); non-CPM: A:8 (61,5%), B:3 (23,1%), C:2 (15,4%)].

The aspiration of haemarthrosis was performed 5 times in the CPM group, and twice in group non-CPM group. We did have wound healing problems. Despite the fact the patients felt the CPM comfortable, there was no considerable difference between the two groups in the amount of total intake of pain medication during staying hospital.

## Discussion

The use of CPM after reconstructive surgery of ruptured ACL gives a greater range of movement in the early postoperative period, but an adequate rehabilitation program without CPM can provide the same result in a longer period.

Despite the fact that the CPM gives a comfortable feeling for the patients, it does not decrease significantly the amount of total intake of pain medication.

In some cases the CPM can cause the failure of the graft [1]. By our opinion the CPM does not cause rupture or loosening of the graft, if it is strong enough, placed isometrically and fixed firmly.

## Summary

The CPM gives only a little advantage in the rehabilitation after the ACL replacement.

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## **PROGNOSIS OF UNTREATED LIVER METASTASIS FROM RECTAL CANCER**

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Majority of studies based of treatment of liver metastases from colorectal cancer compare their results to historical controls that include patients having untreated secondary liver tumours. The aim of this study was to show the natural history of patients with liver metastasis from rectal cancer. Data of 303 patients underwent laparotomy between 1984 and 1992 were reviewed. 47 of 57 patients who had liver metastasis at the time of surgery fulfilled the criteria of the study. The mean survival time was 8.5 (1-27) months for all patients, 11 months for patients with solitary hepatic tumour (n=13) and 7.5 months for those with multiple tumours (n=34). Patients who had liver and other distant metastases simultaneously (n=9) survived a shorter time than those with hepatic secondaries only (4 and 9 months respectively). The mean survival time for patients in whom the primary tumour was resected (n=17) was 11 months contrary to 7 months for those who underwent colostomy or exploratory laparotomy, but comparison of survival curves didn't revealed significant difference between the two groups.

Conclusions: The incidence of liver metastases from rectal cancer at the time of laparotomy was 19%. The prognosis was very poor in case of synchronous secondary tumours. Palliative resection of the primary tumour is recommended for selected patients only to control local symptoms.

### **Introduction**

Nowadays there is a tendency to treat the patients with liver metastases from colorectal cancer by surgery with curative intent or to remove the primary tumour even on palliative purpose. In addition many patients with metastatic tumour receive cytostatic treatment to control tumour growth. The majority of studies compare the results of these therapeutic modalities to historical controls that include patients with untreated secondary liver tumours.

The aim of the present study was to evaluate the natural course of patients who had untreated liver metastases from rectal cancer and to assess the results of palliative resection of the rectum carcinoma.

### **Material and Method**

Authors reviewed retrospectively a hospital-based series of patients with rectal cancer who were treated in such a period when the treatment of secondary liver tumours hasn't been widely used. 57 of 303 patients who were studied had hepatic metastases at the time of laparotomy.



Ten patients were excluded because of the operative mortality ( $n=4$ ) or treatment of the liver disease ( $n=6$ ). Among the remaining patients the hepatic metastases were multiple in 34 cases and solitary in 13 cases. There were 8 patients who had hepatic and extrahepatic metastases simultaneously. 17 patients underwent palliative resection of the primary tumour whereas 30 rectum carcinomas were left in situ. The survival was estimated according to Kaplan–Meier method. For comparison of survival curves the long-rank test was used.

## Results

The longest survival time was 27 months. The mean survival time was 8.5 months for all patients, 11 months in case of solitary hepatic metastases and 7.5 months for patients with multiple foci in the liver. Patients underwent colostomy or exploratory laparotomy survived shorter time than is whom the primary tumor was resected (7 and 11 months respectively). Nevertheless the comparison of survival curves didn't reveal any significant difference between these groups of patients ( $p < 0,05$ ). In case of synchronous hepatic and extrahepatic metastases patients presented the poorest survival (4 months in average) contrary to those with liver secondaries only (9 months).

## Discussion

Incidence of liver metastases from colorectal cancer at the time of laparotomy varies from 18 to 25% [1]. The present rate was 19% and the mean survival time was longer than that was reported by others (5.6 months) [1]. The prognosis seemed to be influenced by the amount of metastatic tumour rather than by the number of foci in the liver [1]. In presence of liver metastases the patient's survival hasn't been improved significantly by removing the primary tumour. The poorest prognosis could be seen in patients with synchronous hepatic and extrahepatic metastases. These patients should be managed conservatively rather than by surgery [2]. In selected cases palliative resection of the primary tumour can be recommended to control local symptoms but significant improvement in survival time can't be expected. More aggressive attitude toward the surgical treatment of liver metastases is implemented.

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## OUR PRELIMINARY RESULTS IN APPLICATION OF STOPPA TECHNIQUE FOR RECURRENT GROIN HERNIA

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In 1994 we have started the Stoppa technique which was only used for the recurrent groin hernia repair, when Mersilene mesh was implanted in preperitoneal position from a lower midline incision. From March, 1994 to March, 1996 seventeen Stoppa procedures were performed in our department (14 men, 3 women, mean age of 66 years). Type of hernias: 13 unilaterale, 3 bilaterale recurrent groin hernias and 1 primary bilaterale groin hernia combined with a lower midline incisional hernia. Operations were performed by 7 surgeons. The mean time of the surgery was 85 min. (35–165). The mean postoperative stay in the hospital was 9 days (7–19). The Stoppa technique could be performed in all patients. Serious early postoperative complications didn't occur. The two late recurrences were observed amongst the first five patients. All implanted mesh were well tolerated by the patients. Author believe, this procedure has some advantages: the site of the incision is located in a new place from where the dissection is easier than in the previous incision, the stich fistulas from the previous operation can be avoided, furthermore this method could be applicated for combined hernias located in the lower part of abdomen and it is cheaper than the laparoscopic hernioplasty.

### Introduction

R. Stoppa described his technique in 1973 for recurrent inguinal hernia repair when a Dacron mesh was placed in preperitoneal position from lower midline incision [2]. Since the first report many papers have been dealing with the advantages of this technique [1, 3]. Having known difficulties in repair of the many times recurrent groin hernias, we started the application of Stoppa technique as a hopeful procedure. The aim of the present study was to evaluate our preliminary results with this type of hernioplasty.

### Material and Method

The operation was started with a lower midline incision without opening the peritoneum, which was separated from the abdominal wall extending to the umbilical line (up), to the iliopsoas muscle (lateral) and to the upper part of the foramen obturatum (down). Next step was pulling back the hernial sack towards the abdominal cavity and freeing the spermatic chord. A sized Mersilene mesh was placed in preperitoneal position and it was fixed in place with one or two sutures. Every time a redon drain was left. Urine catheter was placed before surgery. Antibiotic prophylaxis was given to every patients for 48 hours. Patients were kept in their beds for 48 hours.



Patients: 14 men and 3 women were treated, mean age 66 (49–81) years, between March 1994 and March 1996. There were 14 unilateral groin hernia that was first time recurrent in 10 cases, second times recurrent in 3 cases and fourth times recurrent in one case. Three patients had bilateral groin hernia: one side is primary and other side is recurrent in two cases and bilateral primary groin hernia combined with a lower midline incisional recurrent hernia in one case.

The operations were performed by 7 surgeons. The mean time of procedures were 85 (35–165) minutes. The mean postoperative stay in the hospital were 9 (7–19) days.

## Results

There was no operative mortality. The 5 early postoperative complications in 5 patients were the following: wound infection, seroma (required single evacuation), fever during 6 days (cause undiscovered), pneumonia, prolonged auricular fibrillation. The postoperative stay in the hospital was prolonged by these complications (10–12–19–15–12 days respectively). Both of the late complications were recurrence of the hernia in the inguinal region.

## Discussion

Considering our preliminary results and those reported by others, the Stoppa technique is a really useful prosthetic procedure in case of recurrent groin hernia and other lower abdominal postoperative even combined recurrent hernia. This method could be performed in all patients without serious early postoperative complications. The two recurrences were observed amongst the first five patients. All implanted Mersilene mesh were well tolerated by the patients.

Authors believe the Stoppa technique has some advantages: the site of the incision is located in a new place from where the dissection is easier than in the previous incision, the stich fistulas from the previous operation can be avoided, furthermore this method could be applicated for combined hernias in the lower part of abdomen and large area of the weakened transversalis fascia is reinforced by the giant implanted mesh. At present in Hungary this kind of hernioplasty appears more cost effective than the laparoscopic one should be.

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## INTERDISCIPLINARY TREATMENT OF THE MALIGNANT LYMPHOMA OF THE THYROID

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720 patients with malignant tumor of the thyroid were treated at our department between 1950 and 1996. Histological examination revealed 15 cases (2 %) of malignant lymphoma (14 female, 1 male mean age: 69.8 year). In 8 cases Hashimoto thyroiditis, in 1 case chronic lymphocytic thyroiditis was verified beyond the lymphoma. According to Ann Arbor staging, 9 patients were stage I E, 3 II E, 1 III E, and 2 IV E. Radical surgical treatment was performed in 7, palliative in also 7, and only biopsy in one case. Irradiation was administered in 9, chemotherapy in 8 patients. In 5 out of the 7 palliative operated patients tracheostomy was performed. 10 patients were lost. The therapy of the non-Hodgkin lymphoma of the thyroid is debated in the literature. There are some authors, who question the role of surgery. Our experience, based on the longer survival of the patients, who underwent radical operation, support those, who consider the possible surgical treatment as the initial part of the multimodal therapy.

### Introduction

The non-Hodgkin's lymphoma of the thyroid gland is a very rare malignant tumor, which constitutes 2–5% of the malignant diseases of the thyroid. From this it follows that both in its diagnostics and treatment there is no uniform standpoint in the literature. There are authors who question even surgical intervention [3]. Well-chosen procedures of treatment appropriate to the stage of the disease can give the patient optimal survival, contributing to which result is the cooperation of surgery, radiology and hematology.

### Methods

In our Department 720 operations were performed between 1950 and 1996 for malignant thyroid tumors. In the course of the histological evaluation 15 cases (2%) of malignant lymphoma were detected. In 6 cases it was only through histological revision that the diagnosis of malignant lymphoma was established in the material, which were previously considered medullary or small-cell anaplastic carcinomas. We had 1 male and 14 female patients, their average age was 69.8 yr (53–84 yr).



## Results

Most characteristic of the clinical signs was enlargement of the thyroid gland, which showed fast growth during the preoperative 2–3 months, and at the same time caused complaints of compression. Preoperative cytological examination was performed in 6 cases, in 4 of these there was suggestion of malignancy, in 2 cases concrete finding of malignant lymphoma. The staging of the patients was carried out retrospectively on the basis of the available data, according to the Ann Arbor staging. Nine patients were classified into stage IE, 3 into IIE, 1 into IIIE and 2 into IVE.

In 7 patients the surgical intervention was radical. All 7 were in stage IE; 4 patients were treated by irradiation, 2 with cytostatic medicines. In 2 cases subtotal resection was performed (in 1952 and 1965), nevertheless, survival was surprisingly good (23 and 24 yr, respectively). Both patients were given radiotherapy as well. Lobectomy was performed in two cases, the contralateral lobes were intact. One patient out of the two was known to have had recurrent nerve palsy even before the operation. The further 3 patients underwent thyroidectomy. We lost one of these patients 14 months after the operation due to pulmonary metastasis. No recurrent nerve palsy occurred postoperatively, no tracheostoma had to be prepared.

Only palliative intervention was performed in 8 patients. Two out of them was in stage IE, 3 in IIE, 1 in IIIE, and 2 in IVE. In 7 cases the intervention was debulking of the tumor, in one case only biopsy was carried out. We were obliged to prepare tracheostoma in 5 of these patients, 4 were given cytostatic treatment and telecobalt irradiation was administered to 5. One patient was lost on the 2<sup>nd</sup> postoperative day in consequence of left atrial insufficiency. Both patients in stage IVE underwent stomach resection because of gastric lymphoma. They received cytostatic treatment following the healing of the wound. Survival ranged from 1 to 28 months.

The histological findings were centroblastic, centrocytic-centroblastic, immuno-blastic lymphomas. The immunohistochemical examinations demonstrated the B-cell origin of the lymphomas in the majority of the cases. According to the literature, in addition to lymphocytic thyroiditis, the occurrence of non-Hodgkin's lymphoma is significantly increased [1]. According to assumptions, because of the prolonged antigenic stimulus persisting during the chronic inflammation of the thyroid gland, there is higher chance of the malignant transformation of the lymphoid elements. In our material inflammation reaching the level of Hashimoto's thyroiditis was described in 8 cases, and in one case chronic lymphocytic thyroiditis. At the same time, on observing the patients with differentiated papillary thyroid carcinoma it became clear that in the case of concomitant thyroiditis the rate of recurrence and metastases is lower.

Nine of the 15 patients underwent irradiation (in the 50s this meant orthovoltic treatment, later telecobalt). Out of the 10 patients operated on in 15 years 6 were given chemotherapy (BACOP, CVP cure) in the Hematological Section of the 2<sup>nd</sup> Department of Internal Medicine.

Follow-up of our patients was possible through our clinical department with varying lengths of time. In one of the 8 patients undergoing radical surgery bone metastasis was

found, which became radiologically negative after telecobalt irradiation. Another patient developed lung metastasis, and this patient was lost after three months. In the control examinations the thyroid hormone level was checked, then the patients were, corresponding to the findings, supplied with thyroxin substitution.

## Discussion

Malignant lymphoma of the thyroid gland occurred in 2% of the patients in our department, that means that, in agreement with the literary data, it is rarely encountered. Observations on a large number of patients in the literature support the view that in stages IE and IIE operations with appropriate radicality (thyroidectomy, lymph-node dissection) can ensure longer survival. Out of our 12 patients in stages IE and IIE radical surgery was possible in 7 cases. At the same time there are authors who question surgical intervention and recommend it only in cases causing compression, and prefer radio- and chemotherapy [4, 5]. Our experience gained in the treatment of our cases make us join those who regard the possibility of surgery as the initial step in a multimodal therapy [2, 3]. Playing a basic part in the favourable survival rate of patients undergoing radical surgery was the surgical removal of the tumor, in addition to irradiation therapy.

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## CREATION OF AXILLO-AXILLAR BYPASS WITH BIDIRECTIONAL ANASTOMOSES

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Scholz and co-workers reported such type of anastomosis applied in femoro-crural bypass procedures which leads blood flow well into both directions. In vascular surgery practice of the author there were several occasions where this modified anastomosis was favorably applicable. An old man was operated up in this manner whose left common and internal carotid artery and the starting part of the subclavian artery was occluded that caused steal syndrome. Axillo-axillar bypass was done with end to side anastomoses. After the operation blood pressure increased to 155/75 mmHg on both arms the steal phenomena ended. Bidirectional anastomoses make flow from obtuse angle to rectangular.

### Introduction

In 1993 Scholz and co-workers [3] reported such a type of end to side anastomosis that leads blood flow well into both directions. In the practice of vascular surgery we have encountered several situations in which this modified type of anastomosis was favorably applicable. In Hungary we have prepared first axillo-axillaris bypass [1, 2, 4] in 1973 and we have applied it also in indicated case since then.

### Case report

Described below we report the case of our patient. J. Gy. 71 years old men. In his history right hemiparesis and central aphasia, emphysema and chronic bronchitis, hypertension have occurred. The blood pressure on his right arm 160 mmHg and 60 mmHg on the left. He has been feeling dizzy and his left arm has being numb for two months. The left carotid and subclavian artery is not palpable. The aortic arch's DSA have showed the occlusion of the left carotid and subclavian artery and periferic filling of the subclavian artery with significant steal in later phase. After preparing the patient an operation was done in endotracheal anesthesia. We have looked up both axillar arteries under the collarbones and a 6-mm Gore-tex prosthesis bypass was made leading from right to left in the subclavian fat tissue. From the artery a 16–18 mm oval window was cut out and the end of the prosthesis was cut in opposite to each other 10 mm in length. It was sewed with 5–0 Gore-tex string. After the release of the artery preoperative 5 unit's pulse wave increased to 20 units, the blood pressure was 155/75 mmHg on both arms.

The postoperative course was uneventful his wounds healed per primam. Dizziness and numbness has ended.

### Discussion

Narrowing located on the starting section of the subclavian artery can be corrected operatively with reimplantation into the carotid artery (with or without interposition) or with carotico-subclavian bypass. In a patient with decreased tolerance or as it was in our case in absence of the carotid artery axillo-axillar bypass is one possible solution. It has a great hemodynamic disadvantage i. e. on the donor side flow have to turn back in obtuse angle and on the accepting side flow into the vertebral artery is obtuse angle too. Bidirectional anastomoses make flow rectangular on both sides. Hemodynamic effectiveness is supported by the blood pressure measured on both arms.

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## ABOUT STREAMLINED BRACHIAL DIALYSIS SHUNTS

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The authors modified the technics of fistula forming. In such cases where to create a connection on the forearm is impossible one possible modality is to make it between major vessels on the arm. Streamlined connection was made in seven patients between basilic vein and brachial artery in three cases, between cephalic vein and brachial artery in four. There were two men and five women. The age interval was between 58 and 78 years. The longest observation period is 30 months. Until this time the fistulas were suitable for dialysis and had abundant yeald. Because of the number of cases and the observation period has not yet make possible to come to final conclusion their goal was to present technical solution first of all. Their expectation is that with making them streamlined they will manage to create good perfusing and long lasting fistulas.

### Introduction

The "sine qua non" of hemodialysis is well functioning arteriovenosus connection. Classical, nowadays the most frequently applied type is Cimino-Brascia fistula which has several modification. For a vascular surgeon well up in hemodinamics it looks natural to prevent such disadvantageous streaming situation caused by rectangular or obtuse angle ramification. In our practice streamlined connection was created as it was presented earlier [1].

In cases where the ways to create connection on the forearm were used up or it was impossible at all, we constructed it over the elbow. In our practice they were made in "streamlined" form.

### Method

We can choose between two possibilities depending on the vein that looks more suitable for creating a fistula. If the cephalic vien is appropriate it is let in it's bed because it's superficial localization and the easiness for puncture. It is looked for in the cubital fossa and if it is possible we use the join of one tributary's to create a funnellike anastomosis. The brachial artery is looked up at right over the elbow and end to side anastomosis is made. For creating a streamlined bent some adventitial fixing stitches are taken in. The basilic vein is situated deeper and it's puncture is difficult. For this reason anteposition is done. The vein is looked up in the middle or lower third of the arm.

Then it is led to the brachial artery through a tunnel constructed right under the skin where stream lined anastomosis is created. Seven dialysis shunts were done on the arm. There were five women and two men. The age interval was between fifty eight and seventy eight years. In four cases the connection was made with the cephalic vein and ante-position with of the basilic vien in there.

## Results

The fistulas have been working from two to thirty months for on average of fourteen. Two patients died with working fistula after two and eight months respectively. We have checked the blood pressure on both wrist of the patients and it was found decreased with thirty mmHg to the opposite averagly. But it did not cause any complaint.

## Discussion

As it is known from the laws of flow kinetic the loss caused by direction breaking is the least along arctubes. The loss of flow is influenced by the radius of the arc's bend. The loss of two right angles with rather great radius is smaller than one 140–150 degrees breaking's and the 30–40 degrees arc's. Not only the flow loss has importance in the vascular system. Changes producing turbulence has influence on hemostasis too. Dead spaces and coming off of the border layer have role in clot production and in intimal hyperplasia in a longer period. One must hold in his mind that the flow is significantly faster in dialysis fistula. The palpable thrill and auscultatori bruit refer to turbulent flow too. Our idea is supported by the fact that there is only rectangular or acute angle but not obtuse angle ramification in the organism. The number of cases and the observation period has not yet make possible come to final conclusion. Our goal was to present the technical modification first of all. Our expectation is that with taking them stare amlined we shall manage to create good perfusing and long lastind fistulas which are hemodinamicaly more efficient.

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## THE INFLUENCE OF ROUX-Y VERSUS LONGMIRE-GÜTGEMANN RECONSTRUCTION ON THE COMPOSITION OF PANCREATIC JUICE

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Both methods of reconstruction after gastrectomy lead more or less to an insufficiency of pancreas. Therefore investigations on rats should further clarify which defects are obvious after both operation methods. Wistar rats were divided into 3 groups. In 2 groups a gastrectomy was performed while one was reconstructed according to the method of Roux-Y, the other was treated according to the method of Longmire-Güttgemann. The first group was a sham operated control group. 3 months after this operation pancreatic juice was collected over the time of 6 hours. Volume and protein content were determined as well as a differentiation of the proteins by means of the 2D electrophoresis which separates the molecules according to isoelectric focus and the molecular weight. The results show a significant increase of the volume of pancreatic juice after both operations. Whereas the protein content is also altered the number of proteins is significantly decreased. Especially proteins with an alkaline isoelectric focus are significantly diminished. The molecular weight of the proteins is also changed. Low molecular protein fragments which were not observed in the sham operated group are increased especially in the Roux-Y group. This means that the production of enzymes is changed after both operations. The pH optimum as well as the viability of the protein enzymes is shifted. Since the changes are more pronounced after Roux-Y operation signs of pancreatic insufficiency should be expected more frequently after this operation.

### Introduction

Malignant tumors of the stomach make it necessary to perform a gastrectomy with subsequent reconstruction of the passage according to Roux-Y or alternatively according to Longmire-Güttgemann. With the first method the duodenal passage is excluded with the second method the duodenal passage is preserved. In consequence of both methods patients suffer from malabsorption, maldigestion, weight loss and changes of many laboratory parameters which indicate an insufficiency of exocrine and endocrine pancreas function. To get more information about the loss of exocrine function of the pancreas the pancreatic juice was collected from animals operated according to Roux-Y or Longmire-Güttgemann and compared to sham operated animals.

### Methods

Adult Wistar rats were divided into 3 groups. Group 1 were sham operated control animal. In group 2 and 3 a total gastrectomy was performed. Whereas group 2 was reconstructed according to the operation method of Roux-Y group 3 was operated according to the method of Longmire-Güttgemann. 3 months after this intervention the pancreatic juice was collected and the volume and protein content measured under fasting conditions. With the 2D electrophoresis the whole number of different proteins was determined and furthermore the isoelectric focus and the molecular weight of the proteins in pancreatic juice.

## Results

The results show that the total volume of the pancreatic juice is significantly increased after both reconstructive operations. Whereas the total volume of the pancreatic juice over the observation time of 6 hours is  $90 \pm 30$  ml/kg in Roux-Y animals it is increased to  $328 \pm 50$  ml/kg and in Longmire-Güttgemann animals to  $175 \pm 35$  ml/kg. The protein content is also increased in both groups from  $0,46$  g/dl/kg to  $90$  g/dl/kg. The number of proteins in the juice, however, is markedly reduced. Whereas in sham operated animals  $120 \pm 20$  different proteins were counted in the 2D electrophoresis this number is reduced to  $60 \pm 10$  in Roux-Y animals and to  $70 \pm 30$  in Longmire-Güttgemann animals. A marked reduction was also observed in proteins which are working in alkaline milieu in both operation groups.

Furthermore an increase of low molecular protein fragments was observed in Roux-Y animals indicating an altered viability of the pancreatic proteins.

## Discussion

The secretion of pancreatic juice is probably controlled by a feedback mechanism. The presence of trypsin in duodenum induces a decrease in the liberation of CCK and this leads to a diminution of pancreatic juice [2]. In the Roux-Y group the duodenum is excluded from the normal chymus passage which slow down the transport of trypsin to deeper parts of the gut. Consequently the duodenal trypsin concentration is decreased in Roux-Y animals which leads to an increase of secretion of pancreatic juice via CCK liberation. The changed isoelectric focus in both operated groups as well as the increased protein fragments especially in the Roux-Y group indicate a marked alteration in the composition of digestive enzymes. This changes can explain the maldigestion and malabsorption [3] which was observed in human beings [1]. The reason for the changed composition of proteins in the pancreatic juice of both operated groups may be an exhaustion of the exocrine pancreas because the feedback mechanisms are not in proper function.

## Conclusion

1. The secretion of pancreatic juice is significantly increased after gastrectomy and reconstruction of the intestinal passage according to Roux-Y but also according to Longmire-Güttgemann.

2. The protein content is increased but the number of proteins in the juice is decreased.

3. The separation in the 2D electrophoresis shows a shift in the isoelectric focus and an increase of protein fragments especially in the Roux-Y group.

Disturbed feedback mechanisms after operation lead to an exhaustion of the exocrine function of the pancreas.

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## IS THE PRESENCE OF DISTANT METASTASIS ASSOCIATED WITH C-MYC AMPLIFICATION IN GASTRIC CANCER?

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The expression of the c-myc oncogenes has already been reported in human gastric carcinoma. Overexpression can be the consequence of oncogene amplification and often correlates with different prognostic factors. Authors investigated the value of c-myc oncogene amplification in 23 patients (9 male, 14 female, aged 28-85 yrs) with gastric cancer and its correlation to the following clinical and histopathological parameters: grade, TNM stage, Lauren's type, localisation and severity of disease. DNA was isolated from formalin-fixed, paraffin embedded tissue for quantitative dot-blot hybridisation. Amplified c-myc was found in 6 out of 23 cases. Its values ranged from 2.12 up to 18.2 (average 9.1). Significant association was found between the presence of c-myc amplification and distant metastasis (corr. coeff.: 0.5623,  $p < 0.01$ ). High scores of the other parameters also correlated with c-myc, albeit not significantly. The result of cluster analysis, based on the similarity of the parameter values for the individual patients proved that the age was the decisive factor in creating two groups. The distribution of patients into these groups did not seem to coincide with the presence of c-myc amplification or distant metastasis, inspite of the proved correlation between them.

### Introduction

The expression and amplification of the c-myc oncogenes has already been reported in human gastric carcinoma [1, 2]. In this study we attempted to demonstrate the presence of c-myc amplification in patients with gastric cancer and also to investigate the relationship of this amplification to different clinical and histopathological parameters.

### Materials and Methods

Authors investigated the value of c-myc oncogene amplification in 23 patients (9 male, 14 female, aged 28-85, mean 59.6) with gastric cancer and its correlation with the following clinical and histopathological parameters: age, grade, TNM stage, Lauren's type, localisation and the severity of the disease. In order to determine the amplification values for the c-myc oncogene, DNA was isolated from formalin-fixed, paraffin embedded tumour tissue samples for quantitative dot-blot hybridisation as described by Goelz et al [3]. The amplification values were determined by relating the individual hybridisation signals obtained with the c-myc probe to those measured with the beta-actin probe, of which the target sequence is present as a single copy gene in the genome. Some of the parameter values had to be scored for computerised data processing.

According to the localisation of the tumour, patients were ranked into three groups as follows: antrum /1/, proximal and middle third of the stomach /2/ and entire stomach /3/. The score for clinical condition was either one /1/ or two /2/ meaning good and poor condition, respectively. The clinical condition was considered poor in the presence of either anaemia (haemoglobin  $<1.5\text{mmol/l}$ ) or hypalbuminaemia (serum albumin  $<0.46\text{mmol/l}$ ) or weight loss ( $>10\%$ ). Nodal involvement fell into one of four categories (N1–N4) defined as suggested by the Japanese Research Society for Gastric Cancer. In order to reveal association between oncogene amplification and the indicated parameters we used a SPSS/PC statistical software package for calculating linear regression with correlation coefficients as well as t-test for making comparison between patient's groups with and without amplification. Cluster analysis was also performed to investigate the possible role of c-myc amplification in the assortment of patients into the two cluster groups set up by the involvement of all the rest of the parameters.

## Results

Of the 23 samples tested, c-myc oncogene amplification was found in 6 cases. The values varied from 2.12 up to 18.2 (mean 9.1). The only parameter which exhibited significant association with the value of c-myc amplification was the presence of distant metastasis (corr. coeff.: 0.5623,  $p < 0.01$ ). In patients with distant metastasis the average value of c-myc amplification was more than 4-fold higher than that of in the rest of the subjects. Also, significant association was found between the localisation of the tumour in the stomach and, in contrast to the correlation with distant metastasis, the presence and not the value of the c-myc amplification. This is likely attributed to the fact that both the involvement of the entire stomach by the tumour and the oncogene amplification are rather late events in the carcinogenesis. Correlations between the other parameters and the c-myc were weaker which never reached the limit of significance. In multifactorial disorders like gastric cancer the consequence of the interplay of different factors beyond the pair-wise comparison of the studied parameters might be considered. As the results of our performed cluster analysis the age was proved to be the decisive factor in the segregation of patients into two groups. Neither the c-myc amplification, nor the distant metastasis exhibited significantly different distributions in the patients, although both were more pronounced in the cluster group of younger age.

## Discussion

Opinions on the role of the c-myc amplification in the course of gastric cancer is rather controversial. C-myc amplification has already been shown to affect the metastatic potential of gastric and several other carcinomas [2, 4]. The results presented here, reveal significant association of c-myc amplification with the presence of distant metastasis. This is in agreement with the findings by Ranzani et al. [2]. He also claimed, however,



that c-myc amplification can influence tumour progression, that was not justified by our cluster analysis. Of the all studied parameters cluster analysis revealed the importance of patient's age, which is in accordance with the results of clinical trials. In patients below 40 years of age the advanced, undifferentiated lesions usually predominate, while the occurrence of metastasis not more frequent in this type than it is in the differentiated ones [5]. In the light of these findings it is conceivable that the age-related distribution of patients as experienced in the cluster groups does not coincide in this study with the incidence of metastasis development which is likely influenced by c-myc amplification.

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## EXCIMER LASER PHOTOREFRACTIVE KERATECTOMY WITH DIFFERENT ABLATION ZONES

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In this study we would like to introduce the excimer laser, and to demonstrate our results and complications by using different ablation zones during photorefractive keratectomy (PRK) in the correction of myopia and astigmatismus. In 1996 we performed photorefractive keratectomy on 100 myopic eyes of 52 patients (28 females, 24 males). Mean age was 26,21 years (ranged from 19 to 54 years). The preoperative refraction ranged from -1,0 D to -18,0 Diopters. The diameter of the ablation zones were between 5 and 6,5 mm. We evaluated the results and the complications of the surgeries of 100 eyes which were performed with Schwind keratom F excimer laser. After 2 days, 1 week, 1 month, 3 months, and 6 months postoperatively we tested the best uncorrected and corrected visual acuities, and performed intraocular pressure measurement, slit lamp examination as well as corneal topography. The postoperative refractions were between  $\pm 0,5$  to  $\pm 1,0$  Diopters. After six months postoperatively the slit lamp examination showed that 80% of the patients had no corneal haze while 20% had stage I (Hanna) corneal haze. The smaller the diameter of the ablation zone was, the more pronounced the corneal haze and the night-glare were. The photorefractive excimer laser keratectomy is judged to be a safe method, although it might have some side-effects. The different ablation zones of this treatment means an important modification, that not only allows the method to meet the individual requirements, but reduces the chance of the complications as well. Based on the authors' experiences PRK for moderate myopia with large diameter ablation zones appears more predictable than that with smaller ablation zone diameters.

**Keywords:** photorefractive keratectomy, excimer laser treatment, complications, subepithelial haze, ablation zones

### Introduction

Since August 1996 the authors use excimer laser photoablation as a refractive surgical method for the treatment of myopia and astigmatism as a part of myopy surgery profile of the Department of Ophthalmology of the University Medical School of Debrecen [1]. In this study the results of the first 100 operations are summarized, with special respect to ablation zones with different diameters.

### Methods

Before surgery all patients were informed about the procedure and the possible risks, advantages and disadvantages and they signed an informed consent form. Every patient had a preoperative examination that included visual acuity check, slit lamp examination, tonometry, refraction, ophthalmoscopy, corneal topography, pachymetry, measurement



of lacrimal production and break up time of the tear film, and ultrasound examination (both A and B modes).

In 1996 we performed photorefractive keratectomy on 100 myopic eyes of 52 patients (28 females, 24 males). Mean age was 25,21 years (ranged from 19 to 54). The preoperative refraction ranged from -1,0 D to -18,0 Diopters. The diameter of the ablation zones were between 5 and 6,5 mm.

Excimer laser surgery was performed under topical anesthesia. We selected one of the instruments with different diameter to mark the central part of the cornea. Then we removed the epithelium in the ablation zone with a blade. The edges of the removed part must be sharp, and the surface must be completely dry in order to achieve the best results. After this, the patient had to fix a flashing red light during the laser treatment. The Schwind Keratom F has an autopositioning control system. The laser treatment was automatically interrupted if the patients' eye moved from its central position.

During the treatment we selected 5-5,5 mm to 6-6,5 mm diameter ablation zones. In determining the diameter we considered the age of the patient, the refraction and the patient's job.

We treated only one eye at a time, and the other eye after 2 or 3 months. Right after surgery we asked the patients to rest and not to read. Postoperative treatment consisted of pain killers during the first and the second day, antibiotic drops or ointment and a patch until the epithelium healed. Then topical corticosteroid eye drops (dexamethasone or fluorometholone) were used (four times daily in the first month, three times daily in the second month, two times daily in the third month).

We evaluated the results and complications of the 100 eyes which were treated with Schwind keratom F excimer laser. 2 days, 1 week, 1 month, 3 months, and 6 months postoperatively we tested the best uncorrected and corrected visual acuities, and performed intraocular pressure measurements, slit lamp examination, and corneal topography.

## Results

The postoperative refractions were between  $\pm 0,5$  to  $\pm 1,0$  Diopters. The difference between the attempted and the achieved correction were between  $\pm 0,5$  and  $\pm 1,0$  Diopters.

The postoperative refraction in the low myopia group was  $\pm 0,5$  Diopters and in the high myopic group was  $\pm 1,0$  Diopters. After six months postoperatively, the slit lamp examination showed that 80% of the patients had no corneal haze while 20% had stage I (Hanna) corneal haze. The visual acuity examinations were as we expected, and in some cases it was even better.

The preoperative uncorrected visual acuity was between 0,08 and 0,5. After photorefractive keratectomy uncorrected visual acuity improved to 0,8-1,0, except for those who had amblyopia.

According to our results the smaller the diameter of the ablation zone (5-5,5 mm) the larger the number of cases which had more significant corneal haze, and night-glare.

## Discussion

One of the most important step in excimer laser photoablation is the determination of the diameter of the ablation zones.

A diameter for the ablation zone is suggested by the computer, which is based on the Diopters and on the preset value to keep the ablation depth under 150 micrometers. We can change this ablation zone diameter if necessary. Wider zones mean deeper ablations. In determining the diameter of the ablation zone, we also take into consideration the patients' job (whether he works at daylight or not), the activity (whether he drives at nights or not) and the age as well. Since the pupil of young people dilates more in the dark than the pupil of the elderly. We also try not to ablate more than 100 micrometer of the corneal thickness. Based on our experiences and on literature data it is more advisable to use the 6–6,5 mm diameter ablation zone in order to avoid subepithelial haze, and night-glare which especially cause complaints in young adults [2, 4, 5].

Although the treatment is painless, after the ablation most of the patients complained of foreign body sensation, caused by corneal abrasion.

Our clinical results showed that excimer laser PRK is predictable, safe and effective method of refractive surgery to treat mild to moderate myopias.

It is also an effective method in high degree myopia but with less predictability and higher rate of complication (corneal haze, myopic regression, astigmatism).

Photorefractive excimer laser keratectomy is judged to be a safe method although as every surgical procedure it might have some side-effects. The different ablation zones of the treatments mean an important modification, that not only allows the method to meet the individual requirements, but reduces the chance of the complications as well [3].

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## THE ROLE OF DIFFERENT TUMOR MARKERS IN THE EARLY DIAGNOSIS AND PROGNOSIS OF PANCREATIC CARCINOMA AND CHRONIC PANCREATITIS

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The examination of tumor markers in the diagnosis and in the evaluation of progression of tumors has got an increasing significance. The serum level changes of three tumor markers (CEA, CA 19-9, CA 125) were examined before and after the operation in 94 patients operated for pancreatic carcinoma (PC) and chronic pancreatitis (CP) between March 1994 and December 1996 at the 2nd Dept. of Surgery of Debrecen Medical University. From the patients 62 were operated for carcinoma, in 19 cases the tumor was resectable, 43 patients had palliative operation. In 32 patients ductal decompression was performed because of CP. The authors evaluate the serum level changes of the three tumor markers examined in three groups of patients before and after the operation. In conclusion CA 19-9 is the most sensitive marker of PC, the sensitivity was 77.4 %, the specificity was 87.5 %. CEA and CA 125 are not as sensitive markers of PC as CA 19-9, while CEA and CA 125 serum levels are both increased in half of the patients with chronic pancreatitis.

### Introduction

In the last 10 years the examination of tumor markers in the diagnosis and in the evaluation of progression of tumors had got an increasing significance. The usually examined markers in pancreatic diseases are the oncofetal carcinoembryonic antigen (CEA) and two carbohydrate antigens, CA 19-9 and CA 125.

We examined the relation between the three tumor markers and the PC and CP, and the change of the levels of the markers related to progression of the disease.

### Patients and Methods

At the 2<sup>nd</sup> Dept. of Surgery of Debrecen Medical University 94 patients were selected in this study who were operated for PC and CP. Three tumor markers – CEA, CA 19-9, CA 125 – were investigated before and after the operation between March 1994 and December 1996.

From the patients 62 (35 males and 27 females – average year:  $56.4 \pm 20.6$  and  $59.6 \pm 21.8$ ) were operated for carcinoma, 32 (22 males and 10 females – average year:  $44.8 \pm 15.6$  and  $52.4 \pm 13.2$ ) had decompression operation because of CP.

The measurement of CEA and CA 19-9 was performed with quantitative method by LIA-mat technique, immuno-luminometric method. For CA 125 we used IMx Microparticle Enzymimmunoassay (MEIA) technique, with fluorometric method.

## Results

From the 62 patients with PC in 19 the tumor was resectable, 43 patients had palliative operation, and there were 32 patients with CP. The levels of the three tumor markers were examined in three groups of patients before and after the operation:

Group I: operable PC (n=19); groupII: inoperable PC (n=43); groupIII: CP (n=32).

The serum level of CEA increased in 10 patients of the group I, and decreased after the operation. We found increased CEA levels in 23 patients of the group II, and this increase continued after the operation because of the progression of the disease. Elevated CEA levels were found in 15 patients of the group III, and decreased after the operation; in 9 cases CEA level returned to normal.

The serum level of CA 19-9 increased in 15 patients of group I. After the resection of the pancreas the levels decreased highly, in 7 cases returned to normal. Elevated CA 19-9 levels were found in 33 patients of the group II, and this increase was higher than in group I. The levels of CA 19-9 decrease a little immediately after the palliative operation, but lately increased levels were found because of the progression of the disease. In CP the levels of CA 19-9 were not characteristic.

Levels of CA 125 did not increase in the group I. Elevated CA 125 levels were found in 21 cases of the group II, and this increase continued after the operation. Elevated CA 125 were found in 16 cases of the group III. After the decompression operation the levels of the CA 125 decreased, in 12 cases returned to normal.

## Discussion

On the base of the literature the prognosis of PC is poor because of the late discovery of the disease, though the 5 year survival rate has improved (10→30%) in recent years [5].

The diagnostical sensitivity of CA 19-9 is 70-95% in PC, specificity is 78-98% [3, 4], in case of our patients it was 77.4%, and 87.5% respectively. By combination [2] of CA 19-9 and CEA the sensitivity increased to 80.6%.

On the base of the literature in case of resectable PC the increase of CA 19-9 levels is less than in the inoperable cases [4], and we also found this result in our study.

The sensitivity of CEA is 57% [1], in our study we found 53.2%. There are elevated CEA levels in pancreatitis and alcoholic hepatopathy, as well [1].

According the literature the sensitivity of CA 125 in PC is 59% [1], we found 33.9% in our study. On the base of our experiences and the literature concerned there are elevated CA 125 levels in the benign diseases of the pancreas too [1].

## Summary

On the base of the literature and our experiences the measurement of CA 19-9 is the most useful for the early diagnosis of PC and for the differentiation between PC and CP.



After the resection of the pancreas for PC the serum level of CA 19-9 decreases.

In inoperable cases after palliative operations further increase of CA 19-9 was found in the late postoperative period.

By combination of the measurement of CA 19-9 and CEA the sensitivity increases.

The CEA is not as sensitive marker of PC as CA 19-9.

The measurement of CA 125 is not effective to differentiate PC and CP, though after the decompression operation for CP the level of CA 125 decreases.

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## SECOND-LOOK SURGERY (SLO) IN THE MANAGEMENT OF CARCINOMA OF THE OVARY

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There is a permanent controversy on the clinical relevance of second-look laparotomies. In the first approach the majority of clinical experts evaluated this procedure experimental. Our results support the idea of clinical relevance of this procedure as patients with SLOs through the early detection of recurrence really profited from the procedure.

### Introduction

The concept of a second surgical procedure for assesment of disease status after treatment was initially proposed by Wangenstein in 1948, in patients with cancer of the colon. Subsequently, several authors reported their experiences in the management of carcinoma of the ovary with second operation – either laparoscopy or laparotomy.

With all these in mind our intention is to evaluate our experiences with second-look laparotomy to determine whether we could demonstrate any positive impact of the procedure on the outcome.

### Patients and Methods

The number of patients evaluated is 52. The stage distribution is as follows: stage I.: 18, stage II.: 5, stage III.: 18, stage IV.: 11. Histologically 30 patients had serous cystadeno-carcinoma, 7 mucinous cystadenocarcinoma, 4 undifferentiated adenocarcinoma, 4 malignant dysgerminoma, 3 teratoma, 4 patients had borderline adenocarcinoma of epithelial origin.

The indication for "second-look" laparotomy in our study were

1. evaluation of disease with intent of stopping therapy
2. in case of recurrent or persistent disease to perform further tumor debulking and continue chemotherapy with a new regimen.

The details of the surgical techniques of the second-look procedure are the followings.

A vertical lower abdominal incision should be used with the possibility to extend cephaled if necessary to allow examination and biopsy of structures in the upper abdomen.

All fluid in the peritoneal cavity should be aspirated and submitted for cytological examination. If no fluid is present, washing should be taken.

All peritoneal structures have to be carefully examined. Adhesions must be released to allow adequate examination of all parietal and visceral peritoneal surfaces. The intraperitoneal viscera should be examined in a systematic way so that all are palpated or visualised.



If there any suspect area can be found in the pelvis or upper abdomen, biopsy should be taken of the representative areas. We regularly biopsy only the suspect areas and take saline irrigation specimen for cytology. The omentum is removed if this was not part of the primary surgical intervention. In cases with significant amounts of residual tumor an attempt was made to either resect it completely or reduce the bulk as much as possible. Depending on the results of restaging chemotherapy was either stopped, restarted or changed. All patients had initial surgical intervention performed at least for diagnosis. This consisted of abdominal hysterectomy and bilateral salpingo-oophorectomy or laparotomy with biopsy. The goal of the procedure was to perform an extensive tumor reduction occasionally involving resection of some part of gastrointestinal tract and some part of the urinary tract.

Following the primary surgery patients were treated with anti-cancer chemotherapy. The regimens administered were cyclophosphamide + cisplatin, or cyclophosphamid + Adriamycin + cisplatin regiments. As far as the efficacy of the two regimens is concerned, the patient population can be considered homogeneous.

## Results

The distribution of patients according to the indication for second-look operation reflects the strategy followed. At 32 patients SLO was performed with the intention of discontinuation of chemotherapy with the planned number of cycles completed. At 12 patients the indication was the possibility of further tumor debulking. At 8 patients the declaration of resistance to first line chemotherapy should be reinforced by the results of SLO.

The relationship of clinical regression to the surgical regression was also evaluated. Out of 32 patients with clinically complete remission, at the surgical finding the remission proved to be complete at 24 and partial at 8 patients. The distribution of positive findings of intraperitoneal cytology was 21 to 11. The most decisive parameter in this relation is the pathological result: 21 samples proved to be tumor-free out of 32 evaluated.

## Discussion

The results detailed before allows the following conclusions. Considering the occult characteristics of ovarian cancer the only way to evaluate the response to oncotherapy is the surgical pathological evaluation. Our results reinforce this strategy namely the surgical pathological evaluation of response has not only relevance from point of view of research but it has a real everyday clinical importance in the management of patients with ovarian cancer. So it would be a not acceptable standpoint to give up this approach as without clinical relevance.

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## MINIMAL INVASIVE SURGERY

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The advent of laparoscopic cholecystectomy has established a new chapter in surgical treatment with an impact on the various surgical specialities leading to significant changes in surgical practice. The essential attribute of the new approach is the reduction of the trauma of access. Minimal access surgery (MAS) underlies all the benefits of the new approach including the accelerated recovery. Few other developments in surgery have excited so much interest among surgeons and the medical equipment industries alike, and progress during the past 7 years has been impressive though at times lacking direction and in some instances, scientific backing.

The goal is to evaluate the aggressiveness of the different elements of surgery, to compare equal procedures and the difference between conventional and laparoscopic surgery. The aggressiveness of a surgical procedure is a complex issue which includes all the following elements [1]:

- ◆ aesthetics
- ◆ trauma to the peritoneum and abdominal wall
- ◆ cardiac and respiratory problems
- ◆ regulation of the internal environment
- ◆ psychological stress
- ◆ immunology (according to certain recent studies, is more favorable to the laparoscopic approach).

MAS encompasses several approaches: laparoscopic, thoracoscopic, perivisceral endoscopic, endoluminal, intra-articular etc.

In the context of laparoscopic surgery, operations can be categorized as either functional or ablative. Functional operations such as repair (e.g. hernial defects, antireflux surgery), denervation (e.g. sympathectomy, vagotomy), myotomies, adhaesiolysis are ideally situated to the MAS approach. By contrast, ablative operations may pose problems relating to specimen extraction. These are minimal and readily overcome if the organ is hollow and small (e.g. gallbladder, appendix) or if there is a natural anatomical exit for the mobilized specimen (e.g. rectum for colectomy specimens, mediastinum/neck for esophageal resections). However, if the specimen is large or arises in a solid organ which has to be removed in part or whole, the specimen extraction becomes problematic. The options available in this situation are either the creation of an exit wound of sufficient size to enable extraction or morcellation of the specimen using specific instrumentation designed for this purpose [3].



The core strengths of MAS are well documented. The benefits of smoother postoperative period and accelerated recovery have been established beyond question for certain procedures. If applied judiciously, these procedures should bring improved patient outcome and unit costs savings, especially if the reduced period of short-term disability is taken into consideration. Other perceived benefits, such as attenuated transmission of infectious disease and reduced postoperative deep vein thrombosis, remained to be confirmed [2].

The total traumatic insult sustained by a patient undergoing a surgical operation has two components: access trauma related to the exposure of the operative region, and procedural trauma which is the injury inflicted in the execution of the procedure.

The likely benefit of MAS over conventional surgery is dependent on the ratio of access to procedural trauma. The benefit is beyond question in functional operations in relatively inaccessible organs such as esophagus. At the other end of the spectrum are the radical operations with lymphadenectomy. Here the access trauma constitutes a relatively small component of the total operative insult.

- ◆ There are some weaknesses of MAS [2]:
- ◆ Endoscopic surgery takes longer
- ◆ Less efficient
- ◆ Surgeon fatigue and stress
- ◆ More technically demanding
- ◆ Technology dependent
- ◆ Restricted applicability
- ◆ Increased risk of contamination
- ◆ Restricted safe specimen handling and removal.

Two major limitations of endoscopic surgery pertain to tissue approximation and organ extraction, especially when there is a need to restore continuity to gastrointestinal tract. Tissue approximation is substantially more exacting during endoscopic procedures than is conventional open surgery.

The extraction of organs through small endoscopic access wounds raises major problems of potential contamination and in cases of malignancy the risk of tumor-cell implantation [4, 5]. Instances of tumor deposits in the parietal access wounds have now been documented after gallbladder, liver, pancreatic, gastric, colonic and gynecological laparoscopic procedures for cancer. These reports do not prove that laparoscopic surgery entails an increased incidence of tumor-cell implantation in the abdominal wounds, but they do indicate the need for caution and animal studies. On a priori grounds, several factors may predispose to tumor cell implantation in the parietis during laparoscopy and laparoscopic surgery for cancer:

- ◆ Increased handling by instruments and exfoliation
- ◆ Vasodilatation induced by CO<sub>2</sub>
- ◆ Spread of exfoliated cells by the turbulent CO<sub>2</sub> flow into and out of the access ports
- ◆ Fibrin entrapment in the access wounds that can shield cancer cells from host defenses
- ◆ Increased risk of contamination, especially during removal.

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## THE REPLACEMENT OF THE ESOPHAGUS BY MUSCULOCUTANEOUS FLAPS

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If there is no other possibility for the replacement of the whole esophagus, the antethoracic neo-esophagus from musculocutaneous flaps gives the best result compared with the skin tube reconstruction. Two successful cases are discussed.

### Introduction

According to the last therapeutic principles in the treatment of esophagus tumour the whole thoracic esophagus is resected and the anastomosis with the upper esophagus remnant is performed through a lateral collar mediastinotomy. The esophagus is mainly replaced by the stomach, then by the large bowel or small bowel in decreasing frequency [1].

Under unfavorable conditions none of the above mentioned organs is suitable for the replacement of the whole esophagus. (Former stomach operation, inadequate vascular arcade of the bowel.) The situation is similar to the case of an unsuccessful reconstruction. (Necrosis of the transplant.) [5]

To restore the swallowing function in these cases we can construct an antethoracic neo-esophagus from musculocutaneous flaps. This method diminishes the postoperative complications compared with the skin tubes developed at the end of the previous century [2,3].

In our study we deal with two successful cases undergone an antethoracic esophagoplasty.

### Patients and Methods

#### *Case I.*

A 59 years old male underwent a total gastrectomy in another clinic. Local recurrence of the tumour could be verified at the distal third of the esophagus. The tumour was removed without thoracotomy. The large bowel wasn't suitable for the replacement, because in the course of a former operation of the stomach an injury of the colic arcade occurred. For this reason we made the former Roux-en-Y-loop longer. The jejunum was pulled to the chest antethoracally and was marsupialised to the skin some centimeters below the mamilla. In the left lateral neck region and esophagostomy was performed.

#### *Case II.*

A 57 years old man underwent esophageal resection and replacement with stomach because of a middle third tumour of the esophagus. Due to necrosis of the stomach a



Torek operation was performed. Half a year later we replaced the esophagus by the right colon, pulled up antethoracally. Unfortunately the upper 10 cm of the ileocolon necrotised, therefore the colon was sutured out to the skin at the level of the mamilla and again a collar esophagostomy was done. The definitive reconstruction was similar in both patients. The inner layer of the neo-esophagus was created from the skin of the thoracic wall. The axis of the constructed tube was located parasternally. The skin was raised together with the underlying muscle in order to create a reverse pectoral flap so that the suture line of the "skin tube" became covered by the muscle. (According to the method of Borbély.) [1]

The skin defect was covered by a latissimus dorsi musculocutaneous flap shafted from the left.

Both patients healed with a transient mucous fistula. Both of them were able to eat normally after the operation.

### Results and Discussion

The intact stomach is always suitable for total esophageal replacement, but in 1,1% of the cases necrosis may occur. In cases with a preceding operation of the stomach the second choice is the colon. Because of anatomic variations the colon isn't good for the replacement in 1–2% of the cases. Its necrosis rate is about 13,3% [4].

In European populations the jejunum cannot usually be used for the total replacement of the esophagus.

Between 1986 and 1992 at the 1st Surgical Clinic of the Medical University Szeged 130, between 1992 and 1996 at the 1st Surgical Clinic of the Medical University Pécs 153 esophageal resections have been performed.

Only 2 of the 283 cases needed an antethoracal musculocutaneous flap plasty.

The above mentioned plasty results in acceptable function and cosmesis.

The reverse pectoral flap which is covered by the latissimus dorsi musculocutaneous flap strengthens the crucial inner suture layer.

Both the reverse pectoral flap and the excellent blood supply of the latissimus dorsi flap result in a relatively low incidence of complications.

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## **10 YEARS OF COOPERATION WITH THE DEPARTMENT OF EXPERIMENTAL SURGERY, UNIVERSITY MEDICAL SCHOOL OF DEBRECEN: SCIENTIFIC OUTCOME AND IMPACT ON CLINICAL PRACTICE**

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From 1986–1996 several series of experiments were done in cooperation with the Department of Experimental Surgery, University Medical School of Debrecen. Very interesting scientific findings have been achieved in the fields of urethral surgery, continent urinary diversion, alternatives to dialysis, laparoscopy and bladder stimulation. Besides representing a high scientific output nearly all experiments had direct impact on our clinical practice.

### **Introduction**

The main goal of medical science is to improve diagnostic and therapeutic modalities in clinical practice. Experimental surgery has a key position between theoretical and practical application of new methods in medicine. We set out to evaluate ten years of cooperation between clinical urologic departments and the Department of Experimental Surgery University Medical School of Debrecen in terms of scientific output and implementation of new modalities to clinical practice in our department.

### **Investigations**

Since 1986 three functional and three surgical topics were investigated:

1. Comparison of intravesical versus intramuscular electrostimulation of the bladder detrusor.
2. Impact of chronic intramuscular stimulation of the bladder.
3. Pouch dialysis.
4. Surgical treatment of long distance urethral stenosis.
5. Laparoscopic implantation of electrodes into the detrusor muscle.
6. New continent heterotopic small bowel pouch.

### **Results**

**ad. 1.** For electrostimulation of the bladder to induce contractions intravesical stimulation (IVES/Katona) of intramural electrostimulation (IMES/Bradley) may be used. In five female mongrel dogs wire electrodes were implanted into the bladder detrusor as well as a transurethral electrode, which was inserted in generalanesthesia.



Electrostimulation was commenced through both systems using the "UROPLUS A20" (6–20 mAmp, 60–100 Hz, width 8 msec). Intravesical pressure changes were measured via cystostomy. The experiment was repeated after dorsal rhizotomy and after cystectomy. In this setting rises between 10 and 70 cm H<sub>2</sub>O of the intravesical pressure were found. The current needed to induce contractions was 10 to 20% lower when IMES was used. As contractions were induced after dorsal rhizotomy and even after cystectomy the mechanism for both methods appears to be direct stimulation of the detrusor muscle [3, 6].

- ad. 2. We investigated the effect of chronic stimulation of the detrusor in 8 mongrel dogs with intramural wire electrodes considering changes in intravesical pressure, detrusor histology and histochemistry. Stimulation parameters were standardized in all cases (70 Hz, 20 mAmp, 2,5 msec). All canines were cystometrically evaluated prior to and after a three week stimulation period with a 50% and 90% filling status of the bladder. Intravesical pressure changes were recorded with a polygraph. Biopsies for histology and histochemistry were taken in all cases prior to and after chronic stimulation. Intravesical pressures increased by 52,2% at 50% filling and 39% at 90% filling. All dogs tolerated the chronic stimulation well without requiring an anesthesia during stimulation. Histology of the detrusor did not show any significant alteration of mucosal or muscular order. Histochemical staining revealed normal findings. Early dislocation of the electrodes occurred in one case, in two cases electrodes dislocated after 12 and 15 days of stimulation, respectively. Chronic intramural stimulations of the bladder detrusor leads to a significant increase in intravesical pressures, histology and histochemistry did not show major alterations [7, 10].
- ad. 3. The possibility of diffusion of BUN and free water into small bowel pouches was examined and compared to peritoneal dialysis in 8 dogs. Six animals received a small bowel pouch, in two dogs peritoneal dialysis was carried out. 6 weeks postoperatively in all dogs, which had normal kidney functions, 100 ml of 20% Mannitol was instilled into the pouches and the peritoneal cavity, respectively. Samples were drawn after 15, 30, 60 and 90 minutes, after 2 hours the whole contents was drained. In the small bowel pouches an increase of volume of 60% in average was found after 2 hours. The increase in volume from the peritoneal cavity was 150%. The diffusion of BUN in the small bowel pouches reached two thirds of the concentration in the peritoneal dialisate. In dogs with normal kidney functions into both small bowel pouches and into the peritoneal cavity transport of free water and BUN was found with 20% Mannitol as a dialisate. Small bowel may serve as a semipermeable membrane for dialysis into a continent small bowel pouch [8, 11].
- ad. 4. In 21 male mongrel dogs four to ten cm of the urethra were replaced by an inverted autologous vein graft. After a mean observation period of 118 days radiological, endoscopical, macroscopical and histological results were documented. Two animals died perioperatively, in 18 of the 19 remaining

animals micturition was normal. One dog developed high grade meatal stenosis, which ended in urine retention and ascending urinary infection. The gross examination of the graft, however revealed a good result in this case. Other 11 animals showed an ideal result, in five cases satisfactory results were seen. In three animals pronounced stenosis was observed. In summary post mortem examinations showed the neo-urethra to be a tube made up of connective tissue completely lined by urothelium. We have gained a lot of practical experience from the experiments on using a venous graft in urethral surgery. The use of fibrin glue has been implemented into clinical practice for urethral surgery. However, the use of a venous graft has been overtaken by different methods such as pediceled foreskin graft, but still may be an option in select cases [1].

- ad. 5. Five female mongrel dogs were used in an acut animal experiment. Under general anesthesia two monopolar wire electrodes armed with needles on either side were implanted into the bladder wall, the leads of both electrodes were then pulled through the abdominal wall. Filling of the bladder and intravesical pressure measurement were achieved through a suprapubic percutaneous cystostomy. Electrostimulation was carried out using the XEJ-2 experimental electroejaculator. The pressure changes within the bladder following electrostimulation were recorded, the effect of stimulation was observed endoscopically. Electrostimulation of the bladder wall resulted in micturition in all cases showing an initial pressure peak at the commencement of electrostimulation followed by a decrease after onset of evacuation. We believe that laparoscopic implantation of temporary wire electrodes followed by percutaneous electrostimulation may open new possibilities for bladder rehabilitation as well as for diagnostic investigations into the contractile capabilities of the bladder. So far we have not used this modality of implantation, as the indication is very rare. Yet, based on the experience gained from experimental surgery, we will not hesitate to use this method as soon as we see a proper indication for it [2, 9].
- ad. 6 A small bowel continence nipple without the use of specific structures such as the ileocecal region or appendix was investigated. Five female dogs received a small bowel pouch, in which a 6 cm part, which was not detubularized, was used as a continence nipple. This part was tapered to ten french using a GIA. After fenestrating the mesenterium the nipple was incorporated into the pouch in a Gregoire-manouvre. The pouches were continent up to a pressure of 100 cm H<sub>2</sub>O. Based on these experimental studies the continent small bowel pouch developed in cooperation with the Department of Experimental Surgery University Medical School of Debrecen became the method of choice whenever a heterotopic continent urinary diversion is required. So far we have operated 16 patients according to this method and we also know of two patients in Germany being operated in this way. The results in terms of capacity, continence and electrolyte disturbances compare favourably to other intestinal pouches [4, 5].



## Discussion

The scientific output of the cooperation with the Department of Experimental Surgery of University Medical School of Debrecen was presented in 21 oral presentations (Hungary 6, Europe 8, USA 7), publication was commenced in international standard journals and American top journals (some papers are still under revision). Nearly all experimental studies done at the Department of Experimental Surgery had major impact on our clinical practice. One technique has even become method of choice in suitable cases and thereby has replaced the methods which had been used before (the new heterotopic small bowel pouch). Electrostimulation of the bladder both intravesical and intramuscular have been applied in our department in cases of detrusor insufficiency. Occupation with urethral replacement has influenced our policy in urethral surgery and the use of fibrin glue has been implemented in suitable cases. I believe, that the outcome of collaboration between Urology in Vienna and Experimental Surgery in Debrecen can serve as an excellent example for cooperation between clinical and experimental sciences and may be termed particularly fruitful.

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## **INFLAMMATORY MEDIATORS AND SURGICAL TRAUMA REGARDING LAPAROSCOPIC ACCESS: ACUTE PHASE RESPONSE**

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Numerous studies have tried to compare different aspects of patient response to laparoscopic cholecystectomy (LC) versus open cholecystectomy (OC). Our study focused on the acute phase response in order to clarify the better patient recovery following LC. Sixteen patients scheduled for elective cholecystectomy were equally allocated into groups of OC and LC. Blood samples were collected before and for four days after the procedures. Levels of interleukin 6 (IL-6) and C-reactive protein (CRP) were determined by ELISA technique. IL-6 value increased ten fold on the first postoperative day (52.8 pg/ml) in the OC group with a return to baseline value by the fourth postoperative day. In contrast a moderate increase postoperatively (12.1 pg/ml) with a fast normalisation of IL-6 value by the second postoperative day was noted in LC group. A similar pattern was observed in the CRP level. CRP peaked to 84.1 mg/l by the second follow-up day after OC, while only an insignificant rise to 52.7 mg/l was registered in the LC group with again a faster return to baseline value. The marked contrast between the two groups with regard to IL-6 and CRP changes clearly underlines a diminished acute phase response following LC, which verifies LC as probably a less traumatic procedure.

### **Introduction**

In many previous studies it has been shown that laparoscopic cholecystectomy (LC) compares favourably with open cholecystectomy (OC), in respect to hospital stay, post-operative pain, pulmonary and metabolic functions [2, 3]. This is assumed to be as a result of diminished surgical trauma during LC. To quantify such a response to stress and surgical trauma a comparative study of acute phase proteins (namely C-reactive protein, CRP) and cytokines is applicable.

### **Methods**

An unselected number of patients scheduled for elective cholecystectomy were divided into two groups: Group I representing 8 patients operated by OC, group II, 8 laparoscopically operated patients. Chronic cholecystitis was the indication for treatment in every case. Segregation of patients into the two groups was based strictly upon patient preference after consultation. Peripheral blood samples were taken 3 hour before the operation and for four consecutive post-operative days, at the same hour. Using sera isolated from each sample, values of interleukin 6 (IL-6) were determined using the Quantikine Human IL-6 Immunoassay kit (R&D Systems USA). CRP level was also measured as an indication of acute phase response, using an immunological assay (TURBOX tm CRP Orion Diagnostica).



## Results and Discussion

The initial IL-6 values were quite similar between the two groups ( $5.5 \pm 1.3$  pg/ml in OC,  $7.1 \pm 1.2$  pg/ml in LC group). However on the first post-operative day a marked difference was observed. In the OC group the level of IL-6 rose very sharply to a peak of  $52.8 \pm 12.5$  pg/ml ( $p < 0.02$ ), practically ten times that of normal (fig. 1). In the LC group no such response was registered, only a small rise on the first post-operative day ( $12.1 \pm 4.0$  pg/ml) followed by a quick return to base-line level on the following days. In the OC group, although the IL-6 level did decrease much on the second post-operative day, it still maintained a higher value than normal up-until the forth day follow-up. The CRP level rose markedly after OC reaching a peak of 84.1 mg/l by the second post-operative day (fig. 2). This elevation was highly significant ( $p < 0.001$ , ref. range 0–10 mg/l), while in the LC group only an insignificant increase to 52,7 mg/l was recorded. CRP concentration remained elevated in the OC group during the entire observation period, yet it returned to its baseline value in the LC group.

It is well demonstrated that injury caused by surgery is followed by characteristic neuroendocrine, metabolic, acute-phase and immunologic responses [2, 3]. Surgical stress is evoked mainly by afferent nerve signals from the operative site and the release of cytokines from the damaged tissue.  $\text{TNF}\alpha$ , IL-1, and IL-6 are some of the earliest released cytokines. The acute phase response is a general non-specific response to most inflammatory and traumatic processes during which acute phase proteins are produced and secreted. One of the most well known of such proteins is CRP, mainly regulated by IL-6. Generally it is acknowledged that CRP level correlates well with the severity of surgical trauma and operative time. Most studies agree to an accentuated response of both IL-6 and CRP amongst the classically operated group as compared with a laparoscopic one [1,4]. Such a claim has also been clearly verified by the results of our study.

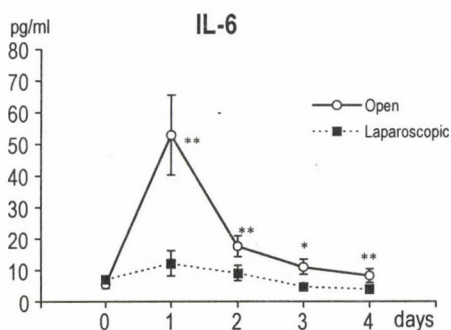


Fig. 1

Post-operative changes of IL-6 level

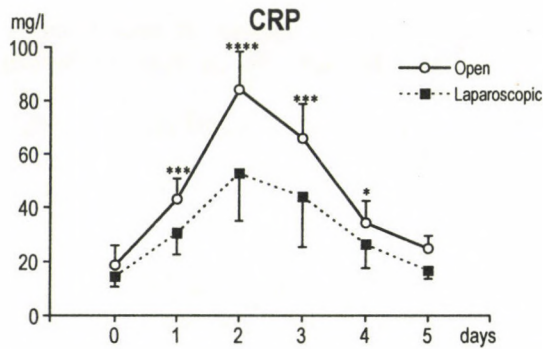


Fig. 2

Post-operative changes of CRP level

### Summary

The aim of our study was to better explain the reasons behind a faster patient recovery following laparoscopic cholecystectomy (LC). Our protocol included measuring pre and post-operative parameters (C-reactive protein, Il-6) to sum up the acute phase response following LC versus operative cholecystectomy (OC). As it will be presented below, indeed acute phase response seems to be less severe following LC, clarifying the better post-operative response at least from an inflammatory point of view.

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## LYMPHADENECTOMY IN GASTROINTESTINAL SURGERY FOR MALIGNANCY

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In a randomised study 25 patients with gastrointestinal surgery combined with extended lymphadenectomy (three field lymphadenectomy in case of esophageal cancer, D<sub>2</sub> lymphadenectomy in case of gastric cancer) has been compared to the same number of patients with limited lymphadenectomy (D<sub>1</sub>). The operation time and the need for blood transfusion has increased in the extended lymphadenectomy group. The complication rate was more than doubled in the extended lymphadenectomy group, due to fluid or lymph collection, lymphatic edema, and infection. The mapping and staging was superior in extended lymphadenectomy group, but increased morbidity and mortality has been found in this group. However the favourable effect of extended lymphadenectomy on survival needs further long-term studies and proofs.

### Introduction

Gastrointestinal malignancy including esophageal cancer has a poor prognosis, and was the most frequent cause of cancer related death world-wide. Japanese investigators started reporting better survival rates for all ages, which they ascribed to early detection and extensive lymphadenectomy [4]. In Japan, so-called *D<sub>2</sub> lymphadenectomy* is employed as standard surgical procedure, while in Western countries a *limited lymphadenectomy* (D<sub>1</sub>) is generally accepted. The Japanese have argued that *D<sub>3</sub> lymphadenectomy* should be performed with advanced gastrointestinal cancer and serosal invasion [3]. However in most Western countries lymph nodes are regarded as indicators, rather than governors of disease [5].

The first randomised trials warned against extended lymph node dissection. The aim of our study directed to analyse the morbidity and mortality after extended lymphadenectomy.

### Methods

Since January, 1, 1995. 25 out of 4004 surgical interventions have been carried out with *extended lymphadenectomy* (three field lymphadenectomy in case of esophageal cancer, D<sub>2</sub> lymphadenectomy in case of gastric cancer, etc.) following gastrointestinal surgical intervention for malignancy (*lymphadenectomy group*). The *control group* consisted of 25 similar gastrointestinal tumours with limited lymphadenectomy. Operating time, blood transfusion, reoperation, median postoperative stay, complication rates, and postoperative death were compared.

## Results

Results are collected in Table 1.

| Morbidity                | Limited lymphadenectomy | Extended lymphadenectomy |
|--------------------------|-------------------------|--------------------------|
| Number of Pts            | 25                      | 25                       |
| Operation time (h)       | 2.1                     | 3.2                      |
| Blood transfusion (unit) | 3                       | 7                        |
| Reoperation              | 2                       | 7                        |
| Postop stay (days)       | 9.8                     | 15.9                     |
| Complication %           | 25                      | 71                       |
| Postop. Death %          | 6                       | 13                       |

## Discussion

We have agreed the four randomised trials carried out in Germany, Netherlands, and Italy, U. K. [1, 2, 5, 6]. The extended lymphadenectomy analysis showed in our practice as well *increased* morbidity and mortality. A beneficial effect of extensive lymphadenectomy on survival remains to be demonstrated in progressive randomised trials. With improved technical skill the complication rate should be cut down in the future.

## Summary

In a randomised study 25 patients with gastrointestinal tumor surgery combined with extended lymphadenectomy has been compared with same number of patients with limited lymphadenectomy. Increased morbidity and mortality has been found connected to extended lymphadenectomy. The mapping and staging was excellent, but the favourable effect of extended lymphadenectomy on survival needs justification in the future.

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## TRANSVERSE HEPATECTOMY IN SURGICAL TREATMENT OF GALLBLADDER CARCINOMA

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In the surgical treatment of gallbladder cancer not only the traditional resections (right trisegmentectomy, lobectomy), but newer, parenchyma sparing multisegmentectomies, resection of 4B, 5, 6, that is *transverse resection* is also justified, as it is shown by demonstrating the 2 first cases in Hungary with transverse hepatectomy. World-wide there is a tendency for more aggressive surgical treatment in case of gallbladder cancer. For this reason we introduced transverse hepatectomy in our surgical practice, and in this paper we demonstrate the technical details of the new procedure. The goal of the transverse resection is to remove the tumour with an adequate margin of resection. The remaining hepatic parenchyma allows good quality of life for the patients till recurrence develops.

### Introduction

Recently segmental liver resections are playing major role in gallbladder and liver tumours surgery [1]. Parenchymal sparing procedure is needed for adequate tumour removal without loss of normal liver function [5]. An excellent example of segmental liver resection is the *transverse hepatectomy*. This resection can be used for gallbladder carcinomas that are invasive to the liver [5, 6].

The surgical treatment of gallbladder cancer is regarded controversial even these days, especially in advanced cases, due to the rapid spread of tumour by lymphatics, and the malignant nature of gallbladder cancer, which is responsible for early recurrence, and development of wide spread metastases. World-wide there is a tendency for more aggressive surgical treatment in case of gallbladder cancer [2, 3, 4]. For this reason we introduced transverse hepatectomy in our surgical practice, and in this paper we demonstrate the technical details of the new procedure.

### Material and Method

Since January 1. 1995. 4004 surgical interventions were carried out at our Department. In 2 patient with gallbladder cancer (T<sub>3</sub>N<sub>1</sub>M<sub>0</sub>) *transverse hepatectomy* was performed at first dissection is carried out on the right side of the umbilical fissure and the portal structures to segment 4B are identified. Next hepatic transection is continued preferably using the ultrasonic dissector to minimise tissue trauma and also to define the main portal vessels in better way. While continuing the dissection along the course of the transverse

plane numerous large branches of the middle and right hepatic veins will be noted crossing into the specimen. Once the main portal vessels are identified in the interior of the liver, the segmental blood supply to segment 5 and 6 are identified, ligated and divided in continuity also. Subsequently the rest of hepatic parenchyma is divided. Previously the cystic duct and artery ligated and divided.

Since good vascular control has been set on the portal trial the we do proceed with inflow occlusion on a routine basis in the conception of bloodless surgery. *Extended lymphadenectomy is added (D<sub>3</sub>).*

## Discussion

In surgery for gallbladder cancer in case of stage T1, T2 or T3 multisegmental resection (mainly 4B, 5, 6 segments) and extended lymphadenectomy is preferable, whenever the T stadium, and histology clarified [2, 3, 4]. The goal of the transverse resection is to remove the tumour with an adequate margin of resection [5, 6]. The remaining hepatic parenchyma allows good quality of life for the patients till recurrence develops.

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## EXPERIENCES WITH DUODENUM PRESERVING PANCREATECTOMY

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According to the principle of surgery for chronic pancreatitis the preservation of pylorus, duodenum or distal part of common bile duct gives the benefit of more physiological intervention. 2 patients with duodenum preserving pancreatotomy are presented. The operation was carried out for chronic pancreatitis. Both patients had jaundice and needed T drainage. Both patients suffered from very severe malnutrition with cahectic condition adding severe pain. None of them proved to be malignant by the frozen section. Previous diabetes, severe chronic inflammation of the whole pancreas, destruction of the pancreatic ductal system and cysts helped the decision-making for ablation of pancreas with preservation of duodenum which seems organsaving procedure. In comparison with the Whipple operation the duodenum-preserving pancreatotomy spares the patient a gastrectomy, a duodenectomy and a resection of distal common bile duct.

### Introduction

Resection in chronic pancreatitis is reserved only for those patients [1] who have failed to respond to conservative treatment, and [2] who are unsuitable for lesser procedures such as cyst drainage or longitudinal pancreato-jejunostomy, and [3] no solution for differential diagnosis between tumour and chronic pancreatitis. Once the decision has been made to undertake a resection, the surgeon must decide the type of resection. The principle is always [1] to *preserve* as much *pancreatic tissue* as possible in order to achieve the believed clinical response [2] to *preserve* the pylorus or *the duodenum* in order to get as physiologic situation as possible. Rarely there is no other alternations only a total ablation of the pancreas with preservation of the duodenum. Our first experiences are published in connection with this procedure.

### Material and Methods

Since January 1, 1995. 2 patients out of 4004 surgical interventions underwent duodenum preserving pancreatotomy for chronic pancreatitis. Both patients had severe jaundice with painfree onset. The nasobiliary decompression or endoprosthesis has failed and question has arisen on both patients according to the nature of disease, and finally both patients had diabetes before. During surgical intervention duodenum preserving pancreatotomy was performed in combination with T tube insertion to the distally narrow common bile duct, as shown in the 2.5 minutes VIDEO.

The demonstrated patients discharged without significant complication with good function of duodenum and biliary tree-Vater papilla.

### Discussion

Duodenum preserving pancreatectomy should be carried out by sharp, careful dissection, avoiding the bile duct and the and the main pancreato-duodenum artery. Due to chronic inflammatory process one count on the distal obstruction of common bile duct, for this reason the effective biliary drainage has to be taken into consideration, as we did on our cases. The basic principle for preservation of duodenum is the negative histology from the head of the pancreas. Duodenum preservation seems an organ saving physiological procedure [4].

### Summary

2 patients with duodenum preserving pancreatectomy are demonstrated. Both had jaundice and needed T drainage. None of them proved to be malignant. Previous diabetes, severe chronic inflammation of the whole pancreas helped the decisionmaking for ablation of pancreas with preservation of duodenum, which seems organ saving procedure. In comparison with the Whipple operation the duodenum-preserving pancreatectomy spares the patient a gastrectomy, a duodenectomy and a resection of the extrapancreatic bile duct.

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## **PREOPERATIVE WORK UP AND THERAPEUTIC SCHEDULE FOR PATIENTS WITH DUPLEX TUMORS**

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Authors analyze the cases of duplex and multiplex tumors among the more than two thousand operated upon patients a year at the Surgical Department of Uzsoki Hospital, Budapest, Hungary. The study enrolls a two years period evaluating the medical history of our patients in hope of a more sophisticated and effective diagnostic and therapeutic regimen. Our experience gained by analyzing data of our patients with synchron tumors shows that the patient's life expectancy is much better if performing a radical multivisceral tumor extirpation at the same sitting even if keeping in mind the higher perioperative risk. In accordance to the above mentioned concept we would like to stress the utmost importance of the interdisciplinary cooperation.

### **Introduction**

By definition we consider lesions for being a duplex or multiplex tumor in case they have: 1. identical histopathology with different locations in the same host, 2. nidentical histopathology with different locations in the same host, 3. identical histopathology on both sides of paired organs, 4. unidentical histopathology on both sides or on one side of paired organs, 5. nidentical histopathology in different organs. Based upon the onset of the tumor lesions there are synchron (parallel onset) or asynchron (divergent onset) tumors [1, 3, 5, 6].

### **Material and Method**

The data of our patients are computer processed so enabling us for a scientific work up. Utilizing our specifically developed programs we selected our patients. Those whom we operated upon via of multivisceral interventions and those whom we had to operate for some reasons in a second sitting too. Finally we picked from this group those patients whom we scheduled for a consequent surgery for an other evident malignancy.

### **Results**

Number of patients admitted to our Department for the past two years was 4937. Number of patients operated upon over this time was 4004. The number of patients

at whom malignant tumor was diagnosed via the surgery was 720. Number of multiplex tumors was: 27. Among tumors 19 were duplex and 8 were triplex tumors. 59% of the multiplex tumors were localized in two different, remote organs. 15% of the multiplex tumors were localized in the counterpart of paired organs. Eleven synchron and 16 asynchron tumors were spotted.

## Discussion

The complexity in determining the entity of multiplex tumors points out the many unanswered questions relating the diagnostics and management of this phenomenon. It is confirmed by reports in the literature that in 5,1% of patients in Europe suffering from malignancies two distinct primary tumors can be found, among which 2,8% are located in different organs [1, 4]. This means that more than half of the multiplex tumors are located in the same organ. Our own observations revealed similar data. We evaluated them from practical points of view in order to adopt observations in everyday practice. The most effective way managing synchron tumors is the correct diagnosis and the simultaneous spotting of the distinct lesions. We would like to emphasize the importance of proper and detailed history taking and physical examination. The highest coincidence of tumors was observed in cases of colorectal malignancies where the coexisting tumor was localized in the course of the colon alike. This underlines the importance of performing thorough irrigoscopic and colonoscopic examination of the complete course of the colon even after having verified the primary tumor. On the scale there are the second most frequent duplex tumors those of the breast malignancies. The bilateral evaluation of the breast is mandatory [5] (mammography, sonography). Beside of the above mentioned localization of the more often observed duplex tumors it is per se obligatory to perform the chest X ray, the abdominal sonography and in case of need the abdominal CT examinations.

Our experience gained by analyzing data of our patients with synchron tumors shows that the patient's life expectancy is much better if performing a radical multivisceral tumor extirpation at the same sitting even if keeping in mind the higher perioperative risk. In accordance to the above mentioned concept we would like to stress the utmost importance of the interdisciplinary cooperation. The oncological department in a tight cooperation with the surgical department offers a great advantage in the complex management of patients with multiplex tumors.

The medical course of our patients with asynchron tumors revealed the importance and proved the efficiency of our postoperative follow up program. It indicated its essential role in the early diagnosis of a second tumor with a later onset. Our good personal experiences with its efficacy permit us to recommend our follow up system to other fellow surgeons to incorporate it in their every day practice.



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## IMPAIRED T CELL FUNCTIONS PRECEDING LYMPHOPROLIFERATIVE DISORDERS IN MICE NEONATALLY TOLERIZED TO TRANSPLANTATION ANTIGENS

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In A/J (H-2<sup>a</sup>) (A) mice, the neonatal i.v. injection of (B10 x A)F<sub>1</sub> spleen cells (SC) induces partial transplantation tolerance (TT) to C57BL/10ScSn (H-2<sup>b</sup>) (B10) skin allografts, chronic host-versus-graft disease (HVGD) and lethal lymphoproliferative disorders (LPD) [2, 3]. They produce anti-T-cell autoantibodies (ATA), and the proliferative responses of their SC to the T cell mitogen Con A are decreased [2, 3]. We found that, similar to ATA [3], the hyporeactivity of T cells developed earlier (at 1-2 weeks of age) than splenomegaly. The proportions of both CD4<sup>+</sup> and CD8<sup>+</sup> T cells were not reduced in the spleens of tolerized mice without manifest LPD. The supernatants (SN) of Con A-stimulated tolerized SC contained no, or only small amounts of interleukin-2 (IL-2). Thus, in the tolerized mice, ATA and T cell deficiency preceded the development of LPD. ATA and the decreased amount of the T cell growth factor IL-2 might play a role in the defective T cell activation.

### Introduction

The neonatal i.v. injection of  $2 \times 10^7$  (B10 x A)F<sub>1</sub> SC induced specific, partial TT to B10 skin allografts in 80% of the inoculated A mice (BAT mice) [2]. In these mice, the chronic HVGD elicited by the F<sub>1</sub> SC was associated with the production of ATA and generalized hyporeactivity of SC, lymph node and thymus cells to T cell mitogens [2, 3]. In >60% of the BAT mice, an often lethal, chronic lymphoproliferative disease (LPD) developed [2]. In this study, we investigated whether: 1) the hyporeactivity of SC to Con A appeared before splenomegaly; 2) it was due to the decreased proportions of CD4<sup>+</sup> and CD8<sup>+</sup> T cells in the spleen; 3) it was associated with a lower production of the T cell growth factor IL-2.

### Methods

Inbred newborn A mice were injected with  $2 \times 10^7$  (B10 x A)F<sub>1</sub> SC. The preparation of SC suspensions, the 72-hour Con A stimulation test, the flow cytometric analysis of CD4<sup>+</sup> and CD8<sup>+</sup> SC, the splenomegaly assay as well as the statistical methods were described earlier [2]. The levels of IL-2 in the SN of tolerized or normal SC stimulated by Con A (5 µg/ml) for 24 hours were measured by a bioassay using an IL-2-dependent CTTL-2 cell line [1].



## Results and Discussion

Splenomegaly started to develop at 2 weeks of age in the BAT mice [spleen weights: BAT:  $61.6 \pm 11.1$  mg; nontolerized (NT) mice:  $44.3 \pm 15.5$  mg;  $p < 0.05$ ]. At 4 weeks, their mean spleen weight was two times, and, at 8 weeks, five times higher, than those of the NT mice.

As determined by  $^3\text{H}$ -thymidine incorporation, the Con A-induced proliferation of the SC of the tolerized mice was markedly reduced already at 2 weeks of age (BAT:  $25,192 \pm 9335$  cpm; NT:  $54,320 \pm 11,415$  cpm;  $p < 0.004$ ). At 2 and 4 weeks of age, the percentages of both  $\text{CD4}^+$  helper and  $\text{CD8}^+$  killer T cells were not reduced in the spleens of the BAT mice (at 2 weeks:  $\text{CD4}^+$ : BAT:  $5.2 \pm 1\%$ , NT:  $5.8 \pm 2.9\%$ ;  $\text{CD8}^+$ : BAT:  $4.2 \pm 0.4\%$ , NT:  $2.7 \pm 0.5\%$ ), suggesting that the hyporeactivity to Con A was of functional origin. At 2 weeks, ATA were already present in the sera of all mice [3]. ATA may occupy or downregulate cell surface receptors of Con A, thereby inhibiting the binding and the effect of the mitogen.

In the first 2 weeks of life no IL-2, and, from 1 to 2 months, only small amounts of IL-2 were detected in the SN of Con A-stimulated tolerized SC (at 2 weeks: BAT:  $0.06 \pm 0.13$  U/ml; NT:  $8.49 \pm 3.57$  U/ml;  $p < 0.001$ ). These results indicated a decreased production and/or increased consumption of IL-2.

In conclusion, in the tolerized mice, the hyporeactivity to Con A developed between 1 and 2 weeks of age, parallel to ATA and preceding LPD. It was not due to a reduction of the numbers of  $\text{CD4}^+$  and  $\text{CD8}^+$  T cells. ATA and the decreased production and/or increased consumption of IL-2 might play a role in the defective T cell activation.

## Acknowledgements

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## EFFECTS OF ANTIENDOTHELIN TREATMENT ON THE EARLY HEMODYNAMIC CHANGES IN HYPERDYNAMIC ENDOTOXEMIA

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We have performed a series of experiments to study the effects of a newly developed antisense homology box-derived endothelin (ET) antagonist peptide (ETR-P1/fl) on the early hemodynamic changes in a hyperdynamic endotoxemic dog model. Mean arterial pressure (MAP), cardiac output (CO) and myocardial contractility (MC) were measured in closed-chest animals. Plasma levels of ET-1,2 were determined by radioimmunoassay. A hyperdynamic circulatory response was elicited with a 2-hour infusion of 5.3 µg/kg of *E. coli* endotoxin (ETX). Control and ETX-treated animals received an infusion of ETR-P1/fl (0.1 mg/kg) iv. ETX treatment decreased MAP and MC, increased initially CO, and a long lasting elevation in the plasma ET level was observed. In ETX-treated animals the administration of ETR-P1/fl significantly prolonged the increase in CO and inhibited the depression of MC. Our results suggest that treatment with the ET antagonist ETR-P1/fl may be advantageous in the early phase of endotoxemia.

### Introduction

The mechanism of cardiovascular collapse in septic or ETX shock has been intensely investigated. It has been demonstrated that ET peptides are important mediators of the circulatory reactions during septic or ETX shock [2]. Although ETs are the most potent vasopressors known up to date, their role in circulatory regulation under normal or septic conditions is still controversial. In our study we used a newly developed "antisense homology box-derived" ET antagonist peptide, which powerfully modifies the ET-A receptor activity in vitro [1]. The antisense homology box theory is based on recent findings, that peptides coded by the sense and the corresponding antisense DNA strands can specifically recognize and bind to each other. After locating these "antisense homology box" regions, on the type A ET receptor, several of the corresponding peptides have been synthesized. Among these ETR-P1/fl peptide proved to be the most potent ET-A receptor antagonist.

### Methods

These experiments were performed on pentobarbital-anesthetized thoracotomised mongrel dogs. Following surgery and the closure of the chest, the animals were breathing spontaneously. Plasma levels of ET-1,2 were determined by radio-immunoassay. MAP and heart rate were monitored, CO was measured by the thermodilution method. The left ventricular pressure and diameter signals were recorded on a computer and MC was



estimated from the slope of the left ventricular end-systolic pressure-diameter relationship. The animals were divided into 4 groups. Group 1 served as the untreated control. In Group 2 the animals received an infusion of ETR-P1/fl (0.1 mg/kg) iv. In Group 3 and 4 a hyperdynamic circulatory response was elicited by a 2-hour infusion of 5.3  $\mu\text{g/kg}$  of *E. coli* ETX (O55:B5). In Group 4 the animals were given ETR-P1/fl (0.1 mg/kg) after the 30th min of the ETX infusion. The observation period was 4 hours after a 30 min control measurements in each groups.

## Results

We observed a long-lasting, 2.5-fold increase in the plasma ET level in both endotoxemic groups. ETR-P1/fl treatment delayed, but did not inhibit the elevation of the plasma ET level. The MAP displayed a steep decline and continued on a lower level in the groups receiving ETX. CO increased initially by about 20%, and peripheral resistance decreased by 35%. These changes subsided in 60 min in Group 3. The administration of ETR-P1/fl peptide prolonged significantly the increase in CO and the decrease in vascular resistance until the end of the observation period. In the ETX-only group MC decreased gradually below the control level after the 60th min of the ETX infusion. Treatment with ETR-P1/fl peptide during endotoxemia inhibited the myocardial depression caused by ETX in Group 4.

## Discussion

Our data demonstrate the participation of ET in the early circulatory response in hyperdynamic endotoxemia. ETR-P1/fl peptide administration during the ETX infusion delays the elevation of the plasma ET level. In our experiments high plasma level of ET and a myocardial depression was observed under endotoxemic conditions. Our results suggest that treatment with the antiendothelin ETR-P1/fl peptide may be advantageous in the early phase of endotoxemia by inhibiting the myocardial depression caused by ETX, and enhancing the compensatory circulatory response.

## Acknowledgements

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## USE OF HARMONIC SCALPEL AT LAPAROSCOPIC CARDIOMYOTOMY. A NEW METHOD

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The laparoscopic cardiomyotomy with anterior fundoplication (Heller–Dor procedure) is accepted for treatment of esophageal achalasia. The crucial point of the procedure is proper myotomy and avoid perforation of the esophagus. Hook cautery is widely accepted to dissect the oesophageal muscle. We'd like to demonstrate our experiences with a new device – Ultrasonically Activated Harmonic Scalpel –, which was used at our operation for achalasia to make the cardiomyotomy. Between December 1993 and December 1996, 11 patients with esophageal achalasia underwent laparoscopic Heller's operation with Dor's antireflux procedures. In one patient we applied the Ultrasonically Activated Harmonic Scalpel (HS) to make the cardiomyotomy. The use of HS and results were evaluated. Application of the Harmonic Scalpel is effective for cardiomyotomy. It can be used more safe than electrocoagulation, because it cause less thermic lesion. It's easy to use at laparoscopic way. A perforation of the esophagus didn't occur. There was no intra-, or postoperative complications. After the operation the patient is free of complains. After our first operation, we have found, that Ultrasonically Activated Scalpel can be applied with safe and good results for the cardiomyotomy at laparoscopic operations for esophageal achalasia.

### Introduction

The laparoscopic cardiomyotomy with anterior fundoplication (Heller–Dor procedure) is accepted for treatment of esophageal achalasia. The procedure consist of longitudinal division of the hyperthropic muscle layer of the lower esophageal sphincter to allow the dysfunctional esophagus to empty, and associated with antireflux anterior semifundoplication according to Dor is very effective in the treatment of esophageal achalasia.[3, 4, 5] Crucial point of the procedure is the proper dissection of the esophageal muscle without perforation. Hook cautery is widely used to dissect the esophageal muscle.[2, 4] We have tried to dissect it with a new method, using Ultrasonically Activated Harmonic Scalpel (Ultracision®). We demonstrate our experiences based on our first one operation.

### Methods

Between December 1993 and December 1996, 11 patients with esophageal achalasia underwent laparoscopic Heller's operation with Dor's antireflux procedures. In one patient we applied the Harmonic Scalpel. A 44 years old woman was submitted to



operation after careful preoperative assessments. He had had clinical, radiologic and manometric signs of esophageal achalasia. Upper GI endoscopy excluded malignancy. We have performed Heller myotomy with a Dor semifundoplication. Dissection of oesophageal muscle was performed by Harmonic Scalpel.

The HS uses mechanical energy rather than electrical energy to achieve dissection of tissues is. There is a transducer in the handpiece that vibrates at 55,000 x/s with a 50-100 micron excursion. A laparoscopic extender with an exchangeable blade carries the energy to tissue. The blade couples with tissue and mechanically denatures protein by disruption of hydrogen bonds within the protein structure, so achieve coagulation, finally the dissection of tissues [1].

## Results and Discussion

There were no intraoperative and postoperative complications. The operation lasted 95 minutes. The perforation of the esophageal mucosa didn't occur. One month after myotomy patient was free of any complaints. Esophageal manometry showed decreased LES pressure.

The use of HS was more safe than electrocoagulation, because it caused less thermic lesion. It was easy to use at laparoscopic way.

After our first operation, we have found, that Ultrasonically Activated Scalpel can be applied with safe and good results for the cardiomyotomy at laparoscopic operations for esophageal achalasia.

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## USE OF HARMONIC SCALPEL FOR DIVISION OF SHORT GASTRIC VESSELS AT LAPAROSCOPIC NISSEN FUNDOPLICATION. A NEW METHOD

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The essential of laparoscopic Nissen fundoplication is creating a loose and tension free wrap requiring mobilisation of the gastric fundus. Division of the short gastric vessels (SGV) is a standard component of that procedure which requires considerable part of the operation time, and despite of a careful dissection sometimes significant blood loss can be occurred. The Ultracision® Harmonic Scalpel (HS) makes the process quicker safer and can cause less intraoperative complication. This study compares our original method of vessel control (at 10 cases, Group 1), to the Ultracision® Harmonic Scalpel (at 10 cases, Group 2) Times for SGV division, estimated blood loss and intraoperative and postoperative complications were evaluated. In the favour for Group 2 a significant reduction was reached in the time required for division of SGV to mobilize the fundus. As the most common postoperative complication, the dysphagia concerns we found significant difference in the two groups and dysphagia was mild at Group 2. Application of HS provide safer, easier and faster division of SGV resulting significant savings of time and less prone to thermic trauma and recommended at LNF operations to avoid potential intra- and postoperative complications.

### Introduction

The laparoscopic Nissen fundoplication (LNF) is widely used for treatment of gastroesophageal reflux disease, and their results comparable to open surgical procedures but with less overall morbidity.[2,4] Many of the technical details of the procedures may vary widely from one surgeons to another. Substantial at LNF is creating a loose and tension free wrap requiring proper dissection in the crural region and mobilisation of gastric fundus. Division of short gastric vessels (SGV) is a standard component of that procedures. It is important whether the SGV is divided, because there are significantly lower incidence of short-time and persistent dysphagia in patients with divided SGV compared to those that did have not divided the SGV. (Nissen-Rossetti procedure [3]). For this reason recently we divide the SGV on all laparoscopic funduplications, in line with other authors [5]. Generally the division of SGV requires considerable part of the intervention, and despite of a careful dissection may lead to additional blood loss. Therefore the aim of this study is to compare our original method of vessel control and division, using EndoHernia clips (EH) and coagulations, to use of the Ultrasonically Activated Harmonic Scalpel (HS) (Ultracision®), a device that incorporates relatively new technology to achieve hemostasis.



## Materials and Methods

After our learning curve at LNF operations we compared experiences gained at our last 20 procedures. Our patients was submitted to operations after careful preoperativ assesment (endoscopy, pH-metry, manometry, clinical evaluation). We have been performed our antireflux operations since September 1993. Our methods and experiences are written elsewhere [4]. Since June 1996 we have possibility to use Harmonic Scalpel (Ultracision®). The HS uses mechanical energy rather than electrical energy to achieve hemostasis. There is a transducer in the handpiece that vibrates at 55,000 x/s with a 50–100 micron excursion. A laparoscopic extender with an exchangeable blade carries the energy to tissue. The blade couples with tissue and mechanically denatures protein by disruption of hydrogen bonds within the protein structure. The disorganised protein forms a sticky coagulum that coapts the vessel walls [1]. We have applied the HS at our last 10 patients for dissection and division of SGV and soft tissue. (Group 1) At Group 2 we used conventional laparoscopic devices for dissection: EH clips and sharp division of vessels and coagulations for hemostasis. All operations were performed by one surgeon who have had experience with the procedure. Times for SGV division and estimated blood loss during this portion of procedure were recorded for all patients. Intraoperative and postoperative complications were evaluated.

## Results and Discussion

In the favour for Group 1 a significant reduction was reached in the time required for division of SGV: the division of SGV was mean 33,5' in Group 1 and mean 21,6' in Group 2. A minimal difference was found between two groups in estimated blood loss: mean 12,3 cc in Group 1 and mean 18,8 cc in Group 2. There was no intraoperative complication, there was no need for transfusion, conversion or splenectomy. There was no evidence for delayed bleeding from a divided vessels. The hospital stay ranged from 4 to 6 days. As the most comon postoperative complication, the dysphagia concerns we found significant differency in two groups. Dysphagia were found at 2 patients and lasted till 8–10 days at Group 1 and at 8 patients were found and lasted till 10–16 days at Group 2, and dysphagia was mild at Group 1.

We conclude that application of HS provide safer easier exposure of the intercrural region, safer and faster division of SGV resulting significant savings of time and less prone to thermic trauma as well as low rates of postoperative dysphagia, so this device can be recomended at LNF operations to avoid potential intra-, and postoperative complications.

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## RESECTION OF GIANT SCHWANNOMA BY COMBINED SURGICAL EXPOSURE

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Contrary to the past experience the giant Schwannoma with symptoms of canalis vertebralis compression has been removed by combined surgical exposure in one sitting. Laminectomy, decompression of the canalis vertebralis and immediately subsequent extracanalicular resection of the tumour by retroperitoneal approach was performed in one sitting by two surgical teams. The advantages of the combined surgical exposure: 1. The affliction of the patients caused by the operation significantly decreased. 2. The expenses of the treatment, nursing and hotel decreased as well. 3. The surgical team of different specialists remove the tumour together in both approaches.

### Introduction

The Surgical Ward of the Uzsoki Street Hospital together with the Neurosurgical Scientific Institute of Hungary, performed 3 operations between 1985 and 1995 because of symptoms of canalis vertebralis compression caused by neurogen tumours. The surgical intervention was done in two steps. First operation done in the Neurosurgical Scientific Institute of Hungary – laminectomy, decompression of the canalis vertebralis. Second operation done in the Surgical Ward of the Uzsoki Street Hospital – extracanalicular resection of the tumour by retroperitoneal approach. 10–14 days later the first operation was followed by the second one. It seriously afflicted the patients and caused a high expense for the hospital. Authors worked out a combined surgical exposure to remove neurogen tumors by one surgical intervention.

### Material and Method

The operation can be demonstrated by the case of the fourth patient. B. L. 69 years old female. She was examined because of the numbness of the left lower limb. The ultrasonic examination of the abdomen, the CT and the MRI proved neurinoma, sized 7.5x10 cm penetrating in the L III–IV. intervertebral space. The operation was performed by a neurosurgeon, an abdominal surgeon and a vascular surgeon team on the 18<sup>th</sup> of September in 1996. The neurosurgeon performed a L–III laminectomy while the patient was in ITN, in abdominal lying position with elevated lumbal vertebrae. The tumour was separated from the neuronal root of the left L–III vertebra. Its size was 1x0,5 cm. The frozen section proved benignoma (neurinoma?). Finishing the closure of the surgical wound, the patient was turned to her right side. The spinal column was being elevated, transmuscular, retroperitoneal exposure was done by the abdominal surgeon.



## Results

The compact tumour sized 10x7.5x6.5 cm raised the left m. ilio-psoas. It was prepared till the foramen vertebral end totally removed without injuring the neuronal root. The operation wound was revised, closed and a redon drain was situated there. After the 90 minutes operation the patient awakened untroubled. She did not need transfusion. She did not show neurologic symptoms. She was symptomfree during the postoperative period and left the hospital on the 9<sup>th</sup> postoperative day. The final histological examination proved Schwannoma. According to her examination, she is still symptomfree. The 3 months CT control is just being done.

## Discussion

The Surgical Ward of the Uzsoki Street Hospital and the Neurosurgical Scientific Institute of Hungary are working together since many years. This collaboration resulted the team work in removing the tumours surrounding the spinal column. Authors state the advantages of the combined surgical exposure: 1. The affliction of the patients caused by the operation significantly decreased. 2. The expenses of the treatment, nursing and hotel decreased too. 3. The surgical team of different specialists remove the tumour together in both approaches. In similar cases authors advise to apply their new surgical method if personal and material conditions were given.

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## DIAGNOSTIC-STAGING LAPAROSCOPY

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Recently instead of the old fashioned, traditional explorative laparotomy the newer up-to-date procedure, the diagnostic-staging laparoscopy has been generally used in the everyday surgical practice of the Authors. Evaluating 32 diagnostic and staging laparoscopy Authors draw the attention to the importance of this procedure which has high diagnostic value, and reduces the complication rate. Biopsy, cytology, frozen section can be done. Authors carries out diagnostic and staging laparoscopy in cases of esophageal, liver, stomach and pancreas tumours just immediately before surgery.

### Introduction

Since 1992 in the Surgical Ward of the Uzsoki Teaching Hospital operations with laparoscope are being done, cholecystectomies are usually performed by laparoscopic method. Nowadays it is used for diagnostic purpose as well. It is almost the only method for abdominal investigation instead of the old, traditional explorative laparotomy. It can be widely used in old patients because its known advantages – short operating time, it hardly afflicts the patient, lack of septic complications etc. – The aim was to study the experience drawn by 32 diagnostic laparoscopies done in the past four years.

### Material and Method

The inspection with the conventional instrument was done through the umbilical region. Biopsy was performed by a second wound through a 6 mm trocar. Diagnostic laparoscopies were done in two cases because of small pelvis (gynecologic) alteration. In 6 cases it was done to prove cholelithiasis and a portal hypertension caused by cirrhosis hepatis. In 24 cases its aim was the verification and staging of intraabdominal tumours (gastro-esophageal, pancreas, hepar, colon tu). The tumour was previously shown by sonography and CT but the hepatic and peritoneal metastasis could not be seen. It was also not known whether the abdominal tumour could had been resected. In half of the cases biopsy, hystology and ascites cytologic examinations were done.



## Results

In 28% unknown hepatic metastases and carcinosis peritonei were proved, so 7 patients could avoid the laparotomy. The details are shown and demonstrated by 5, 6 minutes VIDEO. To decide about the resecability (vascular invasion, retroperitoneal lymph nodes involvement) the inspection gives less information than laparotomy. The patient were hardly afflicted, there was no complication or death. Perforation of a hollow organ, intraabdominal bleeding, septic complication were not seen.

## Discussion

According to other authors, it was also found that diagnostic laparoscopy provides new and correct informations even ultrasonography, CT, angiography, ERCP were done. It can be useful mainly in the diagnosis of small hepatic metastasis and carcinosis peritonei [1, 2, 4] The examination is not afflicting for the patient and means less expense for the hospital than open exploration [3, 5] Its greatest advantage is that numerous patients can avoid the operation. Authors advise according to their experience, laparotomy should precede the operation for tumours of the esophagus, stomach, liver, pancreas and the colon.

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## **SUTURELESS ANASTOMOSIS IN THE SURGERY OF THE GASTROINTESTINAL TRACT**

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The idea of the sutureless anastomosis is not a new one, but only the introduction of the VALTRAC-BAR instrument made the wide clinical application possible. The authors have applied this instrument in the case of 32 patients in a two years period. It was used in intestinal procedures in 28, in gastric resection in 4 occasions, respectively. In one case spontaneously recovered stercoral fistula was observed. According to our experiences, the instrument can be used advantageously in preparing anastomoses in the gastrointestinal tract.

### **Introduction**

It has been more than 100 years, when the idea of the sutureless anastomosis arose [1, 2, 3, 4]. Hardy, who created and used first the VALTRAC-BAR, is quoting Senn's paper – published in JAMA, in 1983 – in his article, where he is drawing up the requirements of the sutureless anastomosis. The VALTRAC-BAR seems to fulfill these requirements.

### **Method**

We have been using the VALTRAC-BAR for preparing sutureless anastomoses since 1995. During the application the enclosed instructions and recommendations were kept in view [3].

The preoperative treatment of the patients was usual intestinal cleaning, gastric lavage, and antibiotic prophylaxis, thrombosis prophylaxis in reasonable cases. After the operation the position of the BAR was checked by native abdominal X-ray examination. The nourishment of the patients after intestinal procedures was usual, but not after gastric operations, where – according to the literature – we gave a fluentpulpy diet.

The types of anastomosis: gastro-duodenostomy:2; gastro-jejunostomy:2; jejuno-jejunostomy:2; ileo-cecostomy:1; ileo-ascendostomy:1; ileo-transversostomy:9; colo-colostomy:17.

### **Results**

In case of 32 patients 34 anastomoses were made with the VALTRAC-BAR instrument. The operations were carried out for malignant disease in 27, for benign disease in 5 cases, respectively. VALTRAC-BAR was used in the case of 1 acute operation for ileus.



Surgical complication was detected in 1 case, on the seventh day postoperatively a stercoral fistula occurred, which recovered spontaneously.

One patient has died in pulmonary embolisation, in spite of thrombosis prophylaxis on the 22nd postoperative day. The ring usually departed between the 17. and 21. day, and was mostly unnoticed by the patients.

## Discussion

The introduction of the VALTRAC–BAR gave a new method to the surgeon in preparing anastomoses in different parts of the alimentary tract. In the beginning we made only intestinal anastomoses in our practice, according to the original proposal. On the base of literary data, the application of the instrument was expanded to the upper gastrointestinal area, where differences were observed in the disease course of the patients in comparison with previous cases. In all 4 cases inconvenience of motility was registered in the form of hiccups and gastric retention, which has lasted for 10 days. On the contrary, X-ray examinations of the upper gastrointestinal passage, carried out on the 2nd day postoperatively, demonstrated appropriate status in all cases. From the complications, mentioned in the literature (ileus, bleeding, suture insufficiency, stenosis) occurred only one – one a spontaneously recovered fistula during the study [2, 5].

By using the measuring equipment, the selection of the appropriate ring doesn't make any trouble in the case of similar bowel ends [5]. In case of different diameters of bowel ends, the dimensions according to the smaller one must be chosen.

According to our experience, that correspond with literary data, the VALTRAC–BAR is advantageous for the surgeon, for the patient and for socioeconomic viewpoints, too. The application is not suitable where there is a great difference between the lumen sizes and in the thickness of the anastomosing ends. In this case a hand made suture must be used.

In current status of the Hungarian sanitation the price of the instrument is a little bit high [5].

## Conclusion

According to our experiences – corresponding to the literature – the VALTRAC–BAR is suitable for preparing sutureless anastomoses on different sections of the gastrointestinal tract.

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## **THE BLOOD SUPPORTING OF NIPPLE-AREOLAR (NAC) COMPLEX PERFORMING FOR MAMMAPLASTIES**

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In case of mammaplasties the blood support of the nipple – areolar complex is one of the most important. The authors give a comprehensive clinical summary of the operating technics which are suitable to correct mastoptosis and breast hypertrophy (or macromastia). After mentioning the anatomy, blood and nerve supply of breast, following the classifying of mastoptosis and breast hypertrophy. Summarizing of the historical development of operating methods, which resulting in modern solutions, and adding Hungarian – related data. The widely used mastopexies and reduction mammaplasties will be analyzed, with demonstration of transposition of NAC using different kind of dermo-glandular flaps, e.g.: Skoog-, Pitanguy-, McKissock-, Strömbeck-, Robbins-, Regnault- and other's method. After discussing the possible postoperative complications, authors underline the necessity of detailed analysis and exact planning in varied clinical cases for achieving wanted functional and aesthetic result. Attaching importance to have more perfect operating techniques.

### **Introduction**

The blood supporting of NAC is essential goal in mammaplasties, because the transposition into the normal anatomical place can be realizable in this way [4].

The recognition of the anatomy and blood supply of the breast made newer operating techniques possible.

These methods result in better functional and aesthetical effects. Planning of mammaplasties call for careful analysis of the breast disorders [6].

### **Methods and Results**

The authors offer a comprehensive clinical summary of the most general and wide-spread methods, which are suitable for correcting different kind of ptosis and macromastia. We would like to underline the importance of detailed knowing and management of mastopexies and reduction mammaplasties as well [1].

Expounding of the anatomy, blood supply and innervation of the breast, with special regard to the periareolar vascular ring, the so called "circulus Halleri" [6].



### *The history of mammaplasty: The main stages [2]*

The basic components of mastopexy.

Classification of breast ptosis.

The basic components of reduction mammaplasty.

Classification of breast hypertrophy or macromastia: according to

♦ predicted volume of excision

♦ shape and consistency [1].

The main postoperative complications:

|                            |      |          |
|----------------------------|------|----------|
| Hematoma:                  | 2–3% |          |
| Glandular or fat necrosis: | 2–4% |          |
| NAC necrosis:              | 1–2% |          |
| NAC changing sensitivity:  | 4–8% |          |
| Skin necrosis:             | 2–3% | [1,4,6]. |

## Discussion

The advantages of modern methods: skin and gland could be shaped without any major undermining of the skin. The NAC transposition is possible via dermo-glandular or glandular flap only. The skin within the NAC-carrying flap has the major part of the dermis left intact, but the NAC can survive on a pure glandular flap without any dermis. We advice, like Climo and others, to preserve a circular dermal ring or "cloak", at least 1,0 cm wide from the areolar margin [1].

## Summary

Many new techniques have been presented recently. These operating solutions have resulted in much more better shaping of the breast, more acceptable scars and aesthetical effects, parallel with reducing of postoperative complications. We would like to emphasize the importance of perfect knowing and using more operating techniques, which could be used to correct different kind of deformities, because only one technique could not be applied to every breast.

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## LEVEL OF SENSITIVITY OF PAIN IN PATIENTS WITH OBESITY

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Our aim was to find out the presence of differences in pain sensitivity level depending on body weight. 206 healthy persons at the age of 18 to 84 were the objects of the research with the help of the special instrument which action was based on the principle of dosage pressure by a needle on the forearm skin and by registration of indecis pressure extents when the patients felt no pain, when they felt slight pain and when they felt violent pain. The patients with normal body weight didn't feel pain when the pressure of a needle was 28,53 g; persons with surplus body weight and fatness of the 1 degree – 46,5 g and persons with fatness of the 2–3 degrees – 61,55 g. Slight pain was registered when the pressure was 40,5 g; 57,6 g and 72,9 g conformably. And the violent pain – 76,5 g; 91,3 g and 116,2 g. Thus the patients with fatness have higher pain sensitivity threshold then people of other categories, so they feel less pain. The older a person is the higher pain sensitivity threshold is.

### Introduction

We noticed that obsessed patients are more sensitive to pain than patient's with normal body weight. To find out how for it is true, we tried to experimently find whether there is any difference between obsessed and normal patients to pain sensitivity.

### Methods

To find out level of pain sensitivity exists a method, which works on principal of pressure of a needle on skin. This method consist's of scale, handle, arrow and spring whose lower end is attached to base. To the upper end of spring a needle and arrow are attached. On base there is a hole through which needle. Moves experimently it is proven that deviation of needle upwards is equal to 9 grams.

Pain sensitivity is measured in following way. Needle end is sterilized before every investigation clean it with 96% ethyl spirit. Investigation is done with patient sitting or lying down. For this end of the needle is attached to the anterior surface of forearm. After this, with forse press, the needle, it will move upwards and arrow with show the measurement on scale. During the experiment some patients did not feel pain at all, some felt mild pain and other's felt very strong pain. Experiment was done on 206 healthy people, out of them 114 mend and 92 women of age 18 to 84 year's. Men were of height from 165 to 191,5 cm and weight from 62 to 110 kg. Women were of height from 153 to



175 cm and weight of 50–110 kg. With the help of Broka-index and our index patients indore there are 3 groups:

- 1 group – normal body weight
- 2 group – extra body weight, obesity I stage
- 3 group – obsessed patient II–III stage.

## Results

Patients of 1 group are not sensitive to pain due to pressure of needle on skin equal to 28,53 g; 2 group – 40,5 g; and 3 group – 61,65. Patients of 1, 2, 3 groups are sensitive to mild pain due to pressure of needle equal to 40,5, 57,6, 72,9 grams, strong pain when pressure is 76,5, 91,8 and 116,2 grams.

Patients with normal body weight are considered to be not sensitive to pain. It is taken as 100%. For 2–3 groups of weight we got following results. Pain is not felt at 142 and 216%, strong pain at 142 and 180%, and very strong at 120–152%. Patients belonging to second and third groups are more resistant to mild and medium stimulation. Sensitivity decreases in strong pain stimulation.

## Discussion

We could find only 2 source of information on this topic. B. Zahorska–Markiewicz et al., [1] where it is proved that obsessed women are less sensitive to than women with normal or low body weight. L. P. Chepky, 1990 [2] proved that in obsessed patient (3–4 stage) pain sensitive is decreased to 15%. Cause for this could decreased in quantity of nerve end in skin and decrease in emitation of nerve fibres.

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## INTERNAL CAROTID STENT IMPLANTATION WITH ANGIOSCOPIC CONTROL

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Stent implantation is a method, which is being used more and more often, mainly in the field of peripheral arteries, but coronary stent implantation is also well-known. The authors apply this procedure for patients, who besides the carotid bifurcation stenosis also suffer from the internal carotid stenosis in a longer section of the artery. The indication are as follows: 1. in the case of internal carotid stenosis in a longer section we assure the flow with the help of carotid thrombendarterectomy and solve the run-off with balloon catheter dilatation and stent implantation. 2. in the case of a stenosis in a short section we use stent implantation to avoid dissection of the intima. With each intervention we perform the carotid bifurcation thrombendarterectomy. The authors made the first intervention 15 months ago, since then we have performed 17 stent implantations. One of the 17 patients developed a temporary stroke (TIA). This is a new method, further cases are needed for long-term experiences. Intervention under eye-control can be carried out with more confidence. As regards to the post-operative medicinal treatment, the administration of thrombocyte aggregation-blockers or heparinoid preparation (e.g.: PPS-SP 54) after the stent implantation has become a routine therapy. Summarized the foregoing, these cases constitute about 10–15% of all carotid operations, therefore the authors would like to make it clear, that this is not a routine method, but a possibility, strictly respecting the above-mentioned indications.

### Introduction

The professional progress of the present is characterized by tending towards the minimally invasive surgery. In the vascular surgical practice a great advance was made by introduction of endoscopic video-systems of fiberglass optics.

The angioscopy as a diagnostic and therapeutic intervention is a generally accepted procedure all over the world [3]. Stent implantation is a method, which is being used more and more often, mainly in the field of peripheral arteries, but coronary stent implantation is also well-known [1].

### Methods

We apply this procedure for patients, who besides the carotid bifurcation stenosis also suffer from the internal carotid stenosis in a longer section of the artery. In these cases we implant a rather long, about 4 cm stent. The other indication is an insecure intimal flap which has been left behind, for this reason we fix the intima with a 1,5–2 cm stent, to prevent the danger of dissection.



*The indication are as follows:*

- ◆ In the case of internal carotid stenosis in a longer section we assure the flow with the help of carotid thrombendarterectomy and solve the run-off with balloon catheter dilatation and stent implantation.
- ◆ In the case of a stenosis in a short section we use stent implantation to avoid dissection of the intima.

With each intervention we perform the carotid bifurcation thrombendarterectomy and use videoangioscopic procedure.

## Results

Relating to complications and long-term results we can only give a report in brief:

We made the first intervention 15 months ago, since then we have performed 17 stent implantations. In 12 patients with indication for a long stent, in 3 patients for fixing the intima, in 2 cases for the simultaneous correction of stenosis and kinking. One of the 17 patients developed a temporary stroke (TIA). In the case of this patient the CT-examination has detected a vertebro-basilar circulation disorder – with good carotid flow. This is a new method, further cases are needed for long-term experiences.

Concerning long-term results it is well-known that the post-operative treatment for stent implanted patients is compulsorily prescribed. The alternatives of this therapy in the perioperative stage are dextran and heparin, for a prolonged treatment thrombocyte aggregation blockers, ASA and heparinoid preparations are used.

The follow-up controls as duplex scan, x-ray examination and haemorheological laboratory tests.

*The advantages of this method are as follows:*

Interventions under eye-control can be carried out with more confidence.

In the case of isolated internal carotid stenosis, the percutaneous stent implantation causes a minor stress, but in the case of a stenosis, which touches upon the common carotid, the carotid bifurcation and the internal carotid, the joint use of the vascular surgical and radiological intervention is much more effective.

As regards to the post-operative medicinal treatment, the administration of thrombocyte aggregation-blockers or heparinoid preparation (e.g.: PPS-SP 54) after the stent implantation has become a routine therapy.

## Discussion

These cases constitute about 10–15% of all carotid operations, therefore we would like to make it clear, that this is not a routine method, but a possibility, strictly respecting the above-mentioned indications. This method is quick, safe. The videoangiography and the postoperative PPS-treatment improve the safety of the procedure.

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## **ENDOGENOUS INTOXICATION SYNDROME WHEN ACUTE PROCESS IN ABDOMINAL CAVITY**

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In the time of simultaneous study of the components of blood of sick patient and animals with acute processes in abdominal cavity it was revealed that in short periods there is increase in value indeces of endogenous intoxication syndrome. The independent index is offered for studying the endotoxycosis of whole blood. It is recommended to use for general and particular characteristics of dynamics during the pathological process.

### **Introduction**

The problem of endogenous intoxication when acute pathology of organs in abdominal cavity *is still actual in surgery nowadays*. The origin and development of endogenous intoxication syndrome is on integral process and finally it often defines the result of the surgical treatment. Nowadays only some of the internal medium indeces are studied. They allow to judge the tendency of endotoxycosis when acute surgical pathology of organs in abdominal cavity is supposed.

#### **Aim**

To define the value of the total endotoxycosis of whole blood in norm and in pathology and its further correction.

### **Material and Method**

We have conducted the research of whole blood preparations of man and dog for the establishment of the total endotoxycosis index. The indeces of a man were studied when peritonitis and ileus (30 observations) and when analogous pathologies of twenty dogs.

The ileus of the dogs was created by volvulus of small intestine loop with its fixation in the forced condition by the special clutch; peritonitis was created by the infection of abdominal cavity with the autophlore suspension 30%. The level of the middle mass molecule (MMM)[1] and sorption ability of erythrocytes (SAE)[2] were studied as the indeces of intoxication.



## Results

This data permits to confirm the hypothesis about the reaction of white and red cells of blood for the inflammatory process. So, in 8–12 hours from the moment of disease (model) this indices had a tendency for increase, as the level of MMM and SAE average on 20% and 28% accordingly.

This state has allowed us to unite the indices into one mathematical formula for the complete appraisal of tendency of endogenous intoxication syndrome. Mathematically the erythrocytic index of intoxication (SEII) which is offered to us looks like the correlation of MMM indices and SAE indices.

$$\text{SEII} = \text{MMM}(\text{conventional units}) : \text{SAE}(\%) \times 100\%.$$

The statistic calculus of variations with the help of electronic computers showed that SEII average is  $0,6214 \pm 0,01$  conventional units, which is considered as a standard.

## Discussion

The definition of the total index of whole blood intoxication when acute processes in abdominal cavity, allows to judge not only about the progressive grown of the pathological process, but also the detoxication reaction of natural systems of an organism.

The study of endotoxycosis index with the help of SEII allows to conduct the necessary correction of the different links of endogenous intoxication more subtly.

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## **SURGICAL TREATMENT OF PANCREATIC HEAD AND PERIAMPULLARY TUMORS**

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The aim of this study was the comparison of the postoperative results of standard Whipple pancreatoduodenectomy (WP), pylorus preserving pancreatoduodenectomy (PPPD) and palliative bypass operation performed for treatment of pancreatic head and periampullary tumors. In the period from Jan. 1992 to 1996 106 patients had tumors located in the head of pancreas and 21 patients had periampullary tumors. The diagnosis was established by ERCP, transabdominal ultrasonography and computer tomography. We assessed the morbidity, mortality, prognostical data of the surgery of pancreatic head and periampullary tumors. Tumor markers such as CEA, CA 19-9 and CA 125 were also studied. The operability rate was 26% in case of pancreatic head tumors and 69% in periampullary tumors. The mortality rate was 6%. Postoperative complications were in 23 patients (18.1%). There was no significant difference between the survival of WP and PPPD group, but we found much better survival in patients with periampullary tumor. After palliative operation the survival rate was 6.1 months in case of pancreatic head carcinoma and 11 months in case of periampullary tumors. Our data provided many evidences about the advantage of PPPD in the patients with malignant periampullary and pancreas head tumors and the long term results and quality of life is much better after PPPD.

### **Introduction**

It is often difficult to accurately differentiate cancer of the head of the pancreas from three other malignant periampullary neoplasms: ampullary carcinoma, duodenal carcinoma, and carcinoma of the distal common bile duct [1]. The aim of this retrospective study was the comparison of operative outcome, nutritional recovery and survival of patients who underwent different operative therapies: the standard Whipple pancreatoduodenectomy (WP), pylorus preserving pancreatoduodenectomy (PPPD) and palliative therapy of these tumors [3].

### **Methods**

In the period from Jan. 1992 to 1996 127 patients were selected to this study, investigated and operated. 106 patients had tumors located in the head of pancreas and 21 patients had periampullary tumors. These included 16 tumors originated from the ampulla of Vater and 5 from the distal common bile duct. These tumors were diagnosed by ERCP, transabdominal ultrasonography and computer tomography. We assessed the morbidity, mortality, prognostical data of pancreatoduodenectomy (WP), pylorus preserving pancreatoduodenectomy (PPPD) and palliative surgical therapy. Tumor markers such as CEA, CA 19-9 and CA 125 were also studied.



## Results

The operability rate was 26% (27 patients) in pancreatic head tumors and 69% (11 patients) in periampullary tumors. Considering 31 resections: 5 W.P, 26 cases PPPD and 7 local excisions of the tumor of the ampulla of Vateri were performed. The mortality rate was 6%. We found that elevated serum level of CA 19-9 is the most sensitive marker of all of the tumor markers of the malignant pancreatic tumors. After non resectional treatment 7 patients (7%) died in the postoperative period. Postoperative complications were in 23 patients (18.1%). Delayed gastric emptying was more common in the PPPD group resulting longer hospitalization. In PPPD group there was a better nutritional recovery and also the increase of both body weight and serum albumin level. There was no significant difference between the survival of WP and PPPD group, but we found much better survival in patients with periampullary tumor. After palliative operation the survival rate was 6.1 months in case of pancreatic head carcinoma and 11 months in case of periampullary tumors.

## Discussion

The surgical treatment of the tumors of the head of the pancreas and of the periampullary tumors are the same, nevertheless the pathological behaviour of the two groups of tumors are different. The majority of patients of these tumors are operative candidates [2]. The Whipple and PPPD operations are safe and effective surgery, resulting significant improvement of quality of life [4]. In case of periampullary tumors the survival is better than in the cases of pancreatic head tumors [5].

Improved surgical techniques and improved perioperative management together decrease the surgical risk. Our data provided many evidences about the advantage of PPPD in the patients with malignant periampullary and pancreas head tumors. There is no any difference between the survival rates of WP and PPPD but the long term results and quality of life is much better after PPPD.

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## IMPROVEMENT OF SWALLOWING ABILITY IN ADVANCED OESOPHAGEAL CANCER

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Without different types of palliation the patients with inoperable oesophageal cancer have a poor quality of life, rapid weight loss which leads to death. The aim of palliation is the complete relief of dysphagia. Our modified procedure is a simplified way of a well known method described by Tytgat in 1986. The prothesis is positioned under continuous visual control using only local anaesthesia. This method is safe and not expensive. During the last three years 73 consecutive patients were treated with palliative fiberoptic intubation with Tygon prothesis. 46 patients had esophageal carcinoma, 19 had gastric, 8 had pulmonary carcinoma obstructing the gullet. Among them 11 patients had bronchoesophageal fistula. The early complications were perforations (7) bleeding (2), and later complications: food impaction (5) tumor overgrowth (5) and tube migration (2). The mortality was 2%. All patients have received antibiotic prevention. Although the improvement of life quality is more important than extension of life, for many patients survival will be prolonged due to improved nutrition as a result of treatment. This study summarizes our experience with this technique and analyzes the problems and complications encountered in our patients.

### Introduction

There is a great importance of the surgical treatment of oesophageal cancer because of the majority of patients and of the increasing morbidity and mortality rates [1]. The predominant symptom is the various severity of swallowing inability that eventually progresses to complete dysphagia with hypersalivation, aspiration, rapid weight loss which eventually lead to death. The results of the surgical procedures of gastrostomy and jejunostomy are uncertain because they are unable to prevent the complications because of the obstruction and aspiration.

The aim of this study is to investigate the aspects of the procedure of palliative endoscopic oesophageal intubation that make possible to avoid gastrostomy and jejunostomy and to investigate the complications related [3].

### Methods

The palliative endoscopic intubation was entered in 1992 in our clinic. The enlargement of the tumorous region of the oesophagus under endoscopic supervision makes us possible to get information about the length of the tumorous region, about the spreading of the tumor to the stomach in case of cardiac tumors. During the procedure we push the Tygon endoprothesis with a rammer to the tumorous stricture under endoscopic control.

In the postoperative period the patients received High Dose Rate (HDR) after loading radiotherapy and telecobalt external treatment.



## Results

The complications were divided into three groups: early, late and the results that were not related to the surgery. The early complications were perforations (7 patients), bleeding (1 patient). Two patients died because of sepsis. The late complications were: food impaction (5 patients) tumor overgrowth (5 patients), tube migration in two cases when the tube moved proximally and was replaced by reintubation. We found the complaints of the reflux in all of the cardial tumorous cases. After the intubation the ability of swallowing improved in all of the cases. Increase of body weight We found increase of body weight in 14 cases. The improvement of quality of life is as important result of the treatment as the improvement of the survival time due to better nutrition. 19 patients received intraluminal after loading radiotherapy.

## Discussion

The surgery of oesophageal tumors depends on the the stage of the disease, the localization of the tumor and on the general state of the patients [2].

In the occasion of complications of endoscopic intubation the operative intubation is preferred [4, 5]. Oesophageal tumors are often multiple, therefore reintubation is often indicated. In the cases of tumors of the cardia the procedure of the intubation is more difficult because of the greater distance and the consistency of the tumors.

On the base of the literature and on our experiences the combined radiotherapy has got great importance. In the cases of bronchooesophageal fistulas the radiotherapy is not offered.

Although the improvement of quality of life is as important as the extension of life and for many patients survival will be prolonged due to improved nutrition as a result of treatment. This study summaries our experience with this technique and analyzes the problems and complications encountered in our patients. This method is safe and not expensive.

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## **MORPHOLOGY OF CYSTIC RENAL LESIONS. LECTIN AND IMMUNO-HISTOCHEMICAL STUDY**

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Renal cystic disease include heritable, developmental and acquired disorders. Morphological features were extensively studied mainly in cases of autosomal dominant polycystic and experimentally induced cystic disorders. We report the immunohistochemical (cytokeratin, epithelial membrane antigen, vimentin, Tamm-Horsfall protein, proliferating cell nuclear antigen) and lectin-binding (soybean agglutinin, Dolichos biflorus agglutinin) profile of cystic kidneys from 9 surgically removed and 21 autopsy cases. The primary renal diseases displayed great diversity. Beside polycystic kidney diseases we studied cysts associated to renal neoplasm, hemodialysis, nephrosis syndrome and chronic transplant rejection. Cystic epithelium demonstrated positive reactions with distal tubular markers (epithelial membrane antigen, cytokeratin) or collecting duct (soybean agglutinin, Dolichos biflorus agglutinin) and Henle loop markers (Tamm-Horsfall protein) but the latter in lesser extent. The large number of the vimentin positive cases are suggestive to dedifferentiation or cellular regeneration. The former might be underlined by the diffuse cytoplasmic or basolateral membrane staining of the epithelial membrane antigen in some cystic epithelial cells. Not the cystic epithelium but rather the neighbouring non-dilated tubular cells and interstitial cells presented proliferative activity which was most intense in areas where vimentin and variable nephron segment markers in the same tissue were expressed. Positive reaction of the type IV basement membrane collagen and the rate of the inflammation failed to show similar connection. This finding suggests the importance of the inflammatory cells in the development and/or expansion of the cysts.

### **Introduction**

Cystic renal conditions may occur in different human diseases. Beside the genetically determined autosomal dominant and recessive disorders cortical and medullary, solitaer or multilocular forms are known. Acquired cysts may be associated with renal tumours and hemodialysis. The importance of renal cysts is underlined by the morbidity and mortality data. Nearly half a million people suffer from polycystic kidney disease in the United States and being responsible for 10–12% of end stage renal failure. The genetic background of autosomal dominant and recessive polycystic kidney diseases is now well established. In autosomal dominant polycystic kidney disease the most common chromosomal mutations are localised to the short arm of chromosome 16 or to the long arm of chromosome 4 [1]. The mechanism by which cysts develop is still controversial. The earliest theories supported the role of epithelial hyperplasia which may act in accordance with growth factors and oncogenes [2]. Several biochemical and morphological studies emphasized the altered composition of basement membrane and extracellular matrix in congenital or acquired cystic renal disorders [3]. Another possible mechanism of cyst formation is a change in cell polarity which was demonstrated by the mislocation of Na/K-ATPase to the apical membrane of the cystic epithelium.



## Materials and Methods

Kidney tissues from 30 cases were studied. 9 kidneys were surgically removed and 21 were autopsy cases. Clinical information and the macroscopic appearance of the cysts were obtained from the medical reports and the surgical pathology or autopsy reports. The primary renal disorders and the morphological appearance of the cysts is shown in Table 1.

Table 1.  
The primary renal disorders and the morphological appearance of the cysts

| Primary Renal Disease        |    | Morphology of the Cyst |    |
|------------------------------|----|------------------------|----|
| Cystic kidney disease        | 4  | polycystic             | 3  |
| Chronic inflammatory disease | 4  | multicystic            | 8  |
| Transplant rejection         | 3  | solitaer cyst          | 9  |
| Renal tumour                 | 3  | tubular dilation       | 10 |
| No clinical history          | 16 |                        |    |

Samples were processed in the usual manner, embedded in paraffin and sections were stained with Haematoxylin-eosin (HE).

Immunoperoxidase reactions were performed using the following antibodies: rabbit anti human cytokeratin, mouse anti human epithelial membrane antigen, mouse anti vimentin, mouse anti human type IV collagen, anti lysozyme, mouse anti proliferating cell nuclear antigen, rabbit anti human Tamm-Horsfall protein. Endogenous biotin blocking was applied in all cases. Reactions were visualized using avidin-biotin-peroxidase complex and Vector Red as chromogen.

Lectin binding studies were also performed on paraffin embedded materials. Sections were incubated with peroxidase labeled dolichos biflorus and soybean agglutinin.

Resulting data were analyzed by statistical methods.

## Results

Histology revealed segmental tubular dilation beside the cysts in many cases. Interstitial and pericystic lymphocytic infiltration was seen in 12 of 30. The lining epithelium varied from columnar or cuboidal to flattened. In 3 cases with large unilocular solitaer cyst no epithelium was found. Papillary like epithelial proliferation was present in a few cysts. Most of the epithelial cells had eosinophilic cytoplasm but foci of clear cytoplasm were also visible. There was a significant connection between the primary renal disease and the morphology of the cysts. Kidneys with no previous clinical history of renal disease and rejected kidney transplants represented only segmental tubular dilation. The chronic inflammatory cases were characterised by solitaer or multicystic lesions while the neoplastic kidneys by multilocular cysts.

Distal tubular markers were the dominating features in all cysts. Proximal tubular and Henle loop markers were present rarely in each groups but never in the neoplastic kidneys. Markers characteristic for the collecting ducts were also detectable but with a lesser intensity and especially when the distal tubular markers were weakly positive. The amount of the type IV collagen demonstrated an opposite connection with the morphological appearance. Basement membrane collagen was increased in those cases where no previous renal disease was found, while its amount was less in the polycystic kidneys. Mesenchymal marker, vimentin was expressed in the multicystic and polycystic disorders especially beside the presence of collecting duct markers. Proliferative activity and the presence of inflammation showed no characteristic relation to any of the morphological data.

### Discussion

While the morphology and molecular biology of the genetically determined polycystic kidney disease is well established [4, 5] there are not enough data on the acquired cysts. Our results could not determine significant characteristics for any cystic categories. Although the primary renal disease and the morphological appearance of the cysts demonstrated significant connection. Naturally the number of our cases for significant correlations was limited the similar immunohistochemical reactions suggest similar or common mechanism of cystogenesis allowing to study these factors in non inherited disorders as well.

### Acknowledgements

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## **PROSPECTIVE RANDOMIZED TRIAL COMPARING SHOULDICE AND BASSINI-KIRSCHNER OPERATION TECHNIQUE IN PRIMARY INGUINAL HERNIA REPAIR**

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The authors conducted a prospective randomized trial to compare the Shouldice and the Bassini-Kirschner technique between April, 1994 and December, 1995. During this period 129 adult patients, mean age 54 (17-87) years underwent operation on primary inguinal hernias in their department. 63 Shouldice and 66 Bassini-Kirschner operations were performed by 17 surgeons. The duration of surgery, the technique of anesthesia, the perioperative complications, the duration of postoperative care, then one year after the operation the recurrence rate and the patient's subjective complains were investigated. 85 patients of 129 were examined one year after the operation in spite of that all the patients were invited for control. Both operations gave almost the same results in the perioperative period and nearly identical recurrence rate (4.44% in Shouldice and 5.0% in Bassini-Kirschner group). The patient's subjective complains were also very similar one year after the operation. The authors could not find significant difference in the results of the two types of surgery although they were well experienced with the Bassini-Kirschner operation and just starting to practice the Shouldice procedure. These facts suggest that having more experience with the Shouldice operation makes available the extreme low recurrence rate published by several authors.

### **Introduction**

Before 1994 the standard surgical technique used for primary inguinal hernioplasty in our department was the Bassini (published in 1880), or the Bassini-Kirschner operation. In the spring of 1994 we decided to start a comparative randomized trial with the aim to search a possible new standard decreasing the recurrence rate, the hospital stay, the duration of recovery. For this trial the Shouldice method (published in 1945) seemed to be the most promising after reading about the excellent results published by several authors.

### **Patients and Methods**

All adult patients with primary inguinal (unilateral, or bilateral) hernias were included in the randomization which based on their date of birth. Using this algorithm we tried to keep our surgeons not to be influenced by the individual intraoperative situation which could have seen to be more favorable for one of the two methods [1, 4].

This way 63 patients, 61 male, 2 female, age 52 (18-85) years, Body Mass Index (BMI) 27 (23-31) underwent Shouldice operation and 66 patients, 60 male, 6 female, age 54 (17-87) years, BMI 26 (19-31) were operated according to the Bassini-Kirschner method.

The type of anesthesia depended on the overall health condition and the accompanying illnesses of the patient. General and spinal anesthesia was preferred to local anesthesia, so in the Shouldice group 19 narcosis, 21 spinal anaesthesia, 2 local anaesthesia, 1 epidural anaesthesia and in the Bassini-Kirschner group 12 narcosis, 22 spinal anaesthesia, 4 local anaesthesia were carried out.

Performing the original Shouldice operation with four layers (duplicating the transversal fascia) we used continuous suture of Prolene 2/0.

The standard Bassini-Kirschner operations were performed using Mersilene 1/0 suture.

We compared the duration of surgery in the two groups dividing them into two parts taking into consideration whether the hernias were unilateral, or bilateral. The mean duration in case of unilateral hernias was 61 (35–90) minutes in the Shouldice ( $n = 56$ ) and 45 (25–80) minutes in the Bassini-Kirschner group ( $n = 61$ ). In case of bilateral hernias – where on both sides the same type of surgery was performed – the mean duration time was 105 (55–170) minutes in the Shouldice group ( $n = 7$ ) and 88 (35–90) minutes in the Bassini-Kirschner group ( $n = 5$ ).

The operations were performed by 17 surgeons of our department, 5 consultant surgeons performing 38 Shouldice and 41 Bassini-Kirschner hernioplasties and 12 assistant professors and residents performing 25 Shouldice and 25 Bassini-Kirschner operations. The postoperative hospital stay was 5,4 days in both of the two groups with a range of 3–11 in Shouldice and 4–7 in Bassini-Kirschner group.

All the patients were invited one year after the operation for a control examination where recurrences, subjective complains and possible late postoperative complications were investigated. We examined only 85 patients of 129 (66%), 45 of 63 (71%) in Shouldice and 40 of 66 (60%) in Bassini-Kirschner group due to that only so many patients came to our outpatient department after they had received our letter sent to them.

We defined recurrence as a weakness of the operated area that needs further surgical treatment, other weaknesses of the abdominal wall we did not consider as recurrences.

## Results

The perioperative complication rate was 11 (17,4%) to 7 (10,6%) between the Shouldice and the Bassini-Kirschner group. Among these complications we detected fever (after the second postoperative day) without any other symptoms two times in Shouldice and one time in Bassini-Kirschner group. One minimal haematoma was detected in each group, which were treated conservatively. One wound suppuration in Shouldice group and one pneumonia, two epididymitis in the Bassini-Kirschner group occurred. There was significant difference between the two groups only in occurrence of scrotal edema manifesting 7 times in Shouldice and only 2 times in Bassini-Kirschner group and one of the 7 in Shouldice group persisted as a hydrocele needing further surgery. We had no any other sever complications neither intraoperative nor early postoperative.

Two recurrences of 45 (4,44%) in Shouldice and 2 recurrences of 40 (5,0%) in Bassini-Kirschner group occurred. One of the two recurrences in Shouldice group and both of the two recurrences in Bassini-Kirschner group were treated by Stoppa operation which is a surgery performing mesh implantation in extraperitoneal position with only two-four steaches for fixation via an inferior median laparotomy.



Weakness not needing repeated surgery was detected four times in both of the two groups.

There was no occurrence of testicular atrophy in both groups.

The patient's subjective complaints were pain during physical loading (3–3), local twinge (4–2) and hypaesthesia (5–6) – Shouldice group's data first.

## Discussion

There was no significant difference between the two methods in the perioperative and early postoperative period except in the duration of the operation which comes of the more preparative technique and perhaps of the less experience with this operation.

The cause of the very similar recurrence rate in contrast to the international literature describing much fewer recurrences after Shouldice hernioplasty [1, 2, 3] could be that we involved into this study our first 63 Shouldice operations while we had the experience of years (in case of some consultants of decades) with the Bassini–Kirschner operation.

The personality of the surgeon did not influence the results and in spite of the more difficult technique the surgeon in training performed also the Shouldice procedure with the same characteristic as consultants.

## Conclusions

Summarizing our experiences after performing 63 Shouldice operations and following the patients for at least one year after the surgery we decided to continue our randomized trial, because having more practice we hope to achieve or approach the extreme low recurrence rate published many times by several authors in the international literature.

Nevertheless the longer duration of the operation our colleagues came to like the preparative and more precise technique of the Shouldice procedure, and if having more practice will decrease the recurrence rate, the behalf of our patients also requests us to recommend this "new" hernioplasty technique.

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## JEJUNAL NUTRITION

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Contrary to the past experience of forced parenteral nutrition nowadays the enteral [jejunal] nutrition enjoys priority. It is not questionable, that well adjusted and controlled application of fluid, ion, fat, carbon hydrate, aminoacid promoted convalescence. The experiences of the Authors supports that enteral nutrition through technically proper outperformed jejunostomy does not increase complication rate and beside well controlled food administration provides the physiologic stimulates of food, the method is relatively easy and cost effective. For this reason the Authors initiated jejunostomy at the end of larger interventions such as Akyama procedure, total gastrectomy, multivisceral interventions, pancreatectomy, operations for massive gastrointestinal bleeding and finally reoperations with extreme negative N-balance and with the chance of inability of oral feeding for several days.

### Introduction

Postoperative nutrition after operations on the upper gastrointestinal tract occurs according to the rules of near physiologic early enteral nutrition supported by special literature [1, 2, 3, 4, 5, 6, 7].

### Materials and Methods

Authors review experience gained from 5 case of jejunostomy during 1,5 years on our department of surgery. In our practice we place jejunostomy to all patients undergoing major surgery, in case of complication and first reoperation respectively. By practical consideration density of nutritives requires a tube most proper measure of 14Ch [J-tube]. On the postoperative 2<sup>nd</sup> day at the same time of the starting of intestinal activity, but as initial stimulus as well, we begin nourishing through the probe with food value of 2000 kcal. Preventing obstruction we wash through the tube each time. In case of good tolerance value is increased to 3000–3500 kcal, parenteral infusion is stopped and continued enterally. In terms of significant reflux, tenesmus, long term intestinal inactivity jejunostomy operates as a decompressive drainage. Our method is the following. Select the first oral part of jejunum, that could be adopted to the planned site of stoma without tension. Place the tube in through minimal enterotomy, secure it with a purse string suture. Laying the tube orally, suture the jejunum over it making a tunnel. Then fix it to the abdominal wall so that the jejunum could not twist around it.



## Results

Complications observed in 3 cases, each time the problem was the twisted jejunum around the probe, this constituted indication of surgery. Based upon our experiences it is strongly recommended paying attention to the method of technique, each little step could be the cause of latter complications. Choosing the proper size of tube compared to the diameter of intestine, atraumatic surgical technique, preserving circulation of bowels, selecting the right part of jejunum, method of placing and fixing the intestine are important features.

## Discussion

Why has priority immediate jejunal feeding? On the one hand this is a relatively simple intervention and has low rate of complications, on the other hand specific expenses of nutrition respectably lower compared to other methods [2]. The jejunostomy protects anastomoses and the early enteral feeding is the best stimulus releasing postoperative paralysis [7]. It is well adjustable regarding extent of food, fluid-balance and energy turnover, and it promotes physiologic food absorption [1, 6]. There was no significant inanition despite previous difficulties of calorisation with parenteral nutrition [3, 4, 5].

## Summary

Well adjusted and controlled application of fluid, ion, fat, carbon hydrate, aminoacid promoted convalescence. Our experiences supports that enteral nutrition through technically proper outperformed jejunostomy does not increase complication rate and beside well controlled food administration provides the physiologic stimulus of food, the method is relatively easy and cost effective. That is why we initiated jejunostomy in our practice as a routine method of postoperative enteral nutrition.

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## CHANGING CONCEPT AND MODERN TECHNIQUES IN CATARACT SURGERY

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Until the middle of the 80-ies the routine method of cataract surgery was intracapsular extraction (ICCE). Approximately 10 years ago the so called extracapsular cataract extraction (ECCE) started to become more and more widely used. After extracapsular cataract extraction had come into general use, it became possible to implant the IOL behind the iris, into the left in place capsular bag of the original lens. We usually perform extracapsular cataract extraction with posterior chamber lens (PCL) implantation as a routine procedure. In the last few years phacoemulsification started to gain acceptance. During this operation one breaks the nucleus of the lens into pieces with the help of ultrasound, and this way it is possible to remove both the nucleus and the cortex of the lens through a small wound. The first step in learning phacoemulsification is to be able to create a perfectly round hole on the anterior capsule (capsulorhexis). Besides using various manual techniques we introduced diathermal capsulotomy for capsulorhexis. This latter procedure is becoming more and more popular as it is safe, easy to perform, and gives excellent result.

**Keywords:** cataract extraction, intraocular lens implantation, capsulorhexis

In our practice of ophthalmic surgery among eye opening operations we perform the most frequently cataract surgery. Until the end of the 80-ies the so called intracapsular cataract extraction (ICCE) was generally performed. During these operations the whole lens was removed with the help of special forceps or cryoextractor. Though there were intraocular lens (IOL) implantations performed even at that time, in these cases the IOLs were implanted into the anterior chamber and fixed into the angle or onto the iris. These lenses not rarely caused severe complications either by closing the angle or by injuring the cornea or the iris.

In the last 10 years the so called extracapsular cataract extraction (ECCE) started to become more and more widely used. During ECCE the nucleus and the cortical part of the lens are removed through a specially cut aperture of the anterior capsule.

After the extracapsular cataract extraction came into general use, it became possible to implant the IOL behind the iris, into the remaining capsular bag of the original lens. At present we usually perform extracapsular cataract extraction with posterior chamber lens (PCL) implantation as a routine.

In the past few years phacoemulsification started to gain acceptance. During this operation one breaks the nucleus of the lens into pieces with the help of ultrasound, and this way it is possible to remove both the nucleus and the cortex of the lens through a small wound. In order to implant an IOL through this less than 3 mm wide incision there



were smaller diameter or foldable lenses developed. Although this method is definitely more difficult to learn and it requires many special instruments, it has many advantages because of the smaller wound. It can be performed on an outpatient basis, it causes smaller postoperative astigmatism and the time of the postoperative care is shorter. Because of the previously mentioned reasons phacoemulsification can shortly become even more popular.

The essential condition of PCL implantation is to be able to make an as regular and round capsulotomy as possible without angles. The first ever widely used method for this purpose was the "can opener" technique. In this case we prepare the capsulotomy with a cystotome (a specially formed thin disposable injection needle) by performing small circular incisions on the anterior capsule. The disadvantage of this technique is that the edge of the hole created this way is uneven, and can be torn by even a small force. Because of this disadvantage lately a new technique, the capsulorhexis started to become more and more popular. During this procedure we tear a circular hole on the capsule by using a fine capsular forceps. Although this method is suitable for any kind of PCL implantation, it requires sufficient experience. Because of this many special instruments were developed to perform capsulotomy. In Hungary the diathermal capsulotome of ERBE was first used in the Department of Ophthalmology of the University Medical School of Debrecen. With the help of this instrument it is possible to perform a perfectly round capsulotomy easily through a 3 mm wound. By touching the capsule with the thin diathermal needle one can create an aperture of any size. During this procedure the edge of the capsule becomes thicker because of the thermal coagulation, and easily visible and even stronger. This is important, since the manipulations especially during phacoemulsification can cause posterior capsule rupture. According to the experience of our Department the diathermal capsulotome is very useful for expert or even for beginner cataract surgeons in every kind of PCL implantations.

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## THE EFFECTS OF BISARAMIL AND ANTIARRHYTHMICS ON FREE RADICAL GENERATION OF ISOLATED NEUTROPHIL GRANULOCYTES

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The aim of this study was to investigate the effect of bisamil – an antiarrhythmic drug under clinical trials – on free radical generation of isolated polymorph neutrophil granulocytes (PMN) and to compare its activity with well-known antiarrhythmics. PMNs were isolated from healthy beagle dogs, and superoxide radical generation was induced by phorbol-myristate-acetate. Free radical generation capacity of stimulated PMNs were measured. Bisamil exerted a concentration dependent inhibitory effect on stimulated free radical generation. At the investigated concentration range of the antiarrhythmics only propafenone, mexiletine and diltiazem showed similar activity as bisamil, but clear concentration dependency could not be seen in any of the cases. According to the results of this study inhibition of stimulated free radical production by isolated PMNs can not be closely related merely to either membrane stabilizing or Ca-antagonistic activity of drugs. In vitro inhibitory action of bisamil on free radical generation indicates a possible cardioprotective effect existing independently of its antiarrhythmic one. This observation may be important in outlining the range of clinical indications of bisamil as it may also be useful in the treatment of reperfusion injury.

### Introduction

The role of leukocytes in inflammatory process, phagocytosis, has been well known for decades. It has also been recognised that the process of myocardial infarction with reperfusion of previously ischemic myocardium involves components of typical inflammatory reaction. During the early acute inflammatory reaction polymorphonuclear neutrophils – PMNs – undergo a complex series of functional and biochemical alterations. Amongst others, stimulated neutrophils release highly reactive and cytotoxic oxygen radicals. The lipid peroxidation induced by such radicals influences the lipid metabolism of cells and the movement of myocardial calcium ions, therefore they have an arrhythmogenic effect. The realisation of the arrhythmogenic effect of free radicals produced by activated neutrophils raised the question whether antiarrhythmic drugs are able to modify the free radical generation of isolated polymorphonuclear leukocytes.

### Methods

PMNs were isolated from healthy beagle dogs, and their spontaneous and phorbol-myristate-acetate induced superoxide radical production were measured [1]. The following antiarrhythmic compounds were tested: bisamil, disopyramide, lidocaine, procainamide, mexiletine, propafenone, sotalol, amiodarone, verapamil, nifedipine, diltiazem at the concentrations of 10, 25, 50, 75, 100 mg/l.



## Results and Discussion

None of the antiarrhythmics by itself stimulated free radical generation. Bisaramil showed a clear concentration dependent inhibitory effect on stimulated superoxide radical generating capacity of PMNs. Amongst the investigated drugs, mexiletine and propafenon were the only drugs which showed similar activity to bisaramil. Propafenon was able to cause a complete inhibition at high concentrations, but in some cases, it stimulated superoxide radical production of PMNs at lower concentrations.

Membrane stabilizing lidocaine and procainamide were found to have practically no effect on the measured parameters. Ca-antagonists verapamil, nifedipine and diltiazem were found to differ from each other in their activity. Verapamil and nifedipine even increased the free radical generation, while diltiazem beneficially influenced the measured parameters.

Disopyramide and sotalol induced only a slight, but not significant inhibition of free radical production by leukocytes. Amiodarone was the only drug, which stimulated the free radical production of isolated leukocytes at any concentration, but clear concentration-dependent effect could not be observed. This observation can explain its unfavourable side effects too.

## Summary

These results prove that inhibition of stimulated free radical production by isolated PMNs can not be closely connected merely to either membrane stabilizing or Ca-antagonistic activity of drugs. In vitro inhibitory action of bisaramil on free radical generation indicates a possible cardioprotective effect existing independently of its antiarrhythmic one. This observation may have significance in the acute and chronic phases of myocardial infarction as well as in the prevention of reperfusion injury.

## Acknowledgements

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## MONITORING OF PLASMA TOTAL ANTIOXIDANT STATUS IN DIFFERENT DISEASES

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The pathological increase of oxygen free radical generation has already been recognised in more than one hundred diseases. To gain information about the consequences of oxidative stress the investigation of plasma antioxidants seems to be plausible. In our study we used a new kit (RANDOX, England) for measurement of total antioxidant status (TAS) to determine whether it has diagnostic value in comparison with our earlier results of measuring other parameters of oxidative stress in the following diseases: i./ In the group of patients with ischemic heart disease (n=19) the TAS elevated from  $1.08 \pm 0.13$  to  $1.16 \pm 0.11$  mM after 2 weeks of cardioprotective drug administration showing the beneficial effect of drug treatment. ii./ In the group of patients with essential hypertension (n=47) its values were below the normal range ( $1.11 \pm 0.15$  mM) at the time of the first investigation and increased gradually following antihypertensive treatment. iii./ The changes of TAS values of patients who underwent open (n=21) or laparoscopic (n=21) cholecystectomy indicated the less surgical trauma following laparoscopic procedures. Our results suggest that determination of TAS is a valuable and reproducible method to detect the actual antioxidant status in patients.

### Introduction

Oxygen free radicals are generated as intermediate by-products of cellular metabolism and are normally maintained at low levels by the action of free radical scavengers and antioxidants. The pathological increase of oxygen free radical generation has already been recognised in more than one hundred diseases in which the compensatory and regulatory effect of antioxidant system is likely to play a very important role. To get information about the consequences of oxidative stress the investigation of plasma antioxidants seems to be plausible. The major antioxidant defences in plasma include ascorbate, protein thiols, bilirubin, urate, and  $\alpha$ -tocopherol [1, 2]. Synergism exists between these compounds, therefore instead of estimating the effectivity of any individual one, the total antioxidant status (TAS) of plasma has to be determined. In our study we try to investigate whether the determination of plasma TAS mirrors the effectivity of the treatment of patients suffering ischemic heart disease, essential hypertension, or patients who underwent open or laparoscopic cholecystectomy, that is, does it have diagnostic value in comparison with our earlier results measuring other parameters of oxidative stress.

### Methods

RANDOX NX 2332 kit was used to measure total antioxidant status. The method is based on the measurement of a stable radical generation from ABST and metmyoglobin in the presence of hydrogen peroxide [1]. This reaction can be inhibited by antioxidants and a quantitative relationship exists between the absorbance at 600 nm at 3 min and the antioxidant concentration of the added sample or standard (Trolox). The results are expressed in mM Trolox equivalent.



## Results and Discussion

TAS value in normal human plasma was found to be  $1.46 \pm 0.14$  mM [1].

In the case of patients with ischemic heart disease ( $n=19$ ) the TAS was  $1.08 \pm 0.13$  mM before treatment. After 2 weeks of cardioprotective drug administration the mean TAS value elevated to  $1.16 \pm 0.11$  mM. Although in the case of 16 out of 19 patients the TAS increased, the average change proved to be statistically non significant.

The TAS values of patients with essential hypertension ( $n=47$ ) were below the normal range ( $1.11 \pm 0.15$  mM), showing the presence of oxidative stress in such patients. Following antihypertensive treatment the values of TAS elevated in more than half of the patients ( $1.23 \pm 0.12$  mM,  $n=32$ ), and remained unchanged or decreased in 15 patients.

The TAS values of patients who underwent open ( $n=21$ ) or laparoscopic ( $n=21$ ) cholecystectomy were below the control value before the operation ( $1.12 \pm 0.15$ ,  $1.03 \pm 0.14$  mM respectively). A transient decrease was found in TAS during the first 3 postoperative days in patients with open cholecystectomy, while in laparoscopic patients it increased from the second postoperative day and almost reached the normal value ( $1.2 \pm 0.11$  mM) at the fourth postoperative day.

## Summary

A new method (RANDOX Kit) was used to measure the total antioxidant status (TAS) of the sera separated from patients with different diseases. Although the normal range of TAS is very narrow, its shift mirrors the beneficial effect of cardioprotection and antihypertensive treatment. Using this method the patients can be differentiated regarding the different surgical trauma, reflecting the restoration of endogenous antioxidant capacity.

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## THE EFFECTS OF GLUCOCORTICOIDS AND A GLUCOCORTICOID ANTAGONIST (RU 38486) ON EXPERIMENTAL ACUTE PANCREATITIS IN RAT

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The effects of glucocorticoids on acute pancreatitis are a matter of dispute. In animal experiments, dexamethasone and hydrocortisone significantly decreased the serum amylase activities 8 hours after the induction of pancreatitis. In the dexamethasone treated group, the serum IL-6 level was significantly decreased at 4 and 8 hours, while in the hydrocortisone treated group, all the IL-6 values were significantly diminished vs. the control group. As compared to the control, a glucocorticoid antagonist (RU 38486) did not influence the serum amylase activity, but significantly increased the serum IL-6 level. These results suggest that glucocorticoids may play a role in the control of pancreatitis caused by inhibition of cytokine production.

### Introduction

Glucocorticoids have long been implicated as a possible cause of acute pancreatitis, but the etiological association with acute pancreatitis remains controversial [2]. Glucocorticoids are known to be involved in the regulation and control of cytokine production [1,3], and they may therefore play a role in the pathogenesis of acute pancreatitis. The present aim was to study the effects of different glucocorticoids (dexamethasone (D) and hydrocortisone (H)) and a glucocorticoid antagonist (RU 38486) on experimental acute pancreatitis.

### Materials and Methods

Acute pancreatitis was induced by the retrograde administration of 400 µl of Na-taurocholate (5%) into the pancreatic duct (group AP). In group APD, 4 mg/kg of D, and in group APH, 20 mg/kg of H was administered s.c. just before pancreatitis induction. In group APRU, 5 mg/100 g body weight of RU was given s.c. at the moment of pancreatitis induction. Rats were sacrificed by abdominal aorta exsanguination 0, 2, 4 and 8 h following pancreatitis induction. Serum amylase activity and IL-6 level bioassays, pancreatic weight/body weight (pw/bw) measurement and histologic examination were performed.



## Results

In group AP, the amylase activity was significantly elevated at 2 h ( $8974 \pm 372$  vs.  $2040 \pm 220$  U/l), and continuously higher at 4 and 8 h. In groups APD and APH, the amylase activities were significantly decreased vs. group AP at 8 h ( $12444 \pm 2171$  and  $9476 \pm 1094$  vs.  $16800 \pm 705$  U/l). No significant alteration in amylase activity was found in group APRU. The ratio pw/bw was significantly elevated at 2 h in all groups. In group APD, the ratio pw/bw was significantly decreased vs. group AP at 2 h ( $5.94 \pm 0.69$  vs.  $7.66 \pm 0.54$ ). In group AP, the IL-6 level increased continuously, and reached its peak at 8 h ( $13200 \pm 4904$  U/ml). In group APD, the IL-6 level was significantly decreased at 4 and 8 h, while in group APH, all the IL-6 values were significantly diminished vs. group AP. In group APRU, the level of IL-6 was significantly increased at 2 h vs. group AP ( $16640 \pm 3840$  vs.  $2280 \pm 605$  U/ml).

## Conclusion

Glucocorticoid hormones take part in the control of immunopathological processes of acute pancreatitis which are partly mediated by IL-6. Our data underline the possible therapeutic value of exogenous glucocorticoids in the treatment of acute pancreatitis.

## Acknowledgements

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## EXPERIMENTAL INVESTIGATION OF PRESERVATION INJURY IN ANIMAL KIDNEYS AFTER REPERFUSION WITH EURO-COLLINS

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The authors evaluated the pathomorphologic alterations of removed and reperfused dog kidneys by means of light and electronmicroscopic examination. In each sample the following reversible signs were found: Hypereosinophilia (HE), Hydropic dystrophy (HD), Nuclear polymorphism (NP), Epithelial desquamation (ED), Brush border lesion (BBL), Single cell necrosis (SCN), Total tubular epithel necrosis (TTEN), Interstitial edema (IE), Perivascular edema (PE). The irreversible signs were: Basement membrane rupture (BMR), Cellular infiltration (CI), Glomerular mesangial matrix expansion (GME) and vascular lesions (VL). The most severe and mostly irreversible alterations occur in the 54–72 hours after harvesting. The authors emphasize the significance of basement membrane rupture, because the impossibility of tubular epithelial regeneration, the cellular infiltration due to its fibrogenic effect, glomerular lesion because it makes decrease the glomerular filtration rate, proceeding juxtaglomerular cell proliferation and hypertension through renin-angiotensin mechanism and vascular lesions causing renovascular hypertension and tubulopathy. The authors believe that reperfusion injury is very important factor in kidney allograft survival. Its mechanism is similar to the normal necrosis pathway, but the timing is delayed. Further investigations are needed to understand what specific alterations may occurred under blood circulation in the host to reveal more exact cause of primary graft failure after transplantation.

### Introduction

While the normal pathways of tissue destruction in kidney is clearly defined, there are no data about the exact pathognomic findings and their prognostic values in removed and reperfused kidneys. This question holds great importance from the point of view of organ (renal) transplantation. We have no ideas about the histopathologic events take place during the cold ischaemic time of the cadaver renal allograft. To set the exact point of irreversibility is a very hard target, but to get closer to the truth is basic and needs histopathologic analysis [1, 2].

### Aim of the study

To evaluate the pathologic features of irreversible graft failure during the cold ischaemic time after preservation, and also to define the events by time. That could help in considering the viability of the graft even in humans.



## Materials and Methods

In intratracheal narcosis 9 kidneys were removed from 9 dogs, following the standard technique used by our Clinic for human allograft harvesting. The kidneys were reperused immediately on table by Eurocollins. They were stored in three individual sterile sacks, and in ice of appx. 0 Celsius. Samples were taken from every kidneys in 24, 48, and 58–72 hours after harvesting, under sterile conditions. The samples were stored in formaldehyde, and glutaraldehyde (buffered). Light microscopic stains (hematoxylin eosin, PAS, toluidin blue) were performed. Certain samples were investigated by electronmicroscopy.

## Results

The numbers in parenthesis indicate the positive findings of the certain characteristic / the total number of cases, in the 24, 48, and 54–72 hours group. Reversible signs were: Hypereosinophylia (HE) (8/8, 2/8, 0/9); Hydropic dystrophy grade III (HD) (1/8, 5/8, 6/9); Nuclear polymorphism (NP) (8/8, 8/8, 9/9); Epithel desquamation (ED) (8/8, 8/8, 9/9); Brush border lesion (BBL) (8/8, 8/8, 9/9); Single cell necrosis grade II–III (SCN) (1/8, 4/8, 8/9); Total tubular epithel necrosis (TTEN) (1/8, 5/8, 9/9); Interstitial edema (ISE) (6/8, 7/8, 6/9); Perivascular edema (PVE) (0/8, 6/8, 5/9).

Irreversible signs were: Rupture of basement membrane (BMR) (1/8, 5/8, 7/9); Cellular infiltration (CI) (0/8, 1/8, 5/9); Expansion of glomerular mesangial matrix (GME) (0/8, 5/8, 8/9); Glomerular mesangial infiltration (GMI) (0/8, 5/8, 8/9); Vascular lesion (VL) (0/8, 0/8, 1/9).

## Discussion

The most severe alterations occur in the 54–72 hours. HE, NP, and BBL are early signs of cell damage but they are reversible. Epithel desquamation may be the result of artificial damage, not significant. The single cell necrosis, and the total tubular epithel necrosis (if the basalmembrane is intact) are reversible but their appearance increases by time. Irreversible damages are: the basement membrane rupture, because the impossibility of restitution; the cellular infiltration due to its fibrinogenetic effect; glomerular mesangial matrix expansion, because it makes decrease the glomerular filtration rate, which will proceed to juxtaglomerular proliferation causing hypertension through renin-angiotensin mechanism; and the vascular lesion causing renovascular hypertension, which leads to glomerular filtration decreasing, and tubulopathy. Our investigations showed that four different signs are the most reliable markers of irreversible allograft damage after reperfusion with Euro-Collins [3, 4, 5]. We found that this markers do not occur before 48 hours, and are surely present after 54 hours. The electronmicroscopic finding were performed on selected samples of 48 hour group.

*The authors believe that reperfusion injury is very important factor in kidney allograft survival. Its mechanism is similar to the normal necrosis pathway, but the timing is delayed.* Further investigations are needed while the grafts might survive after 48 hours or not, and what specific histological alterations may occur under blood circulation in vivo [6, 7]. This could get us closer to the understanding of many phenomena experienced at bedside like acute tubular necrosis, non viable kidney.

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## INTRAEPITHELIAL NEOPLASMS OF THE PANCREAS

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Intraepithelial neoplasms of the pancreas have been recently described and relatively rare, but these lesions represent a distinct, however pathologically heterogeneous entity with shared clinical features. We analyzed the clinicopathologic and cytogenetic characteristics of eight patients with intraepithelial neoplasms. Based on our hypothesis that tumor ploidy pattern correlates with ploidy, synthetic (S) phase and proliferative fractions of each neoplasm by flow cytometry. Analysis of the nuclear DNA content of pancreatic intraepithelial neoplasms in this study supports our hypothesis. Each neoplasm demonstrated diploid stemline, with a low S-phase fraction. The diploid DNA pattern and the low proliferative activity are consistent with the nonaggressive behavior of the tumors and, in part, explain the favorable prognosis of intraepithelial neoplasms. Intraepithelial neoplasms of the pancreas constitute a rare, but surgically curable, localized disease with a good prognosis following radical resection. The most valuable tool in the diagnosis of these preinvasive lesions is ERCP combined with brush cytology. This study supports the potential value of flow cytometric DNA analysis in determining outcome, as the diploid DNA pattern and low S-phase fractions correlate with the nonaggressive biological behavior.

### Introduction

The purpose of this study was to analyze the clinicopathologic and cytogenetic characteristics of intraepithelial neoplasms of the pancreas. We hypothesized that tumor ploidy pattern correlated with biological behavior, malignant potential and prognosis.

### Methods

The records of eight patients with pancreatic intraepithelial neoplasms presenting between August 1990 and September 1995 were retrospectively reviewed. Nuclear DNA-content, ploidy, synthetic (S) phase and proliferative fractions of each neoplasm were measured by flow cytometry.

### Results

We report 4 cases of pancreatic ductal carcinomas in situ (DCIS), 2 cases of mucinous ductal ectasia (MDE) and 2 cases of atypical ductal hyperplasia (ADH). The average age of the 4 males and 4 females was 55.2 years (range 40 to 77 years). Presenting symptoms (Table 1)

included abdominal pain of greater than one month's duration (n = 6), unplanned weightloss (n = 4), and jaundice (n = 2). Seven patients were previously diagnosed with pancreatitis. Preoperative work-up (Table 2) included abdominal ultrasonography, computed tomography (CT), endoscopic retrograde cholangiopancreatography (ERCP). Routine serum chemistries including tumor-associated antigens CEA and CA-19.9 were within normal limits. All of the tumors demonstrated diploid stemline with a mean S-phase or proliferative fraction of 3.7% and a mean DNA index (DI) of 0.96 (Table 3). All patients had abnormal ERCP studies with filling defects or dilation of the main pancreatic duct. Five patients had identifiable masses on abdominal CT. Four distal pancreatic resections, three pancreaticoduodenectomies, and a pylorus-preserving pancreatoduodenectomy were performed (Table 4). Because routine intraoperative frozen section revealed positive margins, a completion pancreatectomy was performed in addition to a pancreaticoduodenectomy in one case. All patients are alive and well with an average follow up of 38 months.

**Table 1.**  
**Clinical Characteristics of Patients**

| Subtype      | Number   | Average Age (yrs.)        | M:F        | Pain     | Symptoms<br>Weight loss | Jaundice | Chr. Pancr. |
|--------------|----------|---------------------------|------------|----------|-------------------------|----------|-------------|
| DCIS         | 4        | 56.7                      | 3:1        | 3        | 3                       | 1        | 4           |
| MDE          | 2        | 48.5                      | 0:2        | 1        | 0                       | 0        | 1           |
| ADH          | 2        | 51                        | 1:1        | 2        | 1                       | 1        | 2           |
| <b>TOTAL</b> | <b>8</b> | <b>53.2 (range 40–70)</b> | <b>4:4</b> | <b>6</b> | <b>4</b>                | <b>2</b> | <b>7</b>    |

**Table 2.**  
**Diagnostic Workup**

| Procedure | Informative                    | Noninformative |
|-----------|--------------------------------|----------------|
| US        | 3 mass, dilation               | 5              |
| CT        | 3 mass                         | 5              |
| ERCP      | 8 mass, dilation, displacement | 0              |

**Table 3.**  
**Mean values of flow cytometric analysis**

| Subtype      | S-phase (%) | DNA index   | CV (%)     | Ploidy         |
|--------------|-------------|-------------|------------|----------------|
| DCIS         | 3.65        | 0.95        | 4.2        | diploid        |
| MDE          | 6.05        | 1.00        | 5.5        | diploid        |
| ADH          | 1.75        | 0.94        | 4.3        | diploid        |
| <b>TOTAL</b> | <b>3.77</b> | <b>0.96</b> | <b>4.5</b> | <b>diploid</b> |

**Table 4.**  
**Operative Procedures**

| Subtype n      | Whipple  | Distal Pancr. | PPPD     | Compl. Pancr. |
|----------------|----------|---------------|----------|---------------|
| DCIS 4         | 2        | 2             | 0        | 1             |
| MDE 2          | 0        | 1             | 1        | 0             |
| ADH 2          | 1        | 1             | 0        | 0             |
| <b>TOTAL 8</b> | <b>3</b> | <b>4</b>      | <b>1</b> | <b>1</b>      |



## Discussion

Pancreatic intraepithelial ductal neoplasms have been recently described and relatively rare, but these lesions represent a distinct, however pathologically heterogeneous entity with shared clinical features. Presently there is no accepted and consistent pathologic classification. Most authors agree that these low grade malignancies necessitate radical surgical intervention, although no genetic sequence from in situ to invasive disease has been elucidated. Each tumor demonstrated a diploid stemline on flow cytometry confirming our hypothesis that tumor ploidy pattern correlates with biological behavior, malignant potential and prognosis.

## Conclusion

Intraepithelial neoplasms of the pancreas constitute a rare but surgically curable, localized disease. These preinvasive lesions are diagnosed by ERCP with brush cytology, and cured by radical resection. The diploid DNA pattern and low S-phase fractions determined by flow cytometry, a potential prognostic tool, correlate with the nonaggressive biological behavior.

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## THE PART OF MR CHOLANGIOGRAPHY IN BILIARY SURGERY

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The magnetic resonance cholangiography (MRC) is a new none invasive examination procedure which demonstrates well the extrahepatic ducts. The examination can reveal all the anatomical or pathological anomalies of the biliary tracts. The authors performed this examination on 12 patients between 1<sup>st</sup> December 1996 and 31<sup>st</sup> December 1996. In 4 patients there were no pathological changes. Common bile duct stone was found in 1 patient. Sclerosis of the Vater papilla in 1 case. Mirizzi syndrome in 1 case. Carcinoma of the common bile duct in 3 cases. In 2 cases inflammation of the head of the pancreas caused compression on the bile duct. The patients were all operated. The operative and the MRC diagnosis corresponded. Similar examination procedure has not yet been mentioned in Hungary.

**Keywords:** MR cholangiography, common bile duct stone, microlaparotomy.

### Introduction

Uptil recently the none invasive demonstration of the bile ducts happened with the traditional intravenous cholangiography, ultrasonography, isotope (IDA) examination; the invasive method was possible with endoscopic retrograde cholangiopancreatography (ERCP) and percutaneous cholangiography. During cholecystectomy there is the possibility to performe intraoperative cholangiography. Recently CT cholangiography (CTC) is possible in selective cases. The MR cholangiography is a new none invasive procedure which is suitable to examine the biliary tracts and to reveal the causes of biliary tracts obstruction. The aim of our report is to introduce our early experiences with the MRC examination.

### Method

MR system: Philips Gyroscan, T 5-NT 0,5 T. Premedication and contrast material is not needed. Paramagnetic metallic material in the body of patients means contraindication. The MRC examination is a heavily T2 weighted, 3-dimension, turbo spin echo sequence. Slice thickness is 3 mm. Examination time is 7-10 mins.



## Material

We performed MRC examination on 12 patients between 1<sup>st</sup> December 1996 and 31<sup>st</sup> December 1996. The average age was 70,6 years (37–88 years). There were 7 females and 5 males. Ultrasonography proved cholelithiasis in 4 patients, larger biliary tracts-more done 8 mm and the hypersensitivity of the contrast material prompted the examination.

In 3 patients there was no stone identified in the biliary tracts.

We observed sclerosis of the Vater papilla in 80 yrs female patient. Cholecystomies were performed through microlaparotomy (3 cm upper midline laparotomy). Transduodenal sphincterectomy was also performed in the elderly female patients. 4 patients had jaundice when the examination was performed. Common bile duct carcinoma was seen in 3 female patients whose average age was above 80 years, in these cases percutaneous transhepatic drainage was carried out. In 1 patient the jaundice was caused by impacted calculus in the Vater papilla. The inflamed gallbladders were excised through microlaparotomies. The impacted stones in the Vater papilla were extracted through transduodenal sphincterectomy (this was an imbecile female patient).

3 patients had pancreatitis; among them 2 had swollen head of the pancreas that caused external compression on the common bile duct. Before the present admission of a 75 years old male patient, a year before Billroth II. gastric resection was performed on him due to carcinoma. During the examination it was discovered that the compression of the common bile duct was caused by the impactment of a stone in the cystic duct (Mirizzi syndrome). In these 3 cases cholecystectomies were performed through micro- laparotomy. A 75 years old female patient was operated for mechanical ileus. The obstruction was caused by a gallstone impacted in the small bowel just before the ileocecal orifice. It was extracted. The MRC examination was performed after she was healed with identified stone-free biliary tracts. Fistula was not observed. Cholecystectomy was performed through microlaparotomy.

## Discussion

The traditional intravenous cholangiography is almost extinct from the clinical practice because of its poor information and frequent complications. The IDA examination is rather for functional purposes. The specificity and sensitivity of ultrasonography for the judgment of the biliary tract calculus is 83,6% and 55,6% respectively.

The success of the ERCP examination depends on the experience of the operator. The examination is successful in 70–97%. This of course is an invasive procedure with its morbidity and mortality rate between 1–7% and 0,2–1% respectively. Spiral or helical CT is also a new method for biliary tracts examination. The biliary tracts were well demonstrated. The disadvantage in the necessity for contrast material and ionizing rays together with its danger and complications. The intraoperative cholangiography is a tradition. During cholecystectomy with microlaparotomy we performed it at suspects of biliary tract calculus. Out of our 540 cholangiography in 317 cases (58%) and, found biliary tract stones in 51 cases (16%). There was no false positive result. In two cases we could not trace biliary tract stone 91 [4].

Guilbaud [3] performed MRC on 127 patients for common bile duct stones suspect. He found stones in the common bile duct in 79 cases (63%). There were 7 cases of false negative result. There was no false positive result. The sensitivity and specificity of the examination was 91% and 100% respectively. In the 82nd North American Radiology Congress in Chicago in 1996. Varghese [5] reported 60 cases of MRCP examination performed. In 17 cases 28% more information was obtained than in ERCP. Becker [1] among his 60 MRCP examination performed the followings were recorded: cyst of the common bile duct, Mirizzi syndrome, sclerotizing cholangitis, acute and chronic pancreatitis and malign obstructions. Considerable agreement was found between ERCP and the ultimate diagnosis.

Boraschi [2] found diagnostical accuracy and specificity of MRCP examination to be 95% and 100% respectively.

In our department under one month we performed 12 MRCP examinations. In every case the common bile duct was clearly identified. The followings were recorded: 1 case of common bile duct stone; 1 case of Mirizzi syndrome; 3 cases of carcinoma of the common bile duct, and 1 case of sclerosis of the Vater papilla. In every case we were able to carry out the operations with microlaparotomy. According to statistics and our few personal experience we summarize the indication for MRCP examination as follows:

1. In presence of jaundice, if the laboratory examination result indicates obstructions.
2. Cholelithiasis proved with ultrasonography, case history with jaundice, acute pancreatitis, elevated liver functions, common bile duct larger than 8 mm in diameter, small stones in the gallbladder. Age above 70 yrs.
3. Hypersensitivity of the contrast material before cholecystectomy.
4. Pancreatitis with proved gallbladder stones and presence of jaundice.
5. Recurrence of complaints after cholecystectomy.
6. For follow-up examination after injury to the common bile duct.

To our knowledge MRC examination has not yet been performed in Hungary since the domestic equipments are generally not suitable for this. Probably in future the number of MR equipments suitable for MRC will increase, there by giving more possibilities for more and more examinations to be performed.

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## THE LICHTENSTEIN OPEN TENSION-FREE HERNIOPLASTY

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In the department of general surgery, in Szolnok MÁV General Hospital the authors performed 51 open tension-free herniorrhaphies by Lichtenstein method between 1st July 1995 and 31st December 1996. According to this method the rings are closed anteriorly with Dacron mesh. The method is simple and rapid, less painful than any other technique. Apart from two minor complications, our patients recovered without any problem. The method helps to reduce the period of hospital treatment as well as that of sick-leave.

**Keywords:** groin hernia, tension-free hernioplasty, Lichtenstein.

### Introduction

10–15% of operations performed in departments of general surgery is due to inguinal hernias (cit. 3.).

110 years ago Bassini [2] performed for the first time herniorrhaphy with acceptable result. Since then there have been several modifications of the method.

The disadvantage of both the Bassini and the modified methods is closing the rings with tensions, which prompts the recurrences.

Lichtenstein open tension-free hernioplasty was introduced to our department 2 years ago [4]. The aim of this report is to introduce the method and the early recovery results.

### Technique

The operation is carried out under spinal anesthesia. The preparation of canalis inguinalis is similar to that described in the Bassini method. The hernia sac is not opened, neither in direct nor in indirect hernial events. The sacs are inverted. In a case of large hernia, the sac is invaginated by a single pulse-string suture. A Dacron mesh of 3x16 cm is cut accordingly to match the size of the inguinal floor.

The lower part of the mesh is sutured to the inguinal ligament with non adsorbable continuous suture starting from the pubic tubercle. The running suture terminates 3 cm beyond the internal ring.

A slit of about 3 cm is made on the mesh starting from the lateral end of it to the height of the internal ring to allow the emergence of the spermatic cord. The superior edge of the mesh is sutured to the rectus muscle and conjoined free end of the transverses

muscle with similar running suture. The tails of the mesh are tacked with interrupted sutures to the lateral part of the Poupart ligament.

After the completion of the mesh suture, it covers the rings anteriorly, and the spermatic cord exits through a small opening. The external oblique aponeurosis is sutured in front of the spermatic cord with continuous suture.

After few subcutaneous stitches, the skin is closed with clips.

### **Material**

Between 1<sup>st</sup> July 1995 and 31<sup>st</sup> December 1996 we performed 51 cases of groin herniorrhaphies by Lichtenstein method only on male patients. Their average age was 64 yrs (47–78 yrs.). 32 patients had direct hernia, 11 patients had indirect hernia and 8 patient with recurrent hernia. The operations were performed under spinal anaesthesia. There was no administration of antibiotic prophylaxy. The same day after the operations the patients got out of bed and fed. 49 patients did not develop any postoperative problems. The patients were discharged on the second day after the operations. Removing of the stitches was on the 5th postoperative day. After the operations the patients never requested pain relievers. After removing the stitches, the intellectual workers returned to normal working activities. The physical workers resumed work two weeks after the operation. In two elderly patients we observed haematoma in the scrotum. In these two cases, we performed puncture and suction. The period of hospital treatment was 8 days. They returned home healed. We recalled our patients for follow-up after the first two weeks and every half a year. Recurrences were not observed.

### **Discussions**

To introduce a new operational technique, Consideration must be made about its advantages, disadvantages and the frequency of its complications, even determinations must be made about its later results.

The open tension-free groin hernioplasty by Lichtenstein is simple to learn. The technique is not difficult. The conditions for this operation are almost available in all surgical departments. Patients rarely complain of pain after the operation which explains the absence of suture line tension. Few hours after the operation the patients can get out of bed, even they may leave the hospital.

49 out of 51 of our patients were discharged on the 2nd postoperative day.

The intellectual workers may resume duty after removal of the stitches, while the physical worker return to normal activities two weeks later.

The two cases of haematoma in the scrotum should not be attributed to the method. The two patients had mighty scrotal hernia with eventeration. The bleeding could be attributed to the inefficiency of blood clotting.



It is not easy to determine accurately the number of recurrences after groin hernioplasty. The recurrences depends on the chosen method and on the individual who applies it. Also it depends on the difference between the operations and the follow-up period.

50% of recurrences appear in the first 5 years after the first operations [cit. 4.].

Ravich [6] – observed 20% of recurrences 15–20 years after the first operation. A lot of survey was carried out through questionnaires without physical examination on the patients.

Greater number of the patients are not aware of the recurrence. This explains the season the recurrence rate is between 1,9–32% and 0,2–17% for Bassini and Shouldice respectively according to statistics [5].

Amid, Shulman and Lichtenstein [1] operated 3250 patients for original hernias with the techniques introduced by Lichtenstein between 1989 and 1992. The patients were mainly males of age range 18–88 years. Among these patient 2828 (87%) were followed up with physical examination performed. Recurrence was found on four patients (0,14%). [1]

In our department under 18 months 51 operations were performed with the technique written by Lichtenstein.

We called back the patients for follow-up examinations 2 week and 1/2 yr postoperatively. Recurrence has not yet been registered.

In Hungarian scientific literature no article has yet been published about the Lichtenstein Open Tension-free herniorrhaphy.

Considering our favorable personal experiences, we recommend the introduction of this technique.

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## **DISTRIBUTION OF CALCITONIN-CONTAINING PARAFOLLICULAR CELLS OF THE THYROID IN PATIENTS WITH CHRONIC LYMPHOCYTIC THYROIDITIS: A CLINICAL, PATHOLOGICAL AND IMMUNOHISTOCHEMICAL STUDY**

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The C-cell hyperplasia of the thyroid gland is recognized as precursor to medullary carcinoma, particularly in multiple endocrine neoplasias, however it can be associated with hypercalcemic states and follicular tumours as well. The authors analysed 46 of their cases with Hashimoto's and/or lymphocytic thyroiditis from the immunohistological point of view with the aim of determining to what extent is C-cell hyperplasia associated with these pathological pictures. C-cell hyperplasia was demonstrated on sections of intraoperative preparations with the immunoperoxidase method with anti-calcitonin MoAb. Moderate, focal C-cell hyperplasia was found in 17.4% (8 patients), extensive focal hyperplasia similarly in 17.4% (8 patients). Diffuse C-cell hyperplasia occurred in 1 case (2.2%). These results suggest the possibility that in the case of diffuse or more pronounced focal hyperplasia the serum calcitonin concentration of these patients is also elevated. Further clinical and pathological studies are needed to find out whether there is some pathogenetic relationship between chronic lymphocytic thyroiditis and C-cell hyperplasia or whether the finding is coincidental, and to establish what degree of C-cell hyperplasia is associated with elevated serum calcitonin levels. This relationship has been unknown until the present time, whereas it can be of great clinical significance, in part because of the changes in serum calcitonin levels, in part for screening out the MEN IIa type and working out the operating strategy.

### **Introduction**

The parafollicular cells of the thyroid are of neuroendocrine origin and have become known as C-cells, since it is they that produce the calcitonin hormone, which plays an important part in calcium metabolism; their number in thyroids with normal weight is fairly constant [4]. Early studies on C-cell distribution in the normal human thyroid gland showed that multiple clusters of C-cells were present in patients at high risk of hereditary thyroid medullary carcinoma and in patients with primary hyperparathyroidism [7]. It has been recently pointed out that C-cell hyperplasia may be associated with chronic hypergastrinemia in Zollinger-Ellison syndrome, the tumors of the follicular cells [1], the malignant lymphomas of the thyroid gland [8], several non-neoplastic thyroid diseases [6] and also aging [3]. There are some sporadic, mainly casuistic observations that C-cell hyperplasia may be concomitant with Hashimoto's thyroiditis [2]. The aim of the present study is to investigate these questions on a larger patient material.



## Material and Methods

The analysis was performed on the surgical material of 46 patients with chronic lymphocytic Hashimoto's thyroiditis, who were operated on between 1988 and 1993, in part at the 1st Department of Surgery of the University Medical School of Debrecen and, in part at the Surgical Department of St. John's Hospital, Budapest. Indication for surgery was supplied by the compression of the neck organs or suspicion of malignancy. Distribution by sex and age:

*44 females, average age 51 yr (25–91) and 2 males (15 and 51 yr).*

The diagnosis of chronic thyroiditis was confirmed with H/E-stained sections, then the presence of calcitonin was demonstrated by immunohistochemical staining (immunoperoxidase technique, AEC development, hematoxylin nuclear staining). Detection of thyroglobulin and in some cases of chromogranin was also performed. Evaluation of the reaction:

- a/ nodular in small area - if reaction was observed in areas no more than 3 visual fields at low magnification (x10) per section,
- b/ nodular in large area - if there was reaction in the cytoplasm in areas more than 3 but fewer than 10 visual fields per section,
- c/ diffuse distribution - if positivity was encountered over 10 lowmagnification visual fields.

## Results

In the course of the immunohistological identification one could follow well the individual stages of early changes in C-cell distribution in the thyroid follicles: the ones localized to the poles, the even (intrafollicular) and the nodular distributions. In the oncocytes, frequently seen in Hashimoto's thyroiditis, the intensity of immunoreaction, was not uniform. The cause of the varying strength in staining was presumably the inhibition of binding to the neurosecretional granules by the accumulated mitochondria.

Among the 46 cases of lymphocytic thyroiditis calcitonin positivity was found in 17 (37%), out of which 1 was diffuse (2.2%), nodular in small area: 8 (17.4%), nodular in large area: 8 (17.4%).

Because of the retrospective character of this study, calcitonin serum levels were not measured in any of the patients.

In the majority of the patients bilateral subtotal thyroid lobe resection was performed with the exception of two cases: in the first near-total thyroidectomy was done as completing operation, since unilateral subtotal resection had already been performed in a surgical department other than ours, and the final histological examination confirmed, as early as that time, papillary thyroid carcinoma. In the second case total thyroidectomy was performed as primary operation, since the intraoperative frozen section histology suggested medullary carcinoma and Hashimoto's thyroiditis was confirmed only by the final histological finding.

## Discussion

C-cell hyperplasia of the thyroid has become recognised as a precursor of medullary carcinoma, especially in multiple endocrine neoplasia type IIa, IIb, in addition to being associated with hypercalcemic states, high TSH-secretion, hypergastrinemia, when

estrogen is administered, during cimetidin treatment, adjacent to tumors of follicular cells. There are usually no C-cells in thyroid nodules. The C-cell count increases in toxic goiter as well, which can be accounted for by hypercalcemia frequently associated with hyperthyroidism. On the other hand, Hashimoto's thyroiditis is the most common cause of spontaneously occurring hypothyroidism, and as such, it involves high TSH secretion. The concomitant finding of Hashimoto's thyroiditis and C-cell hyperplasia raises questions regarding pathogenesis. Whereas its causal relationship with the malignant lymphoma of the thyroid gland has been cleared up, its role in the pathogenesis of the epithelial thyroid tumors is debated. There are only very few communications [5] on its concomitant occurrence with medullary thyroid carcinoma; in an earlier survey of ours we also found only one case, which was not familial either. Both the earlier investigations and our present study suggest that the frequency of the concomitant occurrence of C-cell hyperplasia and Hashimoto's thyroiditis is low, although it is true that the latter is rarely treated surgically. Anyway, C-cell hyperplasia cannot be detected with routine staining with H/E.

### Conclusions

1. In agreement with the data in the literature, diffuse C-cell hyperplasia occurs in low per cent in Hashimoto's thyroiditis.
2. Focal hyperplasia was observed in much higher per cent.
3. It is to be cleared up whether extensive focal hyperplasia is associated with calcitoninemia and is, as the diffuse case, precursor to MEN.
4. Further clinical and pathological examinations are needed to decide whether association involves a neoplastic potential, or is only the result of the chronic stimulus affecting the neuroendocrine cells.

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## **SURGICAL TREATMENT OF GASTRIC CANCER: A RETROSPECTIVE STUDY WITH SPECIAL REFERENCE TO EPIDEMIOLOGY**

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The present retrospective study gives the analysis of the epidemiological data of 1474 patients with gastric cancer, who were operated on at the 1st Department of Surgery of the University Medical School of Debrecen in the course of 35 years. In spite of the changes in diagnostics and therapeutic management it was impossible to raise, during this period, the rate of resectability: in the first 10 years it was 56%, and 55% in the last five years. There was no improvement in the proportion of curative and palliative resection, either: 50/6 vs 49/6. The number of gastrectomies increased to 22.5% from 17%, in a quarter of the cases, in the last two periods, extended multivisceral interventions were also performed. In the location of resectable carcinomas the number of those spreading over more than one third increased from 2% to 7%, and similar growth was encountered in the rate of diffuse-type carcinomas. The postoperative surgical complications decreased to 18% from 27%, and early postoperative death from 19.6 to 10.1%! In the last two periods 46% of the patients were admitted in advanced stages of tumor (UICC III B or IV), with half a year's or longer histories. Exclusively surgical treatment is not effective in these cases.

### **Introduction**

According to a world-wide survey for the year 1960, Hungary – together with Austria – occupied 5th–6th place in the mortality rate of gastric cancer. This rate has since then decreased on a global scale, which is primarily accounted for by its decrease in incidence, nevertheless, it still is the second most frequent cause of death among the cancer diseases in the world. It is sometimes referred to as "the captain of death". In our study we sought an answer to the questions whether there has been any change, and to what extent, since the publication of the above statistical survey over 35 years ago.

### **Materials and Methods**

During the years 1960–1995, at the 1st Department of Surgery of the University Medical School of Debrecen, 1474 patients were operated on for gastric carcinoma. For the sake of convenience and comparability this long period was divided into intervals of 10+10+10+5 years. Investigated were changes in resectability, tumor location, histological structure, postoperative morbidity and mortality as well as delay in admission.

## Results

The number of patients operated on for gastric cancer showed moderate decrease in the particular periods (483–431–416 and 144). The rate of resectability did not change in any way since the 60s, it was then 56%, and 55% in the last 5 years. Similarly, the proportion of curative and palliative operations also remained unchanged. There was an increase in surgical radicality: the number of gastrectomies rose from 17% to 22.5%. In a quarter of gastrectomies in the last 15 years, surgery, to attain total radicality, had to be extended to the adjacent organs. In the anatomical location of resectable carcinomas the rate of those spreading over more than one third increased. Changes were found in the distribution by the histological types of carcinomas, too: in the 60s 70% were the intestinal, differentiated type, in the 90s this is only 57%, the rest is of diffuse, undifferentiated structure. The differences in the rates are well demonstrated by the WPR (Well/Poorly differentiated Ratio), which decreased to 1.4 from 2.3. Postoperative surgical morbidity decreased from the highest 27% to 18%, whereas early postoperative mortality from 19.6% to 10.1%. In the last two periods 46% of the patients were admitted in an advanced stage of the tumor: after a history of half a year or longer.

## Discussion

In spite of the continuous decrease gastric cancer remains one of the most common malignant diseases in the world. Struggle with it is carried on in international study groups, with the concomitant establishment of national teams. In Hungary there is no such project. Our present study covers the gastric cancer cases of 35 years, which, naturally, does not represent the whole of Hungary. On the other hand, if we compare our study with reports from other regions of our country [3, 4], the results are nearly identical. Márkus et al. reported on a similarly long period (30 yr). In their material the rate of resectability is even lower, 48%.

In Hungary gastric cancer is the 3rd most frequent cause of death. In 1990 the number of deaths was 2895, whereas it was 4298 in 1975 [2]. Lower mortality may be due to increase in surgical radicality and intensive postoperative care. We have not reached the 60% resectability rate during 35 years, whereas in some other countries this rate is higher: 91.4% in Japan, 82.7% in Germany [1, 5]. The cause is – as our study indicates – that nearly half of the patients are admitted in an inoperable stage, i.e. there is a delay in the early detection of the disease or in the institutional medical check-up of the patient.

The present 35-year-long epidemiological study revealed the following tendencies:

- increase in the number of patients over 70,
- increase in the carcinomas spreading over two-thirds of the stomach,
- rise in the rate of infiltrative, diffuse-type cancers,



- rise in the number of multivisceral, expanded operations,
- no change in the resectability rate
- neither in the number of upper-third tumors
- decrease in surgical morbidity and mortality

### Conclusion

There is need of the early recognition of gastric cancers rather than extended en-bloc resections.

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## LYMPHONODAL RESPONSE TO SENSITIZATION WITH 2,4-DINITROCHLOROGENE (DNCB) IN LABORATORY RATS

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White laboratory rats were used for the experiments. Their popliteal lymph nodes were investigated after sensitization with DNCB (2,4-dinitrochlorobenzene) and i.c. injection of 3-H-thymidine and Patent Blue Violet at several intervals following the challenge with the hapten DNCB. Changes of weight of lymph nodes, further uptake of tritiated thymidine by the cells were investigated by auto-radiography, while the content of 3-H-DNA indicating an increased DNA metabolism due to blastic transformation of the small lymphocytes was determined by a liquid scintillation method. The authors found a significantly increased weight of lymph nodes and a higher percentage of labelled cells following antigenic stimulus of i.c. injected DNCB compared to non-sensitized lymph nodes of the control rats.

### Introduction

2,4-dinitrochlorobenzene (DNCB) as an effective substance able to elicit DCH-responses/delayed cutaneous hypersensitivity/when applied topically or intralesionally into accessible skin tumors is widely used for the non-specific immune therapy of melanoma [3]. In a previous paper [1] we have already reported on the histological changes following intralesional injection of DNCB/disintegration of tumor tissue, membranolysis, vacuolization of the cytoplasm, karyopiknosis, peritumoral lymphocytic infiltration/which mainly point to a local necrosis. However, a transitory swelling and tenderness of the regional lymph nodes was also observed during DNCB treatment, indicating a lymphonodal response, the strength of which we think would greatly depend on the actual state of cellular immune defense. Our goal in the present study was to investigate the regional lymphonodal response to sensitization with DNCB on an animal model.

### Materials and Methods

The experiments were carried out on 47 adult laboratory rats/strain Epimys Norvegicus var. alba, CFY inbred colony/of mixed sex, weighing 250–350 g. The animals were given 100 µg in 0.1 ml acetone i. c. into the abdominal wall. A challenge dose of 50 µg in 0.1 ml acetone was injected 12 days later in the same way into the left hind foot-pad. 12–18–24–30–36 and 48 hours later each group of animals (7 rats formed a group) were narcotized with 0,2–0,3 ml Ketanest (Parke–Davis, München) given intraperitoneally. The the animals were administered 0,1 ml of 4 per cent Patent Blue dye (Bleue Patente V, Laboratories André Guerbet, Yuen–Seine, France) mixed up with 925 kBq



3-H-thymidine (specific activity: 925 Gbq/mmol, Radiochemical Center Amersham) in equal amounts of saline i. c. at the site of the previous DNCB application. Five rats serving as controls were only given 3-H-thymidine added to Patent Blue dye in order to visualize the regional popliteal lymph node. Lymph nodes were exposed and removed 50–60 min following the administration of labelled thymidine.

Removed lymph nodes were measured for weight changes, 5 nodes from each group were subjected to homogenization in 5% TCA solution. The homogenates underwent a double extraction in cold TCA each time for one hour duration. After discarding the non-incorporating fraction, the extraction of DNA was performed in 6 ml of 5% TCA at 90 C degrees for one hour. The extract was then cooled and diluted with scintillation fluid and finally its 3-H-DNA content determined by means of a Packard apparatus. Three control lymph nodes were analyzed in the same way.

The rest of lymph nodes from each group were fixed in 4% formol, embedded in paraffin, cut 4  $\mu$  thick, then covered with Ilford G-4 emulsion (Ilford Ltd., G. B.). The exposure lasted 10 days at 4 Celsius degree and was followed by developing and fixing the sections which were finally stained with hematoxylin-eosin and Nissl's procedure. Finally, sections prepared 24 and 48 hours after challenge with DNCB were investigated for the bulk of labelled cells, the number and diameter of germinal centers. Germinal centres, cortex and medulla were chosen as representative regions within the lymph nodes for the estimation of isotope uptake as a function of antigenic stimulus with DNCB. In each region 1000 cells were counted.

## Results

The administration of labelled thymidine by i. c. injection resulted in good labeling of popliteal lymph node cells of the control and DNCB-presensitized rats. The lymphonodal response to antigenic stimulus of i. c. injected DNCB could easily be demonstrated by significantly increased lymph node weight and a higher percentage of labelled cells if compared to the control specimens. The main nodal weight in the controls resulted in 46.5 mg (SD  $\pm$ 2.1) related to the nodal weight in presensitized animals, which averaged 621.7 mg (SD  $\pm$ 11.8). This difference is significant at  $p < 0.01$  (U-test).

Considering the enlargement of germinal centres in samples from DNCB-pretreated animals, the total number of DNA synthesizing cells was markedly increased in the germinal centres after this treatment. (The percentage of labelled cells in resting state was 12.7%, while this value rose to 15.8% and 17.1% respectively in the animals of the pretreated group 24 hrs and 48 hrs following a challenge dosis of DNCB.) It would have been even higher if sparsely labelled areas could have been omitted from the evaluation, just because of the interesting finding that neighboring germinal centres often showed striking differences in labeling. Differences in the labeling of germinal centres can be explained by a comparted perfusion of the node and escape of the labeling material via efferent lymphatics.

However, widening of the cortex and the paracortical area and increase in the percentage of labelled lymphocytes clearly indicate that a blastic transformation of small, 'resting' lymphocytes is taking place, accompanied by an elevated DNA-synthesis. The amount of labelled cells in different lymph node areas, further the number and diameter of germinal centres were found nearly the same at 24 and 48 h following challenge, but significantly increased if compared to representative values of the control specimens. (We have found an isotope uptake of the cortical region in 3.1% in the pretreated animals before administration of the challenge dose, while 24 and 48 hrs after the challenge with DNCB this percentage rose to 6.2% and 7.3% respectively, related to 1000 cells counted. These values for the medullar area yielded 2.8%, 7.1% and 7.9%, respectively.)

The incorporation of thymidine, i. e. the 3-H-DNA content of the lymph nodes was found markedly increased at quantitative measurements using liquid scintillation, already 18 hrs following the injection of the challenge dose of DNCB (cca. 4x, cpm-value of the controls lay at 900 per lymph node, at 16 000 by 18 hrs and reached its maximum by 24 hrs: approximately 5–6 times as much as after 12 hrs following DNCB-challenge. 30–36 hrs later the rate of incorporation sank to the control values, or below. A further slight rising of cpm values may be attributed to recirculating labelled cells.

## Discussion

The antigenic conjugate formed after topically applied DNCB will be bound to the membrane proteins of the epithelial Langerhans cells. These cells have a lot of properties similar to those of macrophages (e. g. they can stimulate allogeneic T-lymphocytes in mixed cultures and carry mouse I-A and human HLA-DR antigens) and migrate easily via afferent lymphatics to the regional nodes, conveying in this way the antigenic stimulus from the periphery [2].

Our experiments suggest that lymph node cells are very sensitive to DNCB stimulation. The accumulation of DNA-synthetizing cells was protracted until the 4. day, while the peak of 3-H-thymidine incorporation was reached earlier, mainly 24 hrs before the acme of DCH-response. These data agree with the observation of Revillard [2], who also found an increase of the number of pyroninophil cells during the first 48 hrs following DNCB exposure, with an incorporation peak of tritiated thymidine at 18–24 hours. The initially shorter duration of the 'response' suggests that it is very likely determined also by the incidental in-flow and cell cycle of reactive cells. Further, this might also be an explanation for the asynchronicity of germinal centres.

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## **THE PROGNOSTIC VALUE OF CA-125 IN EPITHELIAL OVARIAN CANCER PATIENTS DURING AND AFTER CHEMOTHERAPY**

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In the past ten years the investigations on CA-125 levels of epithelial ovarian cancer patients have raised several questions both in the screening and in the follow-up. The predictive value of the test during the postoperative chemotherapy and the follow-up period was the topic in the series of examinations. Our findings are as follows. The decrease of the CA-125 level predicts a long tumour free survival. The permanent high level of CA-125 is a signal of a recurrence within few month after stopping therapy. In case of increase of the CA-125 level an early recurrence can be expected.

### **Introduction**

During the last decade the measurement of the CA-125 levels has got an important role and an increased significance in the follow-up of epithelial ovarian cancer patients [1,2,4]. While in the screening and in the preoperative evaluation it proved to be an ineffective marker used alone, the post-therapy significance of this method has been confirmed as a useful method for early detection of recurrence [2,3].

Our investigations point to the clinical usefulness of the tumour marker CA-125 in predicting the clinical outcome of ovarian cancer.

### **Patients and Methods**

At the Department of Obstetrics and Gynaecology of the University Medical School of Debrecen there were evaluated 35 patients with primary ovarian cancer with the following inclusion criteria:

1. during the monitorisation period one of the results is over the standard of 35 mU/L to prove that the tumour is CA-125 detectable.
2. The tumour status evaluated was complete response (CR) or stable disease (SD).

Patients were followed-up by CA-125 measurements between January 1994 and February 1997. Out of the 35 evaluable patients 54,28 % belonged to the advanced stages (FIGO std. III-IV) with the average age of 50,3 years (range from 19- to 74 years). During and after the standard postoperative chemotherapeutic protocol (CP scheme: Cytoxan/Platidium 750/75 BSA/ mg from the Bristol-Myers Squibb Co.) CA-125 levels were measured with fluorometric microparticle enzymimmunoassay (MEIA) technique. Result was considered positive over the 35 mU/L serum level. Statistical analysis was performed by Rustin, et al [5].

## Results

Out of the 35 patients evaluated at 25 were a decrease of CA125 level (71,43%) observed which was evaluated as a predictor of a good response to the chemotherapeutic regime administered. At the majority of the patients in this group the clinical response was evaluated as CR or SD which means a stable tumour free or an unchanged tumour status. All this is good correlance with CA-125 levels measured. Six patients' tumour marker levels (17,14%) were unchanged and four of those (66%) showed clinical progression. Patients with elevated CA-125 levels (11,43%) indicated resistance for the 1<sup>st</sup> line chemotherapy and 3 of the 4 patients had experienced rapid progression and died (75%) within the follow-up period.

**Table 1.**  
**CA-125 levels and progression**

| Group No | CA-125    | Patient status | No.of.patients | group (%) | %       |
|----------|-----------|----------------|----------------|-----------|---------|
| 1        | decreased | unchanged      | 24             | 96 %      | 71,43 % |
|          |           | progressed     | 1              | 4 %       |         |
| 2        | stable    | unchanged      | 4              | 66 %      | 17,14 % |
|          |           | progressed     | 2              | 33 %      |         |
| 3        | increased | unchanged      | 1              | 25 %      | 11,43 % |
|          |           | progressed     | 3              | 75 %      |         |
| Total:   |           |                | 35             |           | 100%    |

In our opinion unchanged tumour marker levels render recurrence or progression probable that is resistance to the chemotherapy administered. The clinical equivalent of it is rapid progression and early death.

## Discussion

On the basis of the literature of CA-125 and considering our findings of our study we could establish that:

1. In the response categories CR or SD decreased marker levels mean chemo-sensitive disease and good prognosis, recurrence is not probable.
2. In the same response categories the unchanged CA-125 levels indicate the possibility of the early recurrence or progression in the majority of the cases.
3. Elevated marker levels during therapy indicate very early the resistance to the drugs administered predicting a poor prognosis.

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## **PANCREATIC PSEUDOCYSTS ASSOCIATED WITH CHRONIC PANCREATITIS – EARLY AND LATE RESULTS OF 1367 OPERATIONS**

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The authors hereby review the data of 1367 operations for pancreatic pseudocysts. The surgical procedures of choice in particular pancreatic pathologies are analysed in the light of early morbidity and mortality, as well as long term follow-up results. The best operations for pancreatic pseudocysts have been the internal drainage procedures, which resolve the pathological alterations without the necessity of pancreatic resection. The treatment of chronic pancreatitis may require combined surgical procedure, such as cysto-Wirsungo-gastrostomy. The pancreatic resections performed for the treatment of small pseudocysts in the pancreatic head have been superseded by the less invasive blunt, forced cysto-duodenostomies, representing better results secondary to the smaller perioperative risk for the patient. The cyst-to-stomach and cyst-to-duodenum internal drainage techniques are just as effective, but with shorter operation time, than the Roux-en-Y cysto-jejunostomies.

### **Introduction**

Chronic pancreatitis and pancreatic pseudocysts are polyetiologic diseases. The leading complaints in this disease are represented by the consequences of the chronic inflammation of the pancreas: the most important are the formation of pseudocysts, scarring, and calcification, as well as stone formation in the duct of Wirsung.

Surgical treatment is frequently necessary to resolve the above mentioned ductal morphological alterations of chronic pancreatitis, as well as the peri- and intrapancreatic fluid collections. In appropriate situations the minimally invasive endoscopic and ultrasound guided techniques are applicable, and recently favoured [5]. The so called combined surgical procedures are employed to resolve extrapancreatic fluid collections (sterile or infected), pseudocysts, as well as the pathological ductal and duodenal alterations. This will provide hope for the relief of the patient's complaints.

The publications by authors of internationally respected pancreas referral centres agree that whenever possible, internal drainage with or without decompressive procedures is the treatment of choice [3, 4]. Various surgical applications of isolated Roux-en-Y loops have been preferred, since these will avoid the direct communication of the bowel contents with the pseudocyst. Pancreatic head resection with or without duodenum preservation has frequently been performed for the resolution of the inflammatory mass, involving substantial peri- and postoperative risk. The authors previously recommended the newly developed blunt, forced transparenchymal cysto-duodenostomy as a useful and less invasive operative option [1, 2].

To evaluate the early and late result of the operations performed at the 1st Department of Surgery of Semmelweis University Medical School Budapest we conducted the present comprehensive retrospective statistical study.

### Patients and Methods

Authors analysed data of 1155 patients undergoing 1367 operation for pancreatic pseudocysts complicating chronic pancreatitis during the seven year's period among 1987–1993. The age and gender distribution were as follows: 19–84 year (mean 43.57 years), 1095 males (80.1%), 272 females (19.9%). Data were collected from patients' charts. During the evaluation of data the following enrollment criteria were employed: pancreatic pseudocysts detected by diagnostic imaging studies (ultrasound and/or CT scan, supplemented by ERCP in certain cases) requiring surgical treatment.

Patients were listed in groups on the basis of:

1. Nature of pseudocysts (chronic versus pseudocysts secondary to acute exacerbation of pancreatitis within 6 weeks before surgery),
2. Type of surgical procedure (internal vs. external drainage of pseudocyst, vs. resection),
3. Employment of combined versus non-combined surgical procedure.

The early postoperative morbidity (including complications requiring reoperations) and mortality were evaluated. For the purposes of long term follow-up analysis of the late results of treatment, a patients' questionnaire inquiring about their long term well-being and physical condition has been developed. The written answers were statistically analysed using an associated scoring system.

Those patients were enrolled into this follow-up study, who underwent operations for pancreatic pseudocysts at our institute in the first 5 years of this investigation among 1987–1992 ( $n = 832$ ).

Statistical analyses of the data were performed using the chi-square test, data were considered statistically significant if  $p < 0.01$ .

### Results

Of the 1367 operations for pancreatic pseudocysts 62% were of chronic type, and 38% were secondary to acute exacerbations of chronic pancreatitis.

The surgical procedures of choice were drainage procedures in 88%, resection in 12%. The majority (73%) of drainage procedures were internal, directed towards the gastrointestinal tract. The traditional Juras operation (transgastric cysto-gastrostomy 6.0%) has largely replaced in our centre by the less invasive, more up-to-date solutions. Based on favorable results the authors preferred anastomoses performed between the pseudocysts and stomach (posterior cysto-gastrostomy 10.8%), as well as the pseudocyst



and the duodenum (blunt forced cysto-duodenostomy 63.5%) and the cyst and the jejunum (cysto-jejunostomy 2.1%). Additionally at the same time efforts have been made to resolve the morphological alterations of the duct of Wirsung caused by chronic pancreatitis. This has been achieved by pancreatic duct decompression procedures such as cysto-Wirsungo-gastrostomy (17.6%), and sphincteroplasty of the papilla of Vater. These decompressive procedures with the enteral drainage of the pseudocyst represent the previously discussed combined operation group. Their importance is underlined by the statistical fact that 52.5% of the surgical treatments were such combined interventions in our centre.

On the evaluation of our results we have found that the morbidity was 12.9%. Due to the antibiotic prophylaxis, the rate of severe wound infections was 4%, whereas respiratory infections appeared in 5%. Thromboembolic complications have been developed in 1%. The early postoperative mortality was 1.46%, and was significantly more frequent in cases of complications requiring reoperations (which were found indicated in 5% of all the operations), such as insufficiency of the anastomosis, haemorrhage and abscess formation. There were no statistically significant differences regarding complications and early death rate between the combined and non-combined procedures.

In the patient group that have undergone operations the long terms follow up using the standardized questionnaires was completed. 832 patients entered this follow-up study, 132 were not alive at the time of evaluation, 94 did not return the questionnaire. 606 (83%) answers were satisfactory for evaluation with an average of 44 months' follow up period. The late recovery results based on the scoring system were found to be excellent in 23%, good in 36%, satisfactory in 30% and poor in 11%. The late mortality after 4 years follow up was found to be 15.5%.

## Conclusions

The authors would like to make to following observances and suggestions on the basis of their results:

1. The best operations for pseudocysts in our hands have been the internal drainage procedures, which resolve the pathological alterations without the necessity of pancreatic head resection. The treatment of chronic pancreatitis may require combined surgical procedure, such as cysto-Wirsungo-gastrostomy.

2. The pancreatic resections performed for the treatment of small pseudocysts in the pancreatic head have been superseded by the less invasive blunt, forced cysto-duodenostomies, representing better results secondary to the smaller perioperative risk for the patient.

3. The cyst-to-stomach and cyst-to-duodenum internal drainage techniques are just as effective, but with shorter operation time, than the Roux-en-Y cysto-jejunostomies recommended by others in the literature.

4. Despite the higher complication rate, and more frequent reoperations, the procedures for the of the acute pseudocysts (due to exacerbations) do not differ significantly regarding the late results and overall mortality from that of the chronic group.

5. The overall mortality has not been significantly affected by the nature (acute vs. chronic) of the pseudocysts, neither by the combined or secunder (reoperation) nature of the surgical procedures employed.

### Summary

The authors hereby review the data of 1367 operations for pancreatic pseudocysts. The surgical procedures of choice in particular pancreatic pathologies are analyzed in the light of early morbidity and mortality, as well as long term follow-up results.

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## APPLICATION OF MINIMALLY INVASIVE SURGERY IN MAYER-ROKITANSKY-KÜSTER-HAUSER SYNDROME

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With the advancement of endoscopic techniques more and more invasive procedures can be replaced by less harmful interventions. Successful laparoscopic treatment of vaginal agenesis in Mayer-Rokitansky-Küster-Hauser syndrome is described in four patients.

### Introduction

Despite the widespread use of laparoscopy in adult patients, its application is still limited in adolescent and pediatric gynecology. With the advancement of technical facilities and operative skills, laparoscopy proved to be beneficial in numerous fields of adolescent and pediatric gynecology. Mayer-Rokitansky-Küster-Hauser syndrome is the congenital anomaly of the female genital organs secondary to inhibition of the müllerian ducts. Vaginal aplasia and the absence of normal uterus explain primary amenorrhea and sterility. Although there are many possible options available for the creation of a neovagina, it always poses a difficult problem to the gynecologic surgeon. We report four cases of laparoscopic creation of a neovagina.

### Patients and methods

Between March 1994 and April 1996 four women were treated with laparoscopic procedure because of vaginal aplasia at our department. All of them were admitted with the characteristic signs and symptoms of Mayer-Rokitansky-Küster-Hauser syndrome. They were willing to have intercourse after surgery.

Operation was performed under general anaesthesia. Pneumoperitoneum was introduced and a 10 mm trocar was inserted through the umbilical incision with attached camera, additionally with a 5 mm trocar on both sides to enable the insertion of the traction threads. A tunnel was performed by blunt dissection at the end of the vaginal dimple in which a mold was inserted. Its two traction threads were grasped by a forceps inserted preperitoneally from the trocar to the end of the tunnel. The end of the sutures were attached to the tension device located outside the abdomen. Traction was applied to the threads for 7-8 days and tension was readjusted daily.

### Results

No intra- or postoperative complication occurred. Blood loss was minimal in all cases. Patients had their first intercourse 6-8 weeks after surgery. Six months after the

operation they presented with regular sexual activity. The vagina was 7–8 cm long with acceptable width and appearance. Routine bimanual and speculum examination could be performed without difficulties.

## Discussion

Vaginal agenesis in Mayer–Rokitansky–Kuster–Hauser syndrome can be treated either with conservative or operative techniques. The multitude of methods described in the literature indicates that the ideal solution has not yet been found [2]. The first steps are common in all surgical procedures: the creation of a vaginal canal by incision of the vaginal dimple and blunt dissection between the urethra, bladder and rectum. Lining the cavity of the neovagina is a question of debate. Several methods have been described requiring laparotomy and bowel surgery to cover the neovagina with different intestinal segments [3]. High morbidity and even mortality has been described using these methods and only exceptionally performed nowadays.

Vecchietti used a Pfannenstiel incision to create a tunnel in the vesicorectal space [5]. An olive is pulled up into the vaginal dimple and the suture threads are led out through this space and the preperitoneal space to the edges of the Pfannenstiel incision. Tension is applied to these threads for 10–14 days. Recently endoscopic surgery seems to offer a reliable alternative to laparotomy in neovagina construction as well, and has significant advantages over the traditional Vecchietti method [1,4].

The aim of vaginoplasty is to create a neovagina that will be satisfying both in appearance and function. At the same time surgeon should avoid risky intervention and try to lower pain and morbidity in postoperative treatment. Laparoscopically assisted neovaginoplasty using the modified Vecchietti method fills these requirements, and in our four cases proved to be an advantageous way of treating Mayer–Rokitansky–Kuster–Hauser syndrome.

## Summary

With a short review of the possible methods maybe used in the case of vaginal agenesis, we report our results on four patients who had a neovaginoplasty performed through a laparoscopically assisted approach, according to the modified Vecchietti method. Minimal invasive surgery is a promising new method treating this special entity frustrating both for patient and doctor.

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## **RESULTS WITH COLLAGEN FLEECE COATED WITH FIBRIN GLUE (TACHOCOMB). A MACROSCOPICAL AND HISTOLOGICAL EXPERIMENTAL STUDY**

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Diffuse bleeding from parenchymatous organs at conventional surgery is eliminated with the usual methods coagulation tamponade or stiches. We performed experimental series at 9 dogs. After resection of spleen, liver, pancreas and kidney, the bleeding surface was covered by collagen fleece coated with fibrin glue (TachoComb). Postoperatively 7 days, 10 days, 14 days and 28 days we made a relaparotomy. Then the results were analysed macroscopically and microscopically. In the abdominal cavity neither significant quantity of blood nor greater adhesions were detected. At all cases the fibrin glue was found on place where it was put before. Histologically a perfect wound healing experienced. The fibrin glue (TachoComb) using at diffuse parenchymatous organs' bleeding give a very good results when the wound area is at least 1 cm beyond the immediate wound margin and the fibrin glue is applied onto the wound and pressed on it for 4-5 minutes.

### **Introduction**

There are situation in conventional or endoscopic surgery when diffuse bleeding becomes a severe problem [2]. This may occur especially during operation involving parenchymal tissue and/or in cases of impaired hemostasis. The diffuse bleeding from parenchymatous organs in conventional surgery has to this day been treated with the usual methods coagulation, tamponade, oversewing or stitching [3].

In the general surgery were most frequently parenchymatous diffuse bleeding from the liver, spleen, pancreas and other parenchymatous organs. Problems that frequently occur in open surgery include diffuse bleeding from the parenchyma as a result of trauma or liver resection, diffuse bleeding of the spleen as well as of other parenchymatous organs [1].

With the development by the pharmaceuticals industry of a collagen fleece coated with fibrin glue (TachoComb) provided an additional method for coping with such situations.

Tachocomb is an absorbable topic hemostyptic, consist of a collagen fleece wich is layered with the components of a fibrin glue: highly concentrated fibrinogen and thrombin imitate last step of the coagulation cascade. On contact with bleeding wounds or other body fluids the coagulation factors dissolve and a link is formed between the collagen surface [4].

## Methods

We performed the animal experimental series at 9 dogs. In all the cases after resection of liver, spleen, pancreas and kidney, the wound surfaces were covered by TachoComb so the fleece was at least 1 cm. greater then the wound area. The size of wound areas was from 2 to 15 cm<sup>2</sup>. To the satisfactory still of bleeding after the application we pressed the fleece onto it immediate 4–5 minutes using a moist surgical glove or a moist pad. Postoperatively 7 days, 10 days, 14 days, and 28 days we made a relaparotomy and then results were analysed macroscopically and microscopically.

## Results and Discussion

Macroscopically in the abdominal cavity neither significant quantity of blood nor greater adhesions were detected. The application of TachoComb has provied very successful. At all the cases the collagen fleece was found on place were it was put befor.

After 14 days unspecific granulation tissue has infiltrated the fibrin glue (TachoComb). After 28 days the fibrin glue has replaced with cell-poor granulation tissue rich in endogenic collagen fibers.

## Summary

The TachoComb using at diffuse parenchymatous organs bleeding give a very good result when the wound area is at least 1 cm. beyond the immediate wound margin and the fibrin glue is applied onto the wound and pressed on it for 4–5 minutes.

The authors have not been postoperativ bleeding or formation of hematomas observed.

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## PLASMA LEVELS OF TNF AND IL-6 FOLLOWING INDUCTION OF ACUTE PANCREATITIS AND PENTOXIFYLLINE TREATMENT IN RATS

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Activation of cytokine cascade is a decisive factor in determining the pathobiology of different inflammatory processes including acute pancreatitis. The purposes of this study were to determine the TNF and IL-6 levels after the induction of acute necrotizing pancreatitis, and to establish the effects of pentoxifylline on the cytokine production and the severity of pancreatitis. Acute necrotizing pancreatitis was induced by the retrograde injection of 200 µl taurocholic acid into the pancreatic duct in male Wistar rats. TNF was titrated in a bioassay on cell line WEHI clone 164. IL-6 was measured via its proliferative action on the IL-6 dependent mouse hybridoma cell line B-9. Seven mg/kg pentoxifylline was administered intraperitoneally at the time of operation and/or 24 hours later. Rats were sacrificed, 48 or 72 hours after the operation. The TNF bioassay revealed high levels of TNF ( $36.6 \pm 6.0$  U/ml) in the control group whereas levels decreased to zero in the pentoxifylline-treated group. The IL-6 bioassay likewise demonstrated high levels of IL-6 in the control group and markedly decreased levels in the pentoxifylline treated group ( $7083 \pm 2844$  pg/ml,  $6463 \pm 1307$  pg/ml vs.  $137.5 \pm 85.5$  pg/ml, respectively,  $p < 0.05$ ). The high mortality observed in the control group (43%) was sharply decreased by pentoxifylline administration to 11%. The data suggest that pentoxifylline is capable of modifying the cytokine production after 48 hours of induction of acute pancreatitis.

### Introduction

The mortality of acute necrotizing pancreatitis is high (more than 10 %) in spite of novel surgical and intensive therapeutic methods. Some authors have outlined the importance of cytokines in the progress of severe inflammatory diseases (severe burns, peritonitis and sepsis) which can lead to a systemic inflammatory response and multiorgan failure. The clinical course of acute necrotizing pancreatitis is very similar to that in the above-mentioned pathologic processes.

The purposes of this study were to determine the TNF and IL-6 levels after the induction of acute necrotizing pancreatitis and to establish the effects of pentoxifylline on the cytokine production and the severity of the pancreatitis.

### Materials and Methods

Male Wistar rats weighing 200 to 260 g were housed in wire bottom cages and fed standard rat chow and water ad libitum. Aether anaesthesia was induced and the abdomen was shaved, prepped and draped in a sterile fashion and a midline incision was

made. The pancreatic duct was cannulated transduodenally and the common bile duct was temporarily closed with a metal clamp. A knot was tightened around the pancreatic duct and the cannula. Then 150  $\mu$ l or 200  $\mu$ l 4% or 6% taurocholic acid (REANAL, Hungary) was injected via the cannula during one minute [2]. After infusion the clamp, knot and the cannula were removed and the duodenal wound closed with a single figure-of-eight 6-0 prolene suture. Sham-operated animals underwent laparotomy and exploration of the duodenum and pancreas. Treated and untreated animals were killed after 6, 24, 48 and 72 hours. Analysis of plasma samples: All blood samples were centrifuged at 2000 rpm for 30 minutes immediately after collection. Serum amylase levels were determined by means of the Phadebas test and are reported in standard units. Wet pancreatic weight to body weight ratios were calculated and reported in mg/g. TNF was titrated in a bioassay on cell line WEHI-164 [3]. IL-6 was measured via its proliferative action on the IL-6 dependent mouse hybridoma cell line B-9 [1]. The activities were calibrated against rm TNF (GENZYME, Cambridge England) and rm IL-6 (SIGMA-Aldrich, Munich) respectively. The pancreata and lungs were subjected to histologic analysis. The pentoxifylline treated group received 7 mg/kg pentoxifylline intraperitoneally at the time of operation and or 24 hours later. Statistical analysis was performed with the Statgraphics programme (STSC INC. Statistical Graphics Corporation, two-sample analysis.)

## Results

The serum amylase activity was significantly high in every group receiving taurocholic acid ( $23200 \pm 2754$ ,  $22157 \pm 3492$ ,  $15226 \pm 2247$ ,  $11266 \pm 622$  U/ml) comparing with sham-operated group. ( $393 \pm 402$ ,  $283 \pm 116$  U/ml) ( $P < 0.05$ ). The wet pancreatic weight and body weight ratio was elevated in the groups treated with taurocholic acid but the difference was not significant. ( $7.04 \pm 1.0$ ,  $6.1 \pm 0.4$  mg/g versus  $4.78 \pm 0.4$ ,  $4.1 \pm 0.8$  mg/g) There was no mortality in the group receiving 200  $\mu$ l 4% taurocholic acid or 150  $\mu$ l 6% taurocholic acid but the mortality increased to 43% in the group receiving 200  $\mu$ l 6% taurocholic acid after 48 hours.

The histologic analysis of the pancreata revealed interstitial oedema and necrosis of the pancreatic acinar cells in the early phase (at 6 hours) and invasion of neutrophil leukocytes and microabscess formation at the late phase (48 hours). The lung histology showed congestion and perivascular oedema at the early phase and neutrophil leukocyte infiltration and hyaline membrane formation at the late phase. Hyaline membrane formation can be considered as an early sign of respiratory distress syndrome.

TNF was detected in early phase (after 6 hours) after injection of 150  $\mu$ l 6% taurocholic acid ( $35.7 \pm 9.9$  U/ml), but not later at 24 or 48 hours. The elevated TNF level 24 and 48 hours after injection of 200  $\mu$ l 6% taurocholic acid ( $35.0 \pm 5.0$ ,  $36.6 \pm 6.0$  U/ml) can be considered as a consequence of severe acute necrotizing pancreatitis.



The IL-6 levels remained elevated at 48 hours after the administration of 200  $\mu$ l 6% taurocholic acid ( $6728 \pm 3442$  pg/ml). In the event of the lower concentration or volume of taurocholic acid the IL-6 levels decreased rapidly after 48 hours ( $612.5 \pm 477$ ,  $535.5 \pm 227.5$  pg/ml, respectively). To summarize these initial results we concluded that this model is suitable for characterizing of acute necrotizing pancreatitis. The mortality attained 43% and histologic analysis demonstrated severe pathologic changes. The TNF level remained elevated and IL-6 level decreased slowly in accordance with the severity of acute necrotizing pancreatitis.

We next attempted to have an influence of cytokine production. Pentoxifylline (TRENTAL) is well known to inhibit the transcription of TNF mRNA in inflammatory processes. We administered 7mg/ kg pentoxifylline intraperitoneally at 24 hours (group 1) and at 0 and 24 hours (group 2) then sacrificed the animals at 48 hours after induction of pancreatitis by intraductal administration of 200  $\mu$ l 6% taurocholic acid. In group 3 Pentoxifylline was administered at 24 hours and samples were taken at 72 hours. Control animals received 200  $\mu$ l 6% taurocholic acid intraductally.

Pancreas weight to body weight ratio and serum amylase level were not changed significantly after pentoxifylline treatment. TNF was not detected in any pentoxifylline treated group or in the 72-hour control group. However, in the 48 hour control group the TNF level was  $36.6 \pm 6.0$  U/ml. The IL-6 level was decreased significantly ( $p < 0.05$ ) in group 2 and 3 ( $137.5 \pm 85.5$  pg/ml and  $71.5 \pm 66.8$ , respectively versus  $6728 \pm 3442$  and  $7083 \pm 2844$  pg/ml) but not in the group 1 ( $9068 \pm 3206$  versus  $6728 \pm 3442$  pg/ml). The high mortality observed in the control groups (43%) was sharply decreased by pentoxifylline administration to 11%.

Our data suggest that pentoxifylline has a beneficial effect in acute necrotizing pancreatitis.

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## COMPARISON BETWEEN CONTINUOUS BRAIN TISSUE MEASUREMENT AND CEREBROVENOUS MEASUREMENT OF $pO_2$ , $pCO_2$ AND pH IN A PORCINE INTRACRANIAL PRESSURE MODEL

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Simultaneous oxygen measurements in brain tissue ( $p_{ti}O_2$ ) and hemoglobin saturation measurement in cerebrovenous blood in patients after severe head injury have shown different results regarding the comparability of the findings in respect to CPP and ICP. This is contrast to theoretical expectations. The aim of this study was to compare continuous  $p_{ti}O_2$  measurement with oxygen partial pressure measurement in sagittal sinus ( $pO_{2cv}$ ) during simultaneously performance in an animal intracranial pressure model. For continuous measurement we used a newly available multisensor probe. We placed a Paratrend 7<sup>®</sup> probe (BSL, High Wycombe, UK) in the left frontoparietal white matter and measured  $p_{ti}O_2$ ,  $pCO_2$  ( $p_{ti}CO_2$ ) pH ( $pH_{ti}$ ) and temperature ( $t_{ti}$ ) while simultaneously measuring these parameters ( $p_{cv}O_2$ ,  $p_{cv}CO_2$ ,  $pH_{cv}$ ,  $t_{cv}$ ) in the sagittal sinus in 9 pigs under general anaesthesia. A fogarty balloon catheter was placed supracerebellar infratentorial and inflated stepwise in order to increase ICP. The baseline levels of  $pO_{2ti}$ ,  $pCO_{2ti}$  und  $pH_{ti}$  in the non-injured brain tissue showed a more extended heterogeneity compared to the findings in cerebrovenous blood. Both,  $pO_{2ti}$  and  $pO_{2cv}$  were significant correlated to the CPP decrease. In both measurement compartments  $pCO_2$  was inverse correlated to the course of CPP and seems the course of pH mainly to determine.  $p_{ti}O_2$  as well as  $p_{cv}O_2$  showed a close correlation to the CPP course and have proven to be qualified to indicate metabolic information about the relation of cerebral blood flow and metabolic cerebral demands. The measurement of  $CO_2$  tension in both measurement compartments shows a distinct heterogeneity of the absolute values and the results are only weak correlated to CPP. Metabolic influence on this parameter could not be revealed in the used experimental approach.

### Introduction

The continuous  $pO_2$  measurement in brain tissue ( $p_{ti}O_2$ ) with Clark type electrodes or multisensor probes, combining fiberoptical sensors to measure  $pCO_2$  and pH, a thermocouple for measuring temperature and a Clark type electrode for measuring  $pO_2$  is increasingly used in neurosurgical patients to monitor the oxygen supply to the brain and to find out prognostic meaning of the measured values [1, 4, 5]. In recent clinical studies comparing the finding of  $p_{ti}O_2$  with simultaneous fiberoptical haemoglobin saturation measurement different correspondence of the result were explored [1, 4]. This is in contrast to theoretical expectations [2].

The aim of this study was to use a newly available multiparameter probe, measuring  $pO_2$ ,  $pCO_2$ , pH and temperature, simultaneously in brain tissue and in the cerebrovenous outflow in a porcine model. The relation between  $p_{ti}O_2$  and  $p_{cv}O_2$  during inducing ICP increase was evaluated. Additionally it was the purpose to gain more insight and experience in the values of oxygen tension in normal brain tissue and cerebrovenous blood and of the new available continuous parameter  $pCO_2$  and pH.



## Methods

### *Anesthesia and Monitoring of Experimental Animals:*

Nine 8-week-old domestic pigs weighing 18–24 kg were used in the present study. All experiments were performed in accordance with the guidelines issued by the Debrecen University Committee on Animal Care based upon: "Principles of laboratory animal care" (MIH publication No. 86–23, revised 1985). Anesthesia was introduced by i.v. drug medication, tracheotomy was carried out and the animals were ventilated volume controlled with a mix of oxygen and room air.

A parenchymal multisensor probe (P7) (Paratrend 7, Biomedical Sensors Ltd., High Wycombe, UK) was inserted into the white matter of the left frontoparietal lobe over a length of about 4 cm. In all animals, the superior sagittal sinus was exposed in the bregma region. A second P7 probe was introduced into the superior sagittal sinus via direct puncture of the sinus. Below the transverse sinus, a 3x3 mm right-sided craniotomy was carried out, the dura was opened, and a Fogarty-type balloon catheter was forwarded onto the supracerebellar infratentorial cortical surface. By inflating the balloon with saline over a period of 22.5 min ICP was increased.

ABP and ICP were continuously monitored, and CPP was calculated. All values of brain tissue measurement by the P7 probe ( $p_{ti}O_2$ ,  $p_{ti}CO_2$ ,  $pH_{ti}$  and  $t_{ti}$ ) as well as the values of the cerebrovenous measurement in the sagittal sinus by the P7 probe ( $p_{cv}O_2$ ,  $p_{cv}CO_2$ ,  $pH_{cv}$  and  $t_{cv}$ ) were digitally downloaded to a terminal program and stored in a 10 second interval on hard disk. The mean values are expressed as the median  $\pm$  standard deviation if not indicated in an other way.

After fixation and coronal cutting of the entire brain the tracts in the frontoparietal white matter made by the p 7 probe were inspected macroscopically and examined by light microscopy.

## Results

### *Findings prior to ICP increase:*

The mean ICP before balloon inflation was 9.44 (6.35) mmHg. CPP was 82.11 (9.85) mmHg. All animals showed a 100% oxygen saturation in the peripheral pulse oximetry. The mean arterial oxygen tension was 142 (25.54) mmHg. The mean  $p_aCO_2$  was 55.36 (6.69) mmHg and the mean  $pH_a$  was 7.34 (0.06). The mean body temperature measured in the arterial compartment was 37.9 (0.6) °C. Mean  $p_{ti}O_2$  was found to be 28 (13) mmHg. Three of the animals showed initial  $p_{ti}O_2$  values below 20 mmHg.

In the sagittal sinus we found a mean  $p_{cv}O_2$  of 43.72 (6.20) mmHg for all animals. There was no significant correlation between the oxygen levels in both cerebral compartments ( $r=0.41$ ). Because of the sensitivity of the  $pCO_2$  measurement in tissue as well as in cerebrovenous blood to changes in arterial  $pCO_2$  it is difficult to compare values between different animals. That's why all values for  $pCO_2$  measurement in cerebral compartments are given as the calculated difference

( $\delta$  values =  $p_a\text{CO}_2$  - compartment  $\text{CO}_2$ ). The mean  $\delta p_{ti}\text{CO}_2$  was distinctly higher with 18.58 (6.96) than  $\delta p_{cv}\text{CO}_2$  of (6.23). Analyzing the correlation between  $p\text{CO}_2$  values in both compartments for all 9 animals revealed a correlation of  $r=0.89$ .

#### *Findings during ICP increase:*

ICP increased led to a reproducible CPP decline in the animal model. The mean CPP decline was 51.49% for all 9 animals. A CPP below 50 mmHg could be reached in every animal during the balloon inflation. The  $p_{ti}\text{O}_2$  and  $p_{cv}\text{O}_2$  measurement were both tightly correlated to the CPP course. The adjusted  $r$  squared ( $r^2$ ) of the relationship between CPP with  $p_{cv}\text{O}_2$  was 95% and with  $p_{ti}\text{O}_2$  it was 93%. Thus the majority of the measured oxygen data in both compartments could be predicted by the course of CPP. Analysis of the absolute oxygen values over the periods when CPP was under 50 mmHg showed the  $p_{cv}\text{O}_2$  measurement to be 24 (8.77) mmHg for all 9 animals. The mean  $p_{ti}\text{O}_2$  level was found to be 10 (4.6) mmHg.

$p\text{CO}_2$  was inversely correlated to CPP in both compartments (tissue:  $r_{\text{men}}=-0.45$ ; sinus:  $r_{\text{men}}=-0.55$ ) and influenced the course of pH mainly (relation between  $p\text{CO}_2$  and pH: tissue:  $r_{\text{men}}=-0.93$ ; sinus:  $r_{\text{men}}=-0.89$ ). These increase of  $p\text{CO}_2$  during CPP decrease amounted to 45 (23) mmHg in the tissue measurement and to 12 (6) mmHg in the cerebrovenous measurement. These findings were not accompanied by changes in arterial  $p\text{CO}_2$ .

#### *Histological examination:*

The macroscopic examination of the catheter insertion tracts after fixation and serial cutting showed no tissue damage in all 4 inspected brains. Light microscopy revealed minimal subarachnoid hemorrhage adjacent to cortical surface in all cases but the tracts themselves were not conspicuous.

## **Discussion**

Van Santbrink found a poor correlation between simultaneous measurement of oxyhemoglobin saturation in the jugular bulb and  $p_{ti}\text{O}_2$  measurement in patients ( $r=0.12$ ) [4]. Kiening also performed such simultaneous measurements but used a more sophisticated approach to find periods of so called "time of good data quality" for analyzing correlation. He thus found a coefficient of correlation of  $r=0.71$  [1].

Both measurement compartments have proven to be sensitive to global changes in cerebral oxygen supply indicated by CPP declines below 60 mmHg in our experimental study. We conclude, that the differences comparing the results between continuous  $p_{ti}\text{O}_2$  measurement in non injured brain areas and simultaneous continuous fiberoptic jugular bulb oximetry seen in clinical studies in severe head injured patients are mainly due to the technical limitations of the current fiberoptic measurement systems and the anatomical difficulties of measuring in the jugular bulb in patients. The introduction of the polarographical measurement of oxygen tension in the cerebrovenous blood could help to overcome the technical limitations in the use of jugular bulb oxygen



measurement. First results with the P7 probe in the jugular bulb in men have demonstrated the feasibility of this measurement approach [3].

In both measurement compartments  $p\text{CO}_2$  was highly sensitive to CPP changes. The  $p\text{CO}_2$  increase was faster in both measurement compartments occurring than the  $p\text{CO}_2$  drop. We suggest that the increase in  $p\text{CO}_2$  during CPP decrease reflects compromised cerebral perfusion. The reduced "wash out" thus leads to an accumulation of metabolic products. Zauner et al. observed an increase of brain  $p\text{CO}_2$  in the ischemic area to 30% after inducing of focal cerebral ischemia in an animal feline model [5].

However, there was no close correlation between CPP decrease and  $p\text{CO}_2$  increase in our experiment. This could be due to the metabolic interactions between reduced substrate delivery (decreased  $p_{\text{t}}\text{O}_2$ ), induction of metabolic shift to intermediate anaerobic glycolytic pathways and compromised "wash out" of  $\text{CO}_2$ . These complex interactions could not be further studied in our experimental approach.

The course of pH during the changes in CPP was tightly inversely correlated to  $p\text{CO}_2$  in brain tissue as well as in the sagittal sinus. We assume in our experiment pH has been mainly ruled by the dynamic of the  $p\text{CO}_2$  levels.

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## DETAILS OF TEACHING, LEARNING AND TRAINING IN LAPAROSCOPIC SURGERY

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The authors discuss the specific details of teaching, learning and training in laparoscopy in 6 main sections, on the basis of their experience gained through basic and advanced courses held for approximately 480 participants at the courses organised at the Department of Experimental Surgery of the University Medical School of Debrecen, between 1989 and 1996. The 6 sections cover the following: 1. Why these courses are needed? 2. Who should participate in them? 3. When courses should be held (continuously for beginners, at an appointed time for advanced participants, and chances for training should be provided at any time, according to demand) 4. What should be taught? 5. Where teaching and training should take place (surgical learning/training centres) and 6. What methods of teaching should be used.

**Keywords:** laparoscopic teaching, learning, training

### 1. Why are special teaching and courses needed ?

Techniques in laparoscopic surgery require special approach, views and skills as they are quite different from open surgery in many respects.

Therefore course participants have a double aim; on one hand they want to learn the new technique, and, on the other hand, they wish to obtain skills in it. These skills can be learnt through practice, but they should always be based on relevant surgical experience [1,2,3]. Several countries have introduced measures or have their own approach concerning the acquisition of certain preliminary training in laparoscopy [5]; in some other countries there are only recommendations about the application of laparoscopy in the clinical practice [2,3].

### 2. Who should participate in the training courses?

Since laparoscopic surgery involves not only the aforementioned special skills but also greater difficulties in comparison with similar, open surgeries, a surgeon should be trained in traditional surgical techniques in the first place, to be able to use laparoscopic techniques. So it cannot be allowed that someone learns basic surgical techniques such as making preperates or sutures using laparoscopy.

The aforementioned surgical skills are also necessary and imperative in the recognition and elimination of complications as a surgical intervention, which cannot be continued using laparoscopy, should be finished using techniques of open surgery. The emphasis therefore is on skills in open surgery which does not necessarily involve a special examination in this field.

### 3. When should these special skills be taught?

It is our belief, that basic courses in laparoscopy for 'beginners' should be provided continuously.



Advanced laparoscopic courses for participants with some skills in the field should be organised at appointed times, and should there be demand, continuous training possibilities could be provided for learning, practising new types of operations on experimental animals i.e. living tissues. The courses could be organised on the basis of individual applications or at appointed times.

#### 4. What should be taught?

It depends on the nature of the course, whether it is a basic or secondary one.

##### Basic courses

*Learning the theoretical fundamentals (via lectures, slides and video)*

- technical requirements: operating principles of machines and devices
- features of surgical techniques, special problems
- role of joint professions, questions of interdisciplinary nature

*Practising basic practical skills*

##### ◆ *Phantom operations using 'pelvi trainer' or in a 'training box'*

Aim: ability to move and orientate in two-dimensional space;  
co-ordinate the hand and eye; perception of depth acuity.

Tasks: picking small objects, such as a match, and putting them to another place;  
taking and pulling threads; preparation of pieces of organs (e.g. a chicken thigh);  
practising on hepatic and cholecystic preparates of animal origin.

Much time should be spent on thorough practice.

##### ◆ *Surgery on animals*

- Performing either a certain type of surgery such as laparoscopic cholecystectomy which is a basic type of surgery, or
- According to our opinion, it is better to practice each basic activity thoroughly:

Tasks: introduction of trocars, proper camera position, holding organs when assisting, learning techniques of preparation, practising techniques in haemostasis, washing out of the surgical area, practising suction, possible injuries and their management

##### ◆ *Surgery on cadavers*

Performing a certain kind of operation but it is usually not lifelike; there is no bleeding.

#### Advanced laparoscopy courses in the frame of workshops

##### ◆ *Learning and practising developed special techniques in operations on animals*

Tasks: intracorporeal knot tying, intracorporeal stapler technique, endostich, ultracision, precision suturing and anastomotic techniques [5, 6]

##### ◆ *Teaching, learning and training of special laparoscopic operations on animals*

Organisation of demonstrative operations in laparoscopic centres

#### 5. Where can laparoscopic technique be practised and surgical skills obtained?

In surgical learning and training centres.

##### ◆ *In model experiments*

Everything can be modelled, but it is not ideal.

##### ◆ *In animal experiments*

Under real surgical conditions, in the form of basic and secondary courses, considering the regulations of the Scientific Ethical Committee for the Protection of Animals in accordance with international standards [4].

- pig: its internal organs are closest to those of humans
- mongrel dog: it is more difficult but it is excellent training

One can cause injury or bleeding in experimental animals, which then should be identified and treated, etc. Practice under these circumstances could be of invaluable use in operations performed on humans in the future. That is why it is felt that sacrificing animals should be forgiven, however, it should never turn out to be a brutal form of massacre by any means. An experimental animal, too, must be given respect – which is a right

of every living being – by enforcing the ethical rules and keeping to the ethical norms. Course participants should be notified of the above.

♦ *In clinical practice*

At departments with great experience in laparoscopic surgery.

## 6. How should courses be conducted?

1. Essential supplementary materials (video, slide, other supplementary material) should be available.
2. Teaching should only be done using good equipment. Instruction about the use of equipment should involve trouble shooting and elimination.
3. Good technique should be taught.
4. The instructor should be self-confident but not an 'exhibitionist'.
5. A simple and clear way of teaching should be chosen (which is extremely difficult!), teaching should be done with a little bit of humour, in a pleasant atmosphere. It should be a pleasure for both parties.
6. In the teaching process the instructor should not criticise participants (it may be discouraging), he should rather let them know what not to do, what is forbidden.
7. Carefully organised schedule and keeping to the schedule. The schedule should reduce or eliminate inactive time, although one can learn by just watching, it is not enough. Each participant should have his/her active period. Result: much more can be learnt in a shorter period.
8. Preliminary training for assistants (circulating and scrub nurses)

The instructor should not depend on the manufacturing companies. In practice it is very difficult as it is the companies which sponsor courses, but if a course is company-dependent, the products of another factory cannot be displayed and, in the end, it is the patient to lose. Keeping these rules is beneficial for the instructor, participant, companies but first of all, the patients.

For many, learning means the learning of the fundamentals, but if one gives it a second thought, he can see that learning should be done on a continuous basis since newer and newer types of laparoscopic surgery and technical equipment have to be used, practised so that, in the possession of adequate experience, they can safely be used in clinical practice, too.

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## PROTECTION OF THE RENAL ARTERY IN NEPHRON-SPARING SURGERY I. PATHOMORPHOLOGICAL STUDY

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It is necessary to clamp the renal artery for some time in renal surgery to preserve the organ. Not only the renal parenchyma but also the wall of the clamped renal artery may be damaged due to known ischaemic-reperfusion causes. Regional venous renal hypothermia induced by intracellular solutions (Sacks II, Euro-Collins) could provide protection against damage of the vessel wall caused by reperfusion or clamping in our experiments, in cases of clamping for 30 minutes, probably because it also ensured the cooling of the surface of the vessel wall. Similar vasoprotective effect could be achieved by systematic antioxidant treatment (MTDQ-DS) and regional renal hypothermia given in combination. Harmful effects of 45-minute clamping could be best avoided by applying antioxidant treatment alone. While there were no significant morphological changes in the renal arteries the persistent endothelial damage may trigger further complications like renal ischaemic condition.

**Keywords:** renal artery clamping, regional venous renal hypothermia, antioxidant treatment, renal artery protection, pathomorphology

### Introduction

On removing renal tumours or treating traumatized kidneys it is inevitable to clamp the renal artery for shorter or longer periods. In interventions involving clamping of the renal artery for longer than 20–30 minutes, it is necessary to perform the operations in superficial or perfusion regional hypothermia to prevent renal damage caused by warm ischaemia. One of the methods of perfusion cooling of the kidney has been elaborated by our team and it involves hypothermia induced by hyperosmolar intercellular solution through the renal vein, where the collateral branches of the renal vein (internal spermatic/ovarian vein and suprarenal vein) can be used, the renal artery being simultaneously clamped. This method of cooling requires immediate nephrotomy to prevent the pathological swelling of the kidney [4].

According to the data in the literature, in continuous regional or in situ cooling of the renal artery, clamping for 90–120 minutes can be done without causing irreversible damage to the renal parenchyma, and the protection of the functioning renal parenchyma can be achieved, i.e. the conditions of nephron-sparing surgery are ensured [3].

However, the nature of changes in the wall of the artery, emerging from the clamping of the renal artery for different periods of time, is still to be studied [1,2]. The aim of this experiment was to reveal more details of this question.

## Material and Methods

Experiments were performed on 36 mongrel dogs of both sexes.

*Operative technique:* The left kidney was isolated following median laparotomy performed in i.m. narcosis induced by Xylavet-Ketamin. The renal artery, the renal vein and its collateral branch (internal spermatic/ovarian vein) were prepared. Next, the renal arteries were gently clamped with artery forceps for 30 or 45 minutes in the various groups of experiments, and the following treatments were applied:

- Group 1 (n= 6): clamping of the renal artery alone for 30 or 45 minutes
- Group 2 (n=12): clamping of the renal artery for 30 or 45 minutes + simultaneous regional venous renal hypothermia in combination with nephrotomy (perfusion and surface cooling)
- Group 3 (n= 6): clamping of the artery for 30 or 45 minutes + simultaneous intravenous antioxidant treatment
- Group 4 (n=12): clamping of the renal artery for 30 or 45 minutes in regional venous renal hypothermia in combination with nephrotomy + simultaneous intravenous antioxidant
- Group 5: intact contralateral renal arteries served as control

*Cooling solutions:* Sacks II or Euro-Collins intracellular hyperosmolar solutions

*Antioxidant treatment:* MTDQ-DS, water-soluble synthetic substance of dihydrokinolin nature – 100 mg/bwt/kg in infusion

*Morphological investigations:* light and electron microscopic evaluation of samples obtained from arteries of both sides on the 3rd postoperative day to study the intactness of endothelial cells, continuity of lamina elastica and appearance of the tunica media.

## Results

(light microscopy = LM, electron microscopy = EM)

Group 1: (clamping only)

*In clamping of the artery for 30 minutes:* LM showed endothelial cells of different sizes, flattened lamina elastica and focal subendothelial fibrosis. EM revealed knobby enlargement of endothelial cells.

*In clamping of the artery for 45 minutes:* LM proved explicit swelling of endothelial cells, hiatus in the continuity of the elastica interna, focal subendothelial fibrosis and, occasionally, necrosis. EM revealed swollen and vacuolated endothelial cells.

Group 2: (clamping + regional hypothermia)

*In clamping for 30 minutes:* LM showed intact endothelium and continuous lamina elastica of wavy course. EM revealed slightly swollen endothelial cells with random vacuolization.

*In clamping for 45 minutes:* LM showed slightly flattened continuous lamina elastica, with necrosis in some regions. EM proved the presence of some vacuolated endothelial cells and lamellar basement membrane in some regions.

Group 3: (clamping + antioxidant treatment)

*In clamping for 30 minutes:* LM revealed swollen endothelial cells in some regions and continuous lamina elastica interna. EM revealed slight vacuolization in endothelial cells and a thicker basement membrane.

*In clamping for 45 minutes:* LM showed swollen endothelial cells some of them being knobby. EM revealed vacuolization with the presence of slightly thicker basement membrane.



Group 4: (clamping + hypothermia + antioxidant treatment)

*In clamping for 30 minutes:* LM showed intact endothelium and elastica interna. EM revealed mild atrophy of endothelial cells accompanied by vacuolization.

*In clamping for 45 minutes:* LM showed slight damage of the lamina elastica, fibromatosis and slight fibrosis. EM revealed slightly thicker basement membrane accompanied by lamellation and presence of knobby endothelial cells.

## Discussion

Parts of the vessels were examined next to and farther away from the site of clamping, i.e. near the aorta and kidney, respectively. The changes described in the results were characteristic of vessel parts on the clamped areas in the treated groups, whereas explicitly grave defects were typical in clamping for 45 minutes in the untreated groups.

Clamping alone, for 30 minutes, did not damage the arterial wall close to the kidney, but clear signs of damage in the immediate surroundings of the clamp were detected.

Clamping for 45 minutes, however, resulted in the flattening of the elastica interna to a great extent and caused subendothelial fibrosis.

The superficial cooling effect of regional venous hypothermia appeared to prevent arterial damage by itself or in combination with antioxidant treatment, but only in clamping lasting no longer than 30 minutes.

Harmful effects of clamping of the renal artery for 45 minutes could be best ruled out by giving antioxidant treatment alone.

It should be noted, that the endothelium of the vessel parts, which seemed to be intact under the light microscope, ultrastructurally always showed vacuolization and swelling along the line of clamping without treatment, and what is more, knobby endothelial cells are suggestive of irreversible damage in cases like this.

*Summing up:* both hypothermia and combined treatment are effective in the protection of the vessel if clamping is for 30 minutes, but in cases of clamping the renal artery for 45 minutes, antioxidant treatment given alone appears to be more favourable.

## Acknowledgements

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## PROTECTION OF THE RENAL ARTERY IN NEPHRON-SPARING SURGERY II. ARTERIAL CONTRACTILITY INVESTIGATIONS

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It has been well known that reperfusion following ischaemia may cause functional and structural damage to not only the organ involved but also the blood vessels supplying that organ. As in organ-sparing renal surgery it is inevitable to clamp the renal artery for some time, it is expected that reperfusion, following the removing of clamping, causes structural changes in the vessel wall which may result in a decrease in arterial function. In our model experiments on animals, the left renal arteries were atraumatically clamped for 30, 45 and 60 minutes. Simultaneously with clamping, perfusion regional renal venous cooling was applied to some of the animals, together with nephrotomy. In some cases cooling was performed in combination with antioxidant treatment. On the 3rd postoperative day renal arteries from both sides were removed, the right, intact ones serving as control. Noradrenaline dose effect curves characterizing vessel contractility were determined to demonstrate functional changes. It was established that cooling the renal artery for only 30 minutes was enough to rule out the damage due to ischaemia-reperfusion. If clamping lasted for 45 minutes, venous cooling of the kidney in combination with antioxidant treatment was necessary to spare arterial function. Clamping for 60 minutes resulted in irreversible/permanent decrease in contractility even if hypothermia and antioxidant treatment were given simultaneously.

**Keywords:** renal artery clamping, venous renal hypothermia, antioxidant protection, contractility changes

### Introduction

In certain surgical interventions performed on the kidneys, it is inevitable to clamp the renal artery. In operations involving clamping of the artery for 30 or more minutes, damage due to hot ischaemia-reperfusion may ensue, therefore these interventions are performed in superficial regional renal cooling. One of the methods of cooling is known as perfusion cooling, when the kidney is perfused with a cooling solution through the collateral branches of the *renal vein*, accompanied by the simultaneous clamping of the renal artery and nephrotomy [5]. This cooling technique, which provides superficial cooling for both the kidney and renal artery, allows clamping of the renal artery for as long as 90–120 minutes without causing irreversible damage to the renal parenchyma. However, the nature and extent of changes in the vessel wall, brought about by the reversible, atraumatic clamping of the renal artery for different periods of time, are still to be studied. Our research team have set out to investigate into the structural and functional changes of the renal artery caused by clamping for various periods. Conclusions about the extent of changes were drawn from changes which had occurred in the contractile properties of vessel preparates, the results being listed later in this article.



Results dealing with light and electronmicroscopical morphological investigations to reveal about the nature of changes are discussed in another article.

## Materials and Methods

### *Operative technique:*

Experiments were performed on mongrel dogs of both sexes, weighing between 15–25 kg. The left kidney was isolated following median laparotomy performed in intramuscular narcosis induced by Xylavet-Ketamin. The renal artery, the renal vein and its collateral branch were prepared. Then the renal artery was gently clamped with artery forceps for 30, 45 or 60 minutes. In some of the experimental animals, simultaneously with the clamping of the renal artery, regional venous hypothermia was induced by perfusing Sacks II or Euro-Collins intracellular solutions through the spermatic/ ovarian vein, according to the method elaborated by our research team earlier [5]. In another group of the animals, together with the clamping of the renal artery and renal cooling of the kidney, simultaneous intravenous antioxidant treatment (MTDQ-DS) was given. The renal arteries from both sides were removed on the 3<sup>rd</sup> postoperative day.

### *Experimental groups:*

- Group 1: control, intact renal artery (C)
- Group 2: clamped renal artery (CL)
- Group 3: clamping + regional hypothermia (CL+HY)
- Group 4: clamping + regional hypothermia + antioxidant treatment (CL+HY+AO)

### *Contractility experiments:*

For the investigation of the contractility of intact and clamped renal arteries, helical strips with a width and length of 1.5–2.5 mm and 12–15 mm, respectively, were prepared from the vessels after the thorough removal of the tunica adventitia. The arterial segments were joined with the isometric sensor of the isolated measuring apparatus purchased from Experimetria Kft, which contained an organ bath composed of physiological saline solution thermostatted at 37 °C, bubbled with a mixture of 95% O<sub>2</sub> and 5% CO<sub>2</sub>. These strips of muscle were then stretched to such extent by which the passive tension emerging from the preparates could simulate mean arterial pressure characteristic under *in vivo* circumstances [1, 2]. The contractility of arterial preparates was characterized by comparing the active tension values induced by noradrenaline in the concentration range of 10<sup>-8</sup>–10<sup>-3</sup> mol/dm<sup>3</sup> [4]. Dose effect curves were prepared by plotting the tension values of the individual noradrenaline concentrations, given in the percentage of the maximum tension generated by a given preparate, against the function of the logarithm of noradrenaline concentration. ED<sub>50</sub> (effective dose) values, representing noradrenaline concentration required for inducing 50% tension, were calculated from the parameters of the curve after fitting a sigmoid curve to the points of measurement using the non-linear regressive technique. Decrease in contractility was demonstrated by the increase in ED<sub>50</sub>.

## Results

Damage in the contractile apparatus of the smooth muscle samples prepared from the vessel wall of the different experimental groups, resulting from ischaemia-reperfusion, is explicitly reflected by the differences in  $ED_{50}$  values shown in Figure 1.

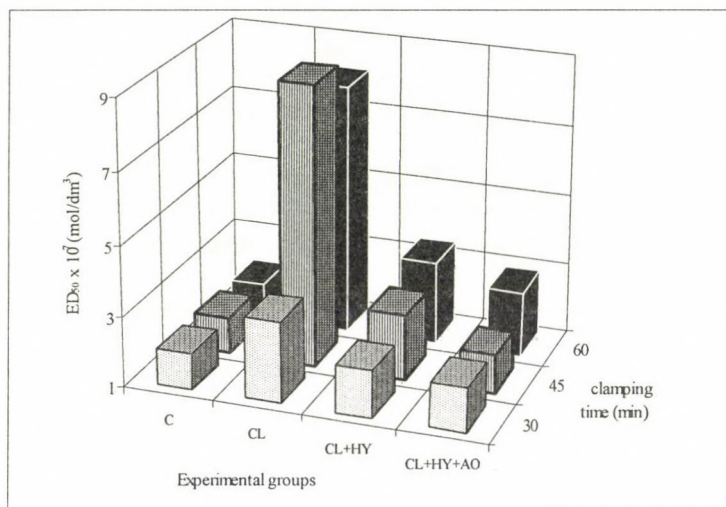


Figure 1

Noradrenaline  $ED_{50}$  values characterizing contractility of renal artery preparates

C: control artery, CL: clamped artery, HY: regional hypothermia, AO: antioxidant treatment

The individual columns represent mean  $ED_{50}$  values derived from 4–6 vessel preparates of 2–3 operations. The control value stands for the mean of 25 preparates.

*Group 1 (C):* Under our experimental circumstances, the noradrenaline  $ED_{50}$  value characterizing intact preparates was  $2 \times 10^{-7} \text{ mol/dm}^3$ .

*Group 2 (CL):* Compared with that of the control preparates, clamping for 30 minutes resulted in over 1.5-time increase in the  $ED_{50}$  value. Clamping for 45 and 60 minutes was accompanied by approximately 4-time increase in  $ED_{50}$ , i.e. a significant decrease in the contractility of the vessel wall and expressed decrease in arterial function were noted, due to clamping.

*Group 3 (CL+HY):* If in situ venous cooling was provided simultaneously with clamping, hardly any difference could be noticed in comparison with the control group when the artery was clamped for 30 minutes: increase in  $ED_{50}$  culminated at 115% in comparison with 163% recorded for samples prepared after clamping but not cooling, which means that hypothermia had a significant protective effect. If clamping lasted for 45 or 60 minutes, cooling could not provide enough protective effect, decrease in contractility was seen at 141% and 166%, respectively.



*Group 4 (CL+HY+AO):* According to our results, intravenous antioxidant treatment provided simultaneously with in situ cooling was of no further protective effect in clamping for a short period of time. However, with vessels clamped for 45 minutes, significant decrease in ED<sub>50</sub> was seen compared to the decrease characteristic of the ED<sub>50</sub> value of preparates which were protected by cooling only. If clamping lasted for 60 minutes, even the combination of cooling and antioxidant treatment proved to be ineffective in providing full protection against the damage, caused by ischaemia reperfusion, in the contractility apparatus of the vessel wall.

## Discussion

It is generally accepted today, that free radicals of oxygen origin are responsible for the damage to the tissues caused by ischaemia-reperfusion. One of the evident ways of avoiding tissue damage lies in the restriction of the formation of free radicals by either decreasing the duration of ischaemia or inducing hypothermia; another way is when the existing free radicals are eliminated by antioxidant treatment [3]. These ways were investigated in our experiments and the results are as follows:

Clamping of the renal artery, generally applied in renal surgery, results in decrease of function, i.e. decrease in the contractility of the renal artery, unless supplementary treatment is provided. If the clamping of the renal artery does not exceed 30 minutes, damage to the artery, represented by decrease in contractility, can be prevented by inducing hypothermia. The significant damage of the artery caused by clamping for 45 minutes can only be avoided if cooling and antioxidant treatment are provided simultaneously. Clamping the renal artery for 60 minutes results in significant damage to the vessel even if simultaneous cooling and antioxidant treatment are available.

## Acknowledgements

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## INTRAOPERATIVE MONITORING OF THE MOTOR PATHWAY USING TRANSTRACHEAL STIMULATION OF THE CERVICAL SPINE IN DOGS

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Although SEP monitoring of the spinal cord has been a well established method recently, not an ultimate, perfectly developed technique for monitoring of the motor system is known so far, particularly, because of the disturbing effect of narcotic drugs and relaxants on the motor evoked potentials. In this study the upper part of the spinal cord was stimulated in 14 anesthetized and relaxed dogs with a cathode attached to the intratracheal tube and an anode fixed to the cervical spinous processes. Single and serial stimuli were applied. Recordings were obtained from the exposed right femoral nerve and quadriceps muscle. Averaging was necessary when using serial stimulations. Responses were consequent and reproducible during regular anesthesia. The origin of the different responses in the spinal cord is discussed. The method seems to be appropriate for intraoperative monitoring of the thoracolumbar spine.

**Keywords:** electric stimulation, intraoperative monitoring, motor response, spinal cord stimulation, transtracheal stimulation.

### Introduction

Electrophysiological monitoring of the spinal cord enables one to make early detection of intraoperative damages during orthopedic and neurosurgical spinal operations. Motor evoked potentials in response to both magnetic and electric stimulations are usually recorded from peripheral nerves or skeletal muscles [1, 5]. It is generally easy in alert patients, but it could be problematic during anesthesia [2, 4]. Stimulation of the spinal cord and recording from peripheral nerve is another appropriate technique of motor monitoring [3]. In this study we made an attempt to stimulate spinal cord in a noninvasive way and tried to record compound myogenic as well as averaged neural responses of the motor pathway.

### Materials and Methods

Transtracheal stimulation of the spinal cord was carried out in 14 mongrel dogs weighing 14-22 kg. (The study was approved by the Regional Scientific Ethical Council for the protection of animal rights.) Anesthesia was introduced by intraperitoneal administration of ketamine  $10 \text{ mg} \times \text{kg}^{-1}$ , xylazine  $1 \text{ mg} \times \text{kg}^{-1}$  and atropine  $0,5 \text{ mg}$  and was maintained with ketamine  $5 \text{ mg} \times \text{kg}^{-1} \times \text{h}^{-1}$  and xylazine  $0,5 \text{ mg} \times \text{kg}^{-1} \times \text{h}^{-1}$ . The animals received atracurium  $0,1 \text{ mg} \times \text{kg}^{-1}$  iv., then they were orotracheally intubated and artificially



ventilated. Atracurium was maintained by  $0,2 \text{ mg} \times \text{kg}^{-1} \times \text{h}^{-1}$ . This dose of relaxant resulted in partial neuromuscular blockade and enable to record muscle action potentials. Heart rate, ECG, blood gases and body temperature were continuously monitored.

The upper cervical part of the spinal cord was stimulated with single and serial stimuli. One of the stimulating electrodes consisting of a  $20 \mu\text{m} \times 1,5 \text{ sq cm}$  thin sheet of Ag-AgCl was attached to the balloon of the intratracheal tube and pressed against the dorsal wall of the trachea with the balloon inflated. The other electrode (a  $0,5 \text{ mm}$  thin bent Ag-AgCl plate of  $4 \text{ sq cm}$ ) was fixed to the shaven and cleaned skin above the

2nd cervical spinous processes. The impedance of stimulating electrodes was kept below  $2 \text{ k}\Omega$ .

Two kinds of stimulation were applied:

(1) Single electric shock with the Digitimer D 160A constant voltage stimulator (Digitimer Ltd., Welwyn Garden City, UK). Reproducible responses could be evoked with 2,5–10 % of the maximum output (1200 V) and with  $100 \mu\text{s}$  time constant. The endotracheal electrode was used as cathode in single stimulation.

(2) Serial stimulations with the constant current stimulator unit of the Amplaid EMG 15 (Madaus Ltd., Freiburg, Germany). Rectangular impulses of  $100 \mu\text{s}$  duration and 11–16 mA were delivered at a stimulus rate of 4 Hz.

Recordings were made with an Amplaid EMG 15 amplifier in single or superimposed mode, with a bandpass of 50–2500 Hz and an analysis time of 200 msec. The gain was adjusted between 2000 – 20000 in order to obtain optimum vertical resolution of the compound action potentials. In cases of serial stimulations one hundred responses were averaged.

The recording electrodes were a pair of Teflon isolated Dantec sensory needles, the active one inserted into the epineurium of the femoral nerve, the reference electrode was subcutaneously 2 cm apart. Recordings were also obtained from the quadriceps muscle with bipolar needle electrodes.

In two animals C4 laminectomy was performed and the spinal cord was directly stimulated with epidural electrodes. Responses evoked by direct epidural and transtracheal stimulations were compared.

## Results

High voltage single electric impulses elicited reproducible bi- or triphasic responses. Depending on the stimulus intensity, latencies varied between 15–18 msec. The amplitudes varied between 150–850  $\mu\text{V}$ . The first potential was frequently followed by a polyphasic second response with longer latency and duration. No significant difference was seen between recordings to direct epidural and transtracheal stimulations. Serial stimulation resulted in a double potential complex starting with a negative peak at 20 msec when recording from the femoral nerve. No changes in vegetative parameters could be recorded during stimulations.

## Discussion

Transcranial electric or magnetic stimulation of the cortex and recording electric responses from the limb muscles are the base of monitoring of motor pathways. Successful monitoring of motor potentials evoked magnetically or electrically could be performed only under special anesthesia. The usual way of intraoperative direct stimulation of the spinal cord is an invasive method. In this study we made an attempt to stimulate spinal cord in a noninvasive way.

The origin of averaged potentials recorded from the femoral nerve during transtracheal spinal cord stimulation is not clear and raises the question of which neural structures may give rise to the early and the late potential complexes. Both efferent and afferent long tracts of the spinal cord get excited at the time of the stimulation. In addition, excitation spreads from the site of stimulation in both rostral and caudal directions. In the explanation of the origin of evoked compound potentials recorded from the femoral nerve, the following possibilities can be considered:

1. Direct excitation of the pyramidal tract elicits short latency motor responses.
2. Antidromic excitation of the pyramidal tract is reflected back from the cortical pyramidal cells evoking double responses from the alpha motoneurons. This repeated stimulation of the lower motoneuron may explain the double responses to single shock.
3. Antidromic excitation of the dorsal white column afferent tracts is represented also in the peripheral response. In view of this unidirectional synaptic transmission in the dorsal horn, the spinothalamic tract is not involved in this event.
4. Very late responses may originate from slow conducting efferent fibers. Flexor reflexes, crossed flexor – extensor reflexes may also contribute to late responses.

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## MODIFICATIONS OF AND SPECIAL OPERATING TRICKS IN THE CLASSICAL TECHNIQUE OF SURGERY AGAINST STRABISMUS

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Even nowadays the idea of most of the operations against strabismus is based on myectomy and reposition of the rectus muscles. At the Department of Ophthalmology of the University Medical School of Debrecen we use mainly these two methods of operation. At our Department we performed 1605 operations against strabismus during the last 10 years. 1269 of our patients had convergent, 336 had divergent strabismus. The majority of the operations were performed on patients less than 6 years of age, under general anesthesia. The outcome of the operation is successful if it results in a situation, in which torque affecting the eyeball stabilizes it in the normal position. The advantage of the combined surgical procedure is that the former muscular balance remains intact, and by relatively small intervention good results can be achieved. In the rectus muscles of squint patients anatomical and histopathological changes could be found, especially if they did not receive pleoptic treatment preoperatively. Depending on the direction of the strabismus one of the muscles is thicker, while the other is thinner, due to hyper- and hypofunction. Our surgical experience of many years showed that by modifying the classical technique of the operations with some fine technical tricks it was possible to increase the success rate. In our film we presented the right way of incising and handling the subconjunctival connective tissue (Tenon capsule) thus making it possible to lay it back to its original place at the end of the operation. This way the chance of postoperative scarring is reduced. We demonstrated how to test the contractility of the muscles by using muscle-hooks, that replaces the forceps test. In case of myectomy we demonstrated the tricks of how to handle the elastic muscle in the easiest and the finest way. In case of reposition we can achieve perfect reconstruction and wound healing by using the shown simple technique. We also take much care of suturing the conjunctiva during operations performed on infants that is important because of their undisciplined behavior.

**Keywords:** strabismus, myectomy, reposition, surgical techniques

According to the latest statistical data the occurrence of strabismus is 5,3–7,4% in Middle-Europe [1]. 60% of squint patients can be rehabilitated by conservative methods, the other 40% only by surgical methods [2]. Patients who had surgical intervention still may have a some residual angle of deviation even when wearing glasses. Our goal is to achieve a near to parallel eye position (angle of deviation less than 10°) by wearing spectacles after surgical intervention.

The majority of surgical procedures against strabismus are still based on the myectomy and the reposition of horizontal rectus muscles.

At the Department of Ophthalmology of the University Medical School of Debrecen we also use these methods. During the last 10 years we performed 1605 operations against strabismus at our Department. 1269 of our squint patients had convergent, 336 had divergent strabismus. Most of the operations were performed under 6 years of age, in general anesthesia.

The outcome of the operation is considered to be successful if it results in a situation, in which torque affecting the eyeball stabilizes it in the normal position [2]. The advantage of the combined surgical procedure lies in the fact that the former muscular balance remains intact, and by relatively small intervention a good result can be achieved.

During the dosage of the operation we try to affect the agonist and the antagonist muscles symmetrically, to the same extent. The dosage is not absolute, it is largely dependent on the surgical technique. Thus every surgeon has to set up his own surgical scheme [4].

In the muscles of our squint patients manifest anatomical and histopathological changes can be found, especially if they did not receive pleoptic treatment preoperatively. Depending on the direction of the strabismus one of the muscles is thicker, while the other is usually thinner, due to hyper- and hypofunction.

Our surgical experience of many years showed that by modifying the classical technique of the operations with some fine technical tricks it was possible to increase the success rate.

We open the conjunctival sack and the Tenon-capsule by one definite scissors-cut, then they are separated from each other in two layers, and not pushed back. Experience of many years' postoperative follow-up shows that the wound heals safely with minimal scarring. We realized that in case of children due to their young age and their lack of discipline safe wound closure is essential, since despite of all our efforts they often rub their eyes, resulting in opening up of the conjunctival wound, and the prolapse of the Tenon-capsule. Thus by taking into consideration the special characteristics of this age-group at the end of the operation we replace the Tenon-capsule (if necessary we cut off the edges that fold back) and in contrast to the general ophthalmic surgical practice [5] we extremely tightly suture the wound edges of the conjunctiva with interrupted stitches. For examining the muscular power most surgeons use forceps, but in order to shorten the operation prefer to pull the muscle by an inserted muscle-hook and by doing this we can replace the forceps-test. In this way we also can better judge if the muscle is thicker or weaker.

By slightly pulling the internal rectus muscle in this way we can also prevent the onset of the oculo-cardial reflex. We observed that bradycardia most frequently developed after a single sudden pull of the muscle. The slight and fine movements by which we examine the muscular resistance help to avoid this dangerous reflex.

Another modification is the application of a safety myostat attached to the muscle behind the inserted Meller-sutures in case of myectomy. Formerly especially in case of an inexperienced surgeon it often occurred, that the separated rectus muscle came out from the Meller-suture and slipped back behind the globe. The safety myostat prevents the muscle from slipping back, and is removed only after the reinsertion of the muscle.

Another useful trick is that the external rectus muscle after resection can be varied by differential tightening of the sutures. The Meller-sutures are usually not stitched back in full length of the muscle insertion line, but only in a closer part.



In case of retroposition we double mark the sclera according to the previous measures, in order to reach accurate repositioning. The first line represents the calculated value, the second behind the first one shows the point where the needle has to be inserted during suturing. The needle (and the stitch) shows up at the first line during the half thickness scleral suture, thus we can be sure that the muscle was put back at the desired distance. It is more comfortable and safer to insert the scleral suture between the two lines, and many authors agree that this is the most critical part of strabismus surgery.

At the Department of Ophthalmology of the University Medical School of Debrecen we are performing operations against strabismus with the implementation of the above mentioned modifications. Most authors agree that similar results can be achieved by various surgical techniques. It is important, however, that each surgeon should know the advantages and disadvantages of his procedure and this is why strabismus surgery needs much experience and is successful only in experienced hands [3,4,5].

The results of the past 10 years justify the correctness of our technique of surgery. Out of 1605 operations against strabismus in 1402 cases the patients had less than  $10^\circ$  of strabismic angle, and only 203 patient had larger angle. It is well known by ophthalmologists that in case of a strabismic angle less than  $10^\circ$  it is possible to fully rehabilitate the function of the eye of the children. Full rehabilitation means the perfect visual acuity of both eyes, good binocular vision, and good cosmetic result.

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## THORACIC AND LUMBAR SYMPATHECTOMY WITH THE APPLICATION OF ROMICRO MINI LAPAROTOMY SET

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The authors present the use of ROMICRO set (originally developed for mini laparotomy) for thoracic and lumbar sympathectomy. They review 3 thoracic and 2 lumbar sympathectomy operations that had good effects and uneventful recoveries. The advantage of the method is that no special instruments are needed and it can be done as a conventional operation.

### Introduction

The development of surgical techniques make it possible to use new diagnostic and therapeutic interventions that are of minimal burden for the patients. In contrast with abdominal surgery, minimal invasive techniques are not widely practised in vascular surgery. One exception is thoracic sympathectomy which can be applied safely with the use of video thoracoscopy. The alternative to the latter is the so called mini thoracotomy which was developed by Jako [2] in Boston.

The disadvantage of both methods is that they require special, expensive equipment which cannot be utilized generally in vascular surgical practice, although Weber [5] applied the Jako set for aorto-bifemoral reconstruction as well.

### Methods

The ROMICRO set developed by Rozsos [3, 4] for cholecystectomy through a mini laparotomy can be used to combine the safe conventional operation technique with minimal invasive technique. The set consists of 5-7 cm wide different length liver retractors, and a 300 watts fibre optics light source lighting the operation site. The surgical exposure is a "mini thoracotomy" modification of the axillary approach advocated by Atkins [1]. A 5-7 cm long incision is made between the 2nd and 3rd rib. The retractor with the light source is introduced proximally through the thoracotomy while the distal retractor keeps the lung out of the way. The preparation, identification of the anatomy and the sympathectomy is done with the hooks and tissue holding forceps that are used for laparoscopic cholecystectomy. A Redivac drain is left behind following closure of the thoracotomy wound.



## Results

In our department last year we carried out 3 operations using the technique described. All cases had good sympathectomy results. The patients had less post operative pain and all wounds were sound.

## Discussion

The advantages of mini thoracotomy are as follows:

- ◆ it does not require special, expensive instruments.
- ◆ conventional and laparoscopic instruments can be combined.
- ◆ there is little trauma or infection to the chest wall.
- ◆ less post operative pain is experienced.
- ◆ the incision can easily be extended if necessary.
- ◆ the operation can be carried out with an excellent light source .

We noted no disadvantage with this method.

We also used these instruments for lumbar sympathectomy in 2 instances. For the latter we used the conventional positioning and a lateral lumbar "mini" split muscle incision was fashioned. Because the light source at the end of the retractor is so good, the operation can also be done safely with the conventional instruments.

Minimal invasive techniques are often hindered by financial constrains. Currently the subsidisation by the OEP does not encourage the use of this technique. Therefore a certain set of instruments that can have multiple usage is vital. ROMICRO set can fulfill this criteria which combines the conventional technique with minimal invasive technique.

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## INTRASTROMAL CORNEAL RING, A NEW REFRACTIVE SURGICAL TECHNIQUE TO DECREASE MYOPIA. EXPERIMENTAL AND CLINICAL RESULTS

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From among the wide range of keratorefractive operations, the authors applied the intrastromal corneal ring (ICR) technique to treat myopia. The results of operations performed on dogs' eyes were evaluated using slit lamp investigations, cornea topography and histological investigations. In the possession of favourable results, this kind of operation was successfully performed on three patients suffering from expressed unilateral myopia, too. The desired optical results (10,0 dioptres) proved to be permanent 3–10 months after surgery and were demonstrated by the patients' visual acuity as well as cornea topographic examinations. The surroundings of the PMMA ring situated intrastromally and the substance of the cornea remained calm and clear, respectively. The authors think that the ICR technique can successfully be applied in the treatment of myopia similarly to refractive surgical interventions such as radial keratotomy (RK) and excimer laser photorefractive keratectomy (PRK), which are widely used methods these days.

**Keywords:** intrastromal corneal ring, refractive surgery in myopia, animal experimental and clinical results

### Introduction

Surgical interventions aimed at changing the refractivity of the cornea are collectively described as keratorefractive surgical techniques. Depending on the surgical technique, the various methods can be classified as follows: *keratotomy*; *keratectomy*; *thermo-coagulation of the cornea*; *keratomileusis* and *epikeratophakia*.

Certain operations (e.g. keratomies) only allow the decrease of the refractivity of the cornea, whereas other methods (e.g. keratomileusis, keratectomy and keratophakia) enable the surgeon to increase or decrease the refractivity of the cornea as desired. In animal experiments, keratophakia was applied to decrease the refractivity of the cornea, but, instead of using a concave lens, a PMMA ring was implanted intrastromally. Anglo-Saxon literature gave the method the name of intrastromal corneal ring (ICR). Experience about the intracorneal ring gained in animal experiments was exploited in our clinical practice.

### Materials and Methods

Operations were performed under veterinary surveillance, on mongrel dogs of medium size, following narcosis induced by Ketamin–Xylasin. A mark concentric to the optic zone was made with a trephine (used in keratoplasty) with a diameter of 7.0 mm. The optic zone itself was marked with a trephine 3.0 mm in diameter. A concentric tunnel was prepared between the two marks, in the half-thickness of the cornea, using a special knife developed by us. The PMMA ring (Medikontur Kft.) was cut through at one site and slipped into the tunnel. After the centring of the ring, the operation was completed by the



administration of subconjunctival Gentamycin and a corticosteroid. The operation was performed on one eye of 4 mongrel dogs each. Both eyes of the animals were enucleated under general anaesthesia. The animals were exterminated by administering intracardial KCl injections. The first and last enucleations were performed 2 and 6 months after the operation, respectively. The enucleated eyes were examined by slit lamp, cornea topography, and as well as histological investigations were performed. Following the evaluation of the animal study results, implantation of the intrastromal corneal ring was also performed in 3 patients with high unilateral myopia.

## Results

Slit lamp investigation: the epithelium of the operated cornea was smooth and glossy. The substance of the cornea was clear, the plastic ring was found in an interlamellary position, in a calm environment. Cornea topographical investigations: the curvature of the operated corneas had become significantly flatter as it was seen in corneal topography (Texas, USA).

Histological investigations: the serial sections were stained with haematoxylin-eosin and according to Van Gieson, following traditional fixing in formalin and sealing/embedding in paraffin. The sections showed scarce fibroblastic reaction round the foreign substance (PMMA), but no signs of rejection were noticed.

After the approval of the Ethic Council of our department and providing the patients with information, the operation was also performed on the eyes of 3 patients suffering from unilateral myopia. To stop progression, support of the sclera had been performed on their eyes. The first patient was operated on 10 months ago, whereas the third one underwent surgery 3 months ago. Optical results have proved to be permanent over the observation period:

| Case No. | Visus before operation        | Visus after operation        | Observation period |
|----------|-------------------------------|------------------------------|--------------------|
| 1.       | -2.0 D = 1.0<br>-12.0 D = 0.6 | -2.0 D = 1.0<br>-2.0 D = 0.8 | 10 months          |
| 2.       | -12.0 D = 0.6<br>-2.0 D = 1.0 | -2.0 D = 0.6<br>-2.0 D = 1.0 | 6 months           |
| 3.       | -5.0 D = 1.0<br>-17.0 D = 0.4 | -5.0 D = 1.0<br>-7.0 D = 0.4 | 3 months           |

The surroundings of the PMMA ring situated in an interlamellary position and the substance of the cornea remained calm and clear, respectively.

## Discussion

Radial keratotomy (RK) and excimer laser photorefractive keratectomy (PRK) are the most often used keratorefractive surgical methods today. Several articles discussing the advantages and disadvantages of RK have been published since the late 1970s. Excimer laser was introduced in ophthalmologic practice in the 1980s. Data collection and publication about experience are still in progress. The publication by Fleming and co-workers (1987) stirred up interest in the ICR technique, too.

Indications of the operation include the reduction or elimination of myopic refractivity disorders. It can be achieved through the proper choice of the thickness and diameter of the ring. Even in cases of expressed myopia, flattening of the cornea takes place without tissue loss, Bowman's membrane always remains intact in the centre of the cornea. Burris and co-workers (1993) described the relationship between the thickness of the ring and changes in refractivity in human cadaver eyes. Mathematical modelling of ICR was done by Fleming and co-workers (1989) and Nagy and co-workers (1995). The effect of the ring on the tissues of the cornea was investigated with light and electron microscopic techniques by Quantock and co-workers (1994, 1995).

Perforation while preparing the tunnel may be a complication accompanying the implantation of the intrastromal corneal ring. A surgically inadequate formation of the tunnel in the half-thickness of the cornea resulting in perforation – either forwards, in the direction of the epithelium, or backwards, into the anterior chamber – renders the completion of the operation impossible.

The results gained so far are promising and have certain advantages in comparison with RK and PRK.

#### ***Advantages of ICR as opposed to RK:***

The central area and edges of the cornea are spared from scarring due to multiple radial incisions.

Incisions do not reach the optic zone even if correction for high myopia is performed.

#### ***Advantages of ICR as opposed to PRK:***

There is no need for a highly expensive excimer laser device.

The intervention avoids the optic zone.

There is no need for prolonged postoperative local treatment with steroids.

No minimum transitional central corneal haze develops.

#### ***Advantages of ICR as opposed to both techniques:***

The optic zone remains sound, intact, even if high myopia is being corrected for.

Over or under-correction can be ruled out by replacing the ring to achieve the desirable effect.

The ring can be removed from the cornea if necessary, e.g. if presbyopia develops.

After the problems of optical design and dosage are solved, ICR appears to be a better technique than the two other ones used so far. As a matter of fact, the centre of the cornea always remains sound, intact, and should presbyopia develop, the original condition can be restored.

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## MULTIMODALITY TREATMENT OF PANCREATIC PSEUDOANEURISMS

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Vascular lesions of pancreatitis manifest in the form of haemorrhage into the pseudocyst (PC), the development of pseudoaneurisms (PA) or splenic lesions. Between 1987 and 1996 31 patients were found to develop vascular lesions either in the form of haemorrhage into a PC (12) or PA (19). Diagnosis of pancreatic PA was established preoperatively in 8 cases only. Gastrointestinal (GI) bleeding manifested in 12 patients, but only in 6 of them was the pancreatic origin of the bleeding considered. All patients were operated. For the management of the lesions resection of the pancreas (11 cases) or ligation of the bleeding vessel with external or internal drainage of the PC was performed (12 cases). Simple external drainage of a haemorrhaged PC in 3, and cystoduodenostomy or cystogastrostomy was performed in 5 cases respectively. Intraoperatively moderate bleeding gave some concern (7 cases), while post operatively pancreatic fistula developed in 9 patients drained externally. All stopped spontaneously. In two cases severe GI bleeding occurred post operatively. In both cases embolization of the bleeding vessels was performed successfully. No operative mortality occurred. The mean follow-up time was 40.6 months (5-106). Five patients died of unrelated causes, 3 patients underwent subsequent pancreatic operation, and 74.2 % of the patients are doing well. Development of pancreatic PA was associated with a longer observation or conservative treatment period. Angiography should be considered whenever severe upper GI bleeding occurs in patients with known pancreatic disease and the source of bleeding is obscure. In selected cases selective embolization of the bleeding site may provide definitive treatment.

### Introduction

During the course of acute and chronic pancreatitis severe complications may occur. Haemorrhage either in the form of GI bleeding or lesion to the vessels in close proximity to the pancreas is observed in between 2 to 10% of the cases [2]. Bleeding occurs most frequently in association with the development of PC. This can be in the form of haemorrhage into the cyst or the development of PA by the erosion of the wall of the vessel in association with the PC [6]. The diagnosis may present difficulties. Complication and mortality rates are high.

### Patients and Methods

In a ten years period between 1987 and 1996 2100 patients were treated with pancreatic PC and/or its complications. Among them 31 patients were found to have developed haemorrhagic lesions during the course of the disease. Data were collected from hospital charts. Etiology of the PC was acute pancreatitis in 7 and chronic in 24 patients respectively. Female/male ratio is 3/28 and average age was 45 years at the time of the operation. Time

elapsed from the onset of the symptoms was an average of 38.8 months. Diagnosis was based upon ultrasonography (US), and occasional CT scan, ERCP and angiography. Many of the patients had previous pancreatic operation.

*Clinical symptoms:* 12 of the patient had GI bleeding. Pancreatic origin as the source of bleeding was suspected only in 6 cases. 11 patient presented anaemia, 20 patients complained of severe pain, 19 had significant loss of body weight. Abdominal mass was palpable in 15 cases, jaundice was observed in 4 patients. 7 presented clinically as acute exacerbation of pancreatitis.

*Diagnostic findings:* US were performed in every patient. Single or multiple PC was verified in all cases except one. PA was suspected in 6 cases when typical US picture of onion like multi-layered haematoma or turbulence within the cyst was seen. Additionally CT was performed in 10 cases, the presence of blood in the cyst had been verified in 4 of them. ERCP had seen actual bleeding from the papilla of Vater in 2 of the 5 examinations performed.

*Surgical management:* In 30 cases the operation was indicated for the management of the pancreatic PC occasionally complicated by a PA or haemorrhage. In a single case the acute operation was performed because of sever GI bleeding susceptibly of duodenal origin. The source was not found intraoperatively. Angiography performed for recurrent bleeding proved the presence of an aneurysm of the splenic artery. Embolization provided definitive treatment. In 20 cases single or multiple pseudocysts were either drained externally or through gastro-enteral anastomosis. In 12 of these eroded vessels were ligated Eleven pancreatic resections were done.

## Results

Ethiology of the PC was acute or chronic pancreatitis in 6 and 24 cases respectively. In one patient neither previous nor present history of pancreatic disease could be verified. The average time of the known pancreatic disease was 38.6 months. The observation period for the PC was 4.7 months. There was no difference between the PA and haemorrhaged PC. All patients with PA had chronic pancreatitis.

Altogether in 9 cases did we suspect the presence of PA preoperatively. One of these proved to be false positive finding. Intraoperatively 20 PA were identified in 19 patients. Ethiology for the disease was chronic pancreatitis in all except one case, where no previous history of pancreatic disease could be disclosed. Of the six angiographic examinations 1 was false negative. Out of the three cases successfully embolised two had to be operated later for repeated bleeding. Intraoperatively in seven cases bleeding from the eroded vessel gave some concern. After evacuation of the haemorrhaged PC the injured vessel was located and ligated. Postoperative complications developed in 16 patients. There was pneumonia in one, wound abscess in one, pancreatic fistula in 10 cases respectively. All fistulae stopped spontaneously within 5–7 days following the administration of octreotide. In two patients reoperation was necessary to manage gastric leakage. In two other cases postoperative bleeding required reintervention, one patient twice. Ligation of the bleeding gastroduodenal artery within the PC was followed by selective embolization



to manage the rebleeding. This too, proved to be temporary solution, because two weeks later the patient was readmitted with GI bleeding again. This time pylorus preserving pancreatoduodenectomy was performed. In the other case selective embolization proved to be definitively effective. All patients recovered.

The follow up period was an average of 40.6 months. During this period 5 patients died of causes unrelated to the operation. Three patients required subsequent operation for their pancreatic disease, two of them for recurrent cysts, in the third case a pylorus preserving pancreatoduodenectomy two weeks after selective embolization of the bleeding gastroduodenal artery.

### Discussion and Comments

Vascular lesions in pancreatic PC are rare but serious complications. Although the incidence reported in some series reaches 10 %, in our 10 years experience of 2100 patients treated with PC the occurrence rate was 1.5 per cent. Characteristic presentation may be intermittent GI bleeding in the form of *wirsungorrhagia* if the PA or haemorrhaged PC communicates with the ductal system [7,5]. Endoscopic verification is rare, in our 12 cases of GI bleeding only 2 could be seen. CT and US may recognise haemorrhage occasionally, but angiography seems to be most effective [4]. This can demonstrate the bleeding site, and may – if necessary – be combined with embolization. In only 50% of our cases did we suspect the presence of a PA without angiography. On exploration the unsuspected opening of a haemorrhaged PC may cause some concern. The amount of blood loss can effectively be decreased by preoperative embolization [1]. Even if embolization may not be successful in all cases or may not provide definitive treatment as reported [3], in most cases the high-risk emergency operation can be avoided.

It seems from our observation that the development of a PA is associated with a longer observation period of chronic PC. Therefore it is advisable, that PC not resolving spontaneously within 6–8 weeks should be treated more actively.

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## **BENEFITS OF CELL SAVER DURING THE OPERATION OF GASTRIC HAEMORRHAGE FOLLOWING REPEATED PANCREATITIS**

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Authors report on a case of repeated pancreatitis causing several characteristic complications and concluded to splenic vein thrombosis, with an enlarged perisplenic vein network. The source of gastrointestinal bleeding is uncommon: originates from the submucous vein of the stomach. Cell saver was used under splenectomy because of great blood loss, and due to hyperimmunisation occurred as consequence of massive transfusion. The benefit of cell saver was clearly evident from both point of view.

### **Introduction**

Cell saver was first used in the 80ties [2]. It reduces the amount of blood need, and also prevents the hyperimmunisation may occur after high volume transfusion of foreign blood. Therefore cell saver usually used in cardiothoracic and vascular surgery, liver transplantation. In our case cell saver was indicated because of both aims to achieve: blood loss, and irregular antibodies in the patient, who had suffered of segmental portal hypertension causing gastrointestinal bleeding.

### **Case report**

The 37 years old female had a long medical history of diabetes mellitus, hyperlipoproteinaemia, recurrent pancreatitis. She had been operated on due to pancreatic pseudocyst: cystogastrostomy, and coecostomy had been performed. As consequence of repeated pancreatitis thrombosis of the splenic vein and segmental portal hypertension occurred years ago. Repeated but unsuccessful trials of splenectomy were taken place in abroad. In 1995 she has been operated on because of gallstone. After an uncomplicated period she was admitted because of acute gastrointestinal hemorrhage, which collapsed her circulation as well. Gastroscopy didn't find any source of bleeding. After repeated bleeding she was operated on with vital indication. Extremely enlarged perisplenic vein network was detected, as well as dilated veins in the stomach mucosa. Partial sclerotherapy of the stomach was performed. In spite of these efforts we were able to maintain her circulatory balance only by massive (2 U/day) transfusion. In summary she received about 16 units of blood. Repeated gastroscopy (with negative result), and



angiography (coeliacography, indirect portography) were indicated on the 12th day of admission, due to shocking bleeding. This showed vena lienalis thrombosis, but free portal stream. By this time irregular antibodies has appeared in the patients sera, and the patient had shivers at blood transfusion therefore transfusion was considered to be dangerous. We decided to perform splenectomy [1, 3]. From left thoracolaparotomy the enlarged spleen was removed with difficulties. During the operation 3U blood was used, and 2400 ml was recirculated by cell saver. The patient recovered.

### Discussion

Cell saver is very useful in operations requiring great amount of blood, or even in those where the patient is hyperimmunised. In our case both causes were present since the patients received 50 units blood during the hospitalisation.. By the time of the appearance of irregular antibodies, and the signs of immunisation, the patient condition deteriorated. The indication for operation was vital [1, 3]. The use of cell saver resolved both problems. We had no circulatory, no recovering problems with the patient. The duration of the operation was almost 4 hours with an acute blood loss of 4000 ml. During the 39 days of her treatment, the patient received 50 units blood.

### Result

The patient is in good condition, has put on weight, she is without any signs of recurrent pancreatitis. Her diabetes, and hyperlipoproteinaemia are balanced with regular check-up, and medical treatment. Gastrointestinal bleeding didn't repeat so far. The size of the spleen was 22x14x5 cm. Histology verified chronic perisplenitis.

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## EVALUATION OF URINARY ENZYMES IN RENAL ALLOGRAFT DAMAGES BY HISTOLOGY EXAMINATION

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Acute allograft rejection (ARE) is one of the most current problem in kidney transplantation. Urinary enzymes (glutathion-S-transferase /GST/, dipeptidil-dipeptidase /DPP/) are frequently used as prognostic factors of ARE. The authors compared the results of light microscopic study (by Banff scheme), and the GST, and DPP secretion in acute rejection. The correlation between the laboratory, and histology findings wasn't significant. Our results suggest that both GST, and DPP are very sensitive, but less specific indicators in ARE, since their activity increases in many other damages as well.

### Introduction

Enzymuria is a frequent finding among renal allograft recipients suffering of acute rejection (ARE). However the value of these urinary enzymes in the diagnosis of ARE remained uncertain. Several investigation had been performed to establish the right values of DPP, GST enzymes in the prognosis, and diagnosis of acute rejection [1,3,5]. The target of the previous experiments were to prove whether the urinary enzymes has elevation prior to acute rejection. The results demonstrated that both enzymes had marked (ARE) two days before the clinical symptoms occurred. Since the successful treatment depends on the early diagnosis, we tried to verify the sensitivity, and specificity of glutathion-S transferase (GST), and dipeptidil peptidase (DPP) monitoring for ARE.

### Aim of the study

The present experiment was destined for eliminating the subjective elements of the diagnosis. Therefore we have selected those patients whom biopsies were taken from. The histopathologic findings and laboratory results became comparable due to their objectivity.

### Patients and Methods

Till the deadline of this abstract 23 graftbiopsies were analyzed by light microscopy, following the standard stains, and technique. Diagnosis, and grading of rejection was set by the Banff-scheme [2]. From every patient urine sample was taken on the morning of the biopsy. DPP, GST-pi, GST-a, gGT urinary enzymes were measured by ELISA, and all values were corrected by the actual urine creatinin [4]. The results were then evaluated in groups, and analyzed statistically. The groups were: acute rejection (ARE), chronic rejection (CR), and tubulopathy (TP).



## Results

In our population there were 17 women and 14 men. The average age was app. 45 years. The renal disease resulted in end stage kidney chronic glomerulonephritis was in 21 cases, chronic pyelonephritis in 8 cases, diabetes mellitus in one and unknown in two. Except one every patients had their first renal allograft, and all grafts were of cadaver origin. The standard immunosuppression meant ciclosporin, and steroid in all cases. In majority of the cases biopsy was taken because of rising creatinin, in three due to diminishing urine. There were 17 cases of ARE, 4 cases of chronic rejection (CR), 8 cases of ischaemic tubulopathy (TP), one recurrent glomerular alteration, one interstitial nephritis, and one anaemic infarct of the kidney.

*Results in the ARE group were:* DPP:  $0.545 \pm 0.632$  U/mmol creat, gGT:  $3.973 \pm 3.215$  U/mmol creat, GST-pi:  $9.07 \pm 9.83$   $\mu$ g/mmol creat, GST-alpha:  $1.66 \pm 3.71$   $\mu$ g/mmol creat. *The results in the CR group were:* DPP:  $0.867 \pm 1.53$ , gGT:  $9.80 \pm 17.2$ , GST-pi:  $7.78 \pm 8.76$ , GST-alpha:  $1.99 \pm 3.44$ . *In the patients with tubulopathy:* DPP:  $0.198 \pm 0.184$ , gGT:  $2.08 \pm 1.33$ , GST-pi:  $10.87 \pm 22.01$ , GST-alpha:  $1.40 \pm 3.33$ . No significant differences were found at all. Almost significant differences were measured in DPP values in ARE vs TP ( $p < 0.086$ ), as well as in gGT in ARE vs CR groups ( $p < 0.08$ ), and in ARE vs TP ( $p < 0.07$ ).

## Discussion

Both enzymes found to be effective markers in ARE. DPP had higher elevation in patients with ARE, then it was in TP, while gGT was almost significantly different in ARE vs CR, and TP groups. The low level of urine GST-pi in tubulopathy may be the consequence of continuous tubuloe epithel damage. The highest GST-pi result was detected in patients with Banff grade III. ARE, showing eosinophilia, which is a frequent finding in steroid resistant rejections. GST-alpha is said to be elevated in acute tubular necrosis. In our cases where the signs of tubular regeneration were all present in the biopsies GST-alpha remained relatively low. Although we should not conclude to significant prognostic value from this material the necessity of further experiments became clear. DPP, GST-pi seems to be very sensitive, but less specific indicators of acute allograft rejection.

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## THE PRINCIPLE AND PRACTICE OF THE MINIMAL INVASIVITY IN THE COURSE OF OUR TRAUMATOLOGICAL WORK

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The authors examine which experiences can be deduced, in the course of their daily accident surgical work, from the minimal invasive surgical treatment of fracture contradicting many times the principles of the surgical treatment of fracture standardized by AO International.

### Introduction

Owing in part to change of biological attitude, in part to financing reasons every manual profession is in quest of the minimal invasive surgical interventions.

This effort affected also the traumatology where the striving after the so called biological osteosynthesis begins to gain ground also in Hungary, so much the more as it hardly requires separate array of instruments – as contrasted with other professions [1].

### Methods

The method is employed since 1995 by a fast widening circle, at the operational treatment of the fractures of extremity bones [1]. The fracture of the humerus diaphysis as well as of its both metaphysis is secured by intramedullary splinting as well as by percutaneous stitching. In the selected cases of fracture of the olecranon we perform percutaneous screwing. The fractures of the ulna and the radius diaphysis is fixed by percutaneous intramedullary splinting [4].

At the osteosynthesis of fracture of neck of femur only the percutaneous screwing will be chosen as the operational solution [3]. In the case of the fracture of femur diaphysis the plate inserted subcutaneous is suitable for the minimal invasive technique applicable by us [2,4]. The treatment of fractures of the tibia is performed by UTN intramedullary nailing [2,4].

In the case of injuries of the external ankle region we choose the percutaneous screwing as well as the subcutaneous plating as the minimal invasive solution [5]. At the treatment of the calcaneus fractures we utilize routinely the Zdravetz-style replacement and the percutaneous screwing.



## Results and Discussion

At the injuries suitable for biological osteosynthesis we don't uncover the fractured end in the traditional way but covered reposition will be performed, exploiting the potentials of the ligament taxis, than those will be secured by Kirschner wire stitching as well as screwing inserted percutaneous, if necessary by plate placed in subcutaneous, in such a manner that the fractured zone will be brought by plate. Screw will be driven in – also percutaneous – only into one-one or two-two holes of the plate [1,4]. In these cases we aim only at the exact reposition of the dislocations in rotation and axis direction, beside the setting of the original bone length [1,4]. The reason why from time to time we disregard the anatomical reposition required by AO is because we want use the advantages of the minimal invasive osteosynthesis.

At the method of the minimal invasive osteosynthesis – because we avoid the traditional uncovering and open reposition of the fractured ends – there is less danger of developing postoperative septic complication, the sliding surfaces don't damage, cicatrize, the vascular supply and innervation as well as periosteum don't damage, hereby the bone healing is stabiler and a better function can be expected following the operation [4].

As disadvantage of the procedure can be mentioned the postoperative outer fixation as well as the greater X-ray loading accompanied by the percutaneous technique necessary in a group of the cases.

## Summary

The short period examined by them and the small number of cases still make no statistical analyse possible. We draw the conclusion that in the selected cases the biological osteosynthesis means a significantly lesser traumatization for the injured person, effectuated with adequate practice the operation time is far shorter, the postoperative complications are fewer, the time of the hospital stay is shorter, the injured can return earlier to his or her work, sport, everyday activity, and there can be expected a faster, more stabile bone healing and consequently the removal of the metal material indicates a considerably lesser – often ambulatory – intervention.

If the financing system of the Social Security endows it properly it can be well used also in the "one day surgery".

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## 10 YEARS EXPERIENCE IN PERFORMING SHOULDICE OPERATION

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206 male patients were operated for primary direct and indirect inguinal hernia, or both, by Shouldice technique at general surgical departments of Madadeni Hospital, Newcastle, South Africa, Pásztó Hospital and Szolnok MÁV Hospital, Hungary between 1986 and 1996. Mean age was 51 yrs  $\pm$  15 yrs (17–91 yrs). The operations were performed by the original way of Shouldice described that type of hernia repair in 1945. 175 patients had spinal and 31 patients had local anesthesia with intravenous fluid and sedation respectively. Studies indicate that collagen metabolic dysfunction plays a major rule in the etiology of groin hernia. Until this is more clearly defined, surgeons will continue to repair groin hernias constitute 15% of operations in general surgery. In approach to groin hernia, the best view for examination of the inguinal region can be obtained by Shouldice technique to decide the proper surgical intervention to repair groin hernia. With low recurrence rate and rapid rehabilitation, author reports 2% of recurrence rate, the Shouldice operation highly recommended.

**Keywords:** Shouldice-operation, recurrence rate

### Introduction

The repair of inguinal hernia continues to be one of the most frequently performed operations in Hungary, equivalent to cholecystectomy and appendectomy, about 10–15% of all at general surgical departments [2]. There can be little question why surgeons avidly read publications on this subject.

### Materials and Methods

206 male patients were operated for primary direct and indirect inguinal hernia, or both, by Shouldice technique at general surgical departments of Madadeni Hospital, Newcastle, South Africa, Pásztó Hospital and Szolnok MÁV Hospital, Hungary between 1986 and 1996. Mean age was 51 yrs  $\pm$  15 yrs (17–91 yrs).

The operations were performed by the original way of Shouldice described that type of hernia repair in 1945 [3]. 175 patient had spinal and 31 patients had local anesthesia with intravenous fluid and sedation respectively. Bilateral hernias were usually operated three weeks apart.

Polymer sutures were choosen to close peritoneal sacs and for closure of the fascia or aponeurosis, a more permanent and inert sutures are required, monofilament nylon or polypropylene were used, as the aponeurosis takes 6 months to regain 60% of its



strengths. For skin closure steel clips were in use. A closed suction drain is placed in the subcuticular tissue if there is likely to be a haematoma [3]. All Shouldice operations were done by a single surgeon, the author.

## Results

None of the patients died within 30 days from the hernia repair. Unfortunately, since the operations were performed in various hospitals, only 70% of patients were checked at follow-up time. No major complications occurred in the postoperative period, two recurrences were revealed in the first postoperative year and one in the third year. Thus we are unable to confirm the proper recurrences rate of total operations but it can be stated that it is about 2–3% considering the data of literature available [1, 4].

## Discussion

Experience with the four-layer Shouldice technique is increasing, with confirmatory reports of rapid rehabilitation and few recurrences. The Shouldice repair for inguinal hernia is an operation that draws from many of the steps introduced in the last 100 years of eminent contributors to surgery, like Bassini – ligation of the sac; Marcy, McVay – division of the inguinal floor; Condon – inclusion of the iliopubic tract in closure and Bassini, Halsted, McVay – closure of the inguinal floor. The most important aspect of the Shouldice operation lies in the dissection demonstrating the presence of all possible hernias and bring about exposure of the structures necessary for an adequate herniorraphy [3]. Infections are rarely over 1% due to the fact that most operations are elective on healthy individuals. In performing hernia repair by Shouldice technique, there is a main task with no tension between the adjacent tissues, not over 1,3 kg pull, and the sutures need only maintain a holding action for about a year until the remodeling process in healing results in a stable aponeurotic structures [3].

The Shouldice operation has many advantages, the lowest recurrence rate of individual surgeon known to have exceptionally large personal experience with Shouldice hernia repair is below 1%, the average of the collected results is about 1,5%. The average hospitalization is about 3 days and returning to work and assuming full duty takes two-three weeks [4].

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## DOSE DEPENDING EFFECT OF THE COMPLEX ACTION HEMOCORRECTOR "LACTOSORBAL" ON THE MOTILITY OF THE DISTAL COLON IN THE PARALITIC ILEUS DOGS

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For the model of paralytic ileus caused by the severe surgery it has been studied the influence of different doses of hemocorrector of "Lactosorbal" on distal colon motility. It has been established that stimulating effect of "Lactosorbal" on the motility of distal colon is of the dose-dependent nature. The results of the current survey are making the ground for multiple use of "Lactosorbal" to reach the most beneficial outcome of severe paralytic ileus resulting from major traumatic surgery in clinic.

### Introduction

Postoperative period in 7–22% of cases is complicated by development of multiple organ failure (MOF) in patients have come through urgent operations. It was established that gut plays the special role in causing and development of MOF, and it is determined as "the motor" of this syndrome [1]. In this case up-to-date principles of intensive care in postoperative period must aim not only at elimination of results of homeostasis gut functions disorders, but also at simultaneous rehabilitation of its motility. As it was shown earlier on the "Lactosorbal" ("LS") transfusions in hemorrhagic shock dogs exercised the influence on central cardiohemodynamic functions and metabolism normalization, thereby were conductive to animals surviving [2].

### Methods

The study was carried out in 10 dogs in which paralytic ileus has developed after severe operation. Distal colon (DC) motility was judged by changings of contractions' frequency (CF), mean amplitude of contractions (MAC) and motor index (MI) being measured by method of tensography. "LS" which is a 5% albumin solution containing 20% sorbit solution, sodium lactate (180.0 mmol/l)  $\text{Na}^+$ ,  $\text{K}^+$ ,  $\text{Ca}^{2+}$ ,  $\text{HCO}_3^-$  in the recipe of Ringer's solution was administrated into v. cephalica antebrachii at the dose of 10.0 ml/kg (1<sup>st</sup> group) and 20.0 ml/kg (2<sup>nd</sup> group) after 24 hrs later the operation.



## Results and Discussion

It was established that "LS" transfusion against the background of complete absence of motility in the 1st group has conducted single quickly disappearing contractions in DC, while in the 2nd group already  $5.7 \pm 1.9$  min later "LS" administration appeared periodical contractions in DC. By this the FC, MAC and MI have reached  $5.6 \pm 2.8$  in 5 min,  $20.7 \pm 5.8$  mmHg and  $5.2 \pm 1.4 \times 5$  min, correspondently, and duration of the effect of action was made  $27.1 \pm 5.8$  min. Complete and steady recovery of DC motility in both groups of dogs was occurred at the 4–6 days after transfusions of "LS". Generalized analysis of literature data enables to conclude that "LS" positive influence on DC motility depend on 20% sorbit solution being in its compound. It was established that sorbit is capable of stimulation of villikinine secretion, which intensifies contractions of intestinal fibres. Besides, the fructose being formed from sorbit in metabolism pathways releases an energy, that is received by muscle membrane of intestine. Cholecystokinetic action of sorbit is also of great importance [3].

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## **STEREOMATIC CONSTANTS OF THE BILIARY TREE IN NORMAL FUNCTIONAL STATE AND DURING EXPERIMENTAL CHOLESTASIS**

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It has been found from the study of cholangiograms and laboratory specimens of biliary systems of human beings and dog's that the decrease in average diameters of biliary ducts during their passage from the hepatic portals to the periphery, is in accordance with the equation  $D = e^{-kz+b}$  ( $z$  - sequence no of the duct,  $D$  - diameter of the duct,  $k$  - rate of change in the diameter,  $b$  - logarithm of diameter when  $z = 0$ ). It has been established that parameter ( $b$ ) defines size of the liver, and parameter ( $k$ ) does not depend upon hepatic dimensions and changes during pathological processes. The use of ( $k$ ) is recommended as an aid in defining the general character of dynamics of the duration of a given pathology.

### **Introduction**

The problem concerning the blockage and obstruction of biliary ducts. From our point of view a more deep and detailed knowledge about the structure and the functional peculiarities of the biliary tree, whether in normal condition or during pathological condition; would have been useful in the search for new diagnostic methods, treatments and prognosis about the severity and duration of a given pathology or defect. Currently only absolute importance of the diameters of bile ducts during normal activity or pathology has been established. Such experiments have been conducted only on the basis of resemblance to the bronchial tree [1].

Aim. To define a mathematical character of the structure of the biliary tree during normal functional activity or disease. The main objective is to use the above equation to create a clear picture of the dynamics of duration of certain illnesses.

### **Materials and Methods**

For the revelations of the regularity of biliary duct structure, our experiments were conducted on the basis of cholangiography and specimens of biliary system of human being and dog. The structure of a normal biliary tree in a human being was studied with the help of corrosive preparations (5 pes) and during extrahepatic cholestasis by the results of intraoperation cholangiograms (10 pes). The structure of a biliary tree of the dog's in it's normal state and by the extrahepatic cholestasis was studied with the help of corrosive preparations (on 5 pes). The extrahepatic cholestasis was created by applying a ligature to the common bile duct, for a duration of 7 days. With the help of ocularmicrometer the diameters of bile ducts were defined to the 7th level. Average diameters were obtained in every order of branches with the help of variation statistical method.



## Results

The results helped us to confirm our hypothesis about the exponential character of changes in the diameter of the biliary ducts from hepatic portals to periphery according to the formula  $D = e^{-kz+b}$  ( $z$  - sequence no of the duct,  $D$  - diameter of the duct,  $k$  - rate of change in the diameter,  $b$  - logarithm of diameter when  $z = 0$ ). In order to calculate the values of ( $k$ ) and ( $b$ ) it is preferable to use the method of least square root. According to the formula  $D = e^{-kz+b}$  have been for every case defined theoretical values of biliary duct diameters (+1%) proves convincingly the exponential characters of biliary tree structure.

In addition it turned out that value of ( $k$ ) is constant and value ( $b$ ) undergoes changes in accordance with hepatic dimensions. Some differences in the structure of the liver and biliary duct network of the human being and dog lead to different values of ( $k$ ). In a human being during normal functional activity  $k = 0,35-0,37$  and in a dog  $k = 0,62-0,64$ . During disease or dysfunction changes take place in the diameter of bile ducts in the form of an exponential curve. Only in this case the value of ( $k$ ) in a human being increases upto  $0,63-0,65$ . During such a process greater deviation of practical values from theoretical values in the primary sequence of bile ducts (2-3%). In a dog a greater percentage of primary ducts is situated extrahepatically; that is why here the deviation is ever greater (5-7%). The diameter of intrahepatic biliary ducts is completely changed in accordance with the exponential curve. And the value of ( $k$ ) increases to  $0,83-0,85$ .

## Conclusion

Commonness in structure and function of biliary systems of a human and a dog is reflected in the exponential character of changes in the diameter of ducts during their passage from hepatic postals to periphery. In this case the value of ( $k$ ) is not dependent on hepatic dimensions and changes only during pathology. So the value reflects the general state of the biliary tree and it can be used for the characteristics of the dynamics which relates to the duration of a pathological process. A greater deflection of values of diameter of extrahepatic ducts from theoretical exponential curve indicates a greater level of damage then to intrahepatic ducts in event of extrahepatic cholestasis.

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## IS DNA ANEUPLOIDY A PROGNOSTIC FACTOR IN GASTRIC CANCER?

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Flow cytometric analysis of DNA ploidy was performed on an archival material obtained from 79 patients with gastric cancer who underwent a potentially curative (R0) stomach resection with D2 lymphadenectomy, and evaluated its relationship to conventional pathologic parameters, TNM stage and prognosis. No significant association between DNA aneuploidy and either patients' sex, depth of tumor infiltration (pT), lymph node involvement (pN), histological type according to Ming, macroscopic type according to Borrmann or tumor localization was found. However, the incidence of DNA aneuploidy was significantly lower in tumors of diffuse type according to Lauren, in tumors of signet ring cell or undifferentiated type according to WHO classification, in poorly differentiated/undifferentiated tumors and in patients younger than 50 years. We found no significant difference in survival between patients with DNA aneuploid tumors and those with DNA diploid tumors. Although the prognosis of patients with tumors of lower DNA index ( $DI < 1.2$ ) tended to be better than for those of higher DNA index ( $DI > 1.2$ ), the difference did not reach a statistically significant level ( $p = 0.09$ ). TNM stage, depth of tumor infiltration (pT) and lymph node involvement (pN) were the only factors that significantly affected survival in univariate analysis and both pT and pN retained their independent prognostic significance in multivariate analysis.

### Introduction

In spite of improvements in early diagnosis and surgical treatment, mortality of patients with gastric cancer remains high. DNA ploidy has recently been shown to have a prognostic relevance in a number of solid cancers and it has been suggested that DNA ploidy can be used as a prognostic factor in gastric cancer as well [1].

The aim of our study was to assess the relationship between DNA ploidy of gastric cancer cells determined by flow cytometry and known histomorphologic parameters, and to evaluate its prognostic significance in patients who underwent a potentially curative (R0) resection of the stomach with D2 lymphadenectomy.

### Patients and Methods

Patients with gastric cancer treated at Department of Gastroenterologic Surgery, University Medical Center in Ljubljana who underwent a potentially curative (R0) resection of the stomach with D2 lymphadenectomy during years 1988 through 1990 were included in the study. Those who died within 30 days after resection and those with



incomplete follow up information were not included in the study. There were 79 patients eligible for the study. The tumors were histologically graded and classified according to the WHO, Lauren and Ming criteria. The pathologic stage was defined according to the UICC TNM classification. DNA ploidy of the tumors was analyzed by flow cytometry using formalin-fixed paraffin-embedded material. Cell suspensions were prepared according to a modification of the Hedley's method as described by Heiden et coworkers [2]. The cell population was considered diploid when exhibiting a single G0/G1 peak with corresponding G2/M peak in DNA histogram. Cell populations showing two or more G0/G1 peaks in DNA histograms were classified as aneuploid and the leftmost peak was considered to represent diploid cells. DNA index (DI) of tumor cells was calculated by dividing the modal channel number of the aneuploid G0/G1 peak by the modal channel of the diploid one. The quality of DNA histograms was quantified by coefficient of variation (CV) for the diploid G0/G1 peak. Samples showing a CV value of 7 or more were excluded from further analysis.

Statistical analysis of the data was performed by the chi – square and the Fisher exact test. Survival distributions were calculated according to method of Kaplan and Meier. The outcomes from different groups of patients were compared by long-rank test. The Cox regression model was used in multivariate analysis of survival data.  $P < 0,05$  was considered statistically significant.

## Results

Evaluable DNA histograms with CVs ranging from 2.92 to 6.69 (mean 4.42) were obtained in 76 out of 79 cases. DNA aneuploidy was identified in 39 cases (51%), whereas 37 cases (49%) were diploid. DNA indexes of aneuploid tumors ranged from 1.11 to 2.29 (mean 1.56).

There was no relationship between DNA ploidy and either patients' sex ( $p > 0.05$ ), localization of primary tumor ( $p > 0.05$ ), depth of tumor involvement (pT) ( $p > 0.05$ ), lymph node involvement (pN) ( $p > 0.05$ ), pattern of tumor growth (Ming) ( $p > 0.05$ ) or macroscopic type (Borrmann) ( $p > 0.05$ ); however, the incidence of DNA aneuploidy was significantly lower in patients younger than 50 years ( $p = 0.026$ ), in tumors of signet ring cell or undifferentiated histology ( $p = 0.020$ ), in G3/G4 tumors ( $p = 0.029$ ), and in tumors of diffuse type ( $p = 0.005$ ). Only depth of tumor invasion (pT), lymph node involvement (pN) and pTNM stage significantly correlated with overall survival in univariate analysis. Both pT and pN retained their independent prognostic significance in multivariate analysis with respective relative risk of 2.76 and 1.62.

There was no significant difference in survival between patients with diploid and those with aneuploid tumors. Survival of patients with lower DNA index ( $DI < 1.2$ ) tended to be better than that of higher DNA index ( $DI > 1.2$ ), but the difference did not reach a statistically significant level ( $p = 0.09$ ).

## Discussion

Flow cytometric analysis of archival paraffin-embedded specimens of gastric carcinoma in patients with known outcome enables a retrospective evaluation of relationship among DNA ploidy of tumor cells, histopathological characteristics and patient survival.

The reported incidence of aneuploidy in gastric carcinoma differs widely, from 27% to 89% [3, 4]. These discrepant results may be partly due to inter-laboratory differences in material (fresh vs. archival), sample preparation and staining, data acquisition, as well as different classification criteria for ploidy determination. In the present series aneuploidy was detected in 51% of cases, an incidence comparable to that reported in other studies using archival material [3, 5]. We found a significant correlation between DNA ploidy and age of the patients, WHO histologic type, histologic grade and Lauren's type, with diploid DNA pattern being more frequent in patients younger than 50 years, in tumors of signet ring cell or undifferentiated histology, in poorly differentiated/undifferentiated (G3/G4) tumors, and in tumors of diffuse type. A higher incidence of aneuploidy in older patients has been reported in several flow cytometric studies of gastric carcinoma [3, 5], and some investigators also noted its association with higher degree of differentiation [6] and Lauren's intestinal type [4]. The latter finding, together with the reported presence of DNA aneuploidy in chronic atrophic gastritis and in severe dysplasia of gastric mucosa [7] which are regarded as precursors of intestinal type of gastric adenocarcinoma, supports Lauren's distinction of two different types of gastric carcinoma, i. e. intestinal and diffuse.

Majority of studies which found DNA ploidy of gastric carcinoma to be of prognostic value included large proportions of tumors in advanced stage [8], therefore it seems that prognostic impact of DNA ploidy is strongest in these tumors. Indeed, results from some studies indicate that ploidy affects survival only in advanced gastric carcinoma [8]. Thus, the fact that stage I tumors comprise a relatively large proportion of the present series, may be responsible for our failure to find an association between DNA ploidy and prognosis. Prognostic influence of DNA ploidy was shown in some studies only in the intestinal and not in the diffuse type of gastric carcinoma [4]. While we were not able to confirm this, our finding of different ploidy pattern suggests that aneuploidy may have different biological significance and different prognostic implication in these two tumor types.

Most investigations on prognostic value of DNA content in gastric carcinoma are based on comparisons between diploid and aneuploid tumors; however, some studies indicate that aneuploid tumors with higher DI carry worse prognosis than those with lower DI [8]. In fact, some authors obtained better prognostication when dividing tumors according to their DI [9]. A similar tendency was observed in our series: difference in survival was more evident when comparing tumors with  $DI < 1.2$  and those with  $DI > 1.2$ , although it did not reach statistical significance.



## Summary

From the results of our study it seems that DNA aneuploidy of gastric cancer has only a limited prognostic value in patients in whom a potentially curative (R0) resection with D2 lymphadenectomy has been performed and whose prognosis is mainly determined by the TNM stage. DNA aneuploidy seems to be the result of tumor progression and becomes an important prognostic factor in stages when the disease is already beyond the reach of current surgical treatment. Flow cytometric determination of DNA content enables observation of changes in cellular DNA during the progression of tumorous growth, but it does not perceive subtle molecular changes which determine the biologic aggressiveness of the tumor.

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## THE USE OF MODIFIED BAYLOR SCORE IN THE PREDICTION OF REBLEEDING IN PEPTIC ULCER HEMORRHAGE

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The upper gastrointestinal bleeding is still an everyday problem. 40–50% of these bleedings are originating from peptic ulcer. The rate of rebleeding after initial hemostasis is 30–50%. In this group of patients we can observe the highest morbidity and mortality. The aim of this work is to select those patients who belong to the high risk group from the point of rebleeding. For this purpose we introduced after a retrospective analysis the modified Baylor score. In this scoring system the age, the number and severity of parallel illnesses, the hemostatus by the admittance, the ulcer size and location and the stigmata of recent hemorrhage are taken into consideration. On the basis of this every patient gets a score between 0 and 31. Based on our retrospective analysis we could establish three grades of risk groups: low risk (0–7), middle risk (8–11) and high risk (12 and over). In the low risk group there was no rebleeding. In the middle risk group we observed 4 rebleedings in 19 patients, while in the high risk group there were 32 rebleedings out of 36 cases. As a conclusion we can state, that the modified Baylor score is capable for the selection of high risk patients for rebleeding. With the early elective operations in these cases the high morbidity and mortality can be reduced.

### Introduction

The treatment of upper gastrointestinal bleeding (UGB) is still a challenging task for the surgeons. The 40–50% of UGBs originate from peptic ulcers according to different authors [2]. The rebleeding after spontaneous cessation of successful initial endoscopic hemostasis remains an important determinant of poor prognosis at these patients. The average rebleeding rate among peptic ulcer bleeders is between 30–50% [1, 2, 3]. The mortality in this group is 6–12 fold higher than is that without rebleeding, and it can reach even 30% [1, 3]. From the point of further improvement in outcome it is important that we be able to predict which patients are likely to rebleed.

### Methods

In the past few years we could read several papers about the possibilities of the prediction of further hemorrhage in case of peptic ulcer bleeding [5]. In our material we also observed an increased rebleeding rate in case of endoscopic stigmata of recent hemorrhage. Saeed et al. published in 1993 the "Baylor score" for this purpose [4]. This scoring system deals with five variables. These are the age, the number and severity of coexisting illnesses for the determination as preendoscopy, and ulcer location and stigmata of recent hemorrhage for the determination as the endoscopy score. The



postendoscopy score is calculated by the sum of the preendoscopy and edoscopy scores. On the basis of this scoring system they distribute the patients from the point of rebleeding for low risk (equal or under 10 points), and high risk (over 10 points) group. We carried out a retrospective analysis of our patients with peptic ulcer bleeding in 1995–96. We determined their Baylor score and their rebleeding rate. According to different authors and our observations as well the patients hemostatus and the ulcer size has also an important predictive value in rebleeding. Accordingly we made a modification of the Baylor score adding this two variables to it, and calculated a modified Baylor score (Table 1). We made a comparison of the two scoring systems.

**Table 1.**  
**The modified Baylor score**

|                              | 0      | 1       | 2      | 3        | 4                  | 5      |
|------------------------------|--------|---------|--------|----------|--------------------|--------|
| <b>Preendoscopy findings</b> |        |         |        |          |                    |        |
| Age                          | < 30   | 30–49   | 50–59  | 60–69    |                    | > 70   |
| Hemoglobin level g/%         | > 120  | 100–120 | 80–99  | 60–79    | < 60               |        |
| Number of illnesses          | 0      | 1       | 2      | 3        | 4                  | 5– > 5 |
| Severity of illnesses        |        |         |        | Chronic* | Acute**            |        |
| <b>Endoscopy findings</b>    |        |         |        |          |                    |        |
| Site of bleeding             |        |         |        |          | Posterior wal bulb |        |
| Stigmata of bleeding         | F/III. | F/II/c  | F/II/b | F/I/b    | F/II/a             | F/I/a  |
| Size of ulcer cm             | < 1    |         | 1–2    |          | > 2                |        |

\* / Presence of a concurrent chronic life-threatening illness

\*\* / Presence of a concurrent acute life-threatening illness

## Results

During the mentioned two years we treated 234 patients because of UGB, among them were 108 peptic ulcer hemorrhage. Rebleeding occurred in 36 cases (33.3%) The average Baylor score among the non rebleeding patients was 5.42, and among the rebleeders 10.83. There were 12 patients out of 70 non rebleeders who belonged into the high risk group, and 18 patients out of the 38 rebleeders, who belonged to the low risk group. Altogether in 30 cases (27.8%) the scoring system gave a false result. According to the modified Baylor score the average score among the non rebleeders was 6.4, and 16.5 in the rebleeding group. There was no rebleeding under 8 points, so we established the low risk group between 0 and 7 points with 53 patients (Table 2).

The 88,9% of rebleeding patients had more than 11 points, and on the other hand, the 94,4% of non rebleeding patients had equal or less than 11 points. So we created a middle risk group between 8 and 11 points. 19 patients were categorized in this group, out of them 4 rebleedings were observed (2<sup>nd</sup> table). The high risk group was created with 12 or more points. 36 patients belonged into this group, out of them 32 rebleeding occurred (Table 3). The risk groups and their modified Baylor score value are shown in the 3<sup>rd</sup> table.

**Table 2.**  
Number of rebleeding according to different risk groups (1995–1996)

| Risk group | Number of patients | Rebleeding | %  |
|------------|--------------------|------------|----|
| Low        | 53                 | 0          | 0  |
| Middle     | 19                 | 4          | 21 |
| High       | 36                 | 32         | 89 |
| Altogether | 108                | 36         | 33 |

**Table 3.**  
Risk groups according to the modified Baylor score

| Risk groups | Value of the score |
|-------------|--------------------|
| Low risk    | 0–7                |
| Middle risk | 8–11               |
| High risk   | 12–31              |

## Discussion

The peptic ulcer bleeding stops spontaneously in 70–80% of patients [1]. In these cases the rebleeding rate is 30–50% according to different authors [1, 2, 3]. The mortality in case of rebleeding is 6–12 fold higher [1, 3]. The problem is how to identify those patients so that elective operation can be performed with the patient in a stable condition, rather than an emergency operation when there is acute hemorrhage. It is understandable that several attempts have been made to identify risk factors for rebleeding in peptic ulcer patients [5]. According to the literature there are several factors influencing rebleeding. Such factors are age, shock by the admittance, number and severity of coexisting illnesses, stigmata of recent hemorrhage observed at the urgent endoscopy, ulcer size and location [5]. It is evident that a combination of clinical and edoscopic risk factors can provide a more reliable prediction of rebleeding rate [1]. Saeed et al. published a scoring system (Baylor Bleeding Score) taking into consideration five aspects for selecting the high risk patients for rebleeding [4]. After analysis of our 108 patients with peptic ulcer bleeding we have found, that with additional two factors and the modification of the distribution of the points the scoring system can be more effective in prediction of rebleeding. These two additional factors are the hemoglobin level by the admittance (which is an objective mirror of the current hemostatus) and the size of the ulcer. With the help of the scoring system we can choose the high risk patients for rebleeding. If we operate them in a stable condition (before rebleeding) we can hopefully reduce the mortality rate.



## Summary

The possibilities of the prediction of rebleeding are discussed in case of peptic ulcer hemorrhage. With the help of a modified Baylor score we can choose the high risk patients. The operation in a stable condition before rebleeding can reduce the mortality rate in this group of patients.

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## **INVESTIGATION OF MICROCIRCULATORY CHANGES IN THE DUODENUM OF DOGS CAUSED BY SURGICAL SUTURE MATERIALS**

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Surgical suture materials play an important role in the safe performance of surgical interventions. In our experiments we made an attempt to investigate what microcirculatory changes result from pulling the thread through the wall of the duodenum in Lembert stitches by including 3 kinds of absorbable and non-absorbable suture materials each (Catgut, Dexon, PDS, Silk, Ethibond, Ethilon). Research is still in the pre-experimental stage. In the long run, we hope to enrich the description of these suture materials by some new details. It could help prevent suture insufficiency, facilitate wound healing and thus, improved surgical safety.

### **Introduction**

Research concerning the application of suture materials has been done for several years at our department. We have published several papers about the effect of suture materials on the body to help surgeons find their way among suture materials and choose the most suitable one in their practice [1, 2].

Last year, we began to study suture materials from a new aspect [3]. It has been common knowledge for a long time, that stitches bring about changes in the microcirculation of organs and tissues. However, no details about the extent of these changes and no data about their relationship with a given suture material have been found in the literature.

Our former experiments with absorbable suture materials included Catgut, PDS and Dexon. On the basis of those experiments it could be concluded that, according to expectations, it was Catgut which had resulted in changes to the greatest extent, and interestingly enough, those changes had been more expressed on the anti-mesenteric side.

The present series of experiments was devoted to the research of non-absorbable suture materials.

### **Materials and Methods**

The experiments were performed on 30 mongrel dogs of approximately the same weight, independently of the age and sex of the animals, after inducing narcosis with intramuscular Calypsovet (ketamin)-Xilavet (xilazin), with the permission of the Scientific Ethical Committee for the Protection of Animals.



The measurements were carried out using an Experimetria TF-01 flow meter which operates on the principle of thermodilution. (In earlier experiments this device gave almost identical results to those gained by a Laser Doppler.)

The duodenum was isolated following upper-middle median laparotomy and two sensors were joined to the bowel at a constant distance from the pylorus, on the mesenteric and antimesenteric sides, respectively. Lembert stitches were placed in between the sensors, applying quick pulling of the thread, without knotting it. Only 5 cm of the 75 cm suture material was pulled through at first instance, the rest (70 cm) was pulled through after balance had set in and the sensors had been heated up. From among the rich variety of suture materials absorbable Catgut, Dexon and PDS, and non-absorbable Silk, Ethibond and Ethilon had been selected. All of the suture materials were of a thickness of 2-0 and length of 75 cm, fitted with a needle of 26 mm with circular diameter. We tried to ensure standard external circumstances in each case. The suture materials were tested in five measurements each.

Microcirculatory changes were measured for 60 minutes after pulling through the thread. Readings were marked in the system of co-ordinates, showing the percentage of microcirculatory changes in the function of time.

## Results

On evaluating the measurements the following could be seen:

- ◆ In the case of Catgut, a continuously rising curve was obtained on both the mesenteric and antimesenteric sides, the greatest change being obtained in 60 minutes, reaching 20.4% (on the antimesenteric side).
- ◆ If PDS was used in the experiment, the maximum of change in tissue flow was seen at 55 minutes, reaching 11.8% (on the antimesenteric side). Flow on the mesenteric side was slightly elevated for 35 minutes, and gradual decrease was seen afterwards.
- ◆ With Dexon, tissue microcirculation reached a high level at 55 minutes on the antimesenteric side, at 19.5%, and, similarly to PDS, it rose slightly for 35 minutes, and then decreased, on the mesenteric side.
- ◆ In all of the three cases, microcirculation increased more significantly on the antimesenteric side.
- ◆ In the case of Silk, flow reached its maximum (20.6%) on the mesenteric side at 20 minutes, next it was stagnant and then it decreased. It gradually increased on the antimesenteric side, reaching nearly 20% at 60 minutes.
- ◆ If Ethibond was used, the maximum was seen at 5.69% at 40 minutes on the antimesenteric side, then decrease followed. On the mesenteric side, the curve was found near 0, or only slight increase was noted.
- ◆ The use of Ethilon resulted in somewhat different curves. In 4 out of the 5 experiments, microcirculation decreased on the antimesenteric side (maximum: 14.4%), on the mesenteric side, however, a slight increase was followed by decrease to be followed by another increase (maximum: 4.4%). The differences between the individual curves were greater than in the case of the other suture materials.

## Discussion

Compared to the results with earlier microcirculatory experiments with absorbable suture materials [3] we could see that the changes induced by the placement of stitches were greater on the antimesenteric side with non-absorbable suture materials, too. The surface of the thread and the rigidity of the suture material are the two main factors to result in microcirculatory changes in the tissues to a greater extent.

However, no close relationship was found between microcirculatory changes and the extent of tissue reaction on the basis of the reaction index of various suture materials in our department.

## Summary

Examining the microcirculatory changes induced by Lembert stitches placed in the duodenum the following were concluded:

- Microcirculatory changes with both absorbable and non-absorbable suture materials were greater on the antimesenteric side.
- There was no detectable difference between absorbable and non-absorbable suture materials with respect to microcirculatory changes.
- It was the smoothness of the thread surface which played a decisive role in changes in microcirculation.
- Based on the experiments, the use of Catgut and Silk resulted in greater microcirculatory changes.

These results, after further experimental support, may add new details to the features of suture materials. This would, as we hope, contribute to the prevention of often unexplainable suture insufficiency, facilitate wound healing and, thus, improve the safety of surgical interventions.

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## LAPAROSCOPIC DEROOOFING OF NONPARASITIC LIVER CYSTS COMPARISON DIFFERENT METHODS

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Between 1982 and 1995 116 patients underwent operations because of NC of the liver, 18 of them were operated on by laparoscopic way. There were 94 male (mean age: 51.9 years) and 66 female (mean age: 54,6 years) patients. The mean size of the cysts were 57.4 mm in diameter (20–140 mm). In 94 cases they were solitary and in 11 they were multiple. In 31 cases we performed an enucleation, in 60 cases a fenestration and in one case a punction of the cysts. A liver resection had to be carried out in two cases. In 18 cases the fenestration of the cysts was performed by laparoscopy and in 10 cases cholecystectomy was simultaneously carried out. The most common complications were fever and wound suppuration. There was no mortality. Another 26 patients with NC have been treated with ultrasound guided punction of the liver cysts. The cysts were solitary in twentythree cases and multiple in three other cases. The number of the cysts were thirtytwo. One case had to be operated on because of recurrence of the cyst. Mortality could not be observed. In the laparotomised group the average time of the hospitalisation was 14.3 days, and among the patients who were operated on by laparoscopic way 7.0 days. An intervention is indicated only in case of severe complaints or the growing of the lesion. Recently we prefer the ultrasound guided punction or the fenestration of the liver cysts by means of the laparoscopic way.

### Introduction

The treatment of benign focal liver diseases (FLD) still belongs to the current problem of surgery today. As to the treatment there is no uniform international practice.

### Patients and Methods

Between 1982 and 1995 116 patients were treated in consequence of non-parasitic liver cysts. Among them there were 94 female (76.6%) and 22 male (23.4%) patients. The average age in female was 54.6 years (20–83), in males 51.9 years (35–78). In 94 cases the cysts were solitary (81.03%), in 11 cases they were multiplex (9.48 %) and in other 11 cases the liver was polycystic (9.48%). Their mean size was 57.4 mm (14–200 mm).

#### Laparotomy

An enucleation was preferred, if the diameter of the cysts was not longer than 10 cm. Having removed the cyst in toto, the parenchymal surfaces were joined by cat-gut sutures. Fenestration was carried out if the cyst were to be found on the surface of the liver. Liver resection were performed, if the cysts were to be found in a well circumscribed area of the liver.

### **Laparoscopy**

In 18 cases the fenestration of the cysts was performed by laparoscopy and in 10 cases cholecystectomy was simultaneously carried out. The cysts operated by laparoscopy were all on the surface of the liver and all of them were bigger than 5 cm.

### **Interventional radiological procedure**

Interventional radiological procedure was applied on 26 patients on account of liver cysts. The number of the treated cysts were 32. Besides US guided punctions US guided drainage as well as sclerotization with aethoxysclerol or pure alcohol were also performed. Following an US guided liver puncture a recurrence often occurred; not more than 17 patients recovered the first puncture.

## **Results**

Fever could be observed in eight cases, leucocytosis in one case, jaundice in three cases, pleuritis and hydrothorax in one case, suppuration of the wound in one case and a sterile abdominal wall disruption also in one case. No complication could be observed on patients treated by interventional radiological procedures. There was no intra- or postoperative mortality in either of the groups. The average time of the hospitalization of the laparotomized patients was 14.3 days, whereas it was 7 days with patients who were operated on by laparoscopy.

## **Discussion**

Literary opinions about the necessity and method of the treatment of liver cysts are rather different. We are inclined to think that cysts larger than 5 cm can be regarded as an indication for the operation, especially if they are the cause of any complaints. Enucleation, fenestration and stitching of the liver cysts are the most frequently used methods of traditional surgical interventions [1]. Percutaneous puncture of the liver cysts also belongs to the routine [2]. Fenestration of the liver cyst by laparoscopy can primarily be performed by cases where the cysts are localized on the surface of the liver or the cyst is covered only by a very thin liver tissue. In our opinion the applicability of this method is not limited by the multiplicity of the cysts or even by hepatomegaly [3]. But when indicating this procedure we must consider advanced liver lesions as well as the perfect blood coagulation. Fenestration by laparoscopy is not limited by the size of the cyst [4].

As a conclusion we propose a wide fenestration used the laparoscopy as a primary intervention because it can be performed easily and has a low morbidity rate. Traditional surgical exploration ought to be reserved for the cases in which intervention by laparoscopy cannot be performed because of technical causes, or owing to intraoperative technical difficulties the operation must be converted.



## Conclusions

Because of the high rate of recurrence and the repeated hospitalization the interventional radiological methods did not prove more favourable than those of surgery. In spite of it with patients in a bad general condition it may be regarded as an applicable method.

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## HOST-VERSUS-GRAFT DISEASE IN MICE AFTER THE INDUCTION OF NEONATAL TRANSPLANTATION TOLERANCE BY TWO DIFFERENT METHODS

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Newborn A mice were injected either with a single i.v. dose (Group A) or with repeated doses of (B10 x A)<sub>F1</sub> semiallogeneic spleen cells (SSC) (Group B). A similar degree of partial transplantation tolerance (TT) to B10 skin allografts was revealed in both groups. No signs of acute, rapidly fatal host-versus-graft disease (HVGD) (anemia, leukocytosis, severe thrombocytopenia, hepatic infarcts, gastrointestinal bleedings) were found, rather a chronic HVGD developed [moderate thrombocytopenia, autoimmune antithymocyte antibodies (ATA)] in both groups. The mortality due to lymphoproliferative disorders (LPD) was significantly higher in Group A. Thus, repeated perinatal injections of (B10 x A)<sub>F1</sub> SSC into A mice did not increase the tolerogenic and the LPD-inducing effect either, and they did not elicit acute HVGD in contrast to observations in other F<sub>1</sub> donor-recipient combinations [1]. Consequently, the development of acute HVGD depends on immunogenetic factors and not on the repeated administration of SSC.

### Introduction

The induction of neonatal TT in certain donor-recipient mouse strain combinations by repeated injections of SSC resulted in anemia, leukocytosis, thrombocytopenia (TP), LPD, T cell deficiency, bleedings and liver infarcts. This rapidly fatal syndrome is due to the immune reaction of the host against donor SSC (HVGD) [1]. In A mice injected with a single dose of (B10 x A)<sub>F1</sub> SSC at birth, we found a partial specific TT to B10 skin allografts, chronic HVGD (ATA, *in vitro* T cell deficiency) and > 60% LPD [2, 4], similar to findings in other strain combinations [3]. The aim of this study was to investigate whether the repeated inoculations of SSC influence the induction of TT, LPD and the course of HVGD (acute or chronic).

### Methods

Inbred A/J (H-2a) mice were injected on the day of birth with  $2 \times 10^7$  (B10 x A)<sub>F1</sub> SSC i.v. (Group A) [4], or, according to Hard [1], i.v. with  $5 \times 10^6$  plus i.p. with  $10^7$  SSC and, on day 7, i.p. with  $10^8$  SSC (Group B). To test the induction of TT, 3-month-old mice were grafted with C57BL/10ScSn (H-2<sup>b</sup>) (B10) tail skin grafts [4]. Mice died or killed at 1 year of age were autopsied. ATA were detected in the sera of mice by indirect immunofluorescence. Values of *p* less than 0.05 were considered significant [2].



## Results and Discussion

In both groups of mice neonatally injected with SSC (A and B), a similar degree of partial TT developed: B10 skin allografts survived significantly longer [Group A:  $48.3 \pm 29.7$  days ( $n=11$ ); Group B:  $35.4 \pm 25.9$  days ( $n=8$ )] than in nontolerized A recipients [ $11.1 \pm 1.7$  days ( $n=26$ )]. The difference between Groups A and B was not significant.

Splenomegaly was palpable at 1 month of age (22/22) in all mice of Group B, while only in 1 of 22 mice of Group A. At 1 year, there was no significant difference between the groups (A: 14/22; B: 12/16). In the majority of mice of both groups, splenomegaly was associated with lymphadenomegaly, hepatomegaly and kidney infiltration. Mortality in Group B was lower (3/16) than in Group A (8/22). Early deaths (<1 month), liver infarcts and gastrointestinal bleedings characteristic to the acute HVGD [1] were not seen.

At 1 month of age, no anemia and significant changes in the leucocyte counts were found in the tolerized mice (Group A:  $3970 \pm 1110/\mu\text{l}$ ; Group B:  $2030 \pm 370/\mu\text{l}$ ; normal A mice:  $2890 \pm 250/\mu\text{l}$ ). Platelet counts were significantly decreased in both groups (A:  $454,000 \pm 115,000/\mu\text{l}$ ; B:  $516,000 \pm 242,000/\mu\text{l}$ ; normal:  $993,000 \pm 45,000/\mu\text{l}$ ).

The serum of each 1-month-old tolerized mouse contained ATA. Based on the 10 times greater staining capacity of their sera, the quantity and affinity of ATA in mice of Group B were higher than those of Group A.

In conclusion, repeated injections of (B10 x A) $F_1$  SSC into A mice at perinatal age did not increase the tolerogenic and the LPD-inducing effect either. Furthermore, in contrast to Hard's observations [1], they did not elicit acute HVGD. Thus, the development of acute HVGD depends on immunogenetic factors and not on the repeated administration of SSC.

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## **SURGICAL CHEMOTHERAPY IN THE MANAGEMENT OF MELANOBLASTOMA OF THE LOWER EXTREMITIES**

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The therapy of advanced melanoblastomas of the lower extremities is limited. Surgery alone is insufficient due to the extent of the tumor, the radicality of mutilating surgery is questionable because of the existing or suspected subclinical metastasis. To avoid amputation, regional chemoperfusion and simultaneous hemofiltration may be the choice of treatment. Between 1993 and 1995 the authors performed surgical chemotherapy on 21 occasions in 14 patients with advanced melanoblastoma of the lower limb. Partial remission of 4 to 11 months developed in 10 patients, 3 patients achieved subjective improvement for 3 to 6 months, 1 patient had disease progression. Simultaneous application of surgical regional chemotherapy and hemofiltration offers an alternative approach in the management of patients suffering from advanced melanoblastoma.

### **Introduction**

In Hungary the incidence of new melanoblastoma cases is 4 to 6 per 100,000 population. In case of large numbers of transitional metastasis of advanced lower limb melanoblastomas no radical surgery can be carried out [2]. Locoregional cancer chemotherapy permits to potentiate the selective drug effect.

### **Methods**

Due to melanoblastoma of the lower extremity, in the National Institute of Oncology, between 1993 and 1995, we performed semi closed chemoperfusion and simultaneous hemofiltration in 16 patients on 24 occasions. For isolated lower limb perfusion the external iliac artery and vein are isolated from oblique incision, excluding the limb circulation by means of tourniquet. In case of semi-closed perfusion and hemofiltration the artery and vein of the tumorous limb are cannulated, the cytostatic drug is administered intraarterially by means of a rolling pump. The filtrated cytostatic-free blood is returned to the circulation via the venous blood supply of the other extremity. It is essential that the extent of the venous suction approaches or reaches that of the arterial supply. Hemofiltration is performed by AK-10 System, Gambro-manufactured equipment, by means F-88 filter. Blood is roll-pumped to the filter at 150 r.p.m., 0-40 mm Hg venous pressure and 200 mm Hg TMP, on the average. For chemotherapy a total dose of 100 mg Adriamycin and 200 mg Alkeran are used, which corresponds to



10 to 25 mg/l dose calculated to the given limb. In case of Adriamycin no heparin is used. Drug pharmacokinetics is investigated every 10 minutes during administration, and every 20 minutes during filtration, based on the blood samples taken [1]. The mean duration of drug administration is 30 minutes, that of hemofiltration is 120 minutes, respectively. Circulation and respiratory parameters, body temperature as well as the extent of arterial oxygenation of the patients are measured by non-invasive methods.

## Results and Discussion

In 12 of our 14 melanoblastoma patients partial remission exceeding 50% was observed 3 weeks after first treatment. The cutaneous metastasis grew smaller and got dried. Superinfection of the exulcerated lesions was eliminated, their surface became crusted. Remission duration lasted for 4 to 11 months, then cutaneous metastasis appeared at other sites, in other foci. Repeated intraarterial therapy led to 8–12-week remission in 7 patients (58%). In 2 cases partial remission less than 50% occurred for 4 and 6 months, respectively.

As adverse reactions, 8 patients developed local complications from erythema to skin necrosis, 2 patients showed peripheral blood picture deviation, the pancytopenia of 1 patient required hematologic treatment. Regional cytostatic treatment and hemofiltration can be performed in all tumors where the arterial and venous blood supply can be isolated. In limb melanoblastomas metastasis formation takes place most frequently via the regional lymphatic vessels. These cases would require isolated regional perfusion and hemofiltration. In case of regional lymph node metastasis the procedure may be attempted after prior regional lymph node block dissection. In such a case surgical chemotherapy is technically more difficult though not contraindicated.

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## TUMOR SURGERY OF THE PELVIC REGION

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During the past ten years the authors operated on 27 tumors of the pelvic region, 12 of them involving the pelvic blade, 6 the periacetabular region, further 9 the os pubis and ischii, respectively. Most of the cases (16) were chondrosarcomas. The mean age of the patients – 13 male and 14 female – was 41 years. As to surgical radicality 11 wide, 10 marginal and 6 intralesional resections were performed. After a mean follow-up period of 3 years (0.5–11 years) 19 patients are alive tumor-free, 2 with tumor, 4 died and 2 were lost to follow-up. As postsurgical complication wound-healing disorder and inguinal hernia occurred in 5 cases, on the surgical field thrombosis with secondary compartment syndrome and renal insufficiency developed in one case. The authors draw the attention to the difficulties and indications of the pelvic resections (internal hemipelvectomies).

### Introduction

One of the greatest challenges for tumor surgeons is to operate on osseal tumors originating from the pelvic region or on soft tissue tumors joining or destructing them. The reconstruction following "internal hemipelvectomy", i. e. partial pelvic resection may be particularly difficult for restoring the walking ability of the patient and for achieving an adequate quality of life. [1]

### Methods

Between 1986 and 1995 we performed "internal hemipelvectomy" while saving the extremity in a total of 27 cases. In our material we had 13 male and 14 female patients, their mean age was 41 years, ranging from 18 to 78 years. In our material an overwhelming majority of tumors were represented by chondrosarcoma (16 patients). In another 4 patients we were compelled to perform a partial pelvic resection due to a giant cell bone tumor. As to surgical radicality, the intervention was led in 11 cases in the healthy tissue, in 8 cases at least one surface of the resection was marginal, in another 2 cases the tumor, due to its large size, could only be extirpated in two parts that means contaminated marginal resection took place. We performed intralesional intervention in 6 patients. We did reconstruction to 3 patients: we implanted pelvic endoprosthesis to 1 patient, in further 2 patients we fixed the femoral head to the ileal stump of the acetabular defect by cerclage, then prepared a pelvic plaster.



## Results

Local recurrence was observed in 6 patients. Complications occurred in 8 cases. After a mean follow-up of 3 years 18 (66%) of our 27 patients are alive tumor-free, in 6 the follow-up period exceeds 5 years.

## Discussion

One should obviously attempt at complete tumor removal; we should not commence on an operation if the prerequisites are not present. For a proper judgement the up-to-date imaging techniques should also be used. In our opinion, hemipelvectomy is indicated if: 1./ the tumor has invaded along the ischiadic nerve into the gluteal muscles, onto the posterior surface of the thigh; 2./ the tumor involves the iliac external, the femoral artery and vein and extends to the abductors via the adductal canal; 3./ the tumor equally infiltrates the E/I, E/II and E/III regions. Although in this case internal hemipelvectomy can be carried out, there is no possibility of a reconstruction, the flail hip offers an extremely poor rehabilitation outcome; 4./ the age and general condition of the patient should be considered individually.

## Summary

Opinions in the literature are controversial as regards the reconstruction of the defects. The defect need not be reconstructed if the pelvic arc remains intact, i.e. the 2-finger-thick osseal arc above the ischiadic incision and the acetabulum are not damaged [2, 3].

Among our 27 patients operated on during 10 years 20 are alive, 18 without a tumor at present. This is an encouraging figure! The prerequisite of the favorable results is to perform the surgery of pelvic tumors in well-equipped centers, with experienced multidisciplinary surgical teams including orthopedic, abdominal surgeons, eventually gynecologists and/or urologists as well.

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## **CHOLECYSTECTOMY THROUGH A MINI LAPAROTOMY ALONGSIDE LAPAROSCOPIC TECHNIQUE**

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The authors present the surgical treatment of gallstones with special instruments and technique through a mini laparotomy, as developed in Kaposvár (Hungary). Despite the fact that the widespread use of laparoscopic cholecystectomy (LC) has succeeded over open cholecystectomy (OC), in their opinion, there are some instances where cholecystectomy through a mini laparotomy (MLC) would be advantageous. Last year (1996), in the authors' department, 32 MLCs were performed in addition to 72 OCs and 176 LCs. Due to unspecified techniques and differing criteria used to define MLC, it is difficult to find any data related to this subject in the literature available. In Hungary, there are two cities – Kaposvár and Szolnok – where only MLCs are performed for the surgical treatment of gallstones. Conversely, the University hospital of Szeged and the County hospital of Békéscsaba use all three procedures i.e. OC, LC and MLC; as is the case in the authors' hospital. In the article, the pros and cons of MLC are compared to those of LC. (The MLC being more cost effective, enables quick conversion to an OC if required, and provides the surgeon with a three dimensional picture, it is also suitable for the surgical treatment of common bile duct stones. However, it is cosmetically worse, obesity can cause technical difficulties, the incidence of hernia formation is higher, and wound healing is affected.) In the authors' opinion, it would be important to establish set criteria in order to screen patients that are unsuitable for LC, and they attempt to do so in this article.

### **Introduction**

The first retrospective and randomised prospective trials proved that laparoscopic cholecystectomy (LC) has a low morbidity and mortality, and that it is in most cases, a safe option for the treatment of gall stones. There are several advantages: little post operative pain, excellent cosmetic results, good post operative respiratory and metabolic functions, a short hospital stay and a quick recovery, to mention but a few. LC could replace conventional cholecystectomy (OC) becoming the "gold standard" according to Sawyers' [5] opinion, but equally he draws attention to some of its pitfalls that need further evaluation. In LCs, comparing to OCs, there are more iatrogenic bile duct injuries, common bile duct stones prove more difficult to treat, it is more cost effective, the operation takes longer, and the surgical trainees do not have the opportunity to learn open cholecystectomy. The society's need for LC is greater than the need for OC due to the quick recovery, which makes further randomised trials more difficult to carry out.

A further method for the treatment of gall stones alongside the two methods mentioned above, is cholecystectomy through a mini laparotomy (up to 6 cm) reported by Dubois [1]. Through the improvement of the instruments used, and his description of the technique, Rozsos' [4] merits are indisputable.



## Material and Methods

Since 1996, we have had available the improved instruments, i.e. special retractors and the 300 watts fibre optics light source with changeable power output connectable to the liver retractors. The cholecystectomy through a mini laparotomy (MLC) is done through an upper midline incision that lies over the area of the Calot triangle, enabling the retraction of the falciform ligament towards the left. Turning the patient to the left decreases the possibility of injuring or clipping the CBD.

In 1996, 32 MLCs were performed in addition to 72 OCs and 176 LCs.

The number of conversions from LC to OC were: 7, LC → MLC were: 3, MLC → OC were: 2. We did not have any CBD injuries.

## Results

All the surgeons in our department adopted the method of MLC. In table 1. we summarised the indications of MLC and OC.

**Table 1.**  
**Indications of OC and MLC as opposed to LC**

| OC                                                                                           | MLC |
|----------------------------------------------------------------------------------------------|-----|
| ⇐ difficult anatomy expected<br>(severe inflammation)<br>(thickened gall bladder wall on US) | ⇐   |
| suspected stones in CBD<br>(dilated CBD on US)                                               | →   |
| ⇐ multiple abdominal surgery in the past                                                     | ⇐   |
| ⇐ coagulopathy                                                                               |     |
| ⇐ cirrhosis                                                                                  | ⇐   |
| ⇐ suspected malignancy                                                                       | ⇐   |
| ⇐ fistula                                                                                    |     |
| anaesthetic indication e.g. unfit patient                                                    | ⇐   |
| technical difficulties with LC                                                               | ⇐   |
| conversion from LC                                                                           | ⇐   |

## Discussion

The problems and complications of LC can be overcome not only by OC, but MLC as well. The randomised studies comparing LCs with MLCs are usually in favour of LCs, although we must admit that these studies and the operations referred to were done by

very experienced surgeons, while the number of MLCs were very low and were not done with the proper technique and instruments advocated in our paper [2, 3].

In Kaposvár and Szolnok only MLCs are performed for the surgical treatment of gall stones. In our Department our aim was to find the place of MLC alongside LC. It would be important to establish set criteria in order to screen patients that are unsuitable for LC. In table 1. we summarised those cases when OC or MLC can be performed as an alternative to LC.

The pros of MLC compared to LC are that it is more cost effective, enables quick conversion to an OC if required, provides a three dimensional picture as in OC, and it is also suitable for the surgical treatment of CBD stones. To adopt the operation it is useful to have experience in LC. (The operating surgeon is on the left side of the patient, as in LCs.) The cons of MLC are that the results are cosmetically worse, obesity can cause technical difficulties, the incidence of hernia formation is higher, and wound healing can be affected. MLC incorporates the advantages of conventional and laparoscopic technique and enables us to have an alternative option alongside OC to avoid iatrogenic injuries, whilst maintaining a minimal invasive operation.

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## CONTINUOUS $pO_2$ AND $pCO_2$ MEASUREMENT IN BRAIN TISSUE AND CEREBROVENOUS BLOOD DURING DIFFERENT INSPIRED OXYGEN SETTINGS. A PORCINE MODEL

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The clinical use of brain tissue oxygen measurement in patients with severe head injury is increasing. It is important to compare the findings in brain tissue with jugular bulb oximetry, to obtain normal values and to find out limitations of the method. We evaluated a newly available multisensor probe simultaneously in the brain tissue and in the sagittal sinus in a porcine animal model. We placed the Paratrend 7<sup>®</sup>-probe (BSL, High Wycombe, UK) in the left frontoparietal white matter and measured  $pO_2$  ( $p_{ti}O_2$ ),  $pCO_2$  ( $p_{ti}CO_2$ ), pH and temperature while simultaneously measuring these parameters ( $p_{cv}O_2$ ,  $p_{cv}CO_2$ ) in the sagittal sinus in 7 pigs under general anaesthesia during a 100% oxygen enhancement. The relation between oxygen increase in brain tissue and in the sagittal sinus showed a coefficient of correlation ( $CC_{mean}$ )  $r_{mean}=0.96$ . The quantitative response in brain tissue was much more sensitive than in the sinus. A close correlation between  $pCO_2$  in brain tissue and sagittal sinus and the increase of the inspired oxygen was seen:  $CC\ p_{ti}CO_2$  to arterial oxygen pressure ( $p_aO_2$ ) -  $r_{mean} = 0.67$ ,  $CC\ p_{cv}CO_2$  to  $p_aO_2$  -  $r_{mean} = 0.88$ . This is important for interpreting measured values and introducing new coefficients for patient monitoring. Newly available continuous brain oxygen measurement methods will allow better understanding of brain metabolism in the future.

### Introduction

Patients with severe head injury are at high risk for developing neuronal damage caused by secondary ischemia [2]. The continuous monitoring of intracranial pressure (ICP) and calculation of cerebral perfusion pressure (CPP) in patients supposed to develop cerebral ischemic events is not sufficient to detect these events [1]. The continuous  $pO_2$  measurement in brain tissue ( $p_{ti}O_2$ ) with Clark type electrodes or multisensor probes, combining fiberoptical sensors to measure  $pCO_2$  and pH, a thermocouple for measuring temperature and a Clark type electrode for measuring  $pO_2$ , is increasingly used in neurosurgical patients to monitor the oxygen supply to the brain and to find out prognostic meanings of the measured values [2, 4, 5].

The continuous measurement of oxygen haemoglobin saturation with fiberoptics in the jugular bulb in neurosurgical patients ( $S_jO_2$ ) is another rather recent technical development. It is, however, already established as a clinical routine in patients with severe head injury and elevated ICP [1]. But this continuous spectrophotometric monitoring method has its limitation is clinical use due to technical artefacts caused by low light intensity, motion artefacts or changes in catheter position during the measurement period [3,4]. The aim of this study was to use a new available multiparameter probe, measuring  $pO_2$ ,  $pCO_2$ , pH and temperature, simultaneously in brain tissue and in the cerebrovenous outflow in a porcine model. So the course of oxygen tension in both measurement compartments, related to physiological variations of ventilator settings, was evaluated and compared. Additionally it was the purpose to gain more insight and experience in the values of oxygen tension in normal brain tissue and cerebrovenous blood and of the new available continuous parameter  $pCO_2$ .

## Methods

**Anesthesia and Monitoring of Experimental Animals:** Seven 8-week-old domestic pigs weighing 18–22 kg were used in the present study. All experiments were performed in accordance with the guidelines issued by the Debrecen University Committee on Animal Care based upon: "Principles of laboratory animal care" (NIH publication Nr 86–23, revised 1985). Anesthesia was induced by i.v. drug medication, tracheotomy was carried out and the animals were ventilated volume controlled with a mix of oxygen and room air.

A parenchymal multisensor probe P7 (Paratrend 7, Biomedical Sensors Ltd., Highwycombe, UK) was inserted into the white matter of the left frontoparietal lobe over a length of about 4 cm. In all animals, the superior sagittal sinus was exposed in the bregma region. A second P7 probe was introduced into the superior sagittal sinus via direct puncture of the sinus. ABP and ICP were continuously monitored, CPP was calculated. All values of brain tissue measurement by the P7 probe ( $p_{ti}O_2$ ,  $p_{ti}CO_2$ ,  $pH_{ti}$  and  $t_{ti}$ ) as well as the values of the cerebrovenous measurement in the sagittal sinus by the P7 probe ( $p_{cv}O_2$ ,  $p_{cv}CO_2$ ,  $pH_{cv}$  and  $t_{cv}$ ) were digitally downloaded to a terminal program and stored in a 10 second interval on hard disk.

**Oxygen challenge:** In all animals a steady state of basic values in tissue measurement and in cerebrovenous measurement was reached after approximately 90 min after catheter insertion. During this period the inspired oxygen ratio ( $FiO_2$ ) was kept constant at 30%. In a one step approach  $FiO_2$  was increased up to 100% over a period of 5 min and afterwards reduced again on 40%. To make the results of the  $FiO_2$  settings comparable with the results of other working groups we calculated the oxygen reactivity coefficient of Van Santbrink (increase in oxygen tension (%) of the cerebral compartment divided by the absolute increase of arterial oxygen tension (mmHg) [4]. The mean values are expressed as the median  $\pm$  standard deviation if not indicated in an other way.

## Results

**Physiological findings prior to  $FiO_2$  increase:** The mean ICP was 8.24 (5.5) mmHg. CPP was 86.07 (10.75) mmHg. All animals showed a 100% oxygen saturation for the peripheral pulse oximetry. The mean arterial oxygen tension showed to be 136 (22.01) mmHg. The mean  $p_aCO_2$  was 54.02 (5.55) mmHg and the mean  $pH_a$  was 7.33 (0.05).  $p_{ti}O_2$  showed to be 25.71 (8.9) and  $p_{cv}O_2$  was 39.14 [4]. Two of the animals showed initial  $p_{ti}O_2$  values below 20 mmHg. There was no significant correlation between the oxygen levels in both cerebral compartments ( $r=0.4$ ).  $PCO_2$  values in tissue as well as in cerebrovenous blood are given as the calculated difference ( $\delta$  values =  $p_aCO_2$  – compartment  $CO_2$ ). The  $\delta p_{ti}CO_2$  was 22.9 (7.3) and showed to be distinctly higher than  $\delta p_{cv}CO_2$  11.22 (7.23) with similar standard deviation in both compartments.

**Findings during  $FiO_2$  increase:** In both cerebral compartments an increased oxygen tension related to the  $FiO_2$  increase was seen. The mean coefficient of correlation ( $CC_{mean}$ ) between arterial  $pO_2$  increase and  $p_{ti}O_2$  was  $r_{mean} = 0.67$ . The relation between  $p_{cv}O_2$  and  $p_aO_2$  showed a  $CC_{mean}:r_{mean} = 0.91$ . Corresponding to this, the correlation between oxygen increase in brain tissue and in the sagittal sinus showed coefficient of correlation  $r_{mean} = 0.96$ . The coefficient of oxygen reactivity ( $O_{2rea}$ ) was calculated for the tissue values as 0.21 (0.12) and for the cerebrovenous values as 0.06 (0.02).

A close correlation between  $pCO_2$  in brain tissue and sagittal sinus and the increase of the inspired oxygen was seen:  $CC_{mean} p_{ti}CO_2$  to arterial oxygen ( $p_aO_2$ ) -  $r_{mean} = 0.67$ ,  $CC: p_{cv}CO_2$  to  $p_aO_2$  -  $r_{mean} = 0.88$ .

## Discussion

**Oxygen measurement:** Brain tissue oximetry is a local measurement approach. Although the global cerebral oxygen consumption ( $CMRO_2$ ) under constant metabolic conditions,



such as under general anesthesia is an almost stable value it is well known that oxygen is heterogeneously distributed to brain areas.

The  $p_{ti}O_2$  results in our experiment prior to  $FiO_2$  manipulations show a mean of 25.71 (8.9) mmHg. Two of the 7 animals had a tissue oxygen tension less than 20 mmHg and one of these animals started with a  $p_{ti}O_2$  of only 9 mmHg at the beginning of the  $FiO_2$  increase. These normal values are lower compared to other animal and human studies [4, 5]. Our experimental data were obtained between 2 and 4 hours after catheter insertion. We suggest, that during the first period of 1 and 12 hours after catheter insertion probably additional heterogeneity of the measurement performance exists. This heterogeneity might be due to the micro compression of the tissue surrounding the catheter site after insertion and results in patients using this monitoring are cautiously to interpret during the early period of measurement.

Cerebrovenous partial oxygen pressure measurement is a global measurement approach. The normal values in our study showed a much less heterogeneity, when compared to the simultaneous tissue measurement. Both measurement compartments have proven to be sensitive to global changes in cerebral oxygen supply in our experimental study. All manipulation of  $FiO_2$  were performed when hemoglobin was saturated to 100% with oxygen in the arterial blood. We conclude, that the increase of arterial oxygen pressure to values higher than necessary to saturate arterial hemoglobin to 100% improves the cerebral oxygen supply and might be beneficial in patients supposed to suffer on cerebral ischemic events. The oxygen partial pressure in brain tissue responded quantitatively more sensitive to the  $FiO_2$  manipulations and showed a 50% heterogeneity. We conclude, that the  $p_{ti}O_2$  measurement is influenced by the different adjacent position to the arterial capillaries of the brain tissue. That indicates that  $p_{ti}O_2$  measurement is giving insight in substrate delivery to the brain but is difficult to interpret regarding the metabolic status of the neurons.

*Findings in  $CO_2$ :* In both measurement compartments  $PCO_2$  was highly positive correlated to the  $FiO_2$  increase. We suggest that the increase in  $pCO_2$  during  $FiO_2$  increase reflects compromised cerebral perfusion due to oxygen vasoreaction. The reduced "wash out" thus leads to an accumulation of metabolic products.  $pCO_2$  should be further explored in relation to other physiological and pathological data to find out the importance of this newly available continuous parameter.

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## MICRO AND MINILAPAROTOMY SURGERY IN THE TREATMENT OF MIRIZZI'S SYNDROME

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The Mirizzi's syndrome presents a difficult surgical challenge because the dense adhesions and edematous inflammatory tissue cause distortion of the normal anatomy in Calot's triangle, leading to a great risk of bile duct injury. Therefore, a controversial issue the surgical strategy for treatment of Mirizzi's syndrome since the introduction of laparoscopic cholecystectomy. The present study was undertaken to elucidate the applicability of microlaparotomy cholecystectomy in the management of Mirizzi's syndrome.

### Introduction

An impacted gallstone in the cystic duct with subsequent inflammation and edema resulting in extrinsic compression of common bile or hepatic duct with jaundice is known as Mirizzi's syndrome should be included in the differential diagnosis of any patient who has extrahepatic biliary obstruction. McSherry et al. [2] classified the Mirizzi's syndrome into two types. Type I lesions involves simple external compression of the common hepatic duct by a stone in the gallbladder neck or cystic duct. A type II lesion involves erosion of a gallbladder calculus into the common hepatic duct with fistula formation.

Csendes et al. [2] classified this syndrome into four distinctive types: Type I: External compression of the common bile duct. Type II. Erosion of less than one third the circumference of the bile duct by a cholecystobiliary fistula. Type III: The fistula involves up to two-thirds of the duct circumference. Type IV: Complete destruction of the duct. These classification schemes may help to define a type specific operative approach for the treatment of Mirizzi's syndrome.

The Mirizzi's syndrome presents a difficult surgical challenge because the dense adhesions and edematous inflammatory tissue cause distortion of the normal anatomy in Calot's triangle, leading to a great risk of bile duct injury. Therefore, a controversial issue the surgical strategy for the treatment of Mirizzi's syndrome since the introduction of laparoscopic cholecystectomy. The present study was undertaken to elucidate the applicability of microlaparotomy cholecystectomy in the management of Mirizzi's syndrome.



## Material and Method

Between December 1990 and December 1996 we operated on 16 patients for Mirizzi's syndrome with micro and minilaparotomy cholecystectomy.

In 14 of these patients had type I of Mirizzi's syndrome, the remaining 2 had type II of this syndrome. In 13 of these patients the gallbladder were removed using 3–4 cm single microlaparotomy incisions. In the remaining 3 patients using 5,5 cm, 8 cm as well as 12 cm long incisions for the removal of the gallbladder, and placement a distal T tube because of stenosis of the common hepatic duct, suture repair of the choledochal defect as well as choledochoplasty.

## Results and Discussion

It is very important to evaluate the amount of time that actually transpired from the onset of the disease to the surgery. In the early stages, presented within 7 days of the acute edema does not make micro-laparotomy cholecystectomy more difficult. In 12 of these patients the microlaparotomy cholecystectomy were done within 7 days of the onset of the obstructive cholecystitis. The postoperative stay of these patients were uneventful and they were discharged home 3 days after surgery. From the remaining 4 patients discharged home from 10 to 12 postoperative days. We conclude that early operation eliminates the serious complications and fistula formation of Mirizzi's syndrome.

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## THE SURGICAL TECHNIQUE OF MICROLAPAROTOMY CHOLECYSTECTOMY

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The authors are demonstrating the surgical technique of microlaparotomy cholecystectomy and the categorisation of minilaparotomy. In their 1575 unselected cases operated for cholelithiasis and their complications, 94% had microlaparotomy cholecystectomy (MLC: less than 4 cm single skin incision). 5,4% required modern minilaparotomy (4 to 6 cm incision) because of choledocholithotomy or bilioenteric fistula: and 0,3% had classical minilaparotomy (6 to 8 cm incision). In only 0,3% they converted into an incision longer than 8 cm.

### Introduction

The conventional and laparoscopic cholecystectomy is as already every day utilized method, the operation procedure is well developed and the instruments used allow a reliable operation. The cholecystectomy performed by minilaparotomy is not yet wide spread procedure, since there is no established method and the instruments are not readily available, as well as the fact that special complications rates are not yet well known. The authors are demonstrating the surgical technique of microlaparotomy cholecystectomy and the categorisation of minilaparotomy.

### Materials and Methods

The gallbladder removal performed by abdominal incision less than 4 cm is via microlaparotomy, the 4-laparoscopic 6 cm by modern mini- and the 6-laparoscopic 8 cm via the conventional minilaparotomy cholecystectomy. For the success of operation a proper light source and the operative exposure are mandatory. For this the conventional lighting retractors are not adequate. It is very important to place the patient correctly on the operating table and to select the appropriate place of the incision.

Since 1988, we have worked on a microsurgical technique for cholecystectomy using single 3 cm microlaparotomy incision. The operation is performed under general anaesthesia, but in high-risk anesthesia patients, it has been performed in thoracal epidural or infiltration anesthesia. The positioning of the patients and the operating table are very important. The xiphoid process is placed above the kidney bar, which is slightly elevated. The head part of the table is tilted 30 degrees forward the patient's left.



A 2 1/2 to 3 cm vertical midline skin incision is made from the base of the anatomic infrasternal triangle toward the xiphoid. This is in the area of the functional "minimal stress triangle". After the linea alba is cut through, the peritoneum is opened from the right of the falciform ligament.

The exposure and brilliant illumination of the operative area are essential for precision surgery. A 300-watt metal halide or xenon light source is used with one large diameter fiberoptic cable. This is attached to the retractor blade. If the Calot triangle lies deep, it can be brought closer to the incisional window by further elevating the kidney bar. The isolation of the cystic duct and artery are done similarly, as in classical cholecystectomy. The surgeon has stereoscopic vision with his own eyes, which can be complimented with binocular magnifying loupes with a simple operating microscope. The surgeon standing on the patient's left can place the appropriate-sized clip on the isolated cystic duct without damaging other structures. With our technique, ligation of the duct also can be early accomplished.

## Results

In our 1575 unselected cases operated for cholelithiasis and their complications, 94% had microlaparotomy cholecystectomy (MLC: less than 4 cm single skin incision). 5.4% required modern minilaparotomy (4 to 6 cm incision) because of choledocholithotomy or bilioenteral fistula; and 0.3% had classical minilaparotomy (6 to 8 cm incision) because of transduodenal sphincterolithotomy, type II of Mirizzi's syndrome. In only 0.3% we converted into an incision larger than 8 cm because of uncontrollable cystic artery hemorrhage or type II of Mirizzi's syndrome. We classified 17% of MLC cases as difficult operations. The majority of these were in the beginning, as we found the best technique for the incisions and the exploration of the operative area, especially in obese patients. Inadequate lighting and hand instruments were other factors. Also included are cases with difficult complicated pathology.

## Discussion

The postoperative pain and recovery in 35% of the patients with modern minilaparotomy (4-to 6 cm incision) in 98% of MLC was similar to patients with simple laparoscopic cholecystectomies. For comparison the MLC, MMLC, and LC patients were placed in the same room postoperatively. The advantages of MLC compared with LC are the less expensive instrumentation, and no need for disposables. The surgeon sees the operating field directly and three dimensionally with brilliant distal illumination. Reports in the medical literature mainly compare minilaparotomies with LC-s without providing the length and the location of the incisions. Therefore, we classify incision up to 4 cm as minilaparotomies, 4 to 6 cm as modern minilaparotomies, and 6 to 4 cm as classical minilaparotomies.

The postoperative pain is less if the location of the incision is anatomically in the infrasternal triangle or functionally in the "minimals stress triangle". Including these data will provide better information for future comparisons of alternative techniques of minimal invasive procedures. The incisions described here may be less painful and could be use full to convert LC-s.

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## THE REMOVAL OF CYSTIC DUCT AND GALLBLADDER REMNANT BY MICROLAPAROTOMY

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The so called "Postcholecystectomy Syndrome" may be due to various pathological biliary causes. While a very small number of patients may have symptoms attributable to problems related to cholecystectomy. Twenty five patients underwent a second operation on the bile ducts after cholecystectomy, cholecystostomy and choledochoduodenostomy by micro and minilaparotomy between December 1990. and December 1996. The second most common causes for reexploration were cystic duct and gallbladder remnants (16%). After incomplete cholecystectomy they usually find that the cystic duct stump and the alot triangle embedded in inflamed scar tussua. For this reason the surgical risk is to high with laparoscopic surgery to reoperate for these pathological changes.

### Introduction

Cholecystectomy is associated with an excellent therapeutic outcome. A small number of patients, however, continue to have a variety of gastrointestinal symptoms. While a very small number of patients may have symptoms attributable to problems related to cholecystectomy, many may have symptoms unrelated to biliary tract surgery. A disorder of the extrahepatic bile ducts may result in persistent symptoms. These so called post-cholecystectomy syndromes may be due to biliary strictures, retained biliary calculi, cystic duct stump syndrome, stenosis or diskinaesia of the sphincter of Oddi, stenosis of bilio-digestive anastomosis with retained stones or sump syndrome.

Postcholecystectomy symptoms caused by cystic stump and gallbladder remnants had been described early in this century and several papers have been published [1, 2]. In spite of this reported entity and pathology its validity is still controversial and recent surgical textbooks do not even mention it [4]. Without emphasizing the importance of the cystic duct syndrome, most surgeons feel that such an entity exist causing postoperative complaints and surgical treatment should be considered to alleviate it.

### Materials and Methods

Twenty five patients underwent a second operation on the bile ducts after cholecystectomy, cholecystostomy and choledochoduodenostomy by micro and minilaparotomy between December 1990 and December 1996. The most common cause

for reoperation was an attempt to retrieve a residual or recurrent common duct stone (48% of the cases). The second most common causes for re-exploration were cystic duct remnant (16%). The fourth cause for reoperation was stenosis of choledochoduodenal anastomosis with sump syndrome (12%). The fifth cause for late reintervention was fistula formation after cholecystostomy (8%).

## Results

In 8 out of 25 patients we found gallbladder remnant or cystic duct stumps causing their symptoms. Among the 8 patients, 3 had laparoscopic cholecystectomies 5 classical cholecystectomies. Six patients had stones in a partial gallbladder or cystic duct stump. One patient had a neurinoma and another patient had a suture granuloma of the cystic duct stump.

## Discussion

After incomplete cholecystectomy we usually find that the cystic duct stump and the Calot triangle embedded in inflamed scar tissue, and the thickened gallbladder remnants were found to be fixed by adhesions. For this reason the surgical risk is too high with laparoscopic surgery to reoperate for these pathological changes. In all 8 cases the pathological cystic duct stumps and gallbladder remnants were removed using 3–4 cm single microlaparotomy incision [3]. The postoperative stay of these patients were uneventful as they were discharged home 2–3 days after surgery. The postoperative course ranges from 6 months to 5 years and six months and the patients are symptomless.

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## THE BASIC AND THE PRACTICAL WAY OF TREATING OF DIABETIC FOOT

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Developed atrophic ulcer and infected alterations of the foot, as a result of complications of DM, according to the available literature, 40–80% of the performed amputations are not necessary even though in practice they do occur. In our practice even the severely altered and infected extremities which look serious are considered as primarily a savable extremity if the conditions are present. The state of circulation of the extremity and the condition of the limb are evaluated carefully, and the sugar level is monitored continuously. According to our experience, every progressing process, the alteration of the host sugar level can be held as responsible. That is why after the early therapeutic period, careful monitoring of the insulin level is a priority. At our out-patient department we are daily confronted during routine wound inspections by cases of necrotizing osteomyelitis which to our experience are doomed for removal. In 1995 at the out-patient section of the vascular surgery ward we saw over 9000 patients, more than 500 of which included patients with diabetic angio/neuropathy complications. The nursing of this group of patients during that year only to 33 large vessel reconstructive operations and 26 cases of amputations. We conclude from the above statistics that not all cases of osteomyelitis cases should lead to limb amputation. Due to the nature of the condition, careful monitoring with early preventive measures, plus family support play a crucial role in the outcome of the condition. This complex process is better handled if special diabetic centres were set-up to monitor patients progress.

### Introduction

According to statistics about 4,5–5,0% of the Hungarians are diabetics and upon this basis diabetes mellitus is considered a common disease.

Developed atrophic ulcer and infected alterations of the foot, as a result of complications of diabetes mellitus (DM), according to the available literature, 40–80% of the performed amputations are not necessary even though in practice they do occur. In other words with diligent nursing and caring with a lot of patience, many of the extremities can be saved [3].

Unfortunately, even nowadays the presence of diabetes mellitus can only be established after the appearance of trophic changes.

Patients are referred to the surgical unit due to the two most common complications of DM namely micro- and macroangiopathy and peripheral neuropathy, no matter how different in severity. Because of the nature of the disease such complications are usually accompanied by other systemic signs (e.g.: stroke, varicosity, hypertension, obesity, etc) which makes the right diagnosis more difficult [1].

Among the radical form of diabetic foot, the most misleading, depending on severity, is the neuropathic form, which initiates dramatic inflammating process combined with microangiopathy. In such cases a well planed therapy can lead to limb preservation [3].

The other radical complication being the combined angiopathy is best handled therapeutically based on angiographic data.

The succesfull treatment of diabetic foot is only achievable under organised coordination of diagnostic and therapeutic teams.

## Patients and Methods

### *Our tasks:*

1. Evaluation of the metabolic status, and accurate monitoring of insulin therapy.
2. Diagnosis of inflammatory processes (wound sampling) and drug therapy.
3. Surgical removal of local necrotic tissue.
4. Surgical removal of inflammatory changes and their open treatment.
5. Accurate diagnosis and prompt therapy of oncomming angiopathic changes.
6. Correct diagnosis (Tunning fork) and interventions of neuropathic changes.
7. Evaluation of hemorheologic status (blood viscosity, lipids, fibrinogen) and their drug therapy [2].
8. After macroangiopathy diagnoses vascular reconstructive operation, if necessary.
9. Physiotherapy has an important role in maintaining limb mobility.
10. Treatment of trophic changes, limb fixation by use of plasters and foot fixation devices is crucial.
11. Informing the patient and his family about the disease, its stages and preventive possibilities in order to achieve an optimal outcome.

Immediate limb amputation is only indicated in septic or irreversible cases, which is why it is not included in our protocol.

## Results

In our practice even the severely altered and infected extremities which look serious are considered as primarily a savable extremity if the conditions are present.

The state of circulation of the extremity and the condition of the limb are evaluated carefully, and the sugar level is monitored contineously.

According to our experience, every progressing process, the alteration of the host sugar level can be held as responsible.

That is why after the early therapeutic period, careful monitoring of the insulin level is a priority.



At our out-patient department we are daily confronted during routine wound inspections by cases of necrotizing osteomyelitis which to our experience are doomed for removal, either on an out-patient basis or by hospitalization.

In 10% of the patients with careful sanitation and resolution of macroangiopathy by vascular surgery, a favourable end-result can be achieved.

As for microangiopathic changes we insist on using laser ultrasonographic technique.

In 1995 at the out-patient section of the vascular surgery ward we saw 9422 patients and 553 of which included patients with diabetic angio/neuropathy complications.

The nursing of this group of patients during that year only to 33 large vessel reconstructive operations and 26 cases of amputations.

We conclude from the above statistics that not all cases of osteomyelitis cases should lead to limb amputation.

Early removal of the infected end in many cases results in a fast healing of the involved site, which ensures a limb saving scheme with accompanied favourable psychological state of the patients in question [4].

## Discussion

The aim of our routine is the early diagnosis of the disease affecting a large population, its complications and preventing severe trophic changes. Complications should be investigated in full and most effective treatments applied.

A patient-informing relationship is very crucial in maintaining a high success rate in therapy.

Development of complications will in turn further complicate the outcome of the main disease leading to a vicious circle of events. For this reason, in such systemic diseases prevention has a very important role in the outcome.

This complex process is better handled if special diabetic centres were set-up to monitor patients progress.

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## OXYGEN FREE RADICALS AND THEIR CLINICAL IMPLICATIONS

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Reactive oxygen species (ROS) have been implicated in a variety of pathological processes. The generation of highly reactive oxygen metabolites is an integral feature of normal cellular metabolism (mitochondrial respiratory chain, phagocytosis, arachidonic acid metabolism, ovulation and fertilization), however their production can multiply during pathological circumstances. Free oxygen radicals act either on the extracellular matrix or directly upon cellular membranes themselves. The fundamental defense of the organism against ROS include scavenger enzymes (superoxide dismutase, catalase, glutathione peroxidase) and lipid- and water soluble antioxidant compound (ascorbic acid, glutathione, albumin, transferrin, etc.). Their role in ischemia-reperfusion models have now been comprehensively investigated and it has become clear that ROS is to be blamed for the bulk of post-ischemic injuries, hence the basis for newly established antioxidant therapy in such cases. Also more and more studies have concluded a pivotal role of ROS in degenerative and inflammatory conditions, post-radiation processes and aging.

Therefore it seems as we are continuously shedding light on the crucial part played by these molecules regarding a wide range of pathologies, we are discovering new therapeutic windows that would clinically assist us in managing such conditions.

Reactive oxygen species (ROS) and peroxidation of biological substrates are known to be involved in a variety of pathologies [2, 4, 11]. Free radicals are defined as molecular species containing a single unpaired electron in their outer shell, and they are important in fighting infections and are crucial for life maintenance. These molecules are far more reactive than molecular oxygen leading to peroxidative damages of biomolecules: lipids, proteins and nucleic acids [9, 3]. The species produced include superoxide anion ( $O_2^-$ ), hydrogen peroxide ( $H_2O_2$ ), hydroxyl radical ( $HO^\bullet$ ), nitric oxide ( $NO^\bullet$ ) and peroxynitrite ( $ONOO^\bullet$ ). ROS are continuously formed in living cells as by-products of normal metabolism, during metabolism of xenobiotics and by irradiation.

ROS can act in the extracellular matrix, where they degrade hyaluronic acid and collagen. This is particularly important in certain extracellular fluids, such as the vitreous of the eye and the synovial fluid, where the glycosaminoglycans, including hyaluronic acid are abundant [4].

Oxygen radicals may also directly damage cell membranes, apparently through the peroxidation of structurally important polyunsaturated fatty acids. This phenomenon – lipid peroxidation – occurs partially through the direct action of the superoxide anion and hydroxyl radicals, but it is also in part due to secondarily derived lipid peroxide radicals, lipid hydroperoxides and other lipid fragmentation products that are themselves active



oxidizing agents. Membrane damage may affect the cellular envelope itself but it may also disrupt the subcellular organelles such as lysosomes and mitochondria [6, 7].

To prevent such a damage, cells and organisms utilize three defense strategies. One involves low molecular weight antioxidants such as ascorbic acid,  $\alpha$ -tocopherol, and glutathione, which can interact directly with ROS and neutralize them. The other two involve a variety of enzymes that either metabolize ROS (superoxide dismutase, catalase, glutathione peroxidase) or repair macromolecular damage to nucleic acids, proteins and lipids (DNA repair enzymes, proteases, lipases) caused by ROS.

Because antioxidant defences are not completely efficient, increased free radical formation in the body is likely to result in damage. The term "oxidative stress" is used referring to this phenomena. If mild oxidative stress occurs, tissues often respond by making extra antioxidant defences. However, severe oxidative stress can cause cell injury and even death [1, 5].

The main sources of ROS following injury (ischemia/reperfusion, thermal-, traumatic-, cold injury, exercise to excess, toxins, radiation, infection) are: 1./ the activated phagocytes (make  $O_2^-$ ,  $H_2O_2$ ,  $NO^\cdot$ ,  $HOCl$ ); 2./ release of arachidonic acid, followed by enzymic peroxide formation (via activation of lipoxygenase, cyclooxygenase enzymes); 3./ metal iron released from storage sites (Fe, Cu) stimulate  $OH^\cdot$  formation and lipid peroxidation; 4./ haem protein release (myoglobin, haemoglobin, cytochrome c), haem proteins react with peroxides to stimulate free radical damage and release Fe; 5./ interference with antioxidant defence systems (GSH loss from cells).

Generally it can be summarized that oxygen free radicals probably play a major role in processes that involve ischemia, ischemia followed by reperfusion, hyperoxygenation, tissue inflammation or irradiation [8, 13].

#### *Post-ischemic reperfusion injury:*

Having recognized the fact that many previous ischemia attributed injuries are in reality due to free-radical mediated reperfusion damage, the possibility of preventing deterioration in many clinical situations is now raised [8, 13]. Most studies have proven that it is the superoxide generated from xanthine oxidase during reperfusion that triggers many of the post-ischemic injuries seen in different organs: intestine, stomach, liver, pancreas, heart, lung, skin, kidney, skeletal muscle and central nervous system. Furthermore it has been shown that such a triggering mechanism is based mainly along the microvascular endothelial cells, even in organs such as the heart and brain [7]. The superoxide radicals generated by this mechanism cause adhesion and activation of the nearby neutrophils via specific adhesion molecules (integrins) which consequently leads to vascular injury through the release of enzymes such as elastase and protease.

Several antioxidants have already been successfully proven to be effective in preventing such free-radical mediated injury. For example allopurinol has shown to improve myocardial contractility following ischemia mainly by inhibition of xanthine oxidase. Additionally allopurinol and glutathione have both effectively proved a reduction in the incidence of post-transplant renal failure. However the therapeutic window for such antioxidant therapy has been shown to be quite narrow, especially regarding myocardial infarction-reperfusion models [2, 10].

*Degenerative conditions*

More and more studies are suggestive of a crucial role of the reactive oxidants in the process of carcinogenesis and consequently the importance of a diet rich in natural antioxidants such as vitamin C, E and B-carotene [12].

Most recently it was established that the oxidation of low density lipoproteins which facilitates its subsequent uptake by subendothelial phagocytes is the rate limiting step in the development of atherosclerosis. A step which is practically a free-radical mediated lipid peroxidation, and quite effectively managed by regular antioxidant intake. Aging too has been recently shown to be in part due to oxidant-mediate damage to metabolic and repair mechanism of the cells, and hence perhaps amenable to control at least partially by use of antioxidants [10].

*Hyperoxygenation syndroms*

Many conditions are seen in clinical practice that can be clearly associated with hyperphysiologic levels of oxygen such as neonatal bronchopulmonary dysplasia, retrolental fibroplasia and ARDS. In such conditions abundant evidence exists to confirm the beneficial effect of an antioxidant therapy.

*Inflammatory conditions*

There are a number of physiologic mechanisms which involve the generation of reactive oxidants such as the synthesis of prostaglandines and leukotrienes via free-radical mediated lipid peroxidation, or the initiation of phagocytosis of microorganisms. The killing of bacteria by tissue phagocytes and circulating neutrophils is facilitated by the initial generation of superoxide radical by a membrane associated NADH oxidase and the subsequent generation of hypochlorous acid [11]. It has even been suggested recently that the xanthine oxidase enzyme on the luminal surface of microvascular endothelium, as mentioned previously, may act as a trigger mechanism in eliminating circulating microorganisms [7]. This mechanism may also explain the hyper-inflammatory triggering of microvascular injury which leads to different form of inflammatory bowel disease, hyperimmune response, such as adult respiratory distress syndrome and multiple organ failure (MOF).

*Radiation damage*

It is a well established fact that a bulk of radiobiologic effect of radiation is due to the generation of reactive oxygen species. This fact has formed the basis of current adjuvant or curative radiotherapy, specially in cases of gastro-intestinal malignancies, where hyperbaric oxygenation and use of radioprotective agents have attracted great interest and promise great potential for the future. Dramatic radioprotection has been found of the bowel mucosa in rats after the topical application of an antioxidant agent [2, 4]. This could have important implications for the protection of the small bowel, colon or rectum during radiation therapy.

In conclusion the oxidant damage represents a fundamental mechanism of tissue injury. The much better understanding of the basic mechanism of free radical mediated human disease promise new therapeutic approaches in the manipulation of ROS mediated tissue injury.



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## CARDIOPROTECTION DURING HEART ISCHEMIA-REPERFUSION

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Oxygen reactive species play a significant role in reperfusion tissue damages. In this study we aimed to investigate the mechanisms of injury regarding changes of neutrophil function. In our experiments the left descending coronary artery (LAD) was ligated in Beagle dogs for 1 hour followed by one hour reperfusion. Animals were divided into two groups: Group I. dogs (n=10) served as control: Group II. the animals (n=10) were treated by cardioprotective drug Bisaramil. Peripheral blood samples were taken for neutrophil isolation before operation and subsequent reperfusion (5 min, 1 hour). The stimulated superoxide radical generating capacity of polymorphonuclear leukocytes (PMN) was measured. The lipid peroxidation (MDA), amount of reduced glutathione (GSH) and activity of superoxide dismutase (SOD) were measured in non-ischemic and ischemic parts of left ventricle. There was no significant changes either in control or in treated animals in respect to changes of neutrophil radical production after one hour LAD ligation, however there was a significant discrepancy ( $p<0,001$ ) between control and treated animals following a 1 hour reperfusion. The values of MDA in the ischemic-area increased characteristically in the Group I. parallel with decrease of scavenger GSH and SOD. In contrast in Group II., where depleted PMN radical production was observed endogenous scavengers were preserved on a higher level. In summary we can conclude that diminished superoxide radical production of circulating neutrophils during reperfusion has beneficial effects on tissue injury caused especially by free radicals.

### Introduction

Coronary reperfusion by means of thrombolytic therapy, percutaneous transluminal angioplasty or bypass surgery is rapidly emerging as the fundamental strategy in the management of acute ischemic syndroms. Experimental studies have demonstrated that although early reperfusion limits or even prevents necrosis it does result in reperfusion injuries such as ventricular arrhythmias, myocardial stunning and lethal cell injuries [1,4]. There is a growing evidence that oxygen reactive species (ORS) play a significant role in the postischemic reperfusion injuries [2]. The aims of present study were: i./ to investigate the cellular activation and tissue injury mechanisms regarding changes of neutrophil radical generating capacity and alterations of lipid peroxidation as well as endogenous scavengers of reperfused heart muscle; ii./ to measure whether the new antiarrhythmic drug Bisaramil [5] – which can exert strong inhibitory action in vitro on superoxide radical production of neutrophils – can lead to protection against ORS mediated myocardial tissue injury in ischemic – reperfusion state.



## Materials and Methods

The left thoracotomy was performed in Beagle dogs (n=20) during general anaesthesia to prepare the left descending coronary artery (LAD) for ligature. After 60 min of ischemic period, LAD-ligature was released for 1 h. Animals were divided into two groups: Group I. contains control animals (n=10) received saline infusion; in Group II. dogs (n=10) were treated by antiarrhythmic drug Bisaramil at a dose of 2 mg/kg several minutes prior to the end of LAD occlusion, than the administration was repeated in the 30th minute of reperfusion. Blood samples were taken for neutrophil (PMN) isolation following LAD ligature and reperfusion, while at the end of reperfusion hearts were removed and tissue samples were cut from ischemic and non-ischemic part of left ventricle. In the tissue homogenates we determined malondialdehyde (MDA), reduced glutathione (GSH) and superoxide dismutase (SOD).

## Results and Discussion

The *in vitro* superoxide radical generating capacity of PMN closely resembles their *in vivo* stimulation [3]. The mediators accumulated during ischemia and reperfusion facilitate the activity of these cells, which can then promote the progression of the infarction. In the control group a tendency of gradual increase of free radical production capacity was seen, while in Bisaramil treated group practically the changes were not significant, indicating an inhibitory effect of drug treatment on stimulation of free radical generation by PMN (Fig. 1). In the tissue samples the extent of tissue damage was evaluated by measuring the changes in parameters (MDA, GSH, SOD). In our experiments the significant increase of MDA concentration was measured in the infarcted area of myocardium compared to the non-infarcted one, indicating the peroxidative damage of membrane lipids and concomitant pathological changes of their function. In the Bisaramil-treated group, however no such change, showing that the membrane structure was better preserved compared to the control group (Fig. 2). In our experiments significant decrease of GSH-concentration was measured in the ischemic-reperfused area of control group, and the same change was found with respect to SOD-activity. On the contrary, in Bisaramil-treated group far less severe biochemical changes were seen regarding the activity of SOD and GSH. Based on our results, we can conclude: i./ Bisaramil has a significant effect on ischemia-reperfusion injury influencing beneficially the ORS mediated damages; ii./ it seems to be that strong inhibitory action of Bisaramil on the neutrophil superoxide radical generating capacity *in vivo* plays important role to reduce the harmful effect of oxygen radical species following early reperfusion damages.

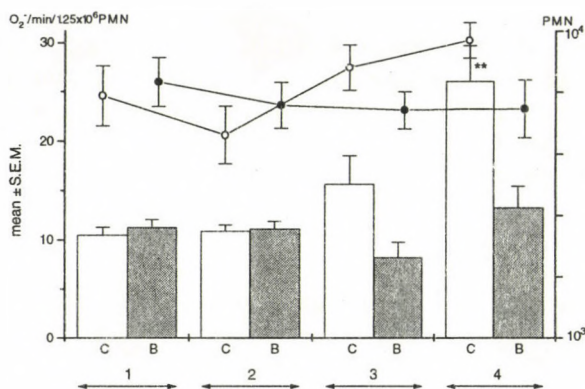


Fig. 1

Changes in the superoxide radical generating capacity of polymorph neutrophil granulocytes and the number of leukocytes isolated from peripheral blood

\*\*  $p < 0.01$  vs basal value of control group. C = control group, B = Bisaramil-treated group.

—●— = leukocyte number in Bisaramil-treated control group

—○— = leukocyte number in the control group

1 = before LAD; 2 = end of LAD; 3 = 5 min reperfusion; 4 = 60 min reperfusion

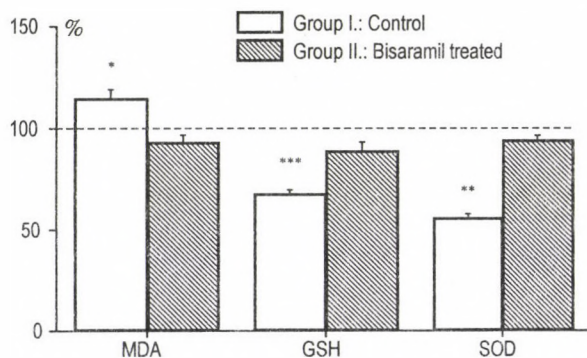


Fig. 2

Comparison of the changes in MDA, GSH and SOD measured in myocardial tissue samples. Significant elevation of lipid peroxidation and depletion of endogenous scavengers were influenced by Bisaramil treatment

(\*  $p < 0.05$ ; \*\*  $p < 0.01$ ; \*\*\*  $p < 0.001$  compared to the value of intact part of the heart)



## Summary

The aim of this study was to know whether antiarrhythmic compound Bisamil which has in vitro inhibitory action on neutrophil radical production, how can influence the free radical mediated tissue injuries following heart ischemia and reperfusion. Our experiments in Beagle dogs clarified that Bisamil infusion significantly inhibited the stimulated radical production of a neutrophils during LAD ligation and reperfusion, which was in a good correlation with better preserved endogenous scavenger content and cellular membrane system.

## Acknowledgements

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## SURGERY OF THE PANCREAS

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The author deal with the surgery of diseases of the pancreas in this article. On the basis of the literature, timing of operation, surgical procedures in acute pancreatitis are discussed. In chronic pancreatitis, results of different decompression operations, resection of the pancreas and endoscopic biliary stenting are evaluated. Regarding the carcinoma of the pancreas, operative methods and factors of survival are the most important questions.

### Introduction

The surgery of the exocrine pancreas can be divided into three main parts:

- surgery of
- 1. acute pancreatitis
- 2. chronic pancreatitis
- 3. tumours of the pancreas.

In the last period the introduction of pancreatic imaging (US, CT, fibre-optic endoscopy) has revolutionized the treatment of diseases of the pancreas. The number of these diseases is increasing. The therapeutic methods have changed, developed which refer to the actuality of this topic / theme.

### Discussion

#### *Acute pancreatitis*

In case of acute edematous pancreatitis mortality is usually less than 1–2%. However, when pancreatitis is characterized by necrosis or hemorrhage, the mortality rises up to 30–50% or higher. This type of the acute pancreatitis has surgical significance.

In the history of surgical treatment of acute severe pancreatitis three periods can be distinguished [8]

1. In the 1930s conservative treatment was recommended for the reason of very high mortality (80–100%) of operative intervention.
2. In the 1970s early operation (within one week) was preferred with aim to resect all areas of necrosis before these lesions become the focus of uncontrollable infection. The mortality rate was 40–80%.
3. From the second half of the 1970s delayed operation (after one week or later) came to the foreground with lower mortality (30–40%).



Regarding the operative methods in the last decade the necrosectomy and postoperative local lavage of the lesser sac were performed in the most centers. This management provides for continuous removal of necrotic tissue, bacteria and different, biologically active materials such as endotoxins, phospholipase A<sub>2</sub>, trypsin, other enzymes and substances [1].

In a prospective study it was showed that sterile pancreatic necrosis, even when extensive and associated with organ failure, could be satisfactorily treated by intensive medical therapy alone including closed peritoneal dialysis [2].

In the Pancreas Club Meeting (San Diego, May. 14, 1995) swiss authors recommended adoption of nonoperative treatment of the acute edematous and sterile necrotizing pancreatitis and indicated surgical intervention for those patients who have secondarily infected necrotic focus in their pancreas [7].

In case of biliary pancreatitis the appropriate treatment involves immediate removal of the bile duct stones, particularly if they are in the papilla. In the last decade endoscopic papillotomy has been accepted as the initial therapy of biliary pancreatitis. This procedure decreases the morbidity and mortality in patients with severe biliary pancreatitis but does not alter the incidence of local and systemic complications [9].

### *Chronic pancreatitis*

In the surgical treatment of chronic pancreatitis decompression operations and different types of resection of the pancreas are used.

Nowadays many surgeons have preferred pancreaticogastrostomy against pancreaticojejunostomy for pain relief in chronic pancreatitis. Performing the anastomosis is easier and the rate of complications is lower. Regarding activation or inactivation of pancreatic enzymes, in a study it was found that the main hydrolytic enzymes of the pancreas are activated when the gastric acidity is over pH 3.1 which normally occurs after ingestion of a meal [13].

For treatment of chronic pancreatitis the classical Whipple resection has become as the standard operation. The disappointing long-term results of Whipple operation have led to the modification of this procedure, introduction of the pylorus-preserving pancreatoduodenectomy. The newest type of resection is the duodenum-preserving pancreatic head resection which was developed to selectively remove the head of the pancreas with preserving the duodenum, pylorus, the body and tail of the pancreas. These types of resection are effective in patients with intractable pain caused by chronic pancreatitis with an inflammatory mass in the head of the pancreas.

Endoscopic biliary stenting is an alternative to surgery for the initial treatment of jaundice and cholangitis in patients with chronic pancreatitis. This procedure is associated with low rate of early complications and in about one – quarter of patients offers definitive treatment [11].

### *Carcinoma of the pancreas*

Cancer of the exocrine pancreas is rarely curable. The 5-year survival rate is about 5% in completely resected patients. Palliative surgical or endoscopic biliary decompression,

open or laparoscopic gastroenteric anastomosis, pain control may improve the quality of life but not affect the overall survival.

The importance of staging of pancreatic exocrine cancer is not great. However, determination of the extent of this disease will be important to make uniform strategy, to review the results of the treatment of pancreatic cancer.

Pancreatoduodenectomy against total pancreatectomy is the accepted surgical treatment for cancer of the pancreas. Postoperative morbidity and mortality, duration of hospital stay are significantly increased after total pancreatectomy and the 5-year survival rate is lower after total removal of the pancreas.

Tumors invading the portal vein may be resected safely during pancreatoduodenectomy and the involvement of this structure is not associated with a poor prognosis.

On the basis of some studies survival after resection is affected by more factors. According to Fortner et al. tumor size is the strongest predictor of prognosis [4]. In another study it was showed that absence or presence of invasion to the anterior capsule of the pancreas, invasion of the retroperitoneal tissue, invasion of the surgical margin of resection and the extent of lymph node metastasis are the most important factors in survival [6]. Conlon et al. found that factors of survival are the followings: differentiation of the tumor, extrapancreatic invasion, perineural invasion and invasion of neighbouring organs [3]. Results of a retrospective study suggest that characteristics of the patient and tumor findings rather than operative procedures affect long-term survival after resection for pancreatic carcinoma [12].

Lymph node metastasis has frequently been found as an important factor in the prognosis. This leads some surgeons to perform an aggressive surgical intervention, including wide lymphadenectomy. Because of considerable morbidity of this procedure german authors offer to make a controlled study on this strategy before general applying in the practice [10].

According to Ishikawa extended pancreatectomy (removing the nerve plexi and connective tissues too) is the most promising procedure at present but its indication should be carefully selected because of the patient's quality of life [5].

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## **THE ROLE OF HIGH RISK HPV LYMPH NODE POSITIVITY IN THE SURGICAL STAGING OF CANCER OF THE UTERINE CERVIX**

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The presence of oncogenic Human Papillomavirus (HPV) DNAs in cervical carcinomas and their normal and metastatic pelvic lymph nodes is studied worldwide. Does the HPV positivity without histological metastasis in the lymph nodes mean an early prognostic indicator in the progress of the disease? The authors analyzed the surgical, histological and virological data of four cervical cancer patients, whose recurrence occurred very early and died soon. After performing radical hysterectomy with precise removal of the pelvic lymph nodes, they assessed the operative specimens by routine histology and detected for HPV types by PCR. All the four lymph nodes harboured HPV-18 subtype in spite of negative histology in three cases. Thus the authors consider that if the lymph nodes contain any type of high-risk HPVs maybe despite negative histology or early stage of cancer we have to treat the patient as if she had an advanced cervical cancer.

### **Introduction**

Cancer of the uterine cervix is one of the most frequent female malignancies worldwide. Human Papillomavirus (HPV) 16, 18 and other high-risk types are strongly associated with the development of invasive cervical carcinoma [3] and present in approximately 90% of cases. Till now the most important prognostic factors of the disease influencing survival were the size of the primary tumor with the clinical stage and especially the histological status of pelvic lymph nodes [2]. However, there is the question of the role of HPV in the progression of cervical cancer, because HPV-DNA presented in cervical carcinomas has been detected in the metastatic lymph nodes as well as in nonmetastatic lymph nodes. The presence and oncogenic subtype of the virus in pelvic lymph nodes could become a significant prognostic factor in evaluating the therapeutic outcome of the disease even if the histology is negative.

### **Patients and Methods**

Our study is about four invasive cervical cancer patients with early tumor recurrence after the treatment, rapid progression of the disease and very short survival. They were screened at the Dept. of Obstetrics and Gynecology of Debrecen Medical University in 1992. After three times local intracavitary irradiations (400, 1700, 1700 reu doses) we performed radical hysterectomy with precise removal of pelvic lymph nodes in all four

cases. After the operation an additional intracavitary radiotherapy to the vaginal stump (400 reu dose) and extended field telecobalt irradiation (40 Gy with 2 Gy/day) were applied. The primary tumors (uterine cervix) and lymph nodes were evaluated by routine histology and the presence and type of HPV-DNA was examined by Polymerase Chain Reaction (PCR) in the two type of samples, respectively. Control examinations were carried out at our outpatient oncological clinic.

## Results

Patient ages were quite low, ranged from 21 to 56 years. According to the etiologic cofactors of cervical cancer, they all belonged to the high risk group in the population (questionable personal hygiene, no history of routine cancer screening, multiparity, frequent vaginal infections, but all were non-smokers). The intraoperative staging confirmed the preoperative one, three patients had FIGO stage II/b and one had stage II/a. The histological examination found squamous cells carcinoma in three cases and adenocarcinoma in one case with the degree of differentiation moderate and poor equally in the primary tumors. However, there was apparent histologic metastasis only in lymph nodes of the case of adenocarcinomatous primary tumor. In the other three cases there was no detectable lymphatic involvement. In spite of these findings, all four patients harboured a high risk subtype of HPV (HPV-18) both in the primary tumor tissue specimens and in the removed pelvic lymph nodes, including the histologically negative lymph nodes! Recurrences occurred in the retroperitoneal lymphatic system first, quite early, between 7–22 months after the primary histological verification and led to the death of the four patients between 2–4 months.

Table 1.  
Patients characteristics

| No.  | Age | Stage | Hystology |            | Grade | HPV type |            | Survival (months)  |                 | Present status |
|------|-----|-------|-----------|------------|-------|----------|------------|--------------------|-----------------|----------------|
|      |     |       | pr. tu.   | lymph node |       | pr. tu.  | lymph node | without recurrence | with recurrence |                |
| I.   | 21  | II/b  | Squam.ca. | neg.       | G III | 18       | 18         | 7                  | 10              | dead           |
| II.  | 33  | II/b  | Squam.ca. | neg.       | G III | 18       | 18         | 7                  | 9               | dead           |
| III. | 35  | II/a  | Squam.ca. | neg.       | G II  | 18       | 18         | 17                 | 21              | dead           |
| IV.  | 56  | II/b  | Adenoca.  | pos.       | G II  | 18       | 18         | 22                 | 24              | dead           |

## Discussion

Success of treatment of cervical cancer depends on prognosis, which is determined by clinicopathologic variables. One of the most reliable well known prognostic factors is pelvic lymph node metastasis. However, there is many cases of invasive cervical cancer in the literature treated at early stages (stage I or II) without pelvic lymph node



metastasis relapse and patients die from their cancer [1,4]. Recently, attention has focused on HPV positivity in pelvic lymph nodes as an early possible prognostic indicator in progression of cervical cancer [5]. Our results seem to confirm this theory, as we detected HPV-18 positivity in lymph nodes, despite negative histological findings and observed early tumor recurrence, rapid progression of the disease with a very short survival.

The above results in agreement with the literature raise the question, is the present FIGO (Federation of International Obstetrics and Gynecology) staging suitable for classifying the different stages of cervical cancer and could it predict the probable outcome of the disease. All things considered, we think that if the lymph nodes contain any type of high-risk HPVs maybe despite negative histology or early stage of cancer we have to treat the patient as if she had an advanced cervical cancer.

The other question is the paraaortic lymph nodes. We think that we have to perform lymphadenectomy of this region, because molecular detection of HPV-DNA in paraaortic nodes maybe helpful to the gynecologic oncologist in planning adjuvant treatment.

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## THE IMPORTANCE OF INCISION-PLANNING AND OPERATION TECHNIQUE DURING ORGAN-PRESERVING AND RADICAL OPERATIONS IN THE CASE OF PATIENTS WITH MAMMARY CANCER

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The authors place a great deal of emphasis on the application of plastic surgery principles in the course of all their operations, especially mammary operations: the incision planning respecting the lines of strength, the atraumatic operation technique (sharp preparation, high-frequency electrocoagulation, tensionless wound closure, and suction drainage from a separate opening). In their organ-preserving operations the radial incision recommended by Veronese is avoided, and the axilla is exposed separately. They do not perform their radical mammary operations according to the customary method (Auchincloss, Patey) either. If necessary they accomplish the tensionless closure of the wound by means of individual incision planning and the preservation (rotation and sliding) of the intact skin of the breast, which is the precondition of the reconstruction that might be performed subsequently. In the course of the follow-up of 295 operations carried out in this manner excellent or good results were obtained in 83% as far as aesthetics and functionality were concerned. Lymphedema did not develop in a single case on account of operation technique.

### Introduction

In our department we place great emphasis on the application of the principles of plastic surgery in the course of all our operations [3].

These are:

- ◆ incision respecting the lines of strength,
- ◆ atraumatic operation technique:
  - sharp preparation performed in the appropriate layer,
  - high-frequency electrocoagulation,
  - tensionless wound closure by means of monofil suturing,
  - suction drainage from a separate opening,
  - a suitably modelled compression-flexible bandage.

All these are particularly important to be applied during our mammary operations, since the female breast by all means also embodies aesthetic values (even in old age). Nowadays we are witnessing the appearance of mammary cancer in ever younger ages-which fact lends even more importance to the above statements.

The emotional attachment of women to their breasts and their fear of losing their breasts are the main reasons why they often present to the surgeon in an advanced stage, sometimes even in a fatally neglected condition.

The spreading of organ-preserving operations and treatments [2, 4] must have originated in the recognition of this fact. However, no matter how widespread is the



expansion of these types of operations if the surgical technique is not appropriate and the „preserved” breast is only at the most the caricature of the original one: in addition to having lost its aesthetical value it is the source of numerous complaints (the pain and itching from hypertrophic scar, the limited motion of the shoulder joint, and the lymphedema of the upper extremity).

The operation technique based on the harmony of oncological principles and cosmetic aspects applied in our department eliminates all this and additionally ensures ideal conditions for potential subsequent reconstructive operations.

### Cases-operation technique:

#### *I. Breast-preserving operations*

We have been performing breast-preserving operations since October 1988 under the following conditions:

1. T 1–2 sized tumor with an upper limit of 3 cm
2. A tumor multiplicity must be ruled out by histological examination (lobular carcinoma!)
3. The tumor-breast proportion shall be appropriate!
4. The axillary block-dissection is done in each case (lymph node positivity was found in 28% of our cases).

The operations are followed by Te-Co irradiation in an obligatory manner. In case of axillary lymph node metastasis a 6-cycle CMF regimen complements the treatment (in addition to a one-year Zoladex therapy in premenopause and a long-term Zitazonium therapy in postmenopause).

In the course of the last eight years (1988–96) 32% of patients (n=94) out of a total of 295 patients operated for breast cancer have been treated by the QUART-method (this rate has increased up to 48% in recent years).

Besides strictly adhering to oncological principles a great deal of emphasis is laid on cosmetic aspects. In accordance with this, we find unacceptable the radial incision (especially within the upper part of the breast) recommended by Veronese and others [4, 1].

We perform quadrantectomies by peri-, paraareolar or submammary curvilinear incisions, and the axilla is exposed by a separate incision led in the skinfolds. Operations carried out in this manner have shown excellent or good results in 83% of cases both in regard to aesthetics and functions.

We attribute a great deal of importance to the atraumatic operation technique in view of both oncological and cosmetic aspects:

- ◆ sharp preparation performed in an appropriate layer,
- ◆ high-frequency electrocoagulation (ligation is performed rarely only in the case of larger vessels exceeding a diameter of 2 mm),
- ◆ suction drainage from a separate opening,
- ◆ tensionless wound closure using monofil sutures (the glandular tissue is not sutured up),
- ◆ a suitably modelled compression, elastic bandage.

The drain is left in place until it sucks fluid (7–10 days).

II. During our *radical operations* the incision is planned individually depending on the location of the tumor, the tumorous infiltration of the skin, the size of the breast, and the width of its base in such a way that the intact skin of the breast is preserved for the

purpose of tensionless closure of the defect. In this manner we might be able to gain a skin flap of up to 10–12 cm width padded with fat, which can be rotated and slid according to preference.

The axillary block-dissection is often performed separately from the incision led in the skinfolds. In this case all breast tissue must be removed through a subcutaneous tunnel between the two operative explorations.

The elements of the atraumatic surgical technique detailed above are strictly observed even during our radical operations. In addition, a lot of emphasis is laid on the protection of a large wound surface against drying out.

In general, a double suction drainage is employed: one in the axilla and the other one at the site of the breast. The volume of the drain is marked daily and the drain is only removed if in the course of 24 hours the volume of the aspirate was less than 20 ml.

### Discussion

Our patients were asked to attend a control examination in January 1997.

86 patients (91%) appeared from the group treated according to the QUART method, while 151 patients (75%) appeared from the group who had undergone the radical operation.

The evaluation was carried out according to functional and aesthetical aspects based on the degree of satisfaction of the patients.

The following were examined:

- ◆ the form and size of the breast operated on (in the organ-preserving group),
- ◆ the change of the quality of life (dressing, wearing swimsuits),
- ◆ the quality of the scar,
- ◆ the condition of the skin of the operated (and irradiated) area (pigmentation, flexibility, and mobility),
- ◆ the movement of the humero-scapular joint (especially in regard to abduction, elevation, and extension),
- ◆ the circumference of the upper extremity on the operated side (lymphedema).

Based on the results the patients were classed in groups with ratings of excellent, good, acceptable, and bad. 83% (n=197) of our patients followed-up were sorted into the groups with excellent and good ratings. In two cases (0,8%) upper lymphedema was detected. In both of these patients repeated „tumor-reducing” operations and irradiation were carried out because of existent inoperable axillary lymph node metastasis. In these cases the venous and lymph circulation disorder was caused by the growing of the (unremovable) tumor mass left in the axilla.



## Summary

In summary we can state that subsequent to the operations performed according to the technique preferred by us (and detailed above) the pain of the wound is minimal, the exercising of the shoulder can already be started the day after the operation, therefore the movement of the humero-scapular joint does not become limited, the operation scar is aesthetic, the skin of the operation area is loose, elastic, with good blood circulation, and padded with fat; consequently it is capable of better tolerating radiotherapy and is suitable for subsequent reconstruction. An additional advantage is that the deformity and dislocation of the remaining breast are the least possible and there is no scar left from the operation on the skin area which is aesthetically valuable. Lymphedema does not develop on the upper extremity because of the operation technique. It is to be hoped from the satisfaction of our patients and the gradual spreading of the organ-preserving operations that our patients with breast cancer will present at our department in ever earlier stages of the disease. After all, this is the crucial question of the problem of breast cancer.

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## THE TOTALLY EXTRAPERITONEAL (TEP) LAPAROSCOPIC HERNIA REPAIR

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In recent years endoscopic techniques using mesh implantation have been added to the many options for the repair of inguinal hernia to diminish postoperative pain, shorten the convalescence period and improve the recurrence figures of the classical repair. The purpose of this paper is to evaluate our first experiences gained by applying the TEP laparoscopic hernia repair. Between March and December 1996, 20 laparoscopic herniorrhaphies were performed with complete extraperitoneal balloon dissection. A large polypropylen prosthesis was inserted to cover all potential defects. The follow-up was 2–10 months. There were 10 indirect, 6 direct, 1 combined direct and indirect, 1 femoral and 2 scrotal hernias. Age (26–86 years) and operative time (52–120 mins) had a wide range. Hospital stay lasted from 1–5 days. Morbidity was low: scrotal emphysema (3), peritoneal lesion (2) and palpable mesh crease (1) occurred in a few cases. No recurrences have been seen so far. It seems that the TEP laparoscopic hernia repair is a highly successful procedure with minimal morbidity. Preliminary results are promising. Further experiences and long term follow-up studies will determine the future of laparoscopic hernia surgery.

### Introduction

Inguinal hernia is one of the most common disorders treated by general surgeons. The inguinal approach described by Bassini was the most usual procedure for several decades. Now there are a variety of accepted techniques for herniorrhaphy. With the advent of laparoscopic general surgery new endoscopic techniques using mesh implantation have been added to the many options for the repair of inguinal hernia. The laparoscopic approach has undergone many variations in technique over the past five years. These techniques were developed in an attempt to diminish postoperative pain, shorten hospital stay and the convalescence period and improve the recurrence figures of the classical repair. The purpose of this paper is to evaluate our first experiences gained by applying the totally extraperitoneal (TEP) laparoscopic hernia repair.

### Methods

Between March and December 1996, 20 laparoscopic herniorrhaphies were performed with complete extraperitoneal balloon dissection. This type of hernioplasty makes use of the anatomical specialities of the rectus muscle vagina, which makes it possible to avoid entering the peritoneal cavity. Three trocars were placed, one parumbilically for



the 0° laparoscope, one in the midline 3–4 cm infraumbilically, and one just beside the spina iliaca anterior superior on the site of the hernia for the operating instruments. For the patchplasty of the inguinal and femoral region a 10x15 cm polypropylen prosthesis was inserted through a 12 mm trocar to cover all potential defects. The operations were usually performed under general anaesthesia but twice under spinal anaesthesia. The follow-up was 2–10 months.

## Results

There were 10 indirect, 6 direct, 1 pantaloon inguinal hernias; 1 femoral and 2 scrotal hernias. Age varied between 26 and 86 years. Operative time ranged from 52 to 120 minutes. Morbidity was low: scrotal emphysema (3), peritoneal lesion (2) and palpable mesh crease (1) occurred only in a few cases. Conversion to classical open repair was made in two cases. Once because of the presence of scar tissues in the extraperitoneal space due to a previous lower abdominal incision; and the other time because of the accidental entering of the laparoscope into the abdominal cavity through a large injury of the posterior rectus sheath. In these cases the hospital stay lasted for five days. Fifteen patients required only an overnight hospitalization, three patients stayed for two days. No recurrences have been seen so far.

## Discussion

Inguinal hernia repair is one of the most common operations in general surgery. There has not been, however, one single approach which has been accepted as a standard. The classical hernia repair usually produces some tension on the suture line, which is responsible for the postoperative pain, quite long convalescence, and relatively high recurrence rate [1, 2].

The recurrence rate significantly improves by tension-free repair methods using mesh [2, 5], but in the case of the groin approach the patients remain uncomfortable and disabled for three or four weeks. These disadvantages can be avoided by laparoscopic methods. Nowadays the two most commonly performed laparoscopic approaches are the transabdominal preperitoneal (TAPP) and the totally extraperitoneal approach (TEP). These methods have a very low recurrence and complication rate [1, 3]. It seems that there are significant advantages to the TEP approach [4]. Unfortunately the laparoscopic approaches require mostly general anaesthesia, furthermore, orientation and identification of inguinal anatomy laparoscopically requires special experiences.

### Summary

The totally extraperitoneal laparoscopic hernia repair was developed in an attempt to diminish postoperative pain, shorten the convalescence period, and equal the recurrence figures of the classical repair techniques. Our preliminary results, based on 20 cases, are promising. Despite the follow-up is very short it will take some time before the true value of this new method can accurately be assessed.

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## THE TRENTAL TREATMENT PREVENTS THE REDUCTION OF SUPEROXIDE DISMUTASE ENZYME (SOD) ACTIVITY IN RATS AFTER COLON SURGERY

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The authors tested the effects of the pentoxifyllin (px, Trental) pre-treatment upon the superoxide dismutase activity of the left colonpart anastomosis of rats. It has been found that the SOD activity of the proximal (4.9 U/g), the anatomical area (1.9 U/g) and the distal (3.1 U/g) intestinal segments considerably decreased, compared to the control (9.16 U/g). In the operated and pre-treated animals with Trental, the SOD activity of all the three intestinal segments increased (proximal 15.5 – anastomosis 5.7 – distal 8.9 U/g) compared to the non treated group.

### Introduction

After intestinal surgery, against the successful operation, the patient recuperation reducing complications, the suture insufficiencies, the adhesions, the inflammation are common. One possible reason of the emerged damage is the relatively wide hypoxical zone in the line of anastomosis emerged by extensive circulatory insufficiency, in which the intracellular free radicals production increased. After reperfusion of the hypoxical zone, the free radicals production temporarily continue to increase, at the background of that there are partly the xantindehydrogenase-xantinoxidase (XD-XO) transformation, partly the activation of the white blood cells [2]. The role of free radicals in gastrointestinal tract (GI) diseases, is well known [5] there are numerous literary data about the protection of SOD and CAT treatment against the damage after reperfusion [4], but it is not known, how the endogenic free radical scavenger enzymatic system – within the elementary arising superoxide anion eliminating SOD enzyme activity – changes in anastomosis. Treatment with pentoxifyllin (Trental) advances the microcirculation of rat colon anastomosis, decreases the inflamed reaction of the peritoneum, the white blood cell (WBC) adhesion, the tumour necrosis factor (TNF-alfa) production and improves the bursting pressure (BP) of anastomosis [1]. Present time it is not known, how the endogenic SOD – enzyme activity – changes in anastomosis after Trental treatment. In recent study after experimental left colon anastomosis, the tendency of SOD enzyme activity of the anastomosis and its periphery were observed in Trental treated and untreated animals.

## Materials and Methods

Pentoxifyllin (Trental inj. CHINOIN) 2.5 mg/kg i.p., Na-Pentobarbital 50 mg/kg SOD-(Orgotein, diagnostic data) 82.0 U/ml (1.64 U/5 µg).

*Animals:* the experiments were performed on male, Wistar (Lati-Gödöllő) rats weighting 200–250 g, were kept in plastic cages (6 rats/cage) under standardized condition (semisynthetic rodent food, temperature 22 °C, duration of light and dark period 12–12 hours, relative humidity about 60%), were fasted 24h before surgery, consumed water ad libitum.

*In vivo groups:* 1. Control, treated with physiological salt solution (n=20), 2. Left colon anastomosis (n=10), 3. Trental treatment, then left colon anastomosis (n=10).

1. Animals of the control group were treated with physiological salt solution by i.p. injections under pentobarbital narcosis.

2. Surgical intervention: rats, anesthetized with pentobarbital, after a median laparotomy the left colon was isolated and the sigma bowel was cut trough transversally, without alteration of mesenterial circulation. Just after cutting trough, the two colon part were matched end to end, and 12 suture were put in the seromucosal layer of the colon. After that the abdomen was closed. The animals were treated with 1 ml/kg physiological salt solution i.p., 24 and 12h before the operation. 3. Animals undergoing the same experimental procedure were treated with 2.5 mg/kg Trental 24h and 12h before the surgery. 1h after the operation from all of the animals under pentobarbital narcosis after the abdominal wall opening 1 cm sized pieces were excised from all the proximal, the anastomotomical, and the distal area, and from a further part appearing uninjured. The examined samples as compared with the anastomosis were signed as: (O) far from the anastomosis, (P) proximal part, (A) anastomosis, (D) distal part. In the control group - comparable - the anatomically similarly located intestinal pieces were observed. The organ samples were frozen and stored on -20 °C until the determination of SOD enzyme. The frozen, 1 g tissue pieces were homogenized with 5 ml distilled water, were centrifuged (13 000 g, 50 minutes), then the enzyme activity were measured using the method modified by Matkovics et al. [3] in the Misra-Fridovich adrenalin-adrenochrom system. The values were given activity / g wet tissue. In vitro experiments were taken to determinate, the rate at which pentoxifyllin effects directly the activation of SOD enzyme. Therefore the tissue homogenates were incubated for 10 minutes with 100 µg, 150 µg or 600 µg pentoxiphillin, then the SOD activity of the sample was measured.

## Results

In vivo in all cases (see P, A, O, D), the SOD activity of samples gained from the intestine of operated animals were decreased considering the values obtained from intestinal homogenate of unoperated rats. Reduction of the SOD enzyme activity both in operated and in treated and operated animals, was observed in the intestinal part taken from the anastomotomical area (operated /op) 22%, Trental treated and operated /T+op/ 67% of the control) meanwhile in the distal and the proximal part of SOD enzyme activity in operated animals was decreased (D op 40%, P op 55%) according to the control. But there was no change in the distal part in treated and operated group (D T+op 100%) and in that group the proximal end the value was a 75% greater than the



control (P T+op 175%). It is interesting to observe, that in the intestinal part, excised very far from the anastomosis, where there was no evidence of tissue injury upon the histological exam, we measured a 50% higher SOD activity in both case of operated (op 150%) and the operated and Trental treated (T+op 144%) animal groups compared to the control. Due to the result of our in vitro exams, was established that the activation of the organ supernatant, incubated with Trental did not show any differences ad compared with the activation of sample without Trental.

## Discussion

In the organism  $O_2^-$  is produced via the metabolization of molecular oxygen in the mitochondrias, in capillary endothelial cells during the xantin-xantinoxidase catalitical reaction and in the white blood cells catalized by NADP/H/-oxidase. In the first case it dismutates via the direct reduction to water therefore it does not make any damage in the organism. The in situ production of free radicals, especially  $O_2^-$  and  $H_2O_2$ , has a major role in the emergence of ischemia-reperfusion injury. The damage in experimental pancreatitis and experimental ischemic heart failure, can be prevented by the pre-treatment with superoxide dismutase or catalase or SOD + catalase. In the GI-tract, beside the  $O_2^-$  produced by xantin-xantinoxidase, the aldehyd oxidase oxygen metabolize producing system plays a major role, too. Upon our experiments we found the endogenic SOD activity of the otherwise low SOD activity intestine, in the anastomical area, in 60 minutes thereafter the colon anastomosis, decreased to one fifth while in the proximal and the distal part to one half compared with the control. The reason is, that in locally the balance of the  $O_2^-$  former and the scavenger systems shift to the production of free radicals, while in the intestinal part excised far from the anastomosis, where in all the animals we received a 30% higher values compared with the control, the eliminating system was the predominant. The Trental prevented the ischemia-reperfusion injury. Whereas our in vitro exams showed, the Trental has no direct scavenger effect, therefore a more complex endogenic SOD activity keeping process result the in vivo protective effect.

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## **CHANGES OF VOLUME SUBSTITUTION FOR THE TREATMENT OF HEMORRHAGE WITHIN 10 YEARS AND THEIR COSTS**

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Whereas 10 years ago blood loss was substituted by whole blood application together with colloidal or cristalloid substitutes, this behavior changed to a distinct therapy according to the changed laboratory parameters with the application of red cell concentrates together with fresh frozen plasma (FFP). By means of two representative operations (resection of sigma and hemicolectomy) the behavior of volume application and the substitution of blood and blood components were controlled for the years 1980 and compared with the behavior of 1990. In addition to that the costs for both behaviors were calculated and compared. The volume substitution of altogether 176 patients was investigated. 87 patients were operated in the year 1980 and 89 patients in the year 1990. 60% sigma resection were observed on both decades. The analysis revealed that the main substitute (60%) was whole blood in the year 1980 whereas in the year 1990 only 3% of the patients were treated with whole blood. A reverse development was observed with the application of red cell concentrates which was only 2% in the year 1980 but 54% in the year 1990. Unexpectedly the consumption of FFP remained nearly constant in both decades whereas the administration of 5% albumin increased from 40% to 80%. Also the behavior with regard to colloidal substitutes changed markedly within the 2 decades. Dextran and gelatin preparations were exclusively applied in the year 1980 and starch preparations in mainly the year 1990. This changed behavior was responsible for an increase of the costs of 100 \$US for every patient. Although the changed behavior can be explained with advantages for the patient but this must be paid by an increase of the costs.

### **Introduction**

From time of the detection of the AB0 blood group system it was possible to treat severe blood loss by whole blood preparations and blood components. But soon it became obvious that with the application of blood and blood components also infectious diseases were transmitted from the donor to the recipient. Since more and more and very new and aggressive infectious diseases [5] were known over the time and the strategies of volume substitution after blood loss were changed towards less blood or only blood components which are necessary and more colloidal and cristalloid substitute solutions [1], it was interesting to investigate the behavior of volume substitution within 2 different decades. For this purpose 2 defined operations were selected in which the operation technique as well as the mean calculated blood loss remained constant. Additionally the costs of the volume substitution were calculated for one patient in each decade.



## Patients and Methods

In the year 1980 a resection of sigma was performed in 49 patients and a hemicolectomy in 38 patients. The average blood loss in this patients was 775 ml and the average in age was 64 years. Ten years later in 1990 56 resections of the sigma were performed and 33 hemicolectomies. The average blood loss was increased to 924 ml and the average age of the patients was 63 years. All volume substitutes were registered beginning from the intraoperative therapy and continuing with the early and late postoperative volume administration.

## Results

The analysis revealed that not only the consumption of blood and blood components was markedly changed within 10 years but also the consumption of colloidal and cristalloid solutions. In the year 1980 the main substitute in 60% of the patients was whole blood whereas ten years later only 3% of the patients were treated with whole blood. The supplementation of patients with red cell concentrates showed a reverse development. Only 2% were used in the year 1980 but 54% in the year 1990. Very unexpected was the fact that FFP consumption remained nearly constant (10%) over the time of 10 years. Also the behavior with regard to colloid substitutes changed markedly within the two decades. Whereas in 1980 only 40% of the patients received 5% albumin it increased to 80% in 1990. Dextran and gelatine preparations were used only in the year 1980 in over 50% and not in 1990, but the substitution with starch preparations increased from 17% in 1980 to 86% in 1990. The administration of glucose and fructose preparations changed also very much within 10 years. 92% of the patients were treated with fructose in the year 1980 and only 4% with glucose, whereas in the year 1990 only 30% were supplied with fructose and 80% with glucose.

Calculating the costs of the changes within the two decades it became obvious that it increased from 500 DM to 650 DM that are about 100 \$US.

## Discussion

The changed behavior with regard to the volume substitution has its roots in different explanations. One main reason is the technical development of blood separation. With that it was possible to supply patients with blood components which were partly free of the risk of infections and a certain deficit could be specifically treated. Adverse reactions which were mainly observed after the application of gelatine or dextran preparations [2, 3, 4] are responsible for the fact that the application of starch preparation increased in 1990. The knowledge about patients with fructose intolerance caused the decrease in fructose supplementation and the increase of glucose consumption in the year 1990. Although the changed behavior in volume substitution diminishes the risk of the patient it must be paid by increased costs.

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## FREE RADICAL REACTIONS IN THE GALLBLADDER

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The changes in the composition of bile can lead to the process of its crystallisation in the gallbladder. In bile model it was shown that inflammation with the generation of reactive oxygen metabolites may induce and influence the cholesterol monohydrate crystal formation within supersaturated bile. The aim of this study was to investigate the ability to detect traces of reactive oxygen metabolites, thiobarbituric acid reactive compounds and dien, in order to compare cholesterol and bilirubin contents in bile and serum during different conditions of inflammation in the gallbladder's wall. In every bile sample a reference to free radical reaction was found. There was an increase in MDA during higher degree of inflammation in the gallbladder, but no alteration in the dien content was observed. In case of common bile duct stones the bilirubin in the serum and in the gallbladder was parallelly high, but in other cases there were no significant correlation. In an occluded gallbladder with hydrops the content of protein was significantly higher in 85% of the cholesterol stones. As a conclusion, free radical reactions in the wall of gallbladder as well as in bile can induce gallstone formation. Further studies are needed to clarify the time which is sufficient to change the composition of bile and the degree of inflammation which lead to the onset of stone formation.

### Introduction

The relationship between biophysical and biological processes of gallbladder bile and free radical reactions is not yet known, even though free radical reactions are involved in many pathological conditions. The aim of the study was to draw the attention to lipid peroxidation reactions in human bile during cholelithiasis.

Free radical reactions was demonstrated in cases of toxic liver injury [4] and in gallbladder carcinoma [5]. Our group showed lipidperoxidation products in rats [2] and a study by Paumgartner's group [3] demonstrated free radical reaction in bile models.

We measured the malondialdehyd, dien, protein, bilirubin and cholesterol contents in bile and tried to find the correlation between serum levels of liver enzymes (SGOT, SGPT, AP) and serum bilirubin level. We tried to compare the free radical reaction products with the degree of inflammation in the gallbladder wall and we examined other gastrointestinal abnormalities (gastritis, HP positivity, bile reflux) to detect whether they have any influence on these products or not.

### Methods

Between September 1995 and September 1996. we collected gallbladder bile from 98 patients (30 man, 68 woman) who underwent laparoscopic and conventional cholecystectomy. Included were 3 samples from obstructing gallbladders with hydrops

and from 2 cases of occluded choledocholithiasis. The bile samples were studied immediately or they were stored at  $-20^{\circ}\text{C}$  until the time of examination.

A new method for chemoluminescence light detection was developed with a Berthold type LB 9501 luminometer [2]. Detector is a fast photon counter with 20 ns resolution spectral sensitivity range 360–620 nm. Quantum efficiency typically 24% at 420 nm. Each bile sample was diluted 10, 100, 1000 times and the natural samples were measured in 40  $\mu\text{l}$  volume. Measuring time was 30 sec. The malondialdehyde content of bile was detected by Pyles et al. method. Bilirubin and thiobarbituric acid reaction was monitored in each sample. Dien conjugates were measured by the recommendations of AOAC method [1] with iso-octane fractionated extraction. Protein content of the preparations was determined by Lowry et al. Cholesterol, bilirubin contents of gall-bladder bile were determined by standard spectrophotometric methods. Statistical analysis was performed with Student's *t* test.

## Results

In every bile sample collected we found free radical reaction products. Dividing the degree of inflammation into minimal, medium and severe forms, the degree the malondialdehyd content increased accordingly. We could not define any correlation between dien content and the degree of inflammation. In an occluded gallbladder the protein content of the gallbaldder bile was higher than in the gallbladder without occlusion. The bilirubin in serum and in bile was paralelly high in case of choledocholithiasis. In case of elevated serum liver enzymes the level of free radical products was also higher than normal, but it was not significant.

## Discussion

It is well known that bile is made by epithelial liver cells in an ammount of approximately 500–800 ml/day. It is concentrated in the gallbladder. In case of liver damage or inflammation of gallbladder the composition of bile changes, while at the same time the bilirubin metabolism may modify, therefore it is supposed that free radical reactions could be detected in bile. Free radical reactions were detected in rats and in bile models. Our results show that the changes in bile composition due to free radical reactions play a significant role in gallstone formation.

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## IN OPHTHALMOLOGY NEW POSSIBILITIES FOR THE USE OF ND:YAG LASER

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Results of the technical development in laser technology created new possibilities in ophthalmic surgery, too. The easy access to various lasers offers an extraordinary opportunity for eye surgeons. At the Department of Ophthalmology of the University Medical School of Debrecen we performed 1400 laser treatments in 1996. Out of that 1100 were retinal Argon laser coagulations because of diabetic retinopathy, 200 YAG laser capsulotomies because of secondary cataract, and 30 laser iridotomies because of glaucoma. Additional 70 laser treatments were performed for special indications. During the laser treatment of the retina and the choroid we use Argon gas lasers, whereas the Nd:YAG laser used in the anterior segment of the eye is a solid-state laser. Our pulse mode modus synchronized Nd:YAG apparatus can produce megawatts of energy in nanoseconds. Authors give an account of the Nd:YAG lasers' possibilities in therapy (capsulotomy, iridotomy), present the most frequent indications of treatments in 1996, and compare it with international literature data. Authors demonstrate the newest principles of the Nd:YAG laser treatment of secondary membranes that are occasionally formed in the anterior chamber especially in the area of the pupil following cataract surgery.

**Keywords:** Argon laser, Nd:YAG laser, capsulotomy, iridectomy, membranotomy

During the past four decades the use of lasers extremely broadened the possibilities in ophthalmic diagnosis and therapy. With the laser beam it is possible to perform an operation on the intact globe. In the optical system of the eye it is possible to focus the laser beam in the desired depth thus the treatment can be done in the appropriate level. The emitted radiation of different wavelengths and different impulse times can concentrate huge energy in a very small area and in a very short time. The basis of the origin of the laser beam is that an outer power-source excite the atoms of the „photoamplifier” material of any lightconducting substance. During the process the excited atoms of high energy emit photons. In order to increase the photon density – or to achieve higher laser energy – one can either decrease the impulse time of the outer exciter power-source, or can combine the photoamplifier substance with the use of resonators (special mirrors and „light-locks”). The method in which the light-lock in the resonator is only opened for some nanoseconds in case of high enough photon density is called Q-connection. If the waves of the same phase between the resonators are synchronized, then the impulse time can be decreased ten times and the transfer of energy in time greatly increases. This method is called modus synchronization [3, 5].

The Nd:YAG laser is a solid-state laser, in which the light conducting substance is an Yttrium-Aluminum-Granite crystal which is polluted with Neodymium. The laser radiation forms on the 1064 nm spectral wavelength of the Neodymium-ion. During the

emission of the laser radiation also unnecessary heat is produced, therefore the efficacy of Nd:YAG lasers is 0,5–1%. The coherency characteristics of Nd:YAG lasers in time and of space are unfavorable, but in a distance of 20–30 cm it is negligible. Since the Nd:YAG laser infrared radiation of 1064 nm is not visible, we often use a He-Ne gas-laser of 633 nm wavelength as an aiming laser. The Nd:YAG laser can produce gigawatts or even terawatts of energy in picoseconds, and has a photodisruptive and photoablative effect in the biological tissue. During photodisruption the effect of the laser beam can raise the temperature of the biological tissue even up to 15000 °C, electrons are released from the atoms, and plasma is formed. The arising hydrodynamic, acoustic and mechanic effects cause a tear in the tissue. In case of photoablation the high energy laser photons break the intramolecular bounds. An increase of temperature is not a part of this process [3].

The Q-connection Nd:YAG laser first was used by Frankhauser in 1981, and ever since this is widely used in ophthalmic surgery [7]. Modus-synchronized Nd:YAG laser instrument was developed and first used by Aron-Rosa (1981) [3]. Both devices were developed mainly for the treatment of the diseases of the anterior segment of the eye.

As every intervention, the YAG laser treatment also has contraindications, such as: nystagmus of great extent, severe blepharospasm, opacity of the cornea or the aqueous humor, active uveitis, hemorrhagic diathesis, and the lack of cooperation of the patient [3, 4, 5].

During YAG laser treatments complications can occur:

- ◆ Cataract formation in phakic eyes as a result of using too high energy or in case of improper focusing. On pseudophakic eyes these are the most frequent causes for IOL damages during YAG capsulotomies, too.
- ◆ Corneal damage may occur in case of slightly cloudy corneas or in case of shallow anterior chamber or in case of improper focusing.
- ◆ Bleeding can be expected even in 20–50% of the cases especially during the treatments of the iris. This is not a major problem as bleeding is usually self-limited.
- ◆ Retinal detachment and macular edema rarely occur as a result of the mechanic pulsewaves generated during the treatment.
- ◆ Intraocular pressure elevation can occur because of the inflammatory reaction after the treatment (early type) or because of angle closure caused by shrinking of goniosynechias (late type).

The most common interventions of the anterior segment of the eye performed by the Nd:YAG laser are the following: iridotomy, trabeculoplasty, transpupillar or transscleral cyclophotocoagulation, laser treatment after filtration surgery, capsulotomy, membranotomy [1, 2, 3, 4, 5].

In 1996 we performed 1400 laser treatments at our Department. In 235 cases we used Nd:YAG laser for the treatment of the anterior segment of the eye. We performed 200 capsulotomies because of secondary cataracts. The opacification of the posterior capsule is a complication of modern cataract surgery. The rate of the formation of opacities on the posterior lens capsule is increasing with time. 4 years after surgery it can occur even



in 41% of the cases. The occurrence is significantly higher in patients under 40 years than in elderly. Beside many other factors (like diabetes mellitus) the type of the implanted IOL can also influence the genesis of the secondary cataract. If the posterior chamber lens is in contact with the posterior capsule the incidence of this complication is lower. Capsulotomy can be performed at least 3 months after cataract surgery. The capsulotomy is not necessary to be larger than 4 mm-s. If there is an extensive pucker on the posterior capsule it is advisable to cut it through, if the opacity is round than it is better to make a round hole or a V shaped hole. The useful energy is between the lowest possible and 3 mJ [3, 4, 5].

We performed laser iridotomy in 30 cases. The indications for this are the same like the ones for normal surgical iridotomy (in cases of acute and chronic angle closure glaucoma or narrow angle). We also perform it on the fellow eye after angle closure glaucoma or malignant glaucoma. YAG iridotomy can be of use in the treatment of pupillary block in phacic or aphacic eyes. The ideal place for the treatment on the iris are the crypts of the iris in the 10–11 o'clock or the 1–2 o'clock sectors at the margins of the outer third and the inner two thirds. These are the places where the stroma of the iris is the thinnest. The applied energy should be less than 5–7 mJ. In order to prevent the complication of bleeding it is advisable to coagulate the area with Ar laser previously [1, 2, 3].

We performed Nd:YAG laser membranotomies in 5 cases. We used this method in cases of fibrin membrane formation in the anterior chamber that were located in the optical zone after complicated IOL implantations or corneal transplantations and that caused anterior synechias. If the membrane is not absorbed after conservative treatment some authors advise the injection of tissue plasminogen activators (tPA) in the anterior chamber. In such not responding cases Nd:YAG laser membranotomy is also a good possibility for the treatment. It is very important to use the minimal effective energy and to focus properly because of the very close location of the lens and the iris, in order to avoid unwanted damages [6].

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## **MUCOSAL PERMEABILITY CHANGES DURING INTESTINAL REPERFUSION INJURY. THE ROLE OF MAST CELLS**

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The objective of this study was to investigate the role of intestinal mast cells in mucosal functional and morphological alterations induced by 30 min segmental ischemia and 120 min reperfusion in anesthetized dogs. The time course of permeability changes of the mucosa to sodium fluorescein (NaFl) in blood-lumen and lumen-blood directions was studied in two separate series of experiments. Local hemodynamics, intramucosal pH (pHi) alterations, mast cell number and degranulation and the degree of tissue injury were determined. The effects of cromolyn (peritoneal-type mast cell stabilizer), quercetin (mucosal-type mast cell stabilizer), and dexamethasone (aspecific membrane stabilizer and mast cell depleter) pretreatments were evaluated. Ischemia-reperfusion induced significant tissue injury, elevated segmental vascular resistance, and decreased pHi. The blood to lumen clearance of NaFl increased significantly during ischemia and reperfusion. Cromolyn and quercetin pretreatment significantly inhibited permeability changes, but did not influence pHi and morphological alterations induced by ischemia-reperfusion. Dexamethasone pretreatment did not influence the number of mast cells, however, the degree of mast cell degranulation and the degree of mucosal damage decreased. These results demonstrate that mast cells or mast cell-induced reactions contribute to the mucosal permeability alterations and barrier lesions during reperfusion, but play a minor role in reperfusion-induced structural injury.

### **Introduction**

Several data support the notion that mast cell degranulation contributes to the tissue response elicited by ischemia-reperfusion, but the role of the mucosal mast cell system in the pathophysiology of postischemic mucosal barrier lesions is poorly understood [1]. The damage of the protective mucosa might range from reversible permeability changes to complete transmural necrosis, and the exact impact of mast cell-induced reactions in postocclusive tissue damage remains unclear. Our first aim was to characterize the ischemia-induced functional and morphological changes in the canine small intestine during the reperfusion phase following a period of complete arterial occlusion. To this purpose we have characterized reperfusion-induced local hemodynamic, pHi and permeability changes of an ileal segment and mast cell distribution and morphological consequences of the ischemia-reperfusion challenge were evaluated histologically. In the second part of our study, we investigated the effects of mast cell-targeted pretreatment regimens on ischemia-reperfusion-induced tissue damage. Soda et al. have demonstrated that dexamethasone pretreatment leads to a significant decrease in mucosal mast cell number through a macrophage-dependent mechanism in rats [2]. However, no data are available on this reaction in other species. Thus, we used selective mucosal and



peritoneal-type mast cell stabilizer compounds and dexamethasone to investigate the role of mast cells in intestinal ischemia-induced mucosal permeability alterations in dogs.

### Materials and Methods

Two separate groups of experiments were performed on a total number of 61 dogs (average weight 12.3 kg) under iv sodium pentobarbital anesthesia (30 mg/kg). NaFI clearance of the intestine, a measure of mucosal permeability, was continuously determined according to a modified method of Otamiri et al. (3). Segmental mesenteric vascular resistance (SVR) was calculated from inflow (arterial) and outflow (venous) pressure differences and segmental blood flow. pHi was measured with a balloon catheter (TGS Tonomitor, Tonometrics Inc., Worcester, Massachusetts, U.S.A.) introduced into the ileal lumen. The animals were subjected to 30 min segmental intestinal ischemia and 120 min reperfusion. Mucosal biopsies were evaluated with light microscopy. The samples were stained with hematoxylin-eosin and alcian blue-safranin O to assess mucosal damage and to identify peritoneal and mucosal subtypes of mast cells, respectively. 2 series of experiments were performed to investigate blood-lumen or lumen-blood direction NaFI clearance changes. Group 1 (n=11) and 2 (n=8) served as control, Group 3 (n=7) and 4 (n=7) received the peritoneal-type mast cell stabilizer cromolyn (25 mg/kg iv, Sigma Chemicals, U.S.A.), Group 5 (n=7) and Group 6 (n=7) the mucosal-type mast cell stabilizer quercetin (Sigma, 25 mg/kg iv) pretreatment, Group 7 (n=7) and Group 8 (n=7) was pretreated with dexamethasone (3 mg/kg iv 24 h before the experiments) to deplete intestinal mast cells (2).

### Results and Discussion

Ischemia induced significant, approx. twofold increases in NaFI clearance in blood to lumen direction as compared to baseline values. No elevation was observed in lumen to blood direction during arterial occlusion. NaFI clearance was significantly elevated during reperfusion in both experimental series. Each pretreatment regimen effectively reduced ischemia-reperfusion-induced permeability alterations. Ischemia significantly decreased pHi, increased SVR, and induced severe structural alterations. These parameters were not influenced by the cromolyn and quercetin pretreatments and these compounds did not influence significantly the histological scores of ischemia-reperfusion-induced mucosal injury. Tissue damage was ameliorated by dexamethasone therapy, however, the number of mucosal type mast cells did not change significantly in the villi following this pretreatment.

## Conclusion

Ischemia-induced endothelial cell destruction and enterocyte damage results in structural and functional alterations and leads to a derangement of the mucosal barrier. The mechanism of this process is multifactorial, but activated mast cells might be involved in reversible functional changes induced by intestinal ischemia-reperfusion. These results demonstrate that ischemia-induced mucosal permeability changes could be significantly attenuated by inhibitors of mast cell degranulation.

## Acknowledgements

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## RARE CASE OF THE UTERO-VESICAL FISTULA CAUSED BY INTRAUTERINE CONTRACEPTIVE DEVICE

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The vesico-uterine fistula is a very rare disease. There have only been 150–200 cases. We are reporting on a case in which the chronic fistula was caused by an IUD having been placed 4 years ago and it "wandered" through the bladder. A 30 year-old patient in 1992 and IUD was inserted. She had gynecological controls twice, in 1993 last time. She has problem of urination very often. A cyclical bladder bleeding drew the attention to the disease. In ambulanterely performed cystoscopy we found an IUD perforating towards the interior of bladder in the borderline of its bottom and back wall and was situated in the bladder with its 3/4. We have removed it with forceps. After six weeks of expectation and strict observation did we want to manage the fistula after having consolidated the symptoms of the inflamed surroundings. During the operation we have noticed a wallment size mass of scar between the uterus and the bladder expanding to the height of the orifice of the uterus. The scarily fixed bladder has been separated from the cervix and the scarry wall of the fistula has been cut out. We have brained the cervix towards the vagina and then we've sutured the cervix and the bladder with Dexon 'O' treat, as well. We have interposed a surgical net between the cervix and the bladder followed by blood-clotting and peritonisation. We should take the follows into consideration: careful separation, fine operative technique, and strong well absorbing thread as well as trying to keep the organ. In our opinion the bioplast – interpositum used on our case maker the efficiency of the operation higher.

**Keywords:** utero-vesical fistula, IUD, bioplast-interpositum

### Introduction

The vesico-uterine fistula is a very rare disease. There have only been 150–200 cases introduced in the international literature until now [3, 11, 12, 13].

The gynecological relations of this topic were brought in by Kaser and Ilke in their surgical studies. The studies are considered as epoch-making in literature published in English speaking countries [11, 12, 13]. It was Zelenka [1] who first gave account of a device known as Szontágh–IUD in Hungarian (1965). Studies on this topic are worth mentioning [2,4,7,8,9,10]. However, these papers mention the topic as the cases were complications of some operation being a question on the dividing line of gynecology and urology.

We are reporting on a case in which the chronic fistula was caused by an IUD having been placed 4 years ago and it "wandered" through the bladder.

### Casuistic

Mrs B.Z. 30 year-old patient admitted to our department after several ambulatory examinations on 3<sup>rd</sup> December 1996. Gynecological history: 3 pregnancies,

2 spontaneous births, 1 section caesarean. Then in 1992 an IUD was inserted. She had gynecological controls twice, in 1993 last time. According to her she did not have her period once, next time she had it for longer than a week. Conforming to the examinations there were not essential disorders seen at that time. Uterus is in AVF, clear surroundings, IUD in situ. *At the moment:* she has problems of urination very often, during menses red and cloudy urine, while passing urine she has had pains similar to birth-throes several times. In ambulanterely performed cystoscopy we found an IUD perforating towards the interior of bladder in the borderline of its bottom and back wall and was situated in the bladder with its 3/4. We have removed it with forceps. Following this her permanent complaints disappeared although she had them cyclically during her period. After six weeks of expectation and strict observation did we want to manage the fistula after having consolidated the symptoms of the inflamed surroundings. We have taken endophoto before the operation. *Cystoscopy before the operation:* unhurt outhere urethra, a 19.5 CH device can easily be entered. There is no residuum. An unhurt shaped bladder with a capacity of 150 ml. The mucous membrane is inflamed on the trigonum area, the orifices are split-shaped. There is a fistula of 4–5 mm diameter which is covered by velvety mucous membrane inside. *I.v. urography:* in native photos the shape and size of the kidneys are normal. After giving 40 ml of Uromiro synchronous secretion appeared on both of sides, unhurt cavity, smooth ureter passage and unhurt contour of bladder. *Abdominal and gynecological US:* no essential disorders. *Cystography:* in the photos laterally taken a little "paravasatum" can be seen.

*Laboratory test:* urine density: 1015, pH: 7.8, a: min. op, p:++, s: neg, ubg: normal, sediment: thick mixed bacterial flora, 15–20 leucocyte. Urine culture: *Proteus* genius 10/ml. (After treatment) We: 8 mm/h, Blood-count: Hgb: 7.3 mmol/l, Leucocyte: 4.26 G/l, Htk: 0.40 Kidney functions are within the normal bounds.

*The operation* was performed after proper arrangements on 3 rd January 1997 with an accompanying gynecologist. During the operation we have noticed a wallmet size mass of scar between the uterus and the bladder expanding to the height of the orifice of the uterus. The scarily fixed bladder has been separated from the cervix and the scary wall of the fistula has been cut out. We have brained the cervix towards the vagina and then we've sutured the cervix and the bladder with Dexon 1/0 thread, as well. We have interposed a surgical net between the cervix and the bladder followed by blood-clotting and peritonisation.

Out patient completely recovered after an after on untroubled postoperative disease – process.

## Discussion

Vesico-uterine fistula is the abnormal connection between the bladder and the uterus. There are three types of fistula: vesicocorporal, veisoc-isthmical and vesicocervical. Our case was a vesico-isthmical one. Beside its contraceptive effect IUD cam cause several complication such as: a/ expulsion, b/ bleeding, c/ pain, d/ inflammation, e/ pregnancy, f/ fluor, g/ perforation.



Perforation is a very rare complication, that occurs rather at insertion. The device itself can also perforate the uterus. However, the incorrect insertion technique of the surgeon" probe can cause perforation. At Gynecologic Clinic of University Medical School of Debrecen, [1] there were 2 perforations out of 10,000 IUD insertions, while at Gynecologic Clinic of Medical School of Szeged, [Oroján and his colleagues, 1974] there was only one perforation out of 5,582 [1]. Its most characteristic symptoms are: haematurgia during menses, leaking of urine through vagina with cystitis. There are some which can appear after years without any symptoms like our case.

In order to make diagnosis we thing cystoscopy, abdominal and gynecological U. S, gynecological examination are important.

Cystography does not always fill up the fistulaproperly, as it happened in our case. At the moment we can not adequately explain when the vaginal urine leaking and when bladder bleeding occurs.

According to Yousseff's research [12, 13] the tone of the isthmus can keep up higher pressure in the cavity of uterus than the pressure in the bladder which can explain the flow of blood towards the bladder.

This could explain the fact that cervical fistulas produce rather urinae leaking while the isthmic ones produce bladder bleeding as a consequence. (Our case was an example of the latter).

They can be treated by operation. We should take the follows into consideration: careful separiton, fine operative technique, and strong well absorbing thread as well as trying to keep the organ. In our opinion the bioplast – interpositum used in our case maker the efficiency of the operation higher.

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## ENDOTHELIN-1-INDUCED CIRCULATORY RESPONSE IN THE RAT: THE ROLE OF ETA AND ETB RECEPTORS

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Production of the powerful vasoconstrictor endothelin-1 (ET1) is increased in a number of pathological conditions. This study was performed 1. to assess the effects of a twofold elevation of circulating ET1 on global hemodynamics and cardiac function, and 2. to determine the ET receptor subtypes that are responsible for this action. We have used the ETA receptor-selective antagonist BQ 610, the novel ETA receptor antagonist ETR-P1/fl peptide and the specific ETB receptor antagonist IRL 1038 to investigate the role of these receptor subtypes in mediating circulatory changes induced by ET1 in anesthetized Wistar rats. ET1 infusion produced a significant rise in mean arterial pressure (MAP), elevated total peripheral resistance (TPR), and decreased cardiac output (CO). BQ 610 and ETR-P1/fl pretreatment significantly attenuated the ET1-induced hemodynamic changes. Pretreatment with IRL 1038 had no effect on CO, but significantly reduced MAP and TPR elevation 20 min after ET1 infusion. These results suggest that ET1 may contribute to circulatory failure in conditions with increased ET1 production via a mechanism involving ETA receptors. ETB receptors, albeit to a lesser extent than ETA receptors, are also involved in mediating ET1-induced peripheral vasoconstriction in the rat.

### Introduction

The endothelins (ETs) are a family of 21-amino acid peptides produced by endothelial cells. The ETA receptor on vascular smooth muscle cells mediates vasoconstriction and has a high affinity for ET1, whereas the ETB receptor on endothelial cells and smooth muscle cells mediates vasoconstriction (ETB<sub>2</sub>) and vasodilation (ETB<sub>1</sub> subtype), and has equal affinity for ET1 and ET3 (reviewed in 2). Although the properties of ET1 seem to favour a role for the peptide in the pathomechanism of myocardial depression and ischemia, to date it remains unclear if increases in circulating ET1 concentrations that have been reported in various pathophysiological conditions could be associated with concomitant alterations in myocardial functions. The plasma levels of ET1 are enhanced approx. 2–5 fold during experimental and clinical ischemia, hemorrhage, sepsis or bacteremia, and this suggests that it may mediate vasoconstriction of regional circulatory beds during these conditions [2]. The present experiments were designed to investigate the global hemodynamic effects of ET1 administration which achieves approx. twofold increases in circulating ET1 level, and to determine the ET receptor subtypes that are responsible for this action. We used the selective ETB receptor antagonist IRL 1038, and BQ 610, a compound with specific ETA receptor antagonist properties. ETR-P1/fl is an antisense-homology box-derived peptide which has a potent anti-ETA receptor activity *in vitro* [2] and effectively influences circulatory responses to ET1 in the splanchnic vascular bed (unpublished). Here, we report the first data on the *in vivo* effects of this



novel ET receptor antagonist on exogenous ET1-induced changes in cardiac functions in the intact rat.

## Methods

The experiments were performed on 40 male, tracheotomized Wistar rats (average weight 250 g) anesthetized with sodium pentobarbital (50 mg/kg ip). Polyethylene catheters were inserted into the right femoral artery and right jugular vein for MAP and CO measurements, respectively. A thermistor-tip catheter was introduced into the aortic arch via the right carotid artery, and CO was determined by means of thermodilution. The drop in the blood temperature induced by an injected cold indicator (0.2 ml saline) was measured. CO, TPR, and MAP were calculated by a Cardistar CO-100 computer (Experimetria Co., Budapest). After a stabilization period, cardiovascular parameters were recorded for 5 min to establish baseline variables in all groups. In Group 1-4 a solution of ETA receptor antagonist BQ 610 (homopiperidinyI-carbonyl-Leu-D-Trp(CHO)-D-Trp-OH, Alexis Corp. Laufelfingen, Switzerland, 100 nmol/kg), ETB receptor blocker IRL 1038 (Cys11-Cys15-endothelin-1(11-21), 100 nmol/kg), ETR-P1/fl peptide (VLNLCALSVDYRAVASWRVI, Kurabo Ltd. Osaka, Japan, 100 nmol/kg), or vehicle was infused iv into the systemic circulation over 10 min. In the second series (Group 5-8) 1 nmol/kg ET1 (Alexis Corp.) was infused iv into the systemic circulation, or ET1 infusion was administered 10 min after the end of IRL 1038, BQ 610, or ETR-P1/fl peptide pretreatment, respectively. In pilot studies this dose of ET1 was chosen to approximately double the level of circulating ET1 (from  $1.45 \pm 0.14$  to  $2.49 \pm 0.39$  pmol/L, as determined with Endothelin-1,2 125I high sensitivity radioimmunoassay system, Amersham, UK). The hemodynamic parameters were observed for 60 min in both series.

## Results and Discussion

In the sham-operated group no significant changes were observed in the hemodynamic variables. ET1 induced a significant, 25% rise in MAP, and a concomitant, approx. 20% decrease in CO. Simultaneously, TPR values rose from 1.16 to 1.83 mmHg/ml\*min 60 min post-ET1 infusion. BQ610 pretreatment significantly attenuated the initial rise in ET1-induced MAP elevation, and then MAP values returned rapidly to the baseline level. CO and TPR values remained unchanged as compared to baseline values. The ETR-P1/fl pretreatment had no effect on the early changes, but this pretreatment significantly attenuated the fall in CO and the rise in MAP and TPR 10 min after the administration of ET1. IRL1038 pretreatment had no significant effect on ET1-induced CO changes, but MAP and TPR were significantly lower as compared to the ET1-treated group ( $105 \pm 12$  vs  $143 \pm 18$  mmHg and  $1.12 \pm 0.16$  vs  $1.62 \pm 0.26$  mmHg/ml\*min, respectively).

### Conclusion

Selective blockade of ETA and ETB receptors was partially effective in reducing ET1-induced peripheral circulatory changes. This might also suggest that residual responses to ET1 in the presence of ETR-P1/fl or BQ 610 may have been mediated by unblocked ETB receptors. ET1 could be involved in the induction mechanism of circulatory failure in pathological states with elevated plasma ET1 concentration, and consequently, non selective inhibition of ET receptors by compounds with dual ETA-ETB receptor antagonist properties have therapeutic potential in these conditions.

### Acknowledgements

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## IDIOPATHIC SCOLIOSIS – NEW SURGICAL METHODS OR SEARCH FOR THE REASONS

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Idiopathic scoliosis (IS) is a deformity of the spine whose aetiology is unknown despite of extensive clinical and basic research work. The significance of this disease lies in the consequences of a spine deformity (deformation of the chest, compromise of the cardio-pulmonar function, compression of the neurological elements, severe somatic and psychological sufferings). According to statistical data, one third of the idiopathic scoliotic cases progress and need surgical intervention. Cotrel and Dubousset introduced the three dimensional correction surgical method for the treatment of spine deformities in 1983 (CD method). The authors report on the application of the CD method for the treatment of IS from 1991 to date. After the operation of 36 patients they give an account of good results and report on the modifications of the surgical technique on the basis of their experiences. Aware of the late consequences of the surgical treatment of IS the authors started with the investigation of the aetiology of the disease in order to introduce a causal treatment. As for the aetiological background of IS, data on the role of heritable factors were relevant only. They gave a hint to start with studies aimed at the investigation of genetic determinants of the syndrome. I aberration of chromosome #10 [karyotype: inv(10)(p11q26)]. In one of the cases there was a multiple familial occurrence of the syndrome coupled with the same anomaly of the karyotype. The probands' father and grandfather all had the same pattern of scoliotic deformity and the same aberrant karyotype of chromosome #10 was found both in the proband and his father. Preparation of genomial DNA from peripheral blood of the patients was started. Fragment length polymorphism (RFLP) examination with PCR technique using oligonucleotide primers specific for chromosome #10 and for regulatory genes of left-right body asymmetry is underway.

### Introduction

Hippocrates was the first to write on spinal deformity in medical literature. The term scoliosis was first introduced by Galen in ancient Greek descriptions. The idiopathic form of scoliosis is known from the ancient Greek times and, interestingly, paleopathologists have no accounts of it from earlier ages. IS is a three dimensional deformity of the spine whose aetiology is unknown despite extensive clinical and basic research. It has great practical and clinical significance, as it represents 80% of all types of scoliosis patients. In progressive cases it involves severe locomotory and other organic disorders. The significance of this disease lies in the consequences of the spine deformity which are the follows:

1. Deformation of the chest, compromise of the cardio-pulmonar function;
2. Compression of neurological elements within the spinal canal in severe progressive cases;
3. Early low-back pain;
4. Psychological effects due to the deformed torso.

One third of the IS cases progress and need surgical intervention according to the statistical data. Cotrel and Dubousset [1] introduced the three dimensional correction surgical methods for the treatment of spine deformities in 1983 (CD method). Many similar instrumentations have been developed since that time. We have been applying the CD method since 1991 for the treatment of IS among other diseases and deformities of the spine. During this period we operated on 36 IS patients.

Without a knowledge of the aetiology, one cannot provide causal treatment for the patients suffering from IS. The nowadays surgical methods are not causal treatment procedures, too. In all present forms, symptomatic treatment results only in partial "cure", *i.e.* an alleviation of symptoms, and involves serious compromises. Of the most varied lines of research, including pathological, physiological, histological and biochemical investigations, it was only the clinical genetic data [2,3] that gave some hint for the aetiological background of IS. For this reason we started a clinical and molecular genetic research programme of our patients [5].

## Methods

**Surgical methods.** From 1991 to 1996 we operated on 36 patients suffering from IS. Types of curvatures were the follows: thoracic curves 30, lumbar curves 3, lumbo-sacral curves 1, double major curves 2. The average magnitude of the curves operated were  $66,53^{\circ}$ , ranged  $52-88^{\circ}$ . The average number of fused segments was 9.

The average correction was: 48%, ranged from 17-79%.

The follow up time was 5 years to 1 year, on average 16 months.

There was one lethal complication because of the serious convulsions of a patient in the early post-operative period. In two cases the implants caused decubitus of the skin after 1 and 3 years and the implants had to have been removed. After the removal of implants, the wound infection ceased and there was no loss of correction.

**Genetic examinations.** IS patients were included in our study who suffered from more than  $20^{\circ}$  curvature. Till now we examined 23 families. Their medical and genetic examination consists of the following:

1. Physical orthopaedic surgery examination.
2. Standing X-ray pictures of the thoraco-lumbar spine.
3. The patients completed a questionnaire and anamnestic records were fixed after an oral interview. Pedigree analysis were performed relying on these and the previous physical examination data.
4. Chromosome analysis was performed from leukocyte cultures of peripheral blood.
5. Genomial DNA samples were also prepared from peripheral blood.
6. Fragment length polymorphism (=RFLP) examination with PCR technique with oligonucleotid primers specific of chromosome #10.
7. Searching for RFLP and DNA sequence anomalies with oligonucleotid primers synthesised on the basis of the sequences of genes (*cAct-RIIa*, *Shh*, *HNF3 $\beta$*  and *cNR-1*) regulating left-right body asymmetry [4].



## Results

We introduced a well established three dimensional surgical method for the treatment of IS. After the operation of 36 patients we can give account of good results.

During the surgical procedures we made some modifications of the basic regime of CD technique:

1. In the beginning of our series we performed CT or MRI rotation measurement for surgical planning and check the derotational correction.
2. According to our rotation measurement we determined the apical vertebrae and we used the lower apical vertebra for the position of the strategic one.
3. We forced the increase of thoracic kyphosis and lumbar lordosis to the physiologic range in order to reach better derotational effect of this instrumentation.
4. Sagittal alignment was also corrigible by bending the rods into kyphosis or lordosis after insertion and derotation of them.
5. As a result of comprehensive surgical and clinical genetic examinations, an increased incidence of varying pattern of IS have been found in 10 out of 23 family.
6. Two cases of a clear-cut structural aberration of chromosome #10 [inv(10)(p11q26)] has been established. In one of the cases a multiple familial occurrence of the syndrome coupled with the same anomaly of the karyotype was found. The probands' father and grandfather all had the same pattern of scoliotic deformity. The same aberrant karyotype of chromosome #10 was found both in the proband and his father. No chromosome anomalies of patients affected by IS have been reported in the literature to date. The relevant structural chromosome abnormality observed yields us a safe ground to our molecular genetic investigations.

## Conclusion

1. Every well worked out surgical method needs the surgeon's special evaluation for the individual patients. In our spine surgery method it gave us good correction and well-balanced spine as a result.

2. Surgeons must admit that all the surgical procedures mean some kind of compromise in the treatment *e.g.* scar tissue formation, fusion, hypermobility of the neighbouring segments around fusions and as a consequence early degenerative changes, etc. That is why to find the aetiology of a disease and to apply causal treatment on the basis of it, seems to be the best resolution for orthopaedic surgeons.

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## PREDICTIVE MORPHOLOGICAL FINDINGS IN "ZERO-HOUR" BIOPSIES OF RENAL ALLOGRAFTS

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"Zero-hour" biopsies of 65 donors have been performed since 1994. Donor kidneys were categorized into five groups based on the morphological findings in "zero-hour" biopsies. No morphological abnormalities were found in 38% of the cases (group 1). Arteriosclerosis was present in 31% of donor kidneys (group 2). Specific morphological alterations, i. e. acute tubular necrosis [21.5%], tubulointerstitial nephritis [6.2%] or glomerulonephritis [3.1%] were detectable in the cases remained (group 3-5). During an average of 336 posttransplant days clinical and histological follow up was performed (50 rebiopsies). Statistical data of mismatch (1.4-2.0), average of donor/recipient age (35-42 years), cold and warm ischaemic time (1290 and 66 min) were comparable in all groups. According to our observations: 1. higher creatinin was found in grafts with arteriosclerosis (group 2) ( $p < 0.05$ ), 2. there were more non-viable grafts and longer period of delayed graft function in acute tubular necrosis (group 3), 3. higher creatinin, rejections with the need of rehemodialysis were observed in four cases of tubulointerstitial nephritis (TIN-group 4). Glomerulonephritis (GN-group 5) grafts had only delayed graft function, however these groups were few for statistical evaluation. Biopsy complication in 1/115 cases was found (rebiopsy induced kidney haemorrhage). In conclusion, "zero-hour" biopsies can be useful and safe tools to predict early graft function. Besides "zero-hour" biopsies help the histological interpretation of consecutive graft rebiopsies.

### Introduction

Early graft biopsies (called as "zero-hour" or "one-hour" biopsies) have been performed since 1968 as they seemed to serve as early reliable indicator of the status of the transplanted kidney [4]. Controversial results are published about the possible predictive value of these biopsies. In one hand its predictive role is questioned in early rejection [4], early and late graft function [1]. On the other hand it is suggested for prediction of graft loss [2]. Consensus has been created that these early graft biopsies are useful tools for subsequent biopsy interpretation [1, 3, 4]. The aim of this study is to introduce our observations on "zero-hour" biopsies and to reevaluate its role in clinical transplantation.

### Materials and Methods

During the period of 1994-1996, 67 pretransplant "zero-hour" biopsies (one from a nonheart-beating donor, 66 from cadaver donors) were studied. 65 out of 67 grafts were transplanted (one with severe arteriosclerosis involving also the renal artery and one because of renal cell cancer with otherwise normal renal histology were excluded).



"Zero-hour" biopsies ("wedge-biopsies" of 3x5 mm size from the upper pole of the grafts) were performed at the end of cold ischaemic time. No "zero-hour" biopsies complications were observed. 50 consecutive graft rebiopsies were performed in 33/65 transplanted patients to follow their graft complications during 336 days in average. Indications of graft rebiopsies included: 1. Delayed graft function for more than 7 days, 2. Steroid resistant acute rejection, 3. No adequate response to anti-rejection therapy, 4. Increasing serum creatinin without signs of rejection. Immunosuppression protocol included: 1. Sandimmun or Neoral (10 mg/kg/die) monitored by serum cyclosporin A from day 8.; 2. Azathioprin (1–2 mg/kg/die); 3. Methylprednisolon (1 mg/kg/die, sequentially reduced to 0.15 mg/kg/die from day 61.); 4. Prophylactic anti-lymphocyte globulin (ALG) or anti-thymocyte globulin (ATG). Acute rejection therapy: 3–5x500 mg methylprednisolon, rebiopsy was performed if there was no response, ALG or ATG if rebiopsy proved grade II–III rejection. Morphological analysis was done by light microscopy, immunofluorescence (IgG, IgA, IgM, C3 and MAC [membrane attack complex]) and transmission electron microscopy (TEM) using standard techniques<sup>1</sup>. Acute and/or chronic rejections, cyclosporin nephropathy, acute tubular necrosis were diagnosed on the basis of graft biopsies according to the Banff criteria [5]. Graft thrombosis was suspected by biopsy findings of renal infarction, proved by Doppler-ultrasonography and macroscopic examination of the kidneys after nephrectomy. Clinical follow up was performed by the members of the transplantation team checking of the following parameters regularly: 1. Full laboratory status, 2. Physical examination, 3. Blood pressure, 4. Throat/urine bacteriology, 5. Chest X-ray, 6. ECG, 7. Abdominal ultrasonography. Clinical information was available about donor/recipient age and sex, HLA–B, DR mismatch, pretransplant kidney disease and hemodialysis time of the recipient, blood group of the donor/recipient, periods of handling time, warm/cold ischaemia and non-graft-related clinical complications, treatments and lethal complications.

Definitions: delayed graft function (DGF) was defined as an initial need of hemodialysis. "Good" renal function was classified if the patient had not returned to hemodialysis or died with good renal function during the follow up period.

## Results

Early graft function was monitored during the first two posttransplant months in recipients with renal allografts of different "zero-biopsy" morphology. Higher serum creatinin (266 [100–530]  $\mu\text{M/L}$ ) was observed in recipients with arteriosclerosis (group 1) ( $p < 0.05$ ) and tubulointerstitial nephritis grafts (group 4) (277 [133–600]  $\mu\text{M/L}$ ) (statistically not evaluable). Higher number of non-viable grafts (21.4%) ( $p < 0.05$ ) was present in acute tubular necrosis (ATN – group 3). There were no differences in the frequency of delayed graft function (DGF) (28–30%), but a significantly longer DGF time (18.5 days) ( $p < 0.05$ ) was found in ATN – group 3. All groups were compared to group 1 with normal morphological findings.

Late graft function was monitored by clinical follow up and rebiopsies of viable grafts during an average of 336 posttransplant days. There was no significant difference in graft survival between statistically evaluable groups (normal:78%, AS:70%). This means increased graft loss in AS-group compared to its early period (0% vs 30%). The graft loss is due to higher frequency of rejections (40%) and a need for rehemodialysis (15%) in arteriosclerosis graft. The worsening function was also reflected in high serum creatinin (253 [100–442]  $\mu\text{M/L}$ ) levels of these recipients. Rare morphological forms of "zero-hour" biopsies (TIN, GN) were statistically non evaluable and carried either a bad (TIN) or a good (GN) long term graft survival. There was no significant difference in mismatch, age, sex, blood group, handling time, warm/cold ischaemia time and in clinical complications or therapy between the groups.

Postoperative mortality rate was 4,7% (3/64), overall mortality was 17,2% (11/64) with 10,95% (7/64) extrarenal causes.

## Discussion

"Zero-hour" biopsies of 65 donors have been performed since 1994. Only 38% of the cases showed no morphological abnormalities which motivated us to study and reevaluate the significance of "zero-hour" biopsies.

Based on our findings we support the literature that "zero-hour" biopsies do not predict late graft function and complications [1, 3, 4]. In addition we can conclude that there are potentially predictable morphological parameters of the graft at early stages. Renal allografts with arteriosclerosis had worse early function in their recipients reflected in higher serum creatinin levels compared to grafts with normal morphological findings. Acute tubular necrosis of renal allografts in our material statistically reduced graft viability, prolonged the delayed graft function time period. A similar value of tubular damage predicting graft loss was reported in renal allograft rebiopsies [2].

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## **SPLENIC AUTOTRANSPLANTATION AFTER ABDOMINAL TRAUMA IN CHILDHOOD. CLINICAL AND EXPERIMENTAL DATA**

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Splenectomy is known to increase the risk of overwhelming bacterial infection. There is a decrease in immunoglobulin IgM and T-lymphocytes, primary antibody response to antigen challenge is impaired, altered opsonic function and Tuftsin deficiency are noted. Splenic autotransplantation has been suggested as a method of preserving function and this concept is supported by experiments in animals. Prior to operation on humans the technique was thoroughly elaborated and practised in animal experiments (dogs). After splenectomy, 6–8 thin segments (Furka's "spleen chip") are placed in between the plates of the major omentum. Within the period of ten years out of 52 patients 11 children (4 girls, 7 boys) suffered from abdominal trauma underwent total splenectomy, and then autotransplantation in the Kenézy Hospital in Debrecen, Hungary. In several patients the postoperative follow-up radionuclid imaging, IgM, and Tuftsin levels, and the haematological changes (leukocytes, differential blood count, platelet count, iron level in serum) unambiguously confirmed the function of the splenic tissue.

### **Introduction**

The first spleen resection and the first suture was carried out in 1590 and 1895 by Rosetti and the Russian Zikoff, respectively [7].

There had been no essential change in the treatment of injured spleens for 400 years until 1952 when a change in approach was initiated by King and Shumacker. The causes of death in their patients with sphaerocytosis who died of unimpressible infection were explained by postsplenectomy conditions. It was them who introduced the term "Overwhelming Postsplenectomy Infection" (OPSI) syndrome.

The incidence of this syndrome in adults was first recorded in 1970 [5]. The follow-up examination of patients who had undergone splenectomy revealed uncommonly high rates (4.25%) in the coincidence of sepsis of which 2.5% proved to be lethal. Pneumococcus, Meningococcus and E coli were detected as pathogens.

### **Material and Methods**

Our examinations are divided into two groups. Prior to operation on humans the technique was thoroughly elaborated and practised in animal experiments (dogs). The procedure is as follows: after splenectomy, 6–8 thin segments are placed in between the plates of the major omentum following its lifting and spreading over a large sheet soaked

with physiological salt solution. The hole in the major omentum is closed with fine, absorbable suture material [4].

Since November 1987, 52 patients, 11 children (4 girls, 7 boys) have been operated on at the Kenézy Hospital in Debrecen, following blunt and penetrating abdominal injuries. 5–8 full diameter spleen chips of with of 1–3 mm were placed in between the plates of the omentum in 52 cases (11 children) following splenectomy. [4,8] The chips themselves were spared from stitches but the windows of the omentum were closed in each case. All the abdominal recess were cleaned of blood by careful lavage.

Follow up examinations included haemato-immunological, and isotopic check-ups as well as the determination of Tuftsin levels, on the basis of animal experiments [6].

### Results and Conclusion

The level of Tuftsin, and IgM were noted in 1 case respectively. Howell-Jolly bodies were found in one case too. Isotope scanning did not show functioning splenic tissue in one case. 20 weeks after splenectomy, the haematological changes (leukocytes, differential blood count, platelet count, iron level in serum) were in the normal level, and that unambiguously confirmed the function of the splenic tissue.

Fundamental changes in the approach in treating spleen injuries have taken place over the past decade. More and more knowledge has accumulated about the function of this "mysterious" organ. The spleen has an important role in the so called nonspecific defense mechanism and at the same time it is the major site of T-independent immune reaction, as well as B-lymphocytes. Beyond phagocytosis, it plays a major part in the mechanism of opsonisation by manufacturing a Tuftsin-like substance that is capable of enhancing phagocytosis to a significant degree. This gamma-globulin fraction which is specific for the spleen and is responsible for maximal phagocyte stimulation was discovered by Najjar in 1970 [7].

Autotransplantation in animals under experimental circumstances first took place in 1962 and it was introduced into clinical practice by Cooney in 1979 [1]. The regeneration of autotransplanted splenic tissue can well be observed in animal experiments. Central necrosis takes place on days 1–4, it is followed by vascular regeneration on day 8 and in the 5th week some white pulp can be distinguished in the regenerated splenic tissue. The major omentum is the best place for the replanted spleen slides, as far as favourable revascularisation, portal drainage and bacterial clearance in the omentum are concerned. Furka's spleen chip technique, into an ommental "apron" meets the requirements since the omentum does not undergo angulation, no local circulatory damage develops, revascularisation of spleen chips is undisturbed, and after surgery, the omentum regains its anatomical position [2,3].



The quantity of the autotransplanted splenic tissue is also of crucial importance for immunobiological functioning. The critical mass should be 30–50% of the original bulk of the spleen [1, 9]. In the case of disintegrated spleen and/or hilar rupture immediate splenectomy is a must and it should be followed by autotransplantation in each case unless the patient's condition is haemodynamically under control or there is any other exclusive reason.

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## MINI-STERNOTOMY FOR AORTIC VALVE SURGERY

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In the recent years more and more efforts have been made widely to introduce new techniques in the minimally invasive cardiac surgery. At our Department and the Linköping University Hospital, Cardiothoracic Surgery Department, from August 1996 to January 1997, aortic valve surgery was performed in 23 adult patients (9 female, 14 male), age 28–86 years (mean age 62.5 years). Twenty-two patients had aortic valve replacement, among these, in 3 cases concomitant aortic annulus dilatation was made and in one case reduction-plasty of the dilated ascending aorta. In another one case resection of a sub-aortic membrane was performed. The operations and postoperative period were free of complications in all patients. Following an average 36 hours intensive care all patients were discharged after an average of 11.2 day hospital stay. The authors introduce the new surgical technique and present its advantages and disadvantages. Mini-sternotomy has less detrimental structural and functional effects on the thorax. Moreover, due to its minimal surgical trauma, this less invasive technique reduces patient morbidity, hospital stay and cost of care. Since mini-sternotomy is a safe and advantageous technique, the authors recommend applying this new technique in most of aortic valve operations.

### Introduction

During the past decade rapid development of laparoscopic and video-assisted thoracoscopic techniques provided new perspectives in surgery. Many abdominal and thoracic pathology that, in the past, was amenable only to open surgical interventions, is being treated via less invasive techniques. Decreasing morbidity and mortality, decreasing postoperative pain, rapid recovery and mobilisation, lower cost of hospital care and more cosmetically acceptable results are all promoting application of new surgical techniques. Although minimal invasive interventions are nowadays becoming routinely employed in the speciality fields of obstetrics and gynaecology, general surgery and thoracic surgery, application in cardiac surgery has been limited [5].

Intensive experimental and clinical work have been made during the last few years in many institutions for the introduction of less invasive operative techniques in cardiac surgery [1,2,4,5]. From August 1996, we started simultaneously, at the Cardiac Surgery Department of the Debrecen University Medical School and the Linköping Cardiothoracic Department employing the mini-sternotomy approach in aortic valve operations. This communication details the new technique, the early experiences and results achieved.



## Materials and Methods

From august 1996 to January 1997, this approach was employed at our institutions in 23 patients with aortic valve disease. Patients' mean age was 62.5 years (28–86) and male to female ratio was 14:9. In all cases isolated aortic stenosis or combined aortic valve disease were the indications for operative management. In 3 patients aortic stenosis was associated with aortic annular stenosis and in one case with ascending aortic ectasia. One patient had a sub-aortic membrane. All cases fall within the NYHA II–IV functional stage.

Following premedication with Morphine and Scopolamine the patient is anaesthetised in the supine position and intubated. A mid-sternal skin incision is made from the jugular notch to the level of the IV–V intercostal space. The length of the incision is 12–14 cm. Sternotomy is made in the same line of the skin incision forming an inverted T-shape with an oscillatory saw starting from the jugulum to the fourth intercostal space, where the bone is cut horizontally. Using a thoracic retractor the mediastinum is exposed then the pericardium is incised also to an inverted T-shape and holding sutures are applied to it. Following heparinization, the aorta and the right atrium are cannulated in the usual manner. Left ventricular venting is achieved by cannulating the pulmonary artery trunk. All operations are performed under cardiopulmonary bypass (CPB) with moderate hypothermia (rectal temperature: 30–32°C). Myocardial protection is ensured by 4°C St. Thomas cardioplegic solution and topical cooling. Exploration of the aortic valve is made by curved longitudinal or horizontal aortotomy. Twenty-two patients had aortic valve replacement using either mechanical or bioprosthetic grafts. Among these, in 3 cases simultaneous dilatation of the aortic annulus with a pericardial patch, and in another one case reduction-plasty was made to a dilated ascending aorta. Moreover, resection of a sub-aortic membrane causing significant aortic stenosis was performed.

After completion of the replacement or repair, the aortotomy is closed, and air is removed from the heart by continuous suction through a cannula placed in the aortic root. Cross-clamp is removed, and following reperfusion, the patient is weaned from the CPB and the heart is decannulated. Heparin effect is neutralized with Protamin. A ventricular pacing wire and one pericardial drain tube are placed and the sternum is closed with wire stitches. The incision is closed with absorbable suture material. Drained blood from the mediastinum is re-transfused to the patient during the first 12 hours. Antibiotic prophylaxis is continued for 48 hours after the operation.

## Results

The mean aortic cross-clamp time was 84.1 min (54–125 min), the mean CPB time was 113.9 min (74–164 min), and the mean total operative time was 213.4 min (155–295 min). Most of the patients were weaned from the respirator few hours after the operation and the latest extubation was on the morning of the first postoperative day. The mean amount of blood drained through the mediastinal tube was 355.3 ml (150–850 ml). There were

neither intra- nor postoperative complications or mortality. The average hospital stay was 11.2 day (8–18 day) after which all patients were discharged with healed surgical wound.

## Discussion

Recently, Techniques of laparoscopy and thoracoscopy have revolutionized many areas of general and thoracic surgery [6, 8-10]. These methods have allowed patients undergo increasingly complex procedures without the pain and morbidity associated with standard open surgical techniques. Minimal invasive cardiac surgery is presently under intense investigation and development [5]. Coronary bypass grafting of the anterior arteries with in situ internal thoracic artery bypass grafts through a limited anterior thoracotomy is an operation that is gaining acceptance [7]. Attempts are being done to introduce the less invasive techniques in both the aortic and mitral valves surgery.

Aortic valve operations have been traditionally performed via median sternotomy. In 1996 Gundry et al. in the Loma Linda Medical Center have developed an alternative for this method, that simplifies the traditional technique without jeopardizing surgical results for patients [3]. Investigating and utilizing this new method, from August 1996 to January 1997, we performed mini-sternotomy for aortic valve surgery in 23 patients. According to our early experiences, this approach makes opening and closing of the chest easier and faster providing satisfactory exposure of the aortic root. The main advantage of mini-sternotomy that it has less traumatic structural and functional effects on the thorax, that is postoperative pain is decreased due to the diminished retraction and stress placed on the ribs and sternum. Further advantages are early extubation of patients and earlier discharge from the hospital following a faster recovery. A small wound reduces the potential for infection and blood loss, and reoperation should be less difficult because the pericardium and the heart below the lower half of the sternum remain intact. Furthermore, clearly, a smaller incision is cosmetically more acceptable to patients. Due to the limited operative field and the scanty experience with the new method, cross-clamp time, CPB time and the total operative time were slightly longer than those in traditional sternotomy.

This approach provides access for the surgeon to perform any procedure in case of isolated aortic valve disease. Additional procedures on the aortic root and ascending aorta also may be possible. Aortic valve surgery via mini-sternotomy is an easy and safe procedure. However, defining the true value of this less invasive technique requires continued study.



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## EFFICACY OF PREVENTION OF THROMBOEMBOLIC COMPLICATIONS WITH LMW-HEPARIN IN EXPERIMENT

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The authors used an antithrombotic agent (Nadroparin Calcium) with anti-Xa effect in their experiments to prevent thromboembolic complications in the model of endoprosthetic replacement of the hip joint in mongrel dogs. 10 experimental animals (Group I.) were given doses of 100 A Xa ICU/kg/bwt of Nadroparin Calcium subcutaneously 4 hours prior to the operation and also once a day until the 3rd postoperative day; between the 4th and 10th postoperative days doses of 150 A Xa ICU/kg/bwt Nadroparin Calcium were given. The 10 control animals (Group II.) did not receive anticoagulant treatment. In both groups platelet count, activated partial thromboplastin times (APTT), prothrombin and fibrinogen levels as well as activated factor X inhibition (F Xa) were measured prior to surgery and also until the 14<sup>th</sup> postoperative day. No changes in APTT and prothrombin levels were detected during the experiment, however platelet count and fibrinogen levels as well as the extent of F Xa inhibition showed significant and different changes in groups I. and II. The Group I. which had received thromboembolic prophylaxis did not develop deep venous thrombosis or pulmonary embolism, but the control group did. Based on their investigations, the authors concluded that they had been able to achieve F Xa inhibition by giving the above mentioned doses of Nadroparin Calcium which was enough to prevent thromboembolic complications in their model experiment of implanting hip endoprosthesis.

### Introduction

Deep venous thrombosis (DVT) and pulmonary embolism (PE) are common and important pathological conditions and are of great importance in surgical complications in particular. Following total hip replacement, which is commonly performed in orthopaedic surgery, the incidence of DVT and fatal PE were initially found to be at about 50% and 1-5%, respectively. Significant decrease in the incidence of thromboembolic complications has been noted after the introduction of relevant prophylactic agents, such as low-dose unfractionated Heparin (UFH) as well as applying low molecular weight Heparin preparations (LMWH) in gradually increasing areas in recent years.

According to Thomas, venous thrombosis can only be prevented if inhibition of thrombin formation is achieved. Therefore attention is directed towards a/ the knowledge of inhibitors and anti-activators capable of preventing shifts of balance towards clot formation and having counter effects at several sites of the blood clotting cascade; b/ also their detection, using laboratory techniques, and c/ in cases of thrombosis, detection of changes in their activity.



The aim of the present experimental study was to see what changes of haemostasis are caused by the applied doses of Nadroparin Calcium, what level of F Xa inhibition can be achieved and, also, if this inhibition is enough to prevent thromboembolic complications.

## Methods

Routine exploratory procedures and manipulations were performed in the model of hip endoprosthetic operations on 20 mongrel dogs. After the exarticulation of the hip, the usual outward rotated and adducted position of the femur was maintained for 30 minutes. All of the animals received a single dose of Ampicillin of 50 mg/kg/bwt as prophylactic antibiotic, 1 hour prior to surgery.

The first group of experimental animals (10 dogs) received LMWH (Nadroparin Calcium) subcutaneously doses of 100 A Xa ICU/kg/bwt 4 hours before the operation and once a day until the 3rd postoperative day, and doses of 150 A Xa ICU/kg/bwt between the 4th and 10th postoperative days.

The second group (10 animals) were not given anticoagulant treatment.

In the first group, sampling for laboratory tests (platelet count, APTT, prothrombin and fibrinogen levels, and F Xa inhibition) took place before the operation and then on the 4th, 5th, 7th, 10th, 12th and 14th postoperative days, in 6 and 12 hours following the administration of the drug.

Sampling for the above tests in Group II was performed at the same intervals.

On the 14th postoperative day the animals were dissected following an overdose of narcosis, and thrombi in the veins of the lower extremities as well as emboli in the lungs were searched for. Samples from pathological tissues were sent for histological investigations.

## Results

No significant changes in APTT, prothrombin or fibrinogen levels or platelet count were found in Group I (10 animals treated with Nadroparin Calcium). F Xa inhibition of 0.2–0.3 U/ml and 0.3–0.4 U/ml were measured between the 1st–5th and 6th–11th postoperative days, respectively, this level showing gradual decrease until the 14th postoperative day. On dissection, none of the animals had thrombi in the deep veins or emboli in the lungs.

No significant changes in APTT or prothrombin levels were detected in Group II (10 control animals). F Xa inhibition in this group was practically immeasurable. However, the average initial level of fibrinogen (1.5 g/L) increased significantly, by 29.2% ( $p \leq 0.05$ ) in 5 animals, from the 6th postoperative day. 5 animals showed no significant changes. 1 animal with increased fibrinogen levels was found to have expressed thrombocytopenia ( $p = 0.00086$ ). On dissection, 5 animals had thrombi in the veins of the lower extremity and they were the ones where increase in fibrinogen levels was measured, too. One of these with expressed thrombocytopenia died of fatal PE on the 7<sup>th</sup> postoperative day. Secondary findings of pneumonia were detected in 2 of the 20 experimental animals.

## Discussion

Low-dose heparin therapy introduced by Best in 1950 was first used in a wide range by Kakkar [3] in the 1970s, and he established that UFH could successfully prevent DVT, although there is always a risk of minor haemorrhage when it is applied. However, UFH proved to be less effective in hip endoprosthetic implantation than in abdominal surgery; the incidence of DVT decreased to 20–25%, whereas PE dropped to 1%, compared to earlier figures of 50% and 1–5%, respectively [5].

When it was recognized that heparin-composing polymer chains with different molecular weights (1,500–30,000 Dalton) had different effects on the serin-proteinase inhibition of the blood clotting system [2, 4] the idea of fractionating heparin to prepare an agent more effective than UFH was brought up.

It was demonstrated that the increase in molecular weight increased anticoagulant activity but inhibition of F Xa did not change significantly with the decrease of molecular weight [1, 4]. So it can be stated, that LMWH is a clinically effective antithrombotic agent with lower risks of haemorrhage, its application after total hip replacement could decrease DVT and fatal PE to about 8% and 1%, respectively [5].

## Summary

It can be concluded that if F Xa inhibition of 0.3–0.4 U/ml is achieved from the 4–5th postoperative days through treatment with Nadroparin Calcium in doses applied by us, it can further decrease thromboembolic complications. If F Xa inhibition only of lower level than the above mentioned is achieved and there is a significant increase in fibrinogen levels it calls attention to the risks of the development of thromboembolic complications.

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## LAPAROSCOPIC DISTAL RESECTION OF THE PANCREAS WITH THE PRESERVATION OF THE SPLEEN

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Management of the pancreatic diseases is still a challenge to the laparoscopic technique. Some experience has been gained in the laparoscopic exploration of the pancreas and staging in cancer. Anatomically the accessibility of the distal pancreas provides the laparoscopic approach technically feasible. Patient and method: A case of insuloma in the tail of the pancreas is presented, where distal pancreatic resection was performed laparoscopically with the preservation of the spleen. In a 55 years old female patient with typical clinical symptoms of hyperinsulinism CT identified a 3 cm large solid tumor in the tail of the pancreas. Complete mobilization of the distal pancreas was enhanced by the use of an ultrasonic dissector (UltraCision). The pancreas is detached from the splenic hilum after dividing the splen vessels. The pancreas is transected proximally by laparoscopic linear stapler. Preservation of the short gastric vessels provides the necessary blood supply of the spleen following division of the splenic artery and vein. Thus removal of the spleen is not a necessary step in this procedure. The operation was carried out within 4.5 hours. Postoperative course was uneventful, the patient left the hospital on the 5th postoperative day. Advantages of the procedure were the earlier mobilization and shorter recovery time, less postoperative pain. The procedure can be safely performed with a good experience in both pancreatic and laparoscopic surgery.

**Keywords:** pancreatic resection, laparoscopic surgery, insuloma.

### Introduction

With the development of minimal invasive techniques several procedures besides cholecystectomy, appendectomy and hernioplasty have been accepted and routinely used in recent years [8]. The management of lesions of the pancreas is still a challenge to the laparoscopic technique. As more experience is gained with the exploration of the pancreas, tumor staging and with more advanced laparoscopic surgical techniques reports of laparoscopic management of pancreatic lesions appeared in the literature. [7, 3] The accessibility of the distal pancreas offers the rationale for the utilization of the minimal invasive technique in the management of solitaire benign lesions, like insulomas.[4] Our technique of distal pancreatic resection is presented with the preservation of the spleen.

### Patient and Technique

The 55 years old woman suffered from recurrent attacks of hypoglycaemia. Laboratory examination repeatedly found the serum level of C peptide and insulin near the upper

limit of the normal range. Spiral CT scans showed a 3-cm large solitaire tumour in the tail of the pancreas. The diagnosis of insuloma indicated surgical exploration.

**Surgical technique:** The patient was placed in the prone position with the table tilted to the right with the head side elevated. Five ports were placed. Two 10 mm port was used for the introduction of a 30° laparoscope and a 10-mm liver retractor. A 12-mm port was necessary for the laparoscopic linear stapler (Endoscopic linear stapler 33, Ethicon Endo-Surgery, Inc.). In the left subcostal region a 10 mm port was placed for clip applier and other instruments, and a 5-mm port placed to the left for retractor and suction device. A window is created in the gastrocolic ligament, and then the stomach is elevated ventrally liberating adhesions from the surface of the pancreas. When the anterior surface of the pancreas is free a laparoscopic ultrasound probe is introduced to explore the pancreas and underlying structures. The tumour is localized and the type of procedure is decided; i.e. choice between enucleation and resection. Dissection is started at the lower border of the pancreas, lifting it from the loose retroperitoneal connective tissue. The dissection is carried out till the splenic hilum. The tail of the gland is lifted and the splenic artery and vein at the superior border is dissected. After double clipping and dividing the vessels the pancreas is easily freed from it surrounding. The line of resection is verified proximal to the lesion. At this site the splenic artery and vein are dissected and divided between clips. The endoscopic linear stapler is introduced through the 12-mm port and the body of the pancreas is transected. The resected surface is inspected for leaks of pancreatic duct and bleeding. The specimen is then transferred into a polyethylene bag and is removed by dilating one of the port sites.

## Result

The operation was completed in 4 and a half-hour. The patient required no blood transfusion, estimated intraoperative blood loss was about 200 cc. Histology confirmed the endocrine tumour of uncertain dignity. The postoperative course was uneventful. The patient was mobilized on the first postoperative day, she required no analgesics from then on, and bowel movements were normal from the second day. She left hospital on the 5th postoperative day.

## Comments

The accessibility of the pancreas by laparoscope has been well demonstrated in staging malignancy [1]. Several procedures have been developed for the laparoscopic management of biliary and gastric obstruction [5]. Following experimental studies on pancreatectomy [9] sporadic reports appeared of successfully completed distal pancreatic resection for the treatment of well-located benign lesions like insuloma, cystadenoma, and chronic pancreatitis [2, 6]. The procedures included removal of the spleen as well. In our traditional open surgical technique of distal pancreatic resection we preserve the



spleen routinely in cases of benign diseases. If the sort gastric vessels are not divided the spleen remains viable even if the splenic vessels are transected during dissection of the pancreas from the splenic hilum. We applied the same technique successfully in our laparoscopic distal pancreatectomy.

### Conclusion

Distal pancreatic resection and preservation of the spleen can be safely performed laparoscopically within an acceptable operating time and without complication, given the expertise in both open pancreatic and laparoscopic surgery. All the benefits of laparoscopic approach have been realized. Postoperative recovery was accelerated and hospital stay shortened.

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## INTRACELLULAR FREE $\text{Ca}^{2+}$ ELEVATIONS IN CULTURED ASTROGLIA INDUCED BY NEUROLIGANDS PLAYING A ROLE IN CEREBRAL ISCHEMIA

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For better understanding of glial participation in cerebral ischemia, spectrofluorimetric analysis using the calcium indicator Fura-2AM was applied to examine the role of intracellular free  $\text{Ca}^{2+}$  ( $[\text{Ca}^{2+}]_i$ ) elevation induced by different neuroactive substances in cultured rat brain astrocytes. The activation by the general receptor agonist glutamate resulted in a biphasic cell response in  $[\text{Ca}^{2+}]_i$ . We couldn't observe N-methyl-D-aspartate-evoked  $[\text{Ca}^{2+}]_i$  response at all. Quisqualate triggered a complex  $[\text{Ca}^{2+}]_i$  response in astrocytes consisting of mobilization of  $\text{Ca}^{2+}$  from the intracellular stores and also  $\text{Ca}^{2+}$  influx from the extracellular space. Kainate elicited a markedly different  $\text{Ca}^{2+}$  signal an external  $\text{Ca}^{2+}$ -dependent sustained  $[\text{Ca}^{2+}]_i$  rise resulting from the activation of the ionotropic glutamate receptor. According to our results two types of glutamate receptors, the quisqualate-specific metabotropic and kainate-specific ionotropic receptor, are involved in  $[\text{Ca}^{2+}]_i$  elevation in these cultures. We could monitor agonist-specific cell response to noradrenalin, serotonin, vasopressin and ATP as well in these cultured rat astrocytes.

### Introduction

Astrocytes stabilize cation homeostasis in the neuronal microenvironment. The glutamate uptake by astrocytes protects the neurons against the effect of long lasting glutamate excess in the neuronal microenvironment which would distort the  $\text{Ca}^{2+}$  homeostasis inside the neuron and would consequently lead to its reversible metabolic damage or even to long-term degeneration. While astroglia protects neurons by stabilizing their  $\text{Ca}^{2+}$  homeostasis, glutamate, ischemia etc., elicit a higher and long-term rise of intracellular free  $\text{Ca}^{2+}$  in astrocyte itself resulting in a damage of these cells, too. At the same time, these signal molecules elicit the prompt and transient elevation of intracellular free  $\text{Ca}^{2+}$  level in cultured astroglia. It is a question of profound importance, when and why these physiological  $\text{Ca}^{2+}$  signals become a toxic effect? These questions prompted our present study.

### Methods

Primary cultures of astrocytes were prepared from the cerebral hemispheres of newborn rats by mechanical dissociation and were cultured in Dulbecco's Modified Eagle Medium (HDMEM) (4500 mg/l Glucose, 10% GFCS) for 4–6 weeks at 37 °C in humidified 5%  $\text{CO}_2$  atmosphere. Confluent layers of astroglial cells grown on glass coverslips were loaded with 2  $\mu\text{M}$  Fura-2AM, for 45 min at 37 °C in a  $\text{CO}_2$  incubator.  $[\text{Ca}^{2+}]_i$  measurements were carried out in 20 mM Hepes buffered Tyrode medium (pH 7.4)



containing 1.8 mM calcium. Confluent layers of Fura-2 loaded astroglial cells were monitored in a Hitachi F 2000 spectrofluorimeter at 37 °C. The fluorescence intensities at 340 nm and 380 nm excitation with 495 nm emission were recorded. The  $[Ca^{2+}]_i$  was calculated according to the method described by Grynkiewicz, G. et al. (1985).

## Results

All the neuroligands examined evoked concentration-dependent  $[Ca^{2+}]_i$  changes highly characteristic of the molecule. Glutamate and its analogs induced characteristic and markedly different  $[Ca^{2+}]_i$  responses in these cultures. The response to glutamate consisted of an initial fast transient followed by a sustained rise in  $[Ca^{2+}]_i$ . The plateau phase of the glutamate response in type-1 astrocyte was due to  $Ca^{2+}$  influx, it was completely abolished when glutamate was applied in  $Ca^{2+}$ -free medium. The ionotropic glutamate receptor agonist kainate in  $10^{-6}$ - $10^{-4}$  M concentration elicited an external  $Ca^{2+}$ -dependent  $[Ca^{2+}]_i$  rise in these cultures. The metabotropic glutamate receptor-specific agonist quisqualate produced a biphasic  $[Ca^{2+}]_i$  response consisting of a fast transient peak followed by a slowly decaying sustained rise. Astrocyte revealed a pronounced  $V_1$  receptor-induced increase in cytosolic  $Ca^{2+}$  concentration in response to vasopressin. We could demonstrate astroglial  $[Ca^{2+}]_i$  responses to two neurotransmitters, a rapid, transient rise evoked by  $10^{-5}$  M serotonin, and a rapid but sustained elevation in response to noradrenaline which were due to activation of multiple receptor subtypes.

## Discussion

Cultured Type-1 astroglial cells express an abundance of various membrane receptors for many neuroactive substances like astrocytes in situ. They provide an excellent opportunity to analyze signal transduction mechanisms of this cell type. Type-1 astrocytes cultured on glass coverslip generate characteristic  $Ca^{2+}$  signals in response to different neuroactive substances. In addition, most of these agonists evoke not only physiological  $Ca^{2+}$  signals but long-lasting  $[Ca^{2+}]_i$  elevation as well, depending on the concentration and characteristics of the agonists. This  $[Ca^{2+}]_i$  rise is a recently revealed essential factor in many toxic effects in the CNS.

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## **SPLENECTOMY AND SPLEEN AUTOTRANSPLANTATION DUE TO SPLENIC CYST**

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Splenectomy is known to increase the risk of Overwhelming Postsplenectomy Infection (OPSI). Autotransplantation is one of the possibilities to preserve splenic functions. The authors performed spleen autotransplantations in two cases after the splenectomy of cystigerous spleens. Ten pieces from the intact spleens each sized 10x20x2 mm were implanted in between the plates of the great omentum according to Furka's spleen apron method. The function of the reimplanted splenic tissue was demonstrated by scintigraphic investigations.

### **Introduction**

Some of the aspects of the physiological functioning of the spleen are still unknown but research of the past decades have demonstrated its outstanding role in protecting the body from infections. In 1952, King and Shumacker [3] explained the short-course sepsis of young children, also known as Overwhelming Postsplenectomy Infection (OPSI), by the incidence of splenectomy. Incidence in adults was reported in 1970.

According to investigations, the amount of IgM, number of T-lymphocytes and specific and non-specific immune response decreased after splenectomy. Decrease in the level of proteins such as properdin and tuftsin, stimulating the functioning of phagocytes, was also noted. Mortality due to sepsis increased significantly. On the basis of the above, attempts to preserve the spleen and preserve its function are justifiable. Autotransplantation is one of the possibilities to preserve splenic function.

### **Case report**

Splenectomy and spleen autotransplantation due to splenic cyst were performed in two cases, according to Furka and co-workers [1,2].

**Case 1:** L.S., 19-year-old male, presented at our hospital complaining of pain below the left costal margin which he noticed during work. The ultrasonographic investigation showed a 80x50 mm cyst in his spleen. His laboratory findings and chest X-ray were normal and negative, respectively. His spleen, sized 12x8x5 cm, containing two non-communicating cysts as big as a walnut and green walnut, was removed in right subcostal laparotomy on 15. 02. 1994. Ten pieces from the intact spleen (called Furka's spleen chips), each sized 10x20x2 mm, were implanted in between the plates of the great omentum and the hole was closed. Histological investigation suggested that the cysts were caused by parasites. The patient was discharged on the 7<sup>th</sup> postoperative day, free from complaint. Scintigraphic investigation performed 16 months after the operation showed a functioning reimplanted spleen.



**Case 2:** G. H., 24-year-old male suffered a blunt injury in his lumbar region 3 months prior to his admission. Because of his tensive abdominal pain an ultrasonographic scan was performed which showed a 110 mm structure, inferior to the splenic capsule, providing slightly poorer reflection than that of the substance of the spleen. The change was also demonstrated in the CT scan. No changes in the laboratory findings were observed. His chest X-ray was negative. Splenectomy was performed on 17 September 1996. 10 chips, each with a size of 10x20x2 mm, from the intact substance of the spleen were reimplanted in between the plates of the great omentum. The patient was discharged on the 8th postoperative day, free from complaint.

Histological findings: Two thirds of the removed 15x12x12 cm spleen were occupied by a thick cyst. Other parts of the spleen were of preserved structure. The histological picture corresponded to a multistage splenic rupture. Control scintigraphic investigation is planned in the future.

## Discussion

Spleen autotransplantations in animal experiments were performed by Furka, Mikó and co-workers [1,2,5]. Follow-up examinations demonstrated that, contrary to splenectomies, successful spleen autotransplantations result in normal levels of IgM and tuftsin which play a role in the defence system of the body. Based on their results, spleen autotransplantations due to benign changes in the spleen were performed according to their method in two cases at our hospital, following splenectomy.

In the first of our cases, restoration of splenic function in the reimplanted spleen was proved by isotopic investigation.

Autotransplantation of the spleen is a procedure easy to perform technically and involves little loss of time. If it is successful it can substitute the spleen from an immunobiological point of view, so the body can preserve its ability to protect itself against infections. It is suggested that spleen autotransplantation is performed due to traumatic spleen injuries [4,6] as well as after splenectomy carried out because of benign changes in the spleen. No data in the available literature have been found about autotransplantations following the removal of cystigerous spleens.

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## MONITORING OF GASTRIC ACIDITY FOLLOWING DUCTAL DECOMPRESSION SURGERY FOR CHRONIC PANCREATITIS

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The accepted decompression methods of chronic pancreatitis are the longitudinal pancreaticogastrostomy and the conventional pancreaticojejunostomy. The aim of the present study was to estimate the effect of these types of drainage operations on gastric acidity and to evaluate the clinical results. Between Jan. 1992 to 1996 56 patients with chronic pancreatitis were selected into the investigation who were operated in our clinic. A 24 hour gastric monitoring was taken on every patient before and 6 weeks after the operation. Following a complete postoperative check up we found that both types of operations are effective for pain relief (71%). Retrospectively 83 % of the patients had no digestive problems due to pancreatic enzyme substitution. According to our statistical evaluation of 24 hour gastric pH monitoring test no alteration was detected in gastric pH in both groups pre- and postoperatively. On the basis of pH measuring and evaluated data we consider that pancreaticogastrostomy is a good operation choice to relieve intractable pain in selected patients with chronic pancreatitis associated with duct dilatation.

### Introduction

The most accepted operation in painful pancreatitis is the pancreaticojejunostomy. The longitudinal pancreaticogastrostomy is a more simple operating method in painful chronic pancreatitis, nevertheless it has not spread widely [3]. The aim of the present study was to estimate the effect of these types of drainage operations and to evaluate the clinical results. It is not even known whether the pancreatic enzymes cause any alteration in the gastric acidity following the longitudinal pancreaticogastrostomy [2].

### Methods

Between Jan. 1992 and 1996 56 patients with chronic pancreatitis were selected into the investigation who were operated at the 2<sup>nd</sup> Department of Surgery, Univ. Med. School of Debrecen, Hungary and we performed 37 pancreaticogastrostomy [PG] and 19 pancreaticojejunostomy [PJ]. We have investigated the symptoms, the rate of diabetes mellitus, the results of ERCP, Ultrasound, CT examinations, consumption of alcohol, opiates and tranquilizers, and we recorded the social status previous to surgery. We performed 24 h pH monitoring and statistical analysis. The Wilcoxon's signed rank test was applied.



## Results

There was no operative death within 30 days. Pancreatic stones were present in 22 and 10 cases in the two groups. Pancreatic duct abnormalities were found in all patients. The alcoholic etiology was most common [54 patients]. The result of the operations was considered to be good in 29, fair in 6 and poor in 2 patients in the group of pancreaticogastrostomy and 14, 4, and 1 in the group of pancreaticojejunostomy, respectively. One patient had bleeding from the site of the anastomosis and another had leakage of the anastomosis. They were reoperated. During the observation the number of diabetes mellitus has increased from 9 to 12 in the two groups. Due to the substitution of pancreatic enzymes we did not find steatorrhea postoperatively. The median preoperative pain scores were 115 (30–220) as against 45 (10–190) postoperative scores in the pancreaticogastrostomy group. In the pancreaticojejunostomy group it was 125 (40–230) against 45 (5–200). None of them used opiates after surgery, 5 patients occasionally used tranquilizers. The median preoperative weight was 58.3 kg (42–68) and the median postoperative gain of weight was 3.8 kg in the first group and 59.0 kg (42–70) increased with 4.3 kg in the pancreaticojejunostomy group. The social status also improved postoperatively.

## Discussion

After longitudinal pancreaticogastrostomy we had 78% good results. After pancreaticojejunostomy the rate of good result was 74% which is similar to other investigators [4, 5]. Similarly with the opinion of other authors the results of this study show that longitudinal pancreaticogastrostomy is also an effective way of operation of chronic pancreatitis [1]. On the basis of pH measuring and evaluated data we can say that there is no change in gastric pH and acidity following pancreaticogastrostomy.

The aim of our study was to investigate gastric acidity in the forms of decompression. According to our statistical evaluation of 24 hours gastric pH monitoring test no alteration was detected in gastric pH level in both groups pre- and postoperatively. On the basis of pH measuring and evaluated data we consider that the pancreaticogastrostomy – which is a simple and quick procedure – is a good operation choice to relieve intractable pain in selected patients with chronic pancreatitis.

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## **INFLAMMATORY MEDIATORS AND SURGICAL TRAUMA REGARDING LAPAROSCOPIC ACCESS: NEUTROPHIL FUNCTION**

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Polymorphonuclear leukocytes (PMN) are well recognised as being the principal cells in the inflammatory response reaction. The current investigation was designed to evaluate the stimulated state of neutrophils in patients undergoing open (OC) and laparoscopic cholecystectomy (LC). The superoxide radical generation of isolated PMN and its lag time, and PMN elastase were measured in peripheral venous blood samples collected from 42 patients. The observation period started on the day of hospital admission and ended on the 5 th day. Our results showed that although there were no characteristic changes in the superoxide radical production of PMN in the LC group, we found a marked depletion already by the first day in OC group which persisted during the whole observation period. There was an elevation of PMN elastase on the first postoperative day in both groups, but in the laparoscopically operated patients it decreased considerably on the 3rd postoperative day while in the OC group it maintained a high level. The same discrepancy was present between the two groups on the 5 th day. Decreased free radical production of isolated PMN may reflect depleted neutrophil functional state, while changes of PMN elastase indicates increased harmful potential. These data suggest the differences in neutrophil activation between the two groups can be partially responsible for the better outcome in patients operated by laparoscopic cholecystectomy.

### **Introduction**

There is a growing body of evidence that the better outcome of minimally invasive surgery is due to the diminished acute phase response [1]. Activated polymorphonuclear leukocytes (PMN) play a pivotal role in the aseptic inflammation releasing several pathogenetic agents such as lysosomal proteinases, reactive oxygen species and different cytokines [2,3,4]. The purpose of our study was to evaluate the role of neutrophils in the postoperative inflammatory period measuring the function of polymorphonuclear leukocytes (PMN) by stimulated superoxide radical production and release of PMN elastase following open (OC) and laparoscopic cholecystectomy (LC).

### **Patients and Methods**

In this study 42 otherwise healthy patients scheduled for elective cholecystectomy were selected. Of these, 21 underwent open cholecystectomy and 21 laparoscopic cholecystectomy. Peripheral venous blood samples were taken 3 h before the operation and every day for 5 days following surgery at the same hour. Whole blood were used for isolation of PMN and the superoxide radical generation was stimulated by phorbol-myristate-acetate (PMA). The free radical production of stimulated PMNs and the time lag necessary for their production were determined. PMN elastase was measured in the sera of the same samples by a heterogenous enzyme immunoassay (Reagent Kit, Merck).



The superoxide radical production expressed in nmol/min (normal value:  $8,5 \pm 1,8$  nmol  $O_2$ /min/ $1,5 \cdot 10^{-6}$  PMN), the time lag in minutes (normal value: 1,2–1,8 min) and the values of PMN elastase in mg/l (reference value:  $22 \pm 10$  ng/ml).

## Results and Discussion

The superoxide radical production in correlation with the lag time showed the following features: (a) in the OC group the radical production decreased on the first postoperative day ( $5,05 \pm 0,8$  nmol  $O_2$ /min/ $1,5 \cdot 10^{-6}$  PMN) and remained on this low level during the whole observation period; (b) in the LC group this depression of the radical production on the first day was not so marked ( $6,905 \pm 1,23$  nmol  $O_2$ /min/ $1,5 \cdot 10^{-6}$  PMN) and on the 3rd day it elevated back to the control level. This decreased PMN capability of generating free radicals in OC group suggests a greater neutrophil involvement in the inflammation in contrast with the LC group. The longer lag time in OC group also showed a greater depletion of PMN function compared with the findings in LC group. The values of PMN elastase elevated in both OC and LC groups on the first post-operative day ( $135,1 \pm 9,1$   $\mu$ g/l,  $p < 0,001$ ;  $150,5 \pm 24,8$   $\mu$ g/l,  $p < 0,05$  respectively). On the second day a further increase was registered in both groups, however we found the most significant difference between the two groups by the 3<sup>rd</sup> postoperative day. While the value of PMN elastase in the laparoscopically operated patients decreased considerably ( $116,5 \pm 20,9$   $\mu$ g/l), it maintained a high level in OC group ( $164,6 \pm 18,9$   $\mu$ g/l;  $p < 0,01$ ). Following the 4th postoperative day we still found an elevated enzyme level in the OC group while in the LC group a continuous fall towards the baseline value was noted. These data suggest a faster functional recovery of neutrophils following the laparoscopic procedure.

## Summary

Our study was designed to explore the neutrophil behavior in the postoperative inflammatory response. In order to do so we determined the plasma level of PMN elastase, the stimulated superoxide radical production of isolated neutrophils and the time lag of radical production of PMN following open and laparoscopic cholecystectomy. We found a marked difference in neutrophil function between patients in the two groups. Although the neutrophil status is only one of the many possible factors involved in surgical injury, these results suggest that the shorter recovery period observed after the laparoscopic procedure may partially be explained by the difference in severity of PMN activation influencing the inflammatory response.

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## **POSTOPERATIVE CHEMOEMBOLISM TREATMENT OF PRIMARY AND METASTATIC MALIGNANT HEPATIC TUMOURS**

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Between 1992 and 1996 62 patients were operated for primary malignant and metastatic hepatic tumours. After the operation 31 patients received cytostatical treatment, 9 patients were treated with the method of chemoembolism. 46 patients are alive 30,7 (5-54) months after the operation. 9 patients died 12,5 (3-27) months after the resection of the liver. Authors have favourable experiences on the treatment of chemoembolism.

### **Introduction**

The primary and metastatic malignant hepatic diseases have got an increasing importance in the surgery and in the oncotherapy of the liver. Beside the improvement of the methods of the intensive therapy and the surgical methods the perioperative chemotherapy spreads in an increasing way. These therapies combined together can highly improve the survival parameters of the patients.

### **Patients and Methods**

Between 1992 and 1996 62 patients were operated for primary and metastatic malignant tumours in the 2<sup>nd</sup> Department of Surgery, University Medical School of Debrecen. The resections of the liver were performed in 6 cases because of primary hepatic cancer, in 37 cases because of the metastasis of colorectal tumours, tumours of the pancreas and of the papilla of Vater (in 6 cases), tumours of the stomach (in 3 cases), tumour of the lung, testis, carcinoid of the small intestine (in 1-1 case). The rate of males and females was: 30/25. The average age was 55,5 years in males and 49,2 years in females. 12 operations were performed by CUSA ultrasonic dissector, before these operations we used the traditional finger fracture method. 21 atypical hepatic resections, 25 segment resections, 4 hemihepatectomies and 5 lobectomies were performed. Simultaneously we performed pancreato-duodenectomy or resection of the pancreas combined with splenectomy + lymphadenectomy in 5 cases, resection of the rectum in 5 cases, resection of the colon in 5 cases, gastric resection combined with splenectomy + lymphadenectomy in 3 cases, resection of the lung in 1 patient. After the operation 31 patients received cytostatical treatment. The patients operated for the metastasis of gastric or pancreatic



tumours received 5-FU, Intron-A combination, or EAP scheme, in the cases of colorectal tumours patients received FAM cytostatical treatment. In the case of primary hepatic cancer the combination of Cysplatin – Farmorubycin 5FU was used systematically or as chemoembolism. 22 patients did not received postoperative adjuvant therapy (because of the refusal of the treatment, gravidity, severe intercurrent diseases, etc.).

## Results

The patients operated for primary hepatic cancer are alive (6 cases). The average survival period of the patients who received cytostatical treatment is 18 (5–34) months. The average survival period of the patients who received chemoembolism (2 patients) is 7 (3–11) months. Five of the 7 patients with inoperable primary hepatic tumours are still alive. In this group of patients the average survival period is 5 (3–8) months for the patients who received cytostatical treatment (5 patients). The patients who received chemoembolism (2 patients) are alive 6–10 months after the operation. The two patients who died 3 and 5 months after the operation, had inopeable hepatic tumours and received cytostatical treatment. The patients who had resectional operation for metastasis (22 cases), received cytostatical treatment and 21 patients are still alive 30,7 (5–54) months after the operation. One patient died 6 months after the operation. The patients who received chemoembolism (5 cases) are alive 8.8 (6–10) months after the operation. From the 22 patients who did not received cytostatical treatment, 14 are alive 14.5 (6–32) months after the operation. Eight patients died 11 (3–27) months after the operation.

## Discussion

In the treatment of the patients with primary and metastatic malignant hepatic diseases the directed chemoembolism has got an increasing importance. Huge hepatic tumours can be transformed into operable [1] or the state of the patients can become suitable for hepatic transplantation [5] after the treatment. Others [2] had good experiences on the combination of the cytostatical treatment and the dearterialisation. There were also investigations to combine high dose intraarterial cytostatical treatment and the haemofiltration of the blood taken directly from vena hepatica [3]. Others had good experiences on the combination of immunotherapy and chemotherapy [4].

## Summary

Authors investigated postoperative adjuvant cytostatical treatment and the chemoembolism in cases with primary and metastatic hepatic tumours. On the base of the data available the directed chemoembolism can improve the survival rates and is a smaller

burden to the patients. In certain cases the preoperative cytostatical treatment is advisable to increase the rate of the patients with resectable tumours and the postoperative chemoembolism is also useful to improve the survival parameters.

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## **SURGICAL TREATMENT OF DIVERTICULITIS OF THE SIGMOID**

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This study demonstrates that elective colon surgery for diverticular disease is benign, with a low mortality and morbidity. The acute severe complications of the colonic diverticular disease are characterized by a large mortality and morbidity. The results reported here, as all those published recently on the same subject, are in favor of broadening the indications of colectomy in diverticular disease, before the occurrence of a severe acute complication.

### **Introduction**

The true incidence of colon diverticular disease (CDD) varies in different countries, depending upon factors such as diet, and age of the population. CDD is practically uncommon before the age of 40. About 95 per cent of cases of CDD are located in the sigmoid.

### **Patients**

In the last four years the Surgical, Gynaecological and Vascular Surgical Department of Pasteur Hospital Centre has treated 95 patients with CDD. 59 patients were treated medically. We operated 20 patients in Group A (mean age 60 y.). They were treated by elective colon resection, with primary anastomosis, without postoperative mortality, morbidity 1/20. 16 Hartmann procedures were realized for peritonitis (9), abscesses (3), acute colonic obstruction (3) and a massive colonic bleeding (Group B, mean age 69 y.). Postoperative mortality of Group B was 3/16.6 patients of Group B kept a permanent colostomy.

### **Discussion**

The clinical manifestations of CDD cover a broad spectrum. The most frequent early symptoms are: cramps, constipation, and local pain in the left lower abdomen or in the suprapubic region. Concomitant bacterial inflammation (diverticulitis) may be associated with increased pain, palpable masse, fever. Diverticulitis consists of many microabscesses in the wall of colon with the inflammatory reaction extending through the wall in the area of the diverticulum. The incidence of such inflammation among patients with CDD has been estimated at 15–25 per cent. General peritonitis and septicaemia signify more serious infection or perforation. Gross perforation results in immediate general

faecal contamination of the peritoneum. More frequently, the perforation is contained by tissues in the wall of the colon or its mesentery or is buttressed by inflammatory adhesions to the abdominal or pelvic wall or adjacent viscera: a localized abscess then forms. Attachment of small bowel loop to the inflammatory process may result in development of a fistula. Diverticulitis may be associated with creation of fistula into the Fallopien tubes, vagina or into the urinary bladder. Rarely, CDD may present with massive rectal hemorrhage, acute colon obstruction or palpable mass due to a giant diverticulum [1, 2]. Repeated bouts of localized uncomplicated diverticulitis may thus result in ligneous inflammatory swelling and scarring of the sigmoid and its mesentery with a intractable colon dysfunction and pain.

Many medical diseases predispose patients with diverticulitis to its septic complications: obesity, diabetes, corticosteroid therapy, posttransplantation immunosuppression, AIDS etc.

Physical signs of CDD vary according to the stage and complications.

Colonoscopy is useful in identifying the inflammatory lesion, associated polyps, or adenocarcinoma, but may be dangerous in the acute case of diverticulitis.

The plain films of the abdomen may show normal findings, paralytic ileus, mechanical bowel obstruction, rarely pneumoperitoneum [4].

In patients with chronic or subacute symptoms, a barium enema examination may confirm the presence of diverticula. By suspected acute diverticulitis or its complications barium enema carries the risk of perforation of an inflamed diverticulum or barium contamination of the peritoneal cavity if a perforation is present. Emergency enema using a water-soluble agent may be extremely helpful. Contrast material outside a diverticulum confirms the perforation. However, absence of this finding does not exclude the diagnosis [4].

CT of the abdomen following oral and rectal administration of contrast medium water-soluble is the most reliable examination for diagnosing diverticulitis. Diagnostic findings include visualisation of diverticula, thickening of the bowel wall, fibrosis in the mesentery, thickening of adjacent viscera, extraluminal mass, or abscess with fluid and/or gas [2].

Uncomplicated CDD can be managed by dietary manipulation, and anticholinergic drugs to inhibit peristaltic cramps.

Patients with intractable colon dysfunction and pain, recurrent attacks of local inflammation (two or more), persistent tender abdominal mass, or rapid progression of symptoms and with relative young age (Group A) should be treated by elective resection of sigmoid colon and primary anastomosis [1,2,3]. Preoperative mechanical preparation of the bowel should be undertaken. Perioperative intravenous antibiotics should be administered. Patients with peritonitis or acute colonic obstruction (Group B) should be treated by Hartmann procedure. Acute severe complications of CDD are characterized by a large mortality and morbidity [1,2,3].

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## DIFFICULTIES IN EARLY DIAGNOSIS AND TREATMENT OF UNCOMMON BREAST TUMOURS

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The aim of the current study was to analyse the uncommon histological type tumours, occurred in our department in the last 10 years. In the study period 921 patients were treated for breast malignoma, 47,4% of them in early cancer stage. In the latter group 3 cases were observed with rare histological tumour type: secretory juvenile breast cancer T1N0M0, GI /case I/; primary angiosarcoma T1N0M0, GI /caseII/; planocellular breast cancer T2N0M0,GII /caseIII/. In the case of rare histological type tumours: (1) triplet diagnostic procedures are usually able to result in correct preoperative diagnosis; (2) the adequate treatment has to be determined individually; (3) continuous, long term follow-up is necessary; (4) MRI is an appropriate technique in the detection of recurrences.

### Introduction

The successful treatment of the malignant tumours occurring in the female breast is based on the early diagnosis and adequate surgical and adjuvant therapy of the cancer. The principles of treatment seem to be fixed for today, but both the diagnosis and therapy could be difficult in the case of rare histological type tumours.

The aim of the current study was to analyse the uncommon histological type tumours occurred in our department in the last 10 years.

### Method

In the study period 921 patients were treated for breast malignoma, 47,4% of them in early cancer stage. In the latter group 3 cases were observed with rare histological tumour type: secretory juvenile breast cancer T1N0M0, GI (case I); primary angiosarcoma T1N0M0, GI (case II); planocellular breast cancer T2N0M0, GII (case III). The data of case history was overviewed. The preoperative diagnosis was set up on the findings of "triplet diagnostics": mammography (except case I), breast ultra-sonography, physical examination and fine needle biopsy with cytology (FNB). The reliability of diagnostic procedures was assessed, literary recommendations were taken account in the selection of clinical treatment. Final histological diagnosis was based on traditional light-microscopy on one hand, and on special histochemical reactions on the other hand. Follow-up of the patients is continuous. Physical status, breast US, mammography, X-ray, scintigraphy, MRI are checked regularly.

## Results

The anamnestic data were characteristic in the case of the secretory juvenile breast cancer (young age, brownish nipple discharge, palpable mass), but not in the other two cases. The triplet diagnostic procedures have resulted in correct diagnosis in case II, and were uncertain in case III in determining the tumour type. In case I, only dysplastic malformation was suggested preoperatively, but later the FNB samples were re-analysed and typical cytologic signs of the secretory juvenile breast cancer were observed.

The type of surgical intervention was selected on the basis of preoperative findings (TNM) and literary recommendations: wide excision with lymphadenectomy in case I and II, modified radical mastectomy in case III. Final histological examinations have briefly confirmed the diagnosis in all cases. The supplementary immunohistochemical reactions of alpha-lactalbumine and protein S-100 were typically positive for secretory cancer [3]. Receptor status analysis was carried out only in the latter case and was found to be negative both for oestrogen and progesteron. Adjuvant therapy was administered in case III (chemo + radiotherapy).

Despite of correct treatment, local recurrences were observed 2 years after the operation in case II and III. The lesions were widely re-excised.

After a 4 years follow-up all patients are clinically tumour-free. Although we have few experience, MRI looks to be a very effective method in the postoperative follow-up of "problem" cases.

## Discussion

The cases, presented here, are extremely rare: in the world literature approximately 110 cases of secretory juvenile breast cancer [4], 170 cases of primary angiosarcoma and less than 50 cases of planocellular breast tumour have been published so far.

It is known, that these cases are often misdiagnosed and treated improperly [1]. In our opinion the preoperative triplet diagnostic procedures are able to result in correct diagnosis in theses cases, too.

The surgical and adjuvant therapy have to be indicated individually on the basis of clinical TNM. According to the literature in all of these cases-whether the conditions of a breast conserving technique are valid- wide excision and axillary lymphadenectomy looks to be appropriate treatment [2]. Although there are few data on adjuvant therapy of these tumours, radiotherapy and chemotherapy are not expected to have too much result.

The recurrences, experienced in our study, show that long-term and very close follow-up of these patients is necessary.



## Conclusion

In the case of rare histological type tumours: (1) triplet diagnostic procedures are usually able to result in correct preoperative diagnosis; (2) the adequate treatment has to be determined individually; (3) continuous, long term follow-up is necessary; (4) MRI is an appropriate technique in the detection of recurrences.

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## DIFFERENT OPENING TECHNIQUES IN CATARACT SURGERY

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A retrospective study on the different opening techniques in cataract surgery at our Department in 1996 was carried out. In our everyday practice fornix based conjunctival flap and sclerocorneal oblique or vertical-oblique approach with a center at 12 o'clock was performed. In the case of hemorrhagic diathesis and secondary ACL implantation the corneal approach was preferred. After glaucomatous filtration surgery the incision was made temporally in some cases.

**Keywords:** cataract extraction, opening technique

Since cataract surgery exists ophthalmologists have been discussing how to open the eye. The dramatic revolution in cataract surgery over the last 15 years yielded a number of novelties in this field, too. The goal of this study was to describe the different opening techniques used at the Department of Ophthalmology in Debrecen and to compare them with the experience obtained by other ophthalmologists.

A retrospective study on cataract surgeries performed at our department in 1996 was carried out. Altogether 1128 such operations were performed. Their distribution was as follows:

|                                             |      |        |
|---------------------------------------------|------|--------|
| ◆ manual ECCE with PCL implantation         | 1005 | 89%    |
| ◆ manual ECCE with ACL implantation         | 53   | 4,5%   |
| ◆ phacoemulsification with PCL implantation | 5    | 0,4%   |
| ◆ ICCE with ACL implantation                | 4    | 0,3%   |
| ◆ secondary ACL implantation                | 28   | 2,2%   |
| ◆ manual ECCE                               | 19   | 1,5%   |
| ◆ ICCE                                      | 14   | 1,1%   |
|                                             | 1128 | 100,0% |

### Abbreviations

ECCE=extracapsular cataract extraction, ICCE= intracapsular cataract extraction, PCL= posterior chamber lens, ACL= anterior chamber lens

Various triple procedure techniques in which ECCE with PCL implantation was combined with perforating keratoplasty or with trabeculectomy were not included in this study.

At ECCE, ICCE and secondary ACL implantation as well as during phaco-emulsification the surgical opening of the conjunctiva and the cornea was performed in different ways. In our everyday practice we performed fornix based conjunctival flap and



sclerocorneal oblique or combined (vertical-oblique) approach with a center at 12 o'clock. In 2 cases of phacoemulsification and 1 case of manual ECCE we prepared limbus based conjunctival flap and straight scleral tunnel incision. In 20 secondary ACL implantations, 15 cases with hemorrhagic diathesis, and in 10 cases with previous trabeculectomy we used a corneal incision and left the conjunctiva intact. In 2 other cases with previous trabeculectomy we made the wound temporally in order to avoid the filtration bleb. In one case with previous partial lateral blepharorrhaphy because of lagophthalmos we performed the limbal wound with a nasal approach because the area of the pupil was better approachable from that direction. In case of secondary ACL implantation – to correct preoperativ astigmatism – we slightly deviated from the 12 o'clock approach several times. The extent of incision was the longest in ICCE, i.e. about  $160^\circ$ . In case of manual ECCE it was sufficient to make an incision of  $120^\circ$  in the majority of cases, whereas in cases of secondary ACL implantation and phacoemulsification the length of the wound was 6 mm or less.

The conjunctival flap can be fornix or limbus based. The fornix based flap is easy to prepare, simple to suture, the exposure of surgical field is optimal, but the adaptation to the limbus is variable and there can be a tendency to bleed. The limbus based conjunctival flap takes more time to prepare, suturing is more difficult, the exposure of the surgical field is occasionally problematic, but the adaptation of the conjunctival wound and the covering of the sutures and the incision are optimal [1]. The opening of the anterior chamber can be carried out with scleral, sclerocorneal or corneal approach. At corneal incision there is no bleeding, the trabecular meshwork is not injured, postoperatively we have a deep anterior chamber with little irritation. This technique has some disadvantages, such as the internal opening of the wound is relatively small, wound healing is slower, Descemet's membrane may be detached, there is a corneal scar. Corneal incision is indicated after anti-glaucomatous filtering operations, in cases of secondary ACL implantation or hemorrhagic diathesis, and if peripheral anterior synechiae are present. At scleral or sclerocorneal incision the wound is covered by conjunctiva, the cornea is not touched and the healing process is more rapid, but the incision may bleed, the trabecular meshwork can be injured and the operation technique is more time consuming. Scleral or sclerocorneal approach is indicated in cases of microcornea, corneal dystrophy or peripheral degeneration and in endothelial damage [1]. It is important to study which type of opening helps the cornea to stabilize its curvature most rapidly and which causes minimal postoperative astigmatism. Hennekes [3] carrying out a scleral "W" incision established that the advantages of this opening technique include reduction and control of astigmatism, improved self-sealing and reduced postoperative leakage. Performing scleral tunnel Haberle et al. [2] recommended for cases with preoperative "with-the-rule-astigmatism", surgical wound at 12 o'clock position and singular perpendicular suture, and for cases with "against-the-rule-astigmatism" (especially  $>1.5D$ ) temporal incision. The sclerocorneal and the corneal incisions can be vertical, oblique, combined (vertical-oblique or oblique-vertical) or a step incision. The combined and the step incisions close easily therefore they need less sutures resulting in less postoperative astigmatism [1]. Thygesen et al. did not find a

statistically significant difference in the postoperative astigmatism after corneal and sclerocorneal incision [6]. Pfleger et al. established that making clear corneal incisions of different length the smaller incision group had the least surgically induced astigmatism and axial change [5]. Neumann et al. concluded that the phaco-emulsification procedure with small incision induced significantly less astigmatism and provided faster visual rehabilitation than the manual ECCE procedure [4].

In summary in our everyday practice we perform fornix based conjunctival flap and sclerocorneal oblique or vertical-oblique approach with a centre at 12 o'clock. In the case of hemorrhagic diathesis and secondary ACL implantation we prefer the corneal approach. After filtration surgery it is better to do the incision temporally.

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## NEW INDICATIONS FOR AND TECHNIQS IN VITREORETINAL SURGERY

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Vitreoretinal surgery has become a widely used ophthalmic surgical procedure since the late sixties. However, it remained an intensively developing field of surgical interventions, and indications still become wider and wider. The procedure starts with the removal of vitreous body, blood or inflammatory material from the vitreous cavity. After this, the given retinal disease, such as retinal detachment, macular hole, proliferative diabetic retinopathy, intraocular foreign body, etc. can be properly treated in situ. For that purpose a number of fine intraocular instruments, fluids, gases can be used. While the anatomical success rate can be up to 95 %, the final visual outcome, due to the fact that the retina is not rarely seriously damaged, is less enthusiastic. However, a great number of previously untreatable vitreoretinal diseases can be managed in this way, nowadays.

**Keywords:** vitrectomy, retinal detachment, macular hole, diabetic retinopathy

Vitreoretinal surgery is a relatively new and rapidly growing field of ophthalmic surgical procedures. It is well known from the late sixties, that vitreous body can be removed from the eye without serious consequences. Kasner performed this through the limbus (1968), while Machemer introduced the better pars plana approach (1971). Since the introduction of this new surgical procedure, it has developed very quickly.

The removal of the vitreous body demands a number of high technology instruments: vitreous cutter, fiberoptic lightsource, stereo operating microscope with coaxial illumination, assistant stereo eyepiece, wide angle fundus lenses and foot switches to keep the surgeon's hands free. A great number of specially designed, delicate instruments: intraocular scissors, forceps, membrane peelers, cannulas, laser pipes help the surgeon in this intervention. Nowadays intraocular gases and so called "heavy liquids" became also commercially available. Continuously increasing number of vitreoretinal diseases can be managed with this surgical intervention.

Usually an encircling band is sutured on the sclera above the vitreous base at the beginning of the procedure. It indents the sclera to overcome the expectable concentric contraction of the vitreous base. Temporary keratoprosthesis can be fixed if some corneal opacities makes it necessary. Three pars plana wounds are made with a special sized scleral knife. It must be done at 4 mm's distance from the limbus in a phakic eye, but only at 3.5 mm in an aphakic one. An infusion line is fixed into one of the wounds, usually in the lower-temporal quadrant to maintain a constant intraocular pressure during the whole procedure. The two other wounds are used for intraocular light pipe and manipulators.

After removal of the central part of the vitreous body (core vitrectomy) we use contact or non-contact lenses for visualisation the deeper parts of the eye. Previously, plan-concave contact lenses, or prismatic lenses were used for this purpose. Nowadays, wide angle lenses are also available. Organized blood, pus or foreign body can be removed from the vitreous cavity. Obviously, retinal diseases can only be managed after removal of the vitreous body when the surgeon has good access to the retina. Epiretinal membranes can be peeled off the surface of the retina, blood can be sucked out, foreign body can be removed and it is also possible to enter the subretinal space if it is necessary.

After the cleaning up the vitreous cavity and liberation of the retina, it must be put to its original position. Insufflation of air or injection of heavy fluid can help this procedure. The last step before closing the wounds is fixation of the retina onto the choroid. For this we can use intraocular tamponade with air, expandable gases (Sulfur-hexafluoride, Perfluoromethane, Perfluoroethane, Perfluoropropane), silicone oil, together with endolaser coagulation. Stable postoperative situation and better results can be achieved in this way.

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## TWO METHODS IN THE TREATMENT OF PROSTATE CANCER T<sub>1</sub>-T<sub>2</sub>

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The author reports experience of 82 radical retropubic prostatectomies. In accordance with the length of isolable urethra two methods were applied. In one of the methods the bladder-neck was pulled down to the floor of the pelvis by a synthetic reabsorbable thread (40 cases), in the other method, the urethra-trunk was sewn up to the bladder-neck (42 cases). The early and later complications are dealt with. Their findings: the blood transfusion during intra and perioperative period was identical in both methods. Injury of ureter did not occur, injury of rectum in one case (1,2%) occurred. In the two methods incidence of impotence (85%) and incontinence (15%) were identical. The length of operation was on an average twenty minutes shorter in the pull-down technique but stricture occurred in 4,7%. In the sewing method no stricture occurred. In the opinion of the author the pull-down technique at the short (5-7 mm) urethra-trunk, while the direct sewing-up technique at the long (7-20 mm) urethra-trunk were applied.

**Keywords:** radical prostatectomy, operation technique complications

### Introduction

In the treatment of prostate cancer stage T<sub>1</sub>-T<sub>2</sub>, N<sub>0</sub> M<sub>0</sub> the radical prostatectomy is gaining in importance in spite of relative difficult operation-technique and the frequent later complications. The first operation was performed by Young in 1905 [5]. Since then a number of technique modifications have been made. The surgical intervention can be carried out by retropubic, perineal and sacrococcygeal.

The choice of method depends on the surgical experience, skill and personal qualities.

The radical prostatectomy means the extirpation of prostate, seminal vehicle, ampulla of duct deferent and extirpation of lymphnodes from so called obturatorius triangle.

### Materials and Methods

Between 1991 and 1997 in 82 cases were performed radical prostatectomies because of localized prostate cancer. The patients' average age was 62, no operation was performed above the age of 70.

It is important, the patient to be operated on should be able to live ten more years.

Diagnostic methods: digital rectal palpation, serum prostate specific antigen, transrectal ultrasound examination, transperineal biopsy of prostate

After diagnosis: i.v. urography,  
bone scan examination,  
pelvis computer tomography or magnetic resonance  
examination were made.

The lymphnodes were examined by staging lymphadenectomy before the radical prostatectomy.

If one lymphnode is found positive the radical prostatectomy will not be performed.

Operative methods: in accordance with the length of isolatable urethra two methods were applied.

In one of the methods the bladder-neck was pulled down to the floor of the pelvis by synthetic reabsorbable thread (40 cases), in the other method, the urethra-trunk was sewn up to the bladder-neck (42 cases). On the first day after operation the patients were mobilized, the catheter was removed on the 12–14 th day. The performing of the operation were made difficult:

1. preoperative neoadjuvant treatment
2. preoperative transurethrale resection of prostate.

During the operation the following problems are to be solved:

1. careful decreasing of the bleeding,
2. nerve-sparing,
3. outer constrictor-muscle-sparing.

## Results

Intraoperative complications: it is important the careful decreasing of bleeding. The blood transfusion during the intraoperative period was identical both methods, average 640 ml. 4 patients didn't get transfusion. Injury of ureter did not occur, injury of rectum in one case (1,2%) occurred.

Later complications: wound infections occurred in 5% (4 patients).

In the two methods incidence of impotence 85% (36–35 cases), and incontinence 15% (6–6 cases) were identical. The length of operation was on an average twenty minutes shorter in the pull-down technique, but stricture occurred in 4,7% (2 patients). In the sewing method no stricture occurred.

Comparing the preoperative staging with the pathological staging:

understaging 22% (18%)  
in 12 cases T<sub>1</sub>–T<sub>2</sub>  
in 6 cases T<sub>2</sub>–T<sub>3</sub> were found.

The patient after the operation 3 month undergo laboratory tests. 81 patients (98,7%) live in good general condition, 1 patient died 18 month after the operation, during the operation the prostate cancer crossed the prostate-capsule. The cause of dead was diffuse metastasis.



## Discussion

Early and later complications can be decreased by improving the operation-technique. In decreasing of incontinence is important: the longer the urethra-trunk, the better (10–20 mm). The pull-down technique at the short (5–7 mm) urethra-trunk, while the direct sewing-up technique at the long (7–20 mm) urethra-trunk were applied. In avoiding impotence important role is plaid by the conservation of the neurovasculare-bundle [4].

Comparing data of the last four years concerning 10 million habitants in the USA and in Hungary, it was found, that in Hungary 50 times less radical prostatectomies were performed [1].

It is important to emphasize that radical prostatectomy is the most effective method in the treatment of prostate cancer.

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## **EXPERIENCES WITH ETHANOL INFILTRATION OF THE LIVER METASTASES OF COLORECTAL TUMORS (PRELIMINARY STUDY)**

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With the aid of improvement in imaging technique and with the ability of detection of hepatic tumours, the successful treatment of primary and secondary hepatic tumours using surgical methods has gained importance. Metastasectomies were performed in 16 cases at our department in 1996. In 6 cases atypical resections and/or infiltration with 96% ethanol were performed. In 3 instances ethanol infiltration into the metastases were accomplished during the resection, in 4 cases – when metastases were discovered 1–4 year after the resection of the primary tumours – the same method was used during the relaparotomy. 96% ethanol was injected directly into the metastatic tumours during operations. The early ultrasonograph examinations proved the total destruction of the metastases in diameter of 1–3 cm, and partial necrosis of the large ( $d=3-8$  cm) tumours. Two patients were lost from the follow up. Five patients are still alive after 2–8 months of the ethanol infiltration. In one patient after the ethanol infiltration of metastases  $d=3-5$  cm/ in 6 segments of the liver we observed the dissemination of the tumour.

### **Introduction**

With the aid of improvement in imaging technique and with the ability of detection of hepatic tumours, the successful treatment of primary and secondary hepatic tumours using surgical methods has gained importance. Promising results can be expected with the percutaneous and/or intraoperative ethanol infiltration of tumours, even when the tumour is unresectable, because of its localisation and/or it is multilocular. The elimination of metastatic tumours of the liver is important in the case of colorectal tumours, because – according to several authors [1,2,3] – the rate of the survival period in 5 years significantly increase.

### **Materials and Methods**

96% ethanol was injected directly into the metastatic tumours during operations. Metastasectomies were performed in 16 cases in our department in 1996. In 9 cases atypical resections of the livers, in 6 cases atypical resections and/or infiltration with 96% ethanol were performed. In 3 instances ethanol infiltration into the metastases were accomplished during the resection of the primary tumours, in 4 cases, when metastases were discovered 1–4 year after the resection of the primary tumours, the same method was used during the relaparotomy. In 4 patients the reachable metastases were resected



atypically, in 3 instances the surrounding of the tumours were infiltrated and in one case the unremovable tumour was injected. In one patient, the large tumour ( $d=8\text{cm}$ ) was injected, in one other case six metastases ( $d=3-5\text{cm}$ ), which were located in different segments, were directly infiltrated. In all the 6 cases the basic diseases were colorectal tumours: one rectum-, four sigma- and one transversum adenocarcinoma. In one patient during the investigation we found three tumours in the III.- IV.- V. segments of the liver which were suspected HCC. These tumours were resected and their margins were infiltrated with ethanol. During two operations transarterial catheter implantation were performed in hepatic artery.

In all of the above mentioned cases the ethanol infiltration was used supplementary to eliminate the primary hepatic tumour and/or the unresectable metastases ( $d=1-5\text{cm}$ ) of colorectal tumours. The same method was performed additionally around the removed tumours to prevent the recurrences of the tumours. Ethanol infiltration was also used independently in the cases of multiplex tumours, when the liver resection could not be performed and/or when the conditions of the patients excluded the expansion of the load of surgery. Ages of the patients were between 60-77 years. The number of the ethanol infiltrated primary and secondary tumours altered between 1-6, and their diameter were 1-8 cm. The metastases were most frequently located in the 7 and the 8 segments, and we never performed surgery in the 1<sup>st</sup> segment. The maximal infiltrated volume of the ethanol was 20 ml, which were divided into parts in proportion to the size and the volume of the tumours. (In one case, when six metastases ( $d=3-5\text{ cm}$ ) were treated, 30 ml was injected.) During the treatments systematic side effects or hepatic dysfunction were not observed. Complications were not detected during the postoperative period either.

## Results

The early ultrasonograph examinations proved the total destruction of the metastases in diameter of 1-3 cm, and partial necrosis of the large ( $d=3-8\text{ cm}$ ) tumours. Two patients were lost from the follow up. Five patients are still alive after 2-8 months of the ethanol infiltration. In one patient after the ethanol infiltration of metastases ( $d=3-5\text{ cm}$ ) in 6 segments of the liver we observed the dissemination of the tumour. In other 4 patients, who had atypical resections of the resectable metastases ( $d=1-5\text{ cm}$ ) combined with ethanol infiltration of the surrounding of the tumours and/or the unresectable tumours ( $d=1-3\text{ cm}$ ) were infiltrated, the regression of the metastases were detected. Progressions have not observed, although we know that the period of time after the treatment is short, an one patient was treated with transarteric chemotherapy. The control examination of the patients have performed in every three month using ultrasonography. In the case of appearance of new metastases or progression the ethanol infiltration will be used with ultrasound guided puncture.

## Discussion

This method have been used in our department with the hope that the survival time could be lengthened with partial or total elimination of liver metastases. Although the number of cases is few and the period of follow up is short, our results are promising. Local ethanol injection has several advantages: causes necrosis effective but not selective in the tumour. The applied dose of ethanol (max. 20 ml) does not cause liver dysfunction and does not have systemic side effect. It can be used both percutane and intraoperatively. The disadvantage is that the agent cause tissue necrosis only at the site of injection, and it depends on the doses. In our cases the 1–3 cm tumours were totally destroyed. The larger (d=3–8 cm) tumours were only partially eliminated. The treatment can be repeated with ultrasound guided percutaneous punctions, thus the injection of the residual tumours and new metastases is possible. Overall advantages of the local ethanol injection appear to outweigh its disadvantages, therefore we hope that 96% ethanol infiltration method can be a useful supplementary tool in the treatment of the secondary and primary hepatic tumours.

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## **THE CRYOVARICECTOMY (DEMONSTRATION OF A NEW METHOD)**

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The operating technique of the primary varicosity has changed recently. The subcutaneous methods have been used nowadays. We give account of making 416 cases by cryovaricectomy, which is a quite new method. Using this technic we can remove the dilated venous branches during a 3-4 millimeters wide incision of skin and preserve the sufficient main vein. Summarizing of our advantageous experience: the cryovaricectomy is suitable for principles of minimally invasive surgery, and the operating time is much more briefer, the aesthetic results are best, the attendance far shorter and the postoperative complaints of patients much more fewer.

### **Introduction**

The operating solution of primary varicosity has been changed in the last few years. The subcutaneous methods has come to the front of interesting, for example: using Smetana – instrument, or Várady's-method: The so called "crochet hook" technic. The applying of cryoprobe is a quite modern practice [3, 4].

### **Method**

The authors underline the importance of exact varicectomy, choosing from the other methods. The basic operating technic includes crossectomy in the inguinal bend, stripping of insufficient saphenous vein and localized removing of dilated collateral veins [1,2,5]. This method has been using since spring of 1993 in our department generally.

The principal point of it is removing of main and collateral venous branches by the aid of angiocryoprobe. After placing the freezing probe into cavity of the saphenous vein and using the pedal of appliance, surgeon can make it freeze and than pull out. The smaller branches could be pull out across 3-4 millimeters incision of the skin, and is not required to place the probe into the cavity because they will freeze on the cryoprobe.

The ruptured branches will be coagulated due to freezing effect and haematoma will be reduced.

### Summary

Summarizing experiences of 416 operations in the course of last 4 years:

- ◆ the cryovaricectomy is adequate method like "minimally invasive surgery",
- ◆ the operation is more faster,
- ◆ the cosmetic result is better,
- ◆ the attendance is shorter,
- ◆ the postoperative complications and complaints are less.

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## **A RANDOMIZED COMPARISON BETWEEN MINILAPAROTOMY AND CONVENTIONAL APPROACH FOR AORTOILIAC RECONSTRUCTIVE SURGERY**

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To decrease the surgical stress on patients undergoing aortic surgery the authors developed a less extensive procedure utilizing minilaparotomy and videoendoscopy. From June 1993 through July 1996, patients undergoing surgery for aortoiliac occlusive disease were randomized comparing the minilaparotomy (ML) with conventional approach (CA). Sixtytwo patients participated in this trial, with 37 in the ML group and 25 in CA group. There were no significant differences between the groups in terms of age, sex or comorbid conditions. The incidence of intraoperative complications was similar for both groups. After surgery, nasogastric drainage was significantly ( $p = 0,01$ ) shorter, bowel movement and initiation of alimentation began earlier in ML group. Both groups of patients showed a significant decrease in vital capacity and forced expiration volume postoperatively, but this depression was significantly higher ( $p = 0,05$ ) in CA group. The ML group also had significantly shorter stay in the intensive care unit ( $p = 0,001$ ) and the mean duration of the postoperative hospital stay was also significantly less ( $p = 0,05$ ). Generally, the patients operated by ML method during the postoperative recovery period required less analgesia, and expressed better "overall satisfaction". In long-term follow-up (mean 21 months), there was no significant difference in survival rates between two groups.

### **Introduction**

To establish the feasibility of minilaparotomy approach a randomized, prospective trial was performed that would compare the ML with CA to the aorta for routine infrarenal aortic reconstruction. The study was approved by the university ethics committee, and informed consent was obtained from patients before the operation.

### **Methods**

Between June 1993 and July 1996, patients who were admitted for aortobifemoral bypass implantation were recruited into the study. After obtaining informed consent, sixty-two patients were randomized, with 37 in the ML group and 25 in CA group. There were 32 men and 5 women in the ML group and 21 men and 4 women in CA group. The mean age in the ML group was  $62,3 \pm 8,5$  years and in the CA group  $61,0 \pm 9,7$  years. The incidence of hypertension, abnormal electrocardiogram, diabetes mellitus, chronic obstructive pulmonary disease, cerebrovascular accidents, renal disease and smoking was compared between two groups and there were no significant differences. Operative technique was described in previous publications [2, 5].

## Results

The incidence of intraoperative complications was similar in both groups, with one complication in the ML group (myocardial infarction) and one in CA group (cardiac arrhythmia). There was no intraoperative death. In the ML group three patients died within the first 30 postoperative days. Two of these death were due to myocardial infarction occurring on the third and fourth postoperative day and the other death resulted from an aspiration pneumonia during the third postoperative week. In the CA group two patients died, one from myocardial infarction other from cerebral hemorrhage. Five patients (2 from ML group, 3 from CA group) had clinical or electrocardiographic evidence of infarct within the first 30 days, they recovered fully. One additional patient was treated for urinary problems, and one other also required readmission for conservative treatment of a pancreatitis.

The postoperative recovery was compared in two groups of patients. The most significant difference occurred in the incidence of prolonged ileus defined as a prolonged period of nasogastric intubation (>72 hours). The nasogastric drainage is significantly shorter, bowel movement and initiation of alimentation begins significantly earlier in ML group. Patients can generally take fluids on the first postoperative day, can receive a light meal on the second postoperative day and normal meals thereafter. Intensive care was only in selected cases necessary and the length of stay was significantly shorter in the ML group. The mean duration of the postoperative hospital stay was also significantly less ( $6 \pm 2$  days) compared to the conventional exploration of  $9 \pm 3$  days.

## Discussion

Our results suggest that decreasing exploration can be accomplished without jeopardizing patient outcome and confirm using minilaparotomy approach have not adversely affected safety of the operation. Advantages of the "mini" approach are follows. The small size of incision, the limitation of the exposure and early removal of skin sutures (on 5th postoperative day) all contribute to minimize pain. Because of minimal intraabdominal exposure, dessication and manipulation of the small bowel function. Further advantages of this approach that only one assistant in necessary. All of these aspects may translate to a great reduction in the cost associated with treatment of aortoiliac occlusive disease.

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## EFFECTS OF NITRIC OXIDE SYNTHASE INHIBITION ON THE HEMODYNAMIC CHANGES IN HYPERDYNAMIC ENDOTOXEMIA

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In this study we compared the circulatory effects of the arginine analogue non-specific nitric oxide synthase (NOS) inhibitor N $\omega$ -nitro-L-arginine (NNA), and the specific inducible NOS (iNOS) inhibitor S-methylisothiourea (SMT) and S-(2-aminoethyl)-isothiourea (AEST) in a hyperdynamic endotoxemic dog model. Mean arterial pressure (MAP), cardiac output (CO), and myocardial contractility (MC) were measured. A hyperdynamic circulatory response was elicited with a 2-h infusion of a total dose of 5.3  $\mu$ g/kg E. coli endotoxin (ETX). NOS inhibitory treatment (2mg/kg) was administered from the 45th min of endotoxemia. ETX induced a hyperdynamic circulatory response, and a significant myocardial depression. NNA induced a prolonged, SMT a transient increase in MC, both drugs elevated MAP, but decreased CO. AEST significantly prolonged the elevation in CO, but did not affect MAP. Selective inhibition of the iNOS may be a beneficial treatment in sepsis.

### Introduction

A cascade of inflammatory reactions, including nitric oxide synthesis is activated in sepsis. Nitric oxide (NO) plays an important role both under physiologic and pathologic conditions, and is implicated in the circulatory failure in septic shock. NO, synthesized by the continuously active constitutive enzyme (cNOS) has an important role in neurotransmission in the central nervous system and in peripheral vasoregulation [3]. Inflammatory cytokines or ETX activate the inducible isoform of NOS (iNOS), which produces large amounts of NO [2]. Since NO might contribute to the circulatory failure [3], NOS inhibition could be a beneficial treatment modality in septic shock. The commonly used NOS-inhibitors are arginine-analogue compounds that inhibit both iNOS and cNOS, and increase total peripheral resistance (TPR) and decrease CO [1]. In a rat model, inhibition of iNOS with the novel NOS inhibitors SMT and AEST attenuated the circulatory failure caused by ETX [4]. In this study we compared the circulatory effects of the arginine analogue non-specific NOS inhibitor NNA, and the specific iNOS inhibitor SMT and AEST in the early phase of hyperdynamic endotoxemia.

### Methods

The experiments were performed on pentobarbital-anesthetized dogs. The left femoral artery and vein were cannulated for measuring MAP and for fluid administration, respectively. A Swan-Ganz thermodilution catheter was positioned in the pulmonary artery for measuring CO by thermodilution. TPR was calculated using the standard formula. A Millar tip-micromanometer catheter was placed into the left ventricle to measure left ventricular pressure (LVP). After a left thoracotomy a pair of ultrasonic

crystals was sutured on the myocardium to measure left ventricular diameter (LVD) by sonomicrometry. After surgery the chest was closed, and the animals breathed spontaneously. MC was estimated by the end-systolic pressure-diameter relationship (ESPDR) [3]. The slope of ESPDR was calculated with a computer program. A hyperdynamic circulatory response was elicited with a 2-h infusion of a 5.3 µg/kg dose of *E. coli* ETX (Group 1). The animals were observed for 120 min after ETX-infusion. In Group 2, 3 and 4 NOS-inhibitors were administered from the 45<sup>th</sup> min of the ETX-infusion. Group 2 and 3 received NNA or SMT in a 10-min infusion (2mg/kg iv), respectively. Group 4 was treated with a 2-h infusion of AEST (2mg/kg iv).

## Results

ETX induced a hyperdynamic circulatory response, for approx 90 min. Significant decreases in MAP, and TPR, as well as a significant increase in CO were observed. MC increased initially, but after the 60th min of the ETX-infusion it decreased below the control level. Administration of NNA or SMT elevated MAP, accelerated the decrease in CO, and the increase in TPR. NNA treatment caused a prolonged, and SMT treatment a transient increase in MC. AEST treatment significantly prolonged the elevation in CO, and did not affect MAP.

## Discussion

In our experiments low doses of ETX induced a hyperdynamic circulatory response, characterized by elevation in CO, and a decrease in TPR and MAP. Non-selective inhibition of NOS with NNA had opposing effects on the hemodynamic parameters, since it restored MAP and increased MC, but at the expense of a decrease in CO. NO may play a role in the observed transient myocardial depression, because non-selective NOS-inhibition significantly augmented MC. The similarities between the effects of NNA and SMT suggest an cNOS inhibitory property of SMT. However, AEST prolonged the hyperdynamic circulatory response, and did not show any effect on cNOS in our model. Our data demonstrate that selective iNOS inhibition has a lesser effect on MC, but is more effective in prolonging the compensatory hyperdynamic circulatory reactions during endotoxemia.

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## RECONSTRUCTION OF THE CONSTRICTED ORBITAL CAVITY IN PATIENTS WITH ARTIFICIAL ANOPHTHALMY

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In cases, in which not only the globe of the eye, but the whole conjunctival sack is missing and the eyelids are due to scarring attached either to the orbital tissues and/or to each other, it is not possible to insert a prosthesis. This is a major aesthetic defect. The cavity that allows artificial eye insertion can be formed by surgery. One of the best methods is the orbital cavity reconstruction developed and suggested by the Hungarian István Csapody. He constructed two instruments to perform the operation: a butterfly shaped marker to prepare skin graft with proper size and shape, and an adjustable cone formed spacer to keep the reconstructed socket open during the healing process. We use free autologous split skin graft to line the cavity. If the shapes of the eyelids are intact, and the color of the prosthesis matches the fellow eye and it fits perfectly, then the postoperative cosmetic result can be excellent.

If someone loses one of his eyes because of any reasons, his original or almost original outlook can be restored by wearing an artificial eye sometimes of artistic finish, that is easy to obtain nowadays.

The prosthesis can only be worn, if there is an intact orbital cavity lined by conjunctiva, that can accept the artificial eye. But there are cases, in that not only the eye but the complete conjunctiva is missing as well, and the eyelids are scarred either to the orbital tissues or to each other. This condition is a major cosmetic defect. The possible ways of the correction are the followings. The easiest and the oldest method is the black bandage of one eye. It was popular especially in former times (field marshal Kutuzov, admiral Nelson, general Dajan). Nowadays those, who are in need of it, wear dark glasses instead. This is not very conspicuous, but it has the disadvantage of reducing the vision of the good eye.

Theoretically one can wear a so called ectoprosthesis. The ectoprosthesis consists of eyelids and eyeball made out of acrylate, that are mounted on the posterior part of the glasses, which is kept in place in front of the deformed orbital cavity by the frame of the spectacles. Unfortunately today no one produces that in Hungary. Were it obtainable and most artistically finished, it still would not give the best aesthetic result. The ectoprosthesis can not follow the changes of the color of the skin. In case of blushed, sun tanned or pale face it can be extremely deforming.

The next possibility is the surgery. The operation is not easy, and in many cases the result cosmetically is not the same like the other side. For in most of the cases not only

the conjunctival sack is missing, but the eyelids are deformed as well, or even the eyelashes are partly or completely missing.

Complete symblepharons and ankyloblepharons are usually formed after chemical injuries. There are cases, in which the complete content of the orbital cavity has to be removed because of retrobulbar tumor, thus only the skin of the eyelids remains and covers the orbital cavity. In these cases the situation can even be worsened by the sometimes necessary postoperative irradiation. Unfortunately it also can happen that the conjunctival sack, that after a simple enucleation could accept an artificial eye, begins to shrink suddenly without any obvious reason. In case of children even the bones of the orbit can be delayed in the development.

Ophthalmologists have been concerned about the idea of a surgical solution for a long time. Most ophthalmologists line the cavity with skin. It is very hard to estimate the exact shape and size of the lobe. The problems are folding or stretching of the skin, and both of them results in scarring. Neubauer writes with good reason that there are strikingly many methods described, and there are strikingly few postoperative statistics published.

However there is a good method, the orbital cavity reconstruction of the Hungarian professor István Csapody, which gives the best possible result in all of the cases.

Csapody made a long preparatory work. He prepared moulages of the orbits of cadavers and of the bony orbits of skulls, he made calculations and as a result of these he determined the ideal shape and size of the skin lining the orbital cavity. He developed two special instruments for performing the operation.

1. A butterfly shaped metal cliché, with which help the shape of the skin graft for lining the orbit can be cut out.
2. A spacer constructed out of two quarters of a sphere, on which the skin can be fixed by sutures. The spacer with the skin can be inserted into the orbit, that previously had been freed from scars. The two sphere-quarters can be pulled from each other and according to the size of the orbit it can be fixed in that position. This way the metal spacer stabilizes the skin in the orbital cavity without any wrinkle or stretch.

The course of the operation is as follows. After the usual premedication local anesthetics are given, then we release the eyelids, and remove the orbital scar-tissue. Then the skin graft is cut out. Csapody originally performed the operation with full-thickness free skin graft. Nowadays we use split skin grafts for lining the orbit. Anyhow, this idea had already been raised by Csapody, too. We fix the skin graft on the spacer by some sutures and insert it into the orbital cavity. Then the edge of the skin is stitched to the margins of the eyelids all around. During the last phase of the operation we pack the cavity with one gauze tape. By this we press the skin graft against the bottom of the orbit to the orbital base.

The metal spacer is removed 10 days later, after the removal of the stitches. Until that time the patient must not bend, in order the relatively heavy (14,5 gr.) instrument not to fall out. Then the formed cavity is packed again with one gauze tape for another one week. After the gauze is removed we insert the artificial eye.



If the shapes of the eyelids are intact, and the color of the prosthesis matches the fellow eye and it fits perfectly, then the postoperative cosmetic result can be excellent. Csapody wrote his book about the operation in 1956. Still, the operation is known by a few, performed by a few, no doubt the number of the patients is small, too. The operation, however, is so witty, that it succeeded in 1996, 40 years after the book had been published. The video film about the operation won the first prize on the video-festival of the 9<sup>th</sup> Congress of the Operating Ophthalmologists of Germany in Nürnberg.

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## TREATMENT OF INGROWING TOENAIL WITH SEGMENTAL CHEMICAL ABLATION

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During a 5 year period (1992–1996) 716 segmental chemical ablations using phenol solution of 80 v/v % were carried out because of ingrowing toenail. As a control, Emmert procedure was done in 200 cases. In the present study we discuss the etiology, the surgical technique of the chemical ablation and the results of the intervention. We have found that phenol treatment results in a larger rate of symptomatic relief, lower recurrence rate and better cosmetic results could be achieved. Taking into account the good results, the low financial requirements of the procedure in the treatment of ingrowing toenail, segmental chemical ablation with phenol may be the therapy of choice of the disease.

**Keywords:** ingrowing toenail, surgical and chemical ablation, phenolisation.

### Introduction

Ingrown nail is a common condition occurring at any age. It is not the severity but the frequent incidence of the disease which makes it important to choose the right method of treatment. Wearing uncomfortable tight shoes, improper technique of cutting the nail, familial tendency and inadequate hygiene of the feet and nails should be highlighted among the causes.

Pathophysiology of the disease: It can be seen most often on the great toe that one of the sides of the nail breaks off and this broken piece pierces the nail bed like a thorn. Mechanical irritation causes inflammation. It is evident that conservative treatment will just postpone surgical intervention.

### Materials and Methods

At our department, ingrown nail, which is a common disease among privates, has caused problems. In these cases the disease is caused by poor hygiene and wearing uncomfortable boots all day. The use of fenol solution in the treatment of pilonidal sinus and, on the basis of the literature [3,4,5], in the treatment of ingrown nails was started in the late 1980s. The method of segmental chemical ablation, now considered to be a well established technique in everyday practice, and our results are listed below.

Method of surgical segmental chemical ablation: Oberst's conduction anaesthesia is achieved by 2x1 ml of Lidocain with a concentration of 2%. 2–3 mm of the edge and the



inflamed granulation tissue of the nail are excised longitudinally, together with the matrix, in a bloodless intervention. Excisions are performed with a scalpel.

The use of scissors is discouraged because they may lift the intact nail from its base, too. Then 1–2 drops of 80 v/v % phenol solution are dropped on a gauze plug which is deeply introduced into the place of the resected nail to ensure the destruction of the matrix.

The treatment with phenol solution lasts for 3 minutes. Then the wound is rinsed with physiological saline solution and covered with dressing. From the next day on, the patient is asked to soak his wound in Neomagnol dissolved in water, twice a day for 30 minutes each time. After soaking he should dry his feet and cover his wound with a dry dressing.

During the five-year period between January 1st 1992 and December 31st 1996, 716 cases of surgical segmental chemical ablation using phenol solution of 80 v/v % were carried out at our department. Emmert procedure was performed in 200 cases, as control.

## Results

We observed the period of wound healing. On the 7th postoperative day complete wound healing was seen in more cases treated with phenol solution than with Emmert procedure.

### *Wound healing*

Phenol solution: 500 cases  
no discharge after 7 days  
cuticularization of wound base  
in 87%

Emmert procedure: 200 cases  
no discharge after 7 days  
cuticularization of wound base  
in 71%

The patients's pain was evaluated on the 2nd, 4th and 7th postoperative days. The patients complained of less pain after treatment with phenol solution than after traditional treatment. Even minor analgesics were required only occasionally to decrease postoperative pain.

### *Evaluation of postoperative pain on an empirical scale*

*Phenol solution: 500 cases*

| Pain    | No  | Little | Medium |
|---------|-----|--------|--------|
| 2nd day | 1%  | 28%    | 71%    |
| 4th day | 29% | 57%    | 14%    |
| 7th day | 74% | 26%    | —      |

*Emmert procedure: 200 cases*

| Pain    | No  | Little | Medium |
|---------|-----|--------|--------|
| 2nd day | 5%  | 55%    | 40%    |
| 4th day | 14% | 60%    | 26%    |
| 7th day | 62% | 32%    | 6%     |

Control examination of patient in six month revealed that the number of proportion of recurring cases was lower than that among patients who received traditional treatment.

*Recurrence*

*Phenol solution:* 317 cases of control  
 after 6 months: healed in 96%  
 after 1 year: healed in 94%

*Emmert procedure:* 128 cases of control  
 after 6 months: healed in 94%  
 after 1 year: healed in 91%

It was unnecessary to check-up patients on the 2nd and 4th postoperative days after treatment with phenol solution as the patients could soak their wound in a solution of Neomagnol and put on a new dry dressing in their homes, so check-up is done only once, a week after the intervention.

## Conclusion

Segmental chemical ablation has been successfully applied in the treatment of ingrown nails for over five years. The patients become free of symptoms sooner, the cosmetic results are good and the rate and proportion of recurrence is lower. The intervention is cost-effective.

Considering all the above facts as well as our experience and results, we believe that segmental chemical ablation using combined treatment with phenol solution is an excellent alternative in the treatment of ingrown nails on an outpatient basis.

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## SHALL WE WAIT UNTIL THE HEAD OF THE FEMUR IS COMPLETELY CRUSHED IN IDIOPATHIC NECROSIS OF THE FEMORAL HEAD?

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Although it is of polyetiological nature but of identical pathomechanism, the necrosis of the femoral head has been known for more than a century, and, without treatment, it results in complete necrosis. To stop the progression of the process, load-lifting drilling of the affected area was introduced in the 1970s. Since then, the success of the technique in the early stage of the disease has been justified by countless follow-up examinations and studies. Load-lifting drilling of the affected area in the early stage of the disease yielded similar results at our department in a small clinical sample over 6 years. To ensure permanent drainage, we have used cannulated titanium screws with a diameter of 9 mm for the second year now; besides allowing continuous decompression these screws hold mechanically well and the use of titanium allows MR and CT investigations later on.

**Keywords:** pathomorphology, classification of the necrosis of the femoral head, load-lifting drilling, permanent cannulation

### Introduction

The necrosis of the femoral head results from several factors; however, its pathomechanism invariably includes the circulatory damage of the femoral head. In some cases it is impossible to reveal the cause; this phenomenon is known as primary or idiopathic aseptic necrosis. Several different etiologic factors are recognised in this group and are also known to be risk factors of the disease [1]. In the majority of the cases the disease affects young people and early diagnosis allows us to stop the progression of the disease on the contralateral side, mainly in bilateral processes. The disease develops bilaterally in 40–50% of idiopathic cases and in 80% of cases related to steroid use. The time lapse between the two sides is usually 4–5 years. Since X-ray findings are negative for a long time it is difficult to reveal the necrosis of the head, and by the time the change is noticed the process has progressed to a level which prevents the physician from stopping the progression of the disease even if proper treatment is administered [3].

### Pathomechanism of the disease

The spongiosa of the femoral head consists of beehive-like units, i.e. sinusoids or microcompartments filled with bone marrow and adipose tissue. Each unit is interwoven by a fine network of capillaries to ensure blood supply to bone elements. This closed system is regarded to be a haemodynamic unit, and damage or enlargement in any of its

elements can only take place to the detriment of the other ones. Necrosis of the bone may develop as a result of an interruption in arterial flow, damage to venous flow, intervascular blockage, swelling of the marrow substance or increase of pressure in the sinusoids [1].

Microscopically, necrosis in live bone marrow takes place in a similar manner, independently of etiologic differences. It is of characteristic localisation, i.e. it develops in the craniomedial-ventral portion of the head where the zone of loading is located [3].

Bone marrow necrosis is regarded to be the earliest stage, in which new, circumscribed necrotic foci of the haemopoietic bone marrow and fatty tissue are seen, surrounded by extensive secondary haemorrhage. The necrotic focus is surrounded by ingrowing vascular buds from the intact tissue, and probably this is the stage when the process is still reversible and full regeneration can be expected. Later the necrotic fatty cells trigger the excretion of neutral fats, triglycerides, which then sclerose and fill the already necrosed focus to a significant extent. This corresponds to the solid structure seen in X-rays. In the surroundings of the necrosed tissue circulation may remain stabile; granular tissue grows from the intact trabeculae towards the necrotic area which is therefore surrounded by living osseous tissue and all these processes take place simultaneously. On loading, however, the necrotic subchondral portion is crushed and, depending on the size of necrosis, deformity develops. In the course of the pathological events involving the tissue, a significant increase in pressure in the compartments is detected. Later the pressure begins to decrease because of the presence of crushed bony substance [3].

Two questions arise here: whether avascular necrosis is reversible and if bone can completely repair itself. Under certain conditions, the answer to both questions is 'Yes'. Ischaemia of the bone is reversible in its early stage, pressure in the tissues can be decreased. However, if a case of segmental bone necrosis is considered, the change is irreversible. Diagnosis should concentrate on the details of history and a thorough check-up of the risk factors typical of the clinical picture of the disease. At the beginning, patients complain of vague pain in their hip which increases on loading. Sudden, spastic ischaemic pain is not unknown either, and, in the majority of cases, the patients present to the hospital complaining of greatly limited movement which is supported by X-ray findings of signs of destruction. During the physical examination pain mainly accompanies limited movement due to inward rotation at the early stages [4, 5]. X-ray tests provide poor grounds in revealing circulatory damage of the femoral head; diagnosis can be based on MRI and scintigraphic tests. CT tests inform about the size and location of the already developed necrosis [4].

The treatment of necrosis is self-evident: circulation of the bone should be improved and congestion lifted. Surgically it can be done by drilling the bone, ensuring core depression to improve circulation, bone implantation using the vascular stem technique, various methods of osteotomy and the combination of these techniques [5].

What is the role and what can be expected of load-lifting drilling?

There is hope to avoid the spread of necrosis and crushing of the osseous substance as well as to make small focal necroses heal while the contour of the femoral head is still



intact. The aim is to eliminate compartmental syndrome with the help of decompression and, at the same time, restore microcirculation to the area. The intervention, which represents a minor load, may stop the process in an early stage, therefore this technique is a simple but valuable one. In ideal cases, decompression is indicated in ischaemic necroses of Ficat I-II stage of non-traumatic origin. In the necrosis of the femoral head due to traumatic processes, where the morphology of circulation is damaged, drilling may not result in spectacular [2].

## Materials and Methods

Our department has extensively studied the problem of the necrosis of the femoral head both of traumatic origin and of various etiology since 1990. The typical patient belongs to the younger generation and tends to neglect pain in the hip region in the early stages of the disease. Several questions concerning differential diagnosis, such as uncertain traumatic history, various types of locomotor diseases, changes in the vertebral column, etc., may emerge. Even some of our patients received treatment on the basis of various diagnoses and some of them underwent surgery due to herniated discs. At the beginning, clinical findings may be uninformative. In addition to the details of history, limited movement of the femoral head due to inward rotation is found relatively early. To make the diagnosis, MRI investigation is required as a supplement to a well-structured X-ray picture. Load-lifting drilling has been used in the treatment of the necrosis of the femoral head at our department since 1991. We have treated 27 cases of idiopathic necrosis of the femoral head using core decompression, bilateral drilling being performed in 12 out of the 27 cases. 8 of the patients with necrosis of the femoral head were alcoholics, in 1 case chronic hepatitis was found, increase in body weight exceeding 24% was found in 20% of the patients. Among the 27 patients with necrosis of the femoral head 23 were males, the mean age of the patients being 39.2 years.

Based on the etiology, 24 patients had idiopathic disease and 3 of the patients had received steroid treatment.

Pressure measurements were performed in 20 of the patients during drilling and increased values, exceeding 56 cm, were found in most of them. Histological investigation was performed in 24 patients, all of them supporting the presence of necrosis. After drilling the pain was gone for at least half a year. In Ficat I-II stages the shortest follow-up period after drilling involved 2 years, during which no progression was detected. Classification according to Ficat stages was different on both sides in every case.

Limitations in the extent of this paper do not allow detailed analysis of load-lifting drilling. However, we would like to briefly describe the improved version of the method.

Considering the pathology of idiopathic necrosis of the femoral head as well as the results of load-lifting drilling published in the literature over the past 30 years and the proven regression of the process, we have been searching for a solution which could simultaneously ensure the advantages of load-lifting drilling and improve the stability of

the damaged necrosed femoral head and could prevent it from crushing. That is why permanent drainage of the necrosed femoral head using titanium screws was introduced. A 9 mm cannulated titanium screw, developed by Manninger and his co-workers and used in fractured femoral necks, was introduced to replace drilling and continuous, selective suction was done over 3–5 days after the operation. The force of suction is 60 cm of water. The amount of suction fluid was 30–60 ml on average.

## Discussion

15 titanium screws have been implanted in 13 patients so far (Table 1). Titanium screws were implanted in 2, 7 and 4 patients (6 hips in the latter case) in necroses of Ficat I, Ficat II and Ficat III stage, respectively. The indication for implanting the screw includes permanent mechanical load-lifting as well as continuous cannulation. The intervention is performed with the help of two viewing screens. The pressure in the necrosed focus is measured. Penetration with an 8 mm drill is done at the level of the linea innominata, biopsy for histological investigation is performed and the titanium screw is introduced.

Table 1.

| Stage according to Ficat | Cases (n) | Necrotic process |           | Start of complaint (months) | Follow-up period (months) | Complaint |             | Remarks                                   |
|--------------------------|-----------|------------------|-----------|-----------------------------|---------------------------|-----------|-------------|-------------------------------------------|
|                          |           | uni-or           | bilateral |                             |                           | (n)       | little pain |                                           |
| I.                       | 2         | 1                | 1         | 3                           | 8-15                      | 2         | -           | -                                         |
| II.                      | 7         | 3                | 4         | 3-14                        | 4-15                      | 7         | -           | Contralaterally<br>1 TEP<br>2 osteotomies |
| III.                     | 4         | 2                | 4         | 8-23                        | 4-15                      | 3         | 1           | Contralaterally<br>2 osteotomies          |

Continuous cannulation using titanium screws is thought to be enough in Ficat I–II stages. In Ficat III stage, where the surface of the head is also involved and if the full extent of necrosis seen in anterior, posterior and lateral X-rays does not exceed 160–170 degrees, corrective osteotomy and use of cannulated screws are indicated together.

In necroses of Ficat III stage permanent cannulation alone was used in those patients who refused the extended operation. In one of the patients necrosis of the femoral head developed after steroid treatment following kidney transplantation and the extended operation was disregarded. In the necrosis of the femoral head of Ficat III stage, cannulated titanium screws brought relief, the patients became free of symptoms after the operation and no progression was detected in the 4–15 months of the follow-up period. Untreated necrosis, pain accompanying the crushing of the head and limitation of motion lead to the implantation of prosthesis. However, any solution aimed at the slowing-down of progression, relieving the patient's pain temporarily and maintaining his/her ability to



move is a good one. No progression requiring further intervention in the cannulated patients was seen during the follow-up period.

The past 18 months have been too short to yield a satisfying clinical analysis. Our work is aimed at familiarising this technique of treatment with all those colleagues who are deeply interested in this field.

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## ABOUT THE PRIMARY MALIGNANT TUMORS OF SMALL BOWEL

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Primary malignant tumors of small bowels are relatively rare among the GIA-tumors. There are no specific methods to find these tumors in an early stage. Only the specific radiological examination (double contrast method or CT-scan) or sometimes the specific jejunoscopy can prove the correct diagnosis before the operation. Usually surgeons have to operate because of the emergency situation caused by primary malignant tumors of small bowel. A total of 21 patients were operated on for malignant tumors of small bowels since 1st January, 1986 till 31<sup>st</sup> December, 1995 (during 10 years). 13 of the 21 were urgent cases. 3 perforations and 10 mechanical bowel obstructions were the indications of the acute surgical procedures. The preoperative diagnoses were correct in the eight elective operations. Types of operations: 8 jejunal-resection, 11 ileal-resection, 1 Whipple-operation, 1 ileal-resection with right hemicolectomy. Peri-operative mortality rate was zero. Histological reports: 13 adenocancers, 2 leiomyosarcomas, 5 malignant carcinoids, 1 anaplastic cancer. Lymphomas and tumors of papilla Vateri were excluded from this study. Most of the patients had abdominal symptoms earlier than 8 months before the operations. Earlier diagnosis may give a better chance to operate these tumors in earlier stages, and it can give a better chance for the patients for longer survival.

**Key words:** primary malignant tumor, small bowel

### Introduction

In spite of the fact that the 5-to-6-meters-long small bowel forms 2/3 of the length and around 90% of the surface of the digestive system, the primary malignant tumors of small bowel are rare, they give less than 1% of all GI-tract tumors. Based on histological examination they can be distributed into three main groups: cancers, sarcomas, malignant carcinoids. Concerning the prevalence of cancers and sarcomas opposing opinions exist. Some state that it is the number of cancers and others that it is the number of sarcomas that is prevailing [8].

The tumors of the small bowel are rarely recognised/ diagnosed preoperatively. Up to the middle of the 50's reports were hardly edited on the topic in Hungary. Recently, the number of these increased; however, it is most probably due to the higher number of recognition of these cases and not to the rising number of this type of tumor. In the Hungarian surgical literature the following authors reported articles about malignant tumors of the small bowel studied at their home institutions: Sztankay and Mester [7], Herczeg and Gaál [2], Ihász and colleagues [3], Balázs and Kertész [1], Kiss and Tasnády [4], Petrás and Krutsay [5], and Szabó and colleagues [6].



### Data of patients

At the Surgical Department of the Medical University of Szeged the number of 21 patients were operated on because of primary malignant tumor in the last 10 years. There were 15 males and 6 females. Mean age of the patients was 58,9 years (34–74). The site of the lesions were: 1 case on duodenum, 8 cases on jejunum, 12 tumors on ileum.

Symptoms were observed for 6-24 months prior to the operations. Almost all of the patients attended several institutions throughout the process of examination. However, the real preoperative diagnosis was correct only in eighth cases. Three times morbus Crohn and 2 times retroperitoneal tumors have been "proved" by CT or x-ray examinations, but that were not correct. In the third group of cases the indications of operations were some kind of complications: peritonitis, bowel obstruction.

Types of surgery: 11 ileal resections, 8 jejunal resections, 1 ileal resection with right hemicolectomy, 1 op. sec. Whipple. Early postoperative complications: 7 wound suppurations, 5 urinary infections, 2 bronchopneumonia. Perioperative mortality was zero.

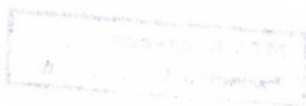
Histological results: 13 adenocancers, 2 leiomyosarcomas, 5 malignant carcinoids, 1 anaplastic malignant tumor.

### Discussion

The clinical manifestations of small intestinal malignant tumors depend upon the location of the tumor. Clinical presentations may include abdominal pain, weakness, weight loss, nausea and vomiting, bowel obstruction, GI hemorrhage, anemia or intestinal perforation. Clinical features of the carcinoid syndrome include cutaneous flushing, episodic watery diarrhea, and paroxysmal dyspnoea.

It is extremely difficult to recognize the malignant tumor of the small bowel with a routine x-ray examination. Maybe the double contrast method can give more chance for the correct diagnosis. Other diagnostic possibilities are: jejunoscopy, abdominal sonography, and computer tomography. In the diagnosis of the tumor of the small bowel selective angiography has been used more and more often. It has a great significance particularly in the diagnosis of jejunum leiomyoma-sarcoma, and also of carcinoid tumors, and reticulosarcoma on other parts of the GIA tract, and in locating the tumors. In case of a recurrent intestinal bleeding selective angiography always has to be carried out. If the traditional examinations do not help in getting the diagnosis and on the basis of clinical symptoms the possibility of a tumor of the small bowel exists, explorative laparotomy is necessary. The early recognition and operation of the malignant tumors of the small bowel is essential concerning the survival rate.

The basic therapy of the malignant tumors of the small bowel is surgery. In general, resection is carried out together with the removal of the mesentrium belonging to the tumor. If the operable tumor is located on the final segment of the ileum hemicolectomy is performed with the removal of that particular ileum-segment. Patients with lesions not



amenable to radical surgical resection should receive palliative bypass to correct the bowel obstruction. The basic treatment of carcinoid tumors is also surgical. According to the relevant literature, we also support the removal of the primary tumor even in case of liver metastasis.

Cancers of the small bowels may be treated with radiation therapy, if curative surgical resection is not possible. However, many GI carcinomas are radioresistent. Chemotherapy may be used in the treatment of small intestinal carcinomas where curative surgical resection is not possible. The principal chemotherapeutic agents have been 5-fluorouracil and nitrosoureas. Chemotherapy of intestinal carcinoid has had limited success. Streptozotocin has shown some efficacy against carcinoid.

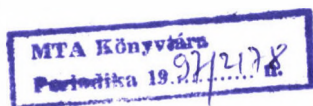
The prognosis of malignant tumors of the small bowel is poor. Due to mild symptoms the patients are operated late. The tumors tend to metastasize routinely to regional lymph nodes as well as hematogenously to liver, lungs, peritoneum, bone, ovarium and other sites. Cancers, as they cause stenosis quickly, are operated earlier; therefore their prognosis is slightly better.

### Conclusion

In case of uncertain abdominal complaints, we should also consider the possibility of a malignant tumor of the small bowel. In that way, it might be possible to decrease the duration of examination time and the preoperative diagnosis could also get more precise. In case of elective operations the risks are smaller. Operations in earlier tumor-stages may produce longer survival rate.

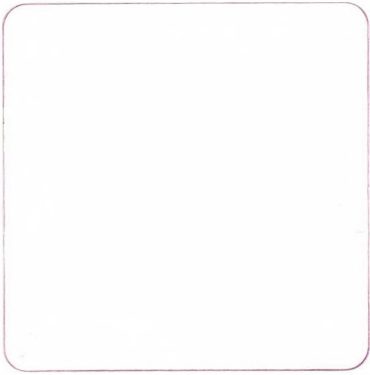
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