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CONTENTS

Advantage of transvaginal over transabdominal sonography. <i>K. Patai, Zs. Jakab, Z. Harkányi and Z. Vigváry</i>	3
A case of Fournier's gangrene. <i>H. Czalbort, L. Hornok and L. Ritter</i>	13
Intraoperative injuries during transperitoneal urological operation. <i>L. Pajor, J. Lip-ták and M. Szücs</i>	17
Ultrastructural changes in the nerve elements in Chron's disease. <i>V. Szabó and Erzsébet Fehér</i>	25
Motor response to electric spatial stimulation of isolated intact and inflamed human appendix. <i>A. Antal, J. Szolcsányi and L. Bartho</i>	33
The potentials of CO ₂ laser in the surgery of the liver, biliary tract and pancreas. <i>T. Tóth and J. Bátorfi</i>	39
A case of multiple cholangiogenic liver abscess due to residual biliary stone cured by percutaneous drainage controlled by CT and endoscopic papillotomy. <i>T. Fazekas, F. I. Todua, M. Y. Vilyavin and A. Bálint</i>	45
Gastrointestinal angiodysplasia. <i>F. Jakab, Márta Balázs, J. Faller and S. Kiss</i>	57
Percutaneous cholecysto-lithotripsy. <i>Cs. Tóth</i>	69
Rupture of the splenic artery aneurysm during pregnancy. <i>D. Hunka, Teréz Csordás and Z. Domány</i>	77
Virus-host studies in human seminal and mouse testicular cells. <i>S. Csata and Gizella Kulcsár</i>	83

Advantage of Transvaginal Over Transabdominal Sonography

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(Received: January 17, 1989)

Results with transvaginal sonography (TVS), a new ultrasound diagnostic method, are reported. A total of 40 patients were comparatively examined by transvaginal and transabdominal sonography. In contrast to transabdominal sonography, the transvaginal examination provided additional information in 35% of the patients. The indications and advantages of transvaginal sonography are summarized as compared with the traditional method. The introduction of the method is recommended in all US laboratories where examinations of the pelvis are performed.

Transvaginal sonography (TVS) is a new endosonographic method, during which a highfrequency (5–7 MHz) transducer of a special shape is introduced into the vaginal fornix. This allows the direct visualization of the pelvic organs, and due to the higher frequency, a higher resolution can be achieved. The scan is richer in detail as opposed to transabdominal sonography (TAS). The advantages of TVS are summarized in Table 1.

TABLE 1
Advantages of TVS

-
1. A greater resolution can be achieved, because the transducer is in the direct proximity of the organ to be examined.
 2. The bladder should not be filled (renal failure, difficulties in urine retention).
 3. Obese patients with thick abdominal wall can be examined more accurately.
 4. Intestines and adnexal structures can be better differentiated.
 5. The structure of the endometrium can be better visualized.
 6. Fetal heart function can be detected at an age of 6 weeks.
 7. The vitelline sac can be seen at 5 weeks.
 8. The structure of the ovaries can be better visualized, the size of the follicles can be judged with greater precision.
 9. The examination takes a shorter time (there is no need to wait for filling of the bladder).
-

The TVS and TAS of 40 patients were performed consecutively and the results of both methods were compared.

TABLE 2

Distribution examinations according to diagnosis

GYNAECOLOGICAL INDICATIONS				
Indication	US finding	No. of cases	Clinical diagnosis	No. of cases
Irregular bleeding	Thick endometrium of irregular structure	5	Endometrial hyperplasia	2
			Endometrial carcinoma	1
			Negative histology	2
Palpable mass/lower abdominal pain	Ovarian cyst	6	Ovarian cyst	8
	Septate cyst of irregular shape	4	Adenocarcinomatous ovarian cyst	2
	Inhomogeneous solid structure in the right adnexal region	1	Ovarian adenocarcinoma	1
	Myomatous trabecules	10	Myoma of the uterus	10
Febrility	Partly cystose, partly solid structure beside the uterus	2	Abscess	2
IUD localization	IUD of favourable location	3		
Endocrine disease	Larger ovaries with small cysts	2	Stein-Leventhal syndrome	2
OBSTETRIC INDICATIONS				
Bleeding	Regular graafian follicle and myoma tubercles	1	6-week intrauterine pregnancy + myomatous uterus	1
Missed abortion	Irregular, empty graafian follicle	1	Missed abortion	1
Extrauterine pregnancy?	Thick endometrium	2	Early intrauterine pregnancy	1
Intrauterine pregnancy	Normal graafian follicle	1	Extrauterine pregnancy	1
			7-week intrauterine pregnancy	1

Patients and Methods

Transabdominal sonography was carried out in 40 patients followed by TVT by a TOSHIBA SONOLAYER SSA-100A apparatus. The TAS studies were performed with filled bladder by a convex 3.75 MHz transducer.

Prior to TVS the patients were informed about the essence and advantages of the method. During the examination there is no need of a filled bladder the patients can be examined without any preparation. The surface of the transducer is smeared with a gel. The patients introduced it themselves into the vaginal fornix without pain. They reported nothing unpleasant during the examination.

During the study a predetermined routine was followed. First, the cervix was brought into the visual field, then the uterus. The width and, structure of the endometrium were studied in detail in each case. After examining the uterus by rotating the transducer somewhat to the left or right the ovaries were brought into the visual field.

The examination was in all cases documented with videoscans or video-prints.

The indications of the study include abnormal bleeding, lower abdominal pain, a palpable pelvic formation, infertility, endocrine disease, abscess or the suspicion of ectopic pregnancy, assumed intrauterine gravidity, missed abortion and the localization of IUD.

The age of the patients ranged between 21 and 62 years.

Results

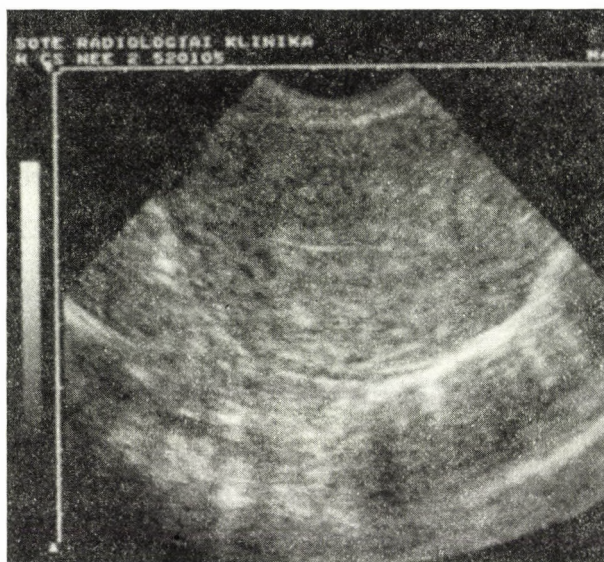
Changes revealed by the examination of 40 patients are shown in Table 2 (Scans 1, 2).

Transvaginal sonography gave additional information as compared to TAS in 14 cases (35%) (Table 3).

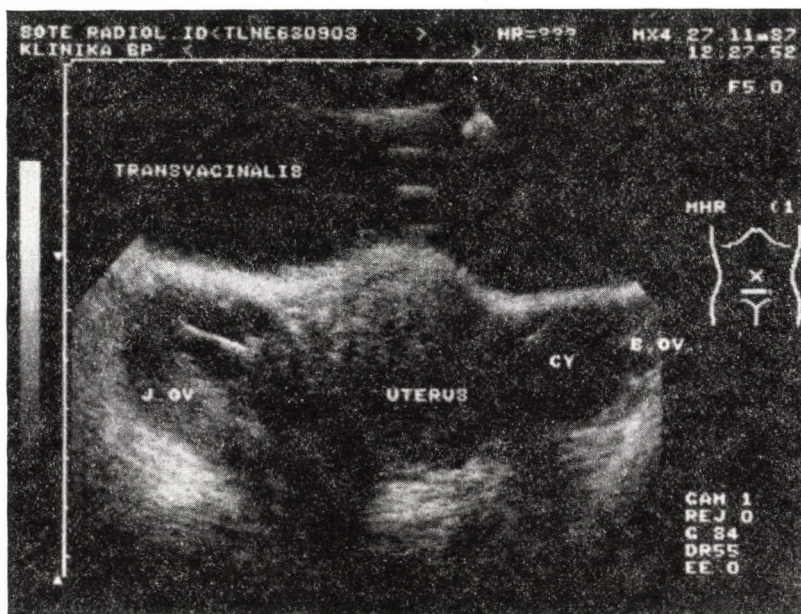
TABLE 3
Comparison of TAS and TVS

TAS provided more information	6 cases (15%)
TVS provided more information	14 cases (35%)
Equal information	20 cases (50%)
Total	40 cases (100%)

Five patients could hardly be examined transabdominally due to obesity or to urine retention disorders. Here, assessable scans were offered only by

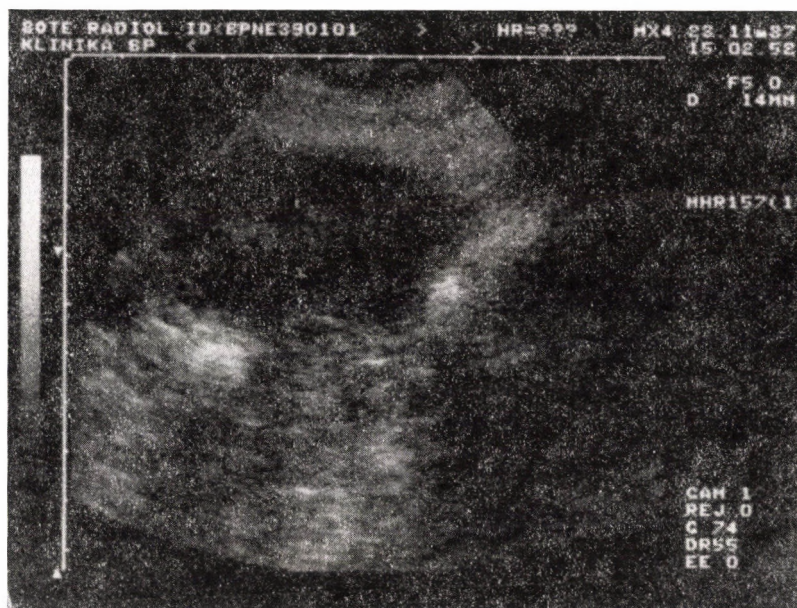


SCAN 1. Normal endometrium, TVS. The young patient's endometrium of a regular structure can be well differentiated in the centre of the uterus



SCAN 2. Ovarian cysts, TVS. Behind the partially filled bladder an uterus of normal size is seen, with cystose structures in both ovaries

TVS. In one case the thickened endometrium of irregular structure could be visualized only by TVS, the histology verified hyperplasia (Scan 3). In a patient dialysed due to chronic renal insufficiency (she could not void spontaneously), only TVS could prove the abscess located on the left side of the uterus (Scan 4). Another female patient having undergone hysterectomy was referred to examination also because of suspicion of an abscess. Transabdominal sonography revealed no circumscribed pathological change in the pelvis, while

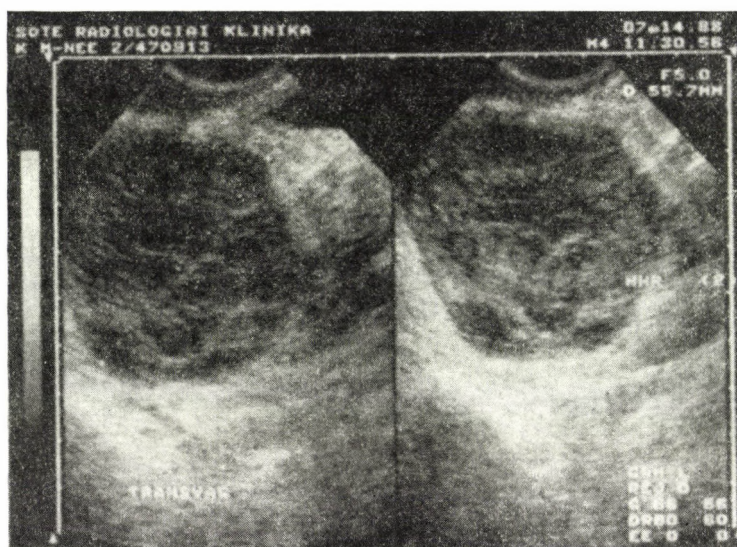


SCAN 3. Endometrial hyperplasia, TVS. The endometrium is thickened, irregular in structure and of uneven contour

TVS verified a 6 cm abscess in the adnexal region. In one case, TVS demonstrated the ovarian origin of a solid structure in the pelvis. In two instances, TAS disclosed an ovarian cyst, TVS showed the cysts to have a thickened wall, with small, irregular sprouts extending into the lumen. In one case of a 7-week intrauterine pregnancy, TVS allowed a better visualization of the parts of the embryo as well as of the vitelline sac (Scan 5).

In myomatous uterus developed in intrauterine pregnancy, TAS showed only the graafian follicle, while the fetal pole and heart function were revealed only by TVS.

In a patient referred to examination due to suspicion of missed abortion, TAS disclosed an empty graafian follicle. TVS could reveal the irregular shape of the graafian follicle with the surrounding cystic structures, fetal echos could not be visualized.



SCAN 4. Abscess, TVS. In the left adnexal region of the dialysed patient, a solid structure of inhomogeneous structure is present



SCAN 5. 7-week intact intrauterine pregnancy, TVS. The parts of the embryo and the vitelline sac are clearly observable

Discussion

Several reports have been concerned with TVS, as a new examination method, reviewing its advantages, and summarizing its major indications [1, 9] (Table 4).

TABLE 4
Indications of TVS

-
1. In all cases if TAS does not give sufficient information.
 2. In difficulties with urine retention and excretion.
 3. Pathological changes of the endometrium.
 4. Pathological changes of the tubes.
 5. Ectopic pregnancy.
 6. Pathological early pregnancies.
 7. Endocrine diseases—accurate visualization of the structure of the ovaries.
 8. Follicle monitoring.
 9. In vitro fertilization—graafian follicle aspiration under US guidance.
 10. Aimed puncture of pelvic effusions.
-

The examination does not require a filled bladder, thus it can be particularly well applied in patients not being able to retain their urine for some causes, as well as in renal insufficiency. Transabdominal sonography is made difficult by obesity, a thick abdominal wall, retroflexed uterus, intestinal loops covering the pelvic organs—these problems can mostly be eliminated by TVS.

Changes in the Uterus

During TVS the first structure to be visualized is the cervix: its alterations like the Naboth cyst, can easily be recognized. The size and structure of the uterus can be well defined, even the tiny myomatous tubercles can be detected. The structure of the endometrium can be better visualized by TVS, the morphological changes during the cycle can be followed clearly and the reactions during hormone treatment can be demonstrated [1, 2, 3, 6, 7]. According to Mendelson et al. [4], the endometrial-myometrial junction can be better visualized by TVS and so the superficial or deep invasion of endometrial carcinomas can be demonstrated with great accuracy. Nishi [15] could determine with great precision the extent of tumour invasion in 11 out of 14 cases. Transvaginal sonography helps in locating intrauterine devices. It can be used in finding "lost" IUDs.

Already a minimal amount (5–10 ml) of free fluid can be detected in the Douglas space.

Ovarian Processes

Transvaginal sonography is to be preferred in visualizing the structure of the ovaries, monitoring follicular growth and recognizing the corpus luteum [9]. The study of ovarian structure is particularly important in various endocrine clinical pictures (e.g. adrenogenital syndrome, Stein-Leventhal syndrome, etc.), and since these diseases are often associated also with obesity, TVS can eliminate technical difficulties. Transvaginal sonography is more beneficial in examining ovaries of atypical location, e.g. in the Douglas space, or postmenopausal ovaries of smaller size. The structure of masses of ovarian origin can be examined with greater precision.

Tubo-ovarian abscesses and hydrosalpinx can be better visualized. One of the most frequent reasons for applying this method is ectopic pregnancy and the detection of early tubal pregnancy. An intact 6-week tubal pregnancy can be easily recognized on the basis of heart function [8].

Pregnancy

Transvaginal sonography is of prime importance in detection of early pathologic pregnancies [8]. Already a 4-week intrauterine pregnancy can be detected by it. At 5 weeks, the vitelline sac can be noted, one week earlier than by TAS. In the 6th week fetal heart function can be registered. The pathologic graafian follicle, incomplete abortion, fetal death and a "pseudo" graafian follicle in ectopic pregnancy can all be early detected. The cervix and the state of the internal and external cervical orifice can be more safely examined.

Artificial Insemination

Transvaginal sonography is also used in in vitro fertilization—in the fetal transfer programme. Oocyte aspiration under transvaginal sonographic control was performed by Wikland et al. [10] in 50 cases. The method is considered to be more beneficial than the transvesical procedure applied up to that time.

Interventions

There is a possibility of the puncture of pelvic effusions under TVS control (Douglas space, peritoneal retention cysts, ovarian cysts).

The procedure is of diagnostic and therapeutic value.

During our studies, TVS provided extra information in 35% of the cases as compared to TAS. Our patients did not indicate any feeling of pain as neither any other unpleasant sensation during the examination.

Difficulties may be caused by the small visual field, the transducer can be moved only laterally and at a small angle because of the anatomical region, and so this may render orientation more difficult than by TAS, the size of more extensive adnexal changes are more difficult to assess. The transvaginal transducers of various types are of different shapes, so having different application fields. In the second and third trimesters of pregnancy TVS is of limited value. Contraindications are an intact hymen, bleeding during pregnancy and vaginal infection.

A TV transducer can be connected to the majority of US devices. Transvaginal sonography is expected to become a routine procedure in the near future in all US laboratories where pelvic examinations are made. It is easy to perform, a radiologist or gynaecologist familiar with US diagnosis can rapidly have a good command of the method enhancing the accuracy of work.

References

1. Bret PM et al.: Transvaginal ultrasound in gynecology 88th Annual Meeting, The American Roentgen Ray Society, San Francisco 8–13 May, 1988, Abstr. p 88
2. Fleischer A et al.: Sonographic depiction of normal and abnormal endometrium with histopathologic correlation. *J Ultrasound Med* 5 : 445, 1986
3. Jakab, Zs et al.: Az endometrium ultrahang morfológiájának változása normális és patológiás állapotokban (Changes in the morphology of endometrial ultrasound in normal and pathologic states). *Magy. Radiol* 62 : 229–235, 1988
4. Mendelson EB et al.: Endometrial abnormalities: evaluation with transvaginal sonography. *AJR* 150 : 139, 1988
5. Nishi M et al.: The application of transvaginal scan for endometrial cancer. Proceedings of EUROSON'87, Helsinki Abstr. p 189, 1987
6. Patai K et al.: Újabb lehetőségek az endometrium non-invasív vizsgálatára (New possibilities for the noninvasive study of the endometrium). *Acta Chir Hung* (in press)
7. Pataki K et al.: Újabb lehetőségek az endometrium korai elváltozásainak felismerésére (New possibilities for the detection of the early changes of the endometrium). *Magy Nőorv L* (in press)
8. Pennell RG et al.: Complicated first-trimester pregnancies: evaluation with endovaginal US versus transabdominal technique. *Radiology* 165 : 79, 1987
9. Timor-Tritsch IE, Carswell H: High-frequency probes aid transvaginal sonography. *Diagnostic Imaging* 98, January, 1987
10. Wikland M et al.: Use of a vaginal transducer for oocyte retrieval in an IVF/ET Program. *J Clin Ultrasound* 15 : 245, 1987

Vorteile der vaginalen Sonographie gegenüber der abdominalen US-Diagnostik

K. PATAI, Zs. JAKAB, Z. HARKÁNYI und Z. VIGVÁRY

Berichtet wird über die Erfahrungen mit einer neuen Ultraschall-diagnostischen Methode der transvaginalen Sonographie.

Anhand des Vergleiches der Ergebnisse von 40 transvaginalen und transabdominalen Ultraschall-untersuchungen wurde folgendes festgestellt.

Im Vergleich zur transabdominalen Untersuchung ergab die transvaginale in 35% der Fälle mehr Informationen. Indikationen und Vorteile der transvaginalen Sonographie im Vergleich zur traditionellen Methode werden zusammengefaßt. Es empfiehlt sich die Einführung der Untersuchungsmethode in sämtlichen UH-Laboratorien, in denen Untersuchungen im kelinen Becken durchgeführt werden.

Преимущества влагалищной сонографии по сравнению с брюшной ультразвуковой диагностикой

К. ПАТАИ, Ж. ЯКАБ, З. ХАРКАНИ и З. ВИГВАРИ

Авторы знакомят с результатами, которых они достигли, применяя новый диагностический метод — трансвагинальную сонографию (TVS).

У 40 больных они провели трансвагинальное и трансабдоминальное исследования и сравнили результаты, полученные при применении обеих методик.

Трансвагинальное исследование по сравнению с трансабдоминальным у 35% больных дало больше информации. Авторы суммируют показания к проведению трансвагинальной сонографии и указывают на достоинства этого метода по сравнению с традиционным. Они рекомендуют введение этого исследовательского метода во всех ультразвуковых лабораториях, где проводятся исследования малого таза.

A Case of Fournier's Gangrene

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Authors report their case of Fournier's gangrene on the basis of their own observations and relying on data of the literature. Complete healing can be expected of immediate radical surgery and of aggressive intensive and antibiotic treatments.

In 1883 Fournier was the first to report on the very rapidly progressing, severe gangrenous process of the external genitals or of their subcutaneous connective tissue [1]. The aetiology of the disease is not always clarified unambiguously, thus it was observed in association with various clinical pictures (like atherosclerosis, panarteritis), following perineal and ureteral injuries, and due to diagnostic or surgical interventions in the rectoanal region (e.g. biopsy, endoscopy) [2].

Case Report

V.I., male patient, aged 38, presented on September 25, 1984 at the surgical consultation of the Polyclinic in Dunakeszi with of rectal complaints. On examination a 2 cm fissure was observed in the posterior commissure at a typical site.

On September 25, 1984, cryo-fissurectomy was performed at the proctological out-patient unit of the 2nd Department of Surgery, Postgraduate University School of Medicine. In view of his urological complaints, he was referred to urological examination where he failed to appear. He was transferred by ambulance on September 29, 1984 to the 2nd Department of Surgery, Postgraduate University Medical School in a septic-toxic state. On examination a definite inflammatory process progressing in both inguinal directions and starting perineally was noted, bursting spontaneously in the perineal region, emptying a sanious, putrid, necrotic discharge.

Intensive treatment was started immediately (Dalacin, Gentamicin, overpressure infusion, a large-dose steroid).

Staining of the wound discharge was found to show gram-positive and -negative cocci, diplococci, gram-negative bacteria and a few gram-positive rods. Anoscopy and rectoscopy revealed an intact cryofissurectomic region, without any pathological change to a depth of 25 cm. During operation, in addition to the perineal, also the periurethral region was opened with extensive exposure as well as the ischiorectal region from a circular radial incision as also the testis and both inguinal regions. Lavage drains and strips were placed in the wounds. On examining the material removed during exposure, debris of vegetable origin was found in the sample proximal to the root of the testes. As he said later, he had piled straw three days prior to his admission. He must have suffered the scrotal injuries at that time.

Lavage with hydrogen was made first every two hours and then, due to the rapid improvement in the patient's condition, 5 times daily. He became afebrile by the following day, his general condition improved gradually, his phlegmon regressed and necrosis became demarcated. During subsequent necrectomies, three-quarters of the scrotum were removed. Later *E. coli*, diphtheroid and *Clostridium perfringens* were cultured from the discharge.

In October 1984, he was discharged in normal condition, free of complaints, with granulating wounds. He was repeatedly admitted on March 14, 1985 because of an anal fistula. On 19 March fistulectomy, rubber interlacing marsupialization were performed. He was discharged after 11 days with clearly granulating wounds. He was completely recovered, after 9 months he became complaint-free and has been active ever since.

Discussion

Fournier's gangrene is a rare disease mainly of young men. It has only been sporadically reported in the world literature. It is not rarely of lethal outcome (e.g. up to 1964, approximately 200 cases had been reported) [4]. Its first sign is intensive pain, with the swelling of the affected surface, with erythema, but very often with high temperature and a septic state by that time. From the appearance of the patient's first symptoms, this severe life-threatening condition may develop within a period of 2-3 days, but also abruptly in a matter of hours [3].

In typical cases, after the onset of erythema, the marked edematous swelling of the perineal tissues, their bluish-purple, occasionally greenish discolouration, the development of fistulas with spontaneous putrid discharge, then extensive skin necrosis and a malignant edematous palpation finding can be noted. According to observations, the inflammation is spreading toward the genitals in the perineal region, less frequently it is of perineal localization [1, 3, 5]. Bacteriological examination most often shows a mixed infection

(*E. coli*, *Staphylococcus aureus* and *albus*, bacterioides, *Klebsiella*, enterococci, *Proteus*, *Citobacter* and *Pseudomonas* strains).

Our case is unique because the trivial injury from where the process had started was revealed by a thoroughgoing histological examination after surgical management.

The three major aspects of surgical management include (i) Local management, radical exposures, removal of the decayed parts, the frequent lavage and cleaning of the exposed region. (ii) If possible, aggressive antibiotic treatment up to starting of an aimed antibiotic therapy. (iii) Intensive treatment.

References

1. Ali Khan S, Smith NL, Gonder M, Ravo B, Sidhart P (1985) Gangrene of male external genitalia in a patient with colorectal disease. *Dis Col Rect* 7:519-522
2. Cunningham BL, Nivatongs S, Shons AR (1979) Fournier's syndrome following anorectal examination and mucosal biopsy. *Dis Col Rect* 22:51-54
3. Czalbert JH, Hornok L, Ritter L (1988) Über einen Fall mit Fournier-Gangran. *Magy Seb* 41:349-350
4. Feller AM, Reimenscheider I, Hörth H (1986) Fournier Gangran. *Colo-proctology* 8:271-273
5. Grimmer H (1964) Akute Gangran der Genitalien/Fournier Gangran. In: Jadasson J: *Handbuch der Haut und Geschlechtskrankheiten*, Vol. V/2 Springer Verlag, Berlin pp 806-832
6. Hauser W (1965) Nicht vereisende Krankheiten des äußeren Genitale. In: Gottron HS, Schöfeld W: *Dermatologie und Venerologie*, Vol V/2. Thieme Verlag, Stuttgart pp 705-753

Über unseren Fall mit einem FOURNIER-Gangrän

J. H. CZALBERT, L. HORNOK und L. RITTER

Aufgrund der eigenen Beobachtungen sowie der Literaturdaten wird der eigene FOURNIER-Gangrän-Fall erläutert. Die restlose Heilung kann von dem sofortigen chirurgischen Eingriff und von der aggressiv-intensiven bzw. von der antibiotischen Behandlung erwartet werden.

«О случае гангрены Фурны

Я. Х. ЦАЛБЕРТ, Л. ХОРНОК и Л. РИТТЕР

Авторы знакомят с случаями гангрены Фурны на основании собственных наблюдений и данных литературы. Можно ожидать полного выздоровления в случае срочного радикального хирургического вмешательства и агрессивного интенсивного или же антибиотического лечения.

Intraoperative Injuries during Transperitoneal Urological Operation

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(Received: April 3, 1990)

The mechanism of development of 19 severe side-injuries arising during 230 transperitoneal urological operations was analysed. During a total of 158 RLAs performed for testicular tumour, vascular injuries—of the aorta, inferior caval vein and renal vessels—were suffered in 10 cases, and injury of the small intestine in one case. In another case, accidental ligation and transection of the ureter were made. During radical nephrectomy, liver and splenic injuries were inflicted in two cases each. The left renal vein was injured also in two cases. In one case the contralateral ureter was ligated. Disregarding the first five cases, the injuries were always made in cases of tumours. After analysing the mistakes, suggestions were put forward for eliminating these complications.

In the recent 10 years, the extensive use of transperitoneal operations in urology have considerably improved the chances of the final recovery of patients with urological tumours.

Reports based on our own experience in Hungary have summarized the advantages of transperitoneal exposure in the surgical management of urological tumours as follows [6]:

- It enables the “en bloc” removal of renal tumours by the primary ligation of vessels and lymphadenectomy [7].
- So the regional lymph nodes of the testicular tumour can be removed from the crus of the diaphragm to the inguinal canal [3].
- It enables the most extensive, if necessary bilateral exposure of the retroperitoneal organs [1, 2].
- It is a possible solution for the concurrent diseases and injuries of the abdominal and retroperitoneal organs.

While enumerating the above advantages, it should also be kept in mind that the transabdominal operations can be associated with specific complications, such as the side-injuries of intra-abdominal organs, the possibility of which is excluded during the traditional retroperitoneal exposure.

It is believed that the causes of injuries, the mechanism of their infliction should be analysed to learn from the mistakes. In this paper only the intra-operative injuries will be dealt with, while other complications, like leakage of lymph, development of haematoma are beyond the scope of this study.

Method and Patients

A total of 238 transabdominal operations were performed at the Department of Urology, Semmelweis University School of Medicine between 1979 and 1988. The indications are shown in Table 1.

TABLE 1

*Transperitoneal operations performed in the recent 10 years (1979–1988)
at the Department of Urology, Semmelweis University Medical School*

RLA	158 cases/12
Radical nephrectomy	52 cases/7
Other, non-tumour operation	28 cases
Total	238 cases

During 238 transperitoneal operations injuries which would have caused a permanent injury to health, or have involved an actual risk of this, occurred in 16 cases (6.7%). The fine details of how the injury occurred were not always recorded in the surgical protocol, while photo documentation is rarely made in an upset and nervous situation. If the permanent health injury had already occurred, at least further deterioration had to be halted by regular control and the required treatment.

Injuries during the Retroperitoneal Lymphadenectomy of Testicular Tumour Patients

The retrospective analyses of retroperitoneal lymphadenectomies have proved vascular injuries to be the most frequent. Some minor vascular injuries, as e.g. those of the internal spermatic artery, or the tearing of the median sacral artery from the aorta, are of no importance, although the surgical management, ligation or suturing of the vessels arising in the posterior side of the large vessels may be technically difficult, particularly at the start of the operation. Namely at the beginning of operation the large vessels, the aorta, the vena cava are anchored through their lumbar vessels, so their posterior sides cannot be reached. A rubber drain is usually introduced under the vena cava and the renal vein to elevate the vessels. In the case of injury, by compression it enables arresting of bleeding. The importance of the azygolumbar vein, a frequently occurring anatomical variation, which runs into the left renal vein, should be pointed out. In general it is of the width of a pencil and if it is injured, it tends to bleed copiously, its stump slipping back into the lumbar musculature, and it is



FIG. 1. Right spermatic vein torn from the vena cava with a "cuff". After clamping of the injury, it was sutured, the picture shows the row of running sutures

difficult to manage. It is better to know the possible vascular anomalies beforehand, thus dissection is cautiously made in the appropriate place. Of the vascular injuries, the large vessel injuries are the most dangerous because of the abrupt loss of blood, particularly the vena cava can bleed frighteningly. The wall of the aorta is thicker, it can be better sutured than the vena cava and there is also a difference in the mechanism of tearing of the lateral branches. It was noted that in general the veins get torn with a lesser or greater "cuff" from the caval vein, while after tearing of the arteries a small nipple remains which can simply be closed by a vascular clamp. Injuries causing the resection of the vena cava occurred in 6 cases (Fig. 1). Cases, where caval resection was consciously made for removal of the tumour are not listed here.

A significant aortic injury occurred only in one case, on the left posterior surface, a 2 cm long Goretex patch involving half of its circumference was sutured by the vascular surgeon. In two cases the renal vein was injured to an extent that no reconstruction was possible, consequently nephrectomy was performed. On dissection, the right renal artery between the two large vessels was transected. The source of bleeding could be clamped and ligated by aortic compression. The renal artery was not possible here to reconstruct, so nephrectomy had to be made. The ureter was, in one case ligated on the left side under the pyeloureteral junction and completely transected. The injury was

recognized still intraoperatively and an end-to-end anastomosis was constructed. In the recent eight years, the anastomosis has gradually narrowed, giving rise to hydronephrosis, however the patient refuses to be operated. In one patient the duodenum was injured but the opening healed without complication after its double-layer closure.

Except for two injuries involving the renal artery and the ureter, the injuries occurred following chemotherapy. The exceptions were, however, among the first five operations, i.e. in the period of accumulating experience (Table 2). The frequency of surgical side-injuries is therefore directly proportional to the progression of the tumour.

TABLE 2
Injuries during 158 RLAs

Aortic patch	1 case II/A
Caval vein injury	6 cases 2 II/B-2 II/C-2 III/A
Nephrectomy due to renal vein injury	2 cases II/C II/A
Nephrectomy due to renal artery injury	1 case I/A
Ureteral injury	1 case I/A
Injury of the small intestine	1 case II/C
Total	12 cases (7.5%) out of 158 cases

Injuries during Transperitoneal Radical Nephrectomies

Some minor vascular injuries occur also during radical transperitoneal nephrectomy but less frequently than during RLA. This may be due to pre-operative angiography. The angiographic "map" facilitates orientation, we are prepared for the vascular variations, as e.g. duplication of renal artery, significant polar vessel, etc. A real danger is assumed to be the injury of the left renal artery in the case of a tumour of the right side. In two of our cases we attempted to ligate the renal artery of a large tumour on the right side between two large vessels and meanwhile the left renal vein was injured. Dissection was made more difficult by the renal arteries being surrounded by tumorous lymph nodes. The opening in the lateral side of the renal vein was clamped and running sutures were placed in closing them. In addition to the transitory increase of renal function values, the patients healed uneventfully. In one case, during radical nephrectomy of the left side, the healthy right ureter was by mistake involved in suturing to close the peritoneum of the posterior side. The patient became anuric, and so percutaneous nephrostomy was made. On the 12th postoperative day the mid-segment of the ureter was

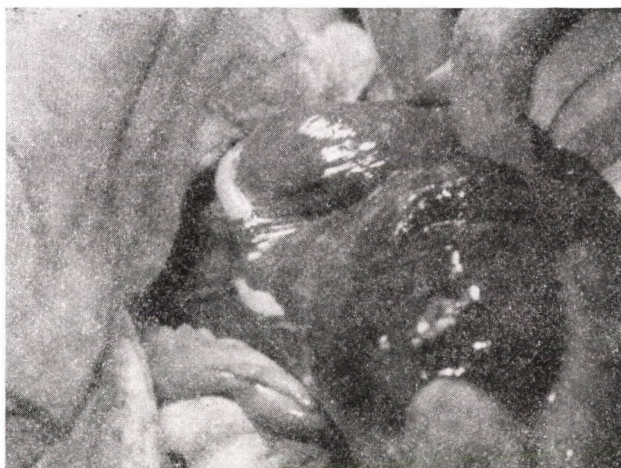


FIG. 2. Typical splenic injury during transperitoneal radical nephrectomy

exposed and deligation was made. During the recent two years no stenosis has developed. Among the intraperitoneal organs the liver parenchyma was torn by the clamp in two cases, these injuries were closed by separate drainage with atraumatic sutures. Splenic injuries occurred also in two cases (Fig. 2), one of the patients suffered also from splenomegaly. The enlarged, hanging, tense spleen is naturally more predisposed to injury. Also splenic injury, can occur due to the pulling of the clamp. A typical mistake is, however, if the splenocolic ligament is not cut sharply but torn and so the rupture can involve also the splenic capsule. Injuries occurring during transperitoneal radical nephrectomies are summarized in Table 3.

TABLE 3

Intraoperative injuries during 52 transperitoneal radical nephrectomies

Injury of the left renal vein	2 cases	$T_2N_1M_0$ and $T_3N_2M_0$
Ureteral ligature	1 case	$T_2N_0M_0$
Splenic injury	2 cases	$T_3N_1M_0$ $T_3N_2M_0$
Liver injury	2 cases	$T_2N_0M_0$ $T_3N_0M_0$
Total	7 cases	(13.4%) out of 52 cases

Discussion

The transperitoneal operations have been performed in our clinic for ten years, thus the processed material also contains the initial injuries arising from a lack of experience. Disregarding the first five cases, side-injuries during RLA occurred only over II/B, while in case of radical nephrectomy in tumours being more extensive than T₃N₁M₀.

It is not possible to prevent subsequent injuries by analysing errors and mistakes, which lead to them, still this is the way to reduce the probability of mistake.

The two pillars of eliminating injuries are:

- to know (to recognize) the anatomy and the variations of the retro-peritoneum from the direction of the abdominal cavity,
- to apply a specific, fine surgical technique during transperitoneal operations.

The atraumatic operative technique excludes the tearing of tissues. The dissector is the most often used manual instrument. It should be placed between the structures, opening it repeatedly, so fashioning the layer. The lymph and blood vessels are knotted or very carefully coagulated. The spilling blood absorbs and destroys the tissues. Large bleeding may start abruptly even with the most cautious dissection. The fast and professional management of bleeding is possible only if the team of surgeons is able to cooperate, if the roles are distinctly demarcated. The „masterful” performance of a clamping at the bottom of a blood pool may result that the wall of an unknown vessel or organ is crushed with the instrument, thus giving rise to further bleeding. In our clinic the first assistant compresses bleeding by the right hand, controlling the aspirator with the left. The task of the operating surgeon is to identify the source of bleeding, to introduce the most apposite clamp and to decide about management, whether a simple ligation would suffice or vascular suturing is necessary. Injury of the vena cava is accompanied by a particularly massive bleeding. The vena cava should be pressed to the spine in both directions from some centimetres from the opening. The clamp is placed on the opening to allow ample room for the sutures. If any kind of vascular injuries need to be closed by ligature, then the thread should not be tugged or stretched during knotting because the thin-walled vessel may get torn.

Ureteral injury and ligature are mistakes not restricted to gynaecological operations. The best way of prevention is if the ureter is exposed, isolated with a thin polyethylene tube being introduced under it, at a characteristic, easily accessible site, like e.g. at the junction of the large vessels. During further dissection, if there is any doubt of the course of the ureter, only the plastic tube should be slightly moved.

For preventing splenic and liver injuries, wet pads should be placed under the clamps.

The task of the urologist performing transperitoneal operations is to possibly avoid injuries, however he should recognize the injury, once it is made, and if, necessary ask by all means for the help of people from the related disciplines, like e.g. surgeon or vascular surgeon.

References

1. Balogh F, Kelemen Zs: A felső húgyutak egy ülésben végzett kétoldali transperitoneális megközelítése (Bilateral transperitoneal approach in the upper respiratory tract performed in one session). *Orv Hetil* 113:931, 1972
2. Bognár F, Szomor L, Szokoly V, Pintér J: A vese és ureter különböző műtéti feltárájáról (Various surgical exposures of the kidney and the ureter). *Urol Nephrol Szle* 7:1, 32, 1980
3. Gerlóczy Gy, Mohácsi L: A retroperitoneális lymphadenectomia jelentősége a here-tumorkok kezelésében (The importance of retroperitoneal lymphadenectomy in treating testicular tumours). *Orv. Hetil* 121:5283, 1980
4. Kisbenedek L, Pajor L, Lipták J, Répássy D: A fejlődési rendellenességek gyakorisága és jelentősége a retroperitoneum sebészetében (The frequency and importance of developmental anomalies in retroperitoneal surgery). *Urol Nephrol Szle* 11:3, 143, 1984
5. Pintér J: A vese és here rosszindulatú daganatai (Malignant tumours of the kidney and the testis). *Orvostudomány* 33:435, 1982
6. Pintér J, Wabrosch G, Eckhardt S: Rosszindulatú urológiai daganatok (Malignant urological tumours). *Medicina*, Budapest 1987
7. Szomor L, Pintér J, Szokoly V, Tóth L: Radikalitást biztosító műtéti feltárások vesedaganat esetén (Surgical exposures ensuring radicality in renal tumours). Paper presented at the Meeting of the Hungarian Urological Society, Budapest 1977

Intraoperative Verletzungen im Laufe transperitonealer urologischer Eingriffe

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Analysiert wurde der Entwicklungsmechanismus von sich im Laufe von 238 transperitonealen urologischen Operationen ausgebildeten 19 schweren Nebenverletzungen. Im Laufe der wegen eines Hodentumors durchgeführten 158 RLA-Eingriffen kam es in 10 Fällen zu einer Gefäßverletzung — Aorta, V. cava, Nierengefäße — in einem Fall zu einer Dünndarmverletzung, während in einem Fall Ureter-Ligatur und Durchtrennung erfolgten. Im Laufe der radikalen Nephrektomien entstanden in je 2 Fällen Leber- bzw. Milzverletzungen; die linke Nierenvene wurde ebenfalls in 2 Fällen verletzt, während in 1 Fall der kontralaterale Ureter unterbunden wurde. Mit Ausnahme der ersten 5 Fälle kamen die Verletzungen ausnahmslos in Fällen mit einem fortgeschrittenen Tumor vor. Nach ausführliche Analyse der Fehler unterbreiteten wir Vorschläge zur Eliminierung dieser Komplikationen.

Интраоперативные повреждения при трансперитонеальных урологических операциях

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Авторы проанализировали в 19 случаях механизм возникновения тяжелых побочных повреждений во время проведения в общей сложности 238 трансперитонеальных урологических операций. В ходе 158 RLA, произведенных по поводу опухоли яичка, в 10 случаях были повреждены сосуды (аорта, полая вена, почечные), в одном случае тонкая кишка; в одном же случае произошли перевязка и перерезка мочеточника. Во время радикальной нефрэктомии в двух случаях повредили печень и еще в двух случаях селезёнку; в двух случаях была повреждена левая почечная вена; в одном случае перевязали мочеточник противоположной стороны. Все повреждения, за исключением первых пяти случаев, произошли при далеко зашедшем опухолевом процессе. После анализа ошибок авторы дают рекомендации относительно того, как можно избежать подобных осложнений.

Ultrastructural Changes in the Nerve Elements in Chron's Disease

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Electron microscopic investigations were carried out to study the nerve elements in the wall of the small intestine in Crohn's disease, comparing it with the control. In the ileum of Crohn's disease only a few synapses were found. The number of nerve terminals were decreased, as well as that of the vesicle population in the remaining nerve terminals. Some of the nerve processes were observed in degeneration. The number of the lysosomes in the nerve cell bodies increased. Inflammatory cells as lymphocytes, plasma cells, mast cells were noted in the total submucosa and in the mucous membrane, their number was also increased. It is suggested that the immunological effector cells and their products could be responsible for changing the neuronal elements.

Introduction

In Crohn's disease epithelial patchy necrosis has recently been reported by Rickert and Carter [15], Dourmashkin et al. [5] and Gebbers and Otto [12] using electron microscopy. An increased level of innervation, the so-called neuromatous hyperplasia, has been known for some time to be present in affected areas [13, 21]. Recently, it has also been demonstrated that vasoactive intestinal polypeptide-containing (VIP) nerves had an abnormally dense population [2, 14, 16, 18, 20]. Endocrine cells were increased in number, but only the serotonin-containing enterochromaffin cells showed statistically significant changes [1].

In contrast with these observations Dvorak et al. [6, 7] have demonstrated severe and widespread autonomic axonal necrosis in Crohn's disease with electron microscopic investigations, and he thought that the autonomic nerve damage might be one of the earliest pathologic changes in Crohn's disease.

Using conventional transmission electron microscopy, we also observed the effect of Crohn's disease on the ultrastructural features of nerve terminals in the small intestine. This investigation is also an attempt to identify the changes in the number of synapses and vesicles of the nerve terminals in Crohn's disease.

Materials and methods

Fresh specimens of adult ileum were taken at surgery from a patient with Crohn's disease. For control, specimens from patients operated with carcinoma were used. Representative samples, measuring approximately

0.5 × 0.5 cm were taken from both involved and macroscopically normal areas from the clear-cut cases of Crohn's disease and from the controls.

All tissues were fixed by immersion for 4 h in Karnovsky fixative solution, post-osmication was carried out for 1 hour in 1% osmium tetroxide and the tissue was then embedded in Durcupan. Ultrathin sections were counterstained with uranyl acetate and lead citrate, and examined with a Tesla BS 500 electron microscope.

All nerves encountered in each thin section were counted, photographed and scored as being normal or damaged. For statistical analysis the number of synapses was counted in areas of 500 μm^2 of myenteric and submucous plexuses for normal and effected areas and was calculated for 100 μm^2 tissue area as the average. The number of nerve processes was also counted the same way. The number of vesicles was counted within 50 nerve profiles for each group.

Results

Varicose nerve fibres could be observed in all layers of the intestinal wall, both within the myenteric and submucous plexuses and in the muscle layers as well as in the tunica mucosa—up to less than 1 μm distance below the epithelial lining of the mucosa. Several nerve fibres were in close apposition to the muscle cells with the space of 100 to 200 nm between the plasma membranes. A large number of vesicle population could be found within the varicose nerve terminals of the control material. Most of the nerve processes contained mainly large granulated vesicles of 80 to 120 nm in diameter with small clear vesicles of 30 to 50 nm in diameter (Fig. 1). Some of these nerve terminals could be observed in synapses on the surface of the cell body or with the dendrites (Figs 1, 2).

In the ileum of Crohn's disease only a few synapses and a very small number of vesicles were found in the nerve terminals as shown in Table 1. The number of nerve processes were also decreased and they contained only microtubules and neurofilaments without vesicles (Fig. 3).

TABLE 1
*The effect of Crohn's disease on the number of synapses
and vesicles in the nerve terminals*

Material	Number of synapses/100 μm^2 tissue area	Number of vesicles/within 50 nerve fibers
Control	12 (100%)	2508 (100%)
Crohn's disease	3 (25%)	728 (29.02%)

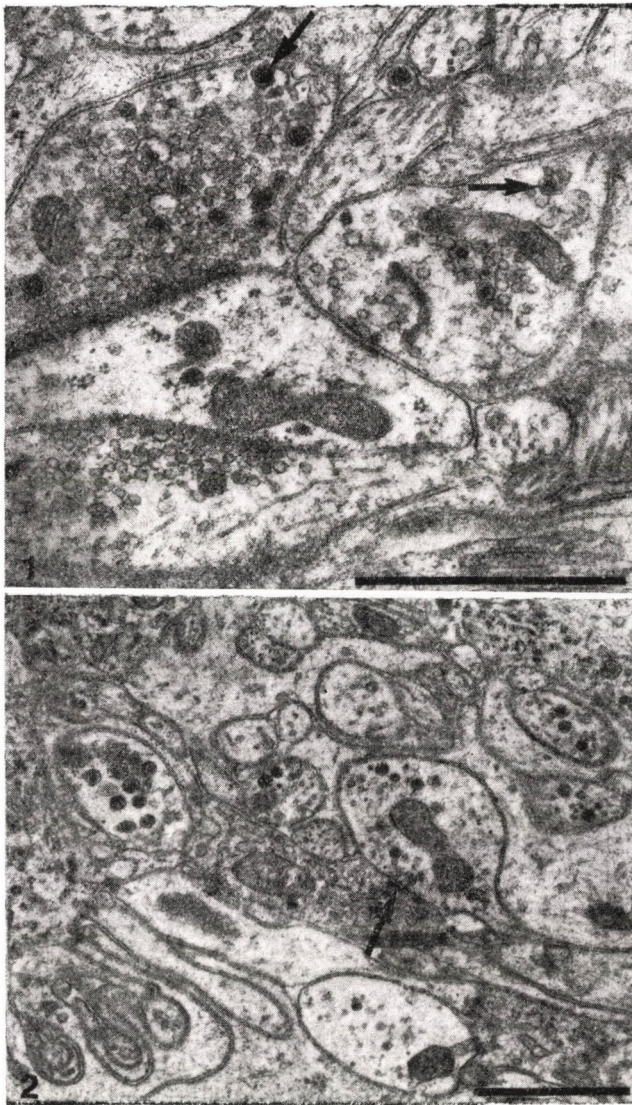


FIG. 1. Three different nerve terminals synapsing on the same dendrite in the control ileum. Arrows show the large granulated vesicles of 80 to 120 nm in diameter. Bar scale = 1 μ m

FIG. 2. A part of the myenteric plexus in the control ileum. Arrow points at the synapse on a dendrite. Bar scale = 1 μ m

The total number of nerve fibres in the tunica mucosa, tela submucosa and in the inner circular muscle layer was 35/100 μ m² (100%); in Crohn's disease it was only 22/100 μ m² (62.8%). In the myenteric and submucous plexuses the total number of the nerve fibres was 85/100 μ m² (100%) in the

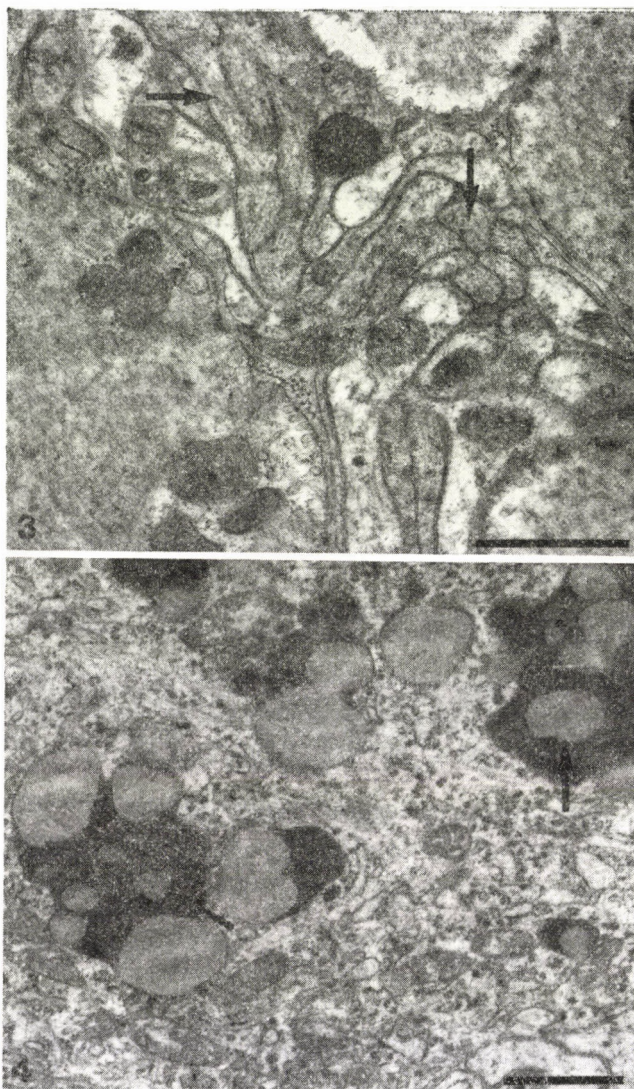


FIG. 3. A nerve bundle of the circular muscle layer in Crohn's disease. Note that the nerve fibres (arrows) contain only microtubules and neurofilaments. Bar scale = $1\ \mu\text{m}$
 FIG. 4. A part of the nerve cell body in the myenteric plexus in the ileum of Crohn's disease. Arrows show the large lysosomes in the cytoplasm. Bar scale = $1\ \mu\text{m}$

control materials, however, in Crohn's disease the nerve terminals were 57/100 μm^2 (67%).

The number of lysosomes was increased in the nerve cell bodies (Fig. 4). Some of the nerve fibres were observed to be in degeneration. Necrotic axons



FIG. 5. A part of the tela submucosa in the ileum in Crohn's disease. Arrows show the nerve bundle in a close situation to the inflammatory cells. LYC = lymphocyte; MC = mast cell; Ly C = lymph capillary. Bar scale = 1 μ m

were mainly found in close proximity to inflammatory cells. These inflammatory cells as lymphocytes, plasma cells, mast cells and eosinophils were mainly observed in the tela submucosa and in the tunica mucosa. The nerve fibres were closely situated to these cells (Fig. 5). The mast cells were occasionally degranulating.

Discussion

Using light microscopy a substantial increase in ganglion cells in Crohn's disease [4] has been observed and therefore it was thought that the autonomic nerves were involved in this inflammatory disease [13, 21]. An increased number of vasoactive intestinal polypeptide (VIP) containing nerve elements was also observed in Crohn's disease. It would be a secondary reaction in severe transmural inflammatory processes, as seen in Crohn's disease which might act as an irritant stimulus for the proliferation of intrinsic nerves. It should be borne in mind, however, that the increasing number of neuronal cell bodies and fibers seen in Crohn's disease might be due to the functional changes with increased content of product within cells and fibres allowing more to be visualized by immunocytochemistry.

Electron microscopic studies of nerve fibres in the small intestine have shown that many nerve fibres contain a large number of vesicles as described previously [8, 9, 10, 11]. In contrast to the light microscopic observations, the number of the synapses, nerve terminals as well as the vesicle population was decreased in Crohn's disease. This discrepancy may be due either to the higher resolution of the electron microscope, or to the different stages of the disease. In the early stages the proliferation of nerves may dominate, while, at later stages the decrease and the degeneration of nerve elements are more expressed and manifest. Dvorak et al. have shown with electron microscopy [6, 7] that severe and extensive autonomic axonal necrosis is a characteristic feature of Crohn's disease and they concluded that axonal necrosis is independent of local inflammation. In chronic pancreatitis Bockman et al. [3] have found also the same axonal degeneration. Therefore, according to our opinion these neural changes were the consequence of the inflammatory process. In the gut, the destruction of intrinsic neuronal elements was associated with Chaga's disease, Hirschsprung's disease, cathartics and chronic idiopathic intestinal pseudo-obstruction [17, 19]. The immunological effector cells and their products could be responsible for these changes. It is also possible, that viral agents with predilection for the autonomic nervous system were responsible for the degeneration and the decreasing of the nerve fibers [6]. In summary, our results confirm that Crohn's disease caused a degeneration of nerve fibres and marked changes in the number of nerve terminals and vesicles with the decrease in the number of synapses. This is thought to be of clinical importance.

References

1. Bishop AE, Pietroletti R, Taat CW: Increased population of endocrine cells in Crohn's ileitis. *Virchows Arch A* 410:391-396, 1987
2. Bishop AE, Polak JM, Bryant MG, Bloom SR, Hamilton S: Abnormalities of vasoactive intestinal polypeptide-containing nerves in Crohn's disease. *Gastroenterology* 79:853-860, 1980
3. Bockman DE, Buchler M, Malfertheiner P, Beger HG: Analysis of nerves in chronic pancreatitis. *Gastroenterology* 94:1459-1469, 1988
4. Davies DR, Dockerty MB, Mayo CW: The myenteric plexus in regional enteritis: a study of ganglion cells in the ileum in 24 cases. *Surg Gynecol Obstet* 101:208-211, 1955
5. Dourmashkin RD, Davies H, Wells C, Shah D, Price A, O'Moraini C, Levi J: Epithelial patchy necrosis in Crohn's disease. *Hum Pathol* 14:643-648, 1983
6. Dvorak AM, Osage JE, Monahan RA, Dickersin GR: Crohn's disease: transmission electron microscopic studies. III. Target tissues. Proliferation of an injury to smooth muscle and the autonomic nervous system. *Hum Pathol* 11:620-634, 1980
7. Dvorak AM, Silen W: Differentiation between Crohn's disease and other inflammatory conditions by electron microscopy. *Ann Surg* 207:53-63, 1985
8. Fehér E, Csányi K: Ultra-architectonics of the neural plexus in chronically isolated small intestine. *Acta Anat* 90:617-628, 1974
9. Fehér E, Vajda J: Degeneration analysis of the extrinsic nerve elements of the small intestine. *Acta Anat* 87:97-109, 1974
10. Gabella G: Fine structure of the myenteric plexus in the guinea-pig ileum. *J Anat* 111:69-97, 1972
11. Gabella G: On the ultrastructure of the enteric nerve ganglia. In: *Basic science in gastroenterology. Structure of the gut*, eds, Polak JM, Bloom SR, Wright NA, Daly MJ, Glaxo Group Research Limited Ware, Herts, UK 1982, pp 193-203
12. Gebbers JO, Otto HF: Alterations of the intestinal mucosal block in ulcerative colitis and Crohn's disease. Immunological and ultrastructural findings and considerations of the pathogenesis. *Klin Pädiat* 197:341-348, 1985
13. Morson BC, Dawson IMP: Inflammatory disorders. In: *Gastrointestinal pathology*, eds, Morson BC, Dawson IMP, Blackwell Scientific Press, Oxford 1982, pp 243-298
14. O'Marain C, Bishop AE, McGregor GP, Levi AJ, Bloom SR, Polak JM, Peters TJ: Vasoactive intestinal peptide concentrations and immunocytochemical studies in rectal biopsies from patients with inflammatory bowel disease. *Gut* 25:57-61, 1984
15. Rickert RR, Caite HW: The "early" ulcerative lesion in Crohn's disease: Correlative light- and scanning electron microscopic studies. *J Clin Gastroenterol* 2:712-715, 1980
16. Schmitz-Reinhardt B, Lohse AW, Arnold R: VIP tissue content in colonic biopsies from normal patients compared with Crohn's disease and ulcerative colitis. *Reg Pept Suppl* 3:540, 1985
17. Schuffer MD, Jonak Z: Chronic idiopathic intestinal pseudo-obstruction caused by a degenerative disorder of a myenteric plexus: the use of Smith's method to define the neuropathology. *Gastroenterology* 82:476-486, 1982
18. Sjöklund K, Schaffalitzky de Muckadell OB, Fahrenkrug F, Häkanson R, Peterson BG, Sundler F: Peptide-containing nerve fibers in the gut wall in Crohn's disease. *Gut* 24:724-733, 1983
19. Smith B: Disorders of the myenteric plexus. *Gut* 11: 271-274, 1970
20. Spaepen M, Van Gompel A, Bormans V, Peters TL, Van Trappen G: Vasoactive intestinal polypeptide (VIP), somatostatin and substance P concentrations in colonic biopsies from patients with Crohn's disease. *Dig Dis Sci* 29:825-832, 1984
21. Whitehead R: Pathology of Crohn's disease of the colon. In: *Inflammatory bowel disease*, eds, Kirsner JB, Shorter RG, Lea and Febiger, Philadelphia 1975, pp 182-198

Ultrastrukturelle Änderungen der Nervelemente bei CROHNscher-Krankheit

V. SZABÓ und Erzsébet FEHÉR

Mittels Elektronenmikroskop wurden die Nervelemente der Dünndarmwand bei CHRONscher Krankheit untersucht und mit den Kontrollschnitten verglichen. Bei CHRONscher Krankheit waren im Ileum nur einige Synapsen vorzufinden. Die Zahl der Nervenfasern hat sich verringert, ebenso wie die Zahl der Vesikulen in den übriggebliebenen Nervenfasern. Einige Nervenfortsätze sind degeneriert. In den Nervenzellen stieg die Zahl der Lysosome an. In der Tela submucosa und in der Schleimhaut sind entzündliche Zellen, Lymphzellen, Plasmazellen in ebenfalls erhöhter Zahl vorzufinden. Für die sich in den Nervenzellen abgespielten Änderungen sind annehmbar die immunologischen Effektorzellen und ihre Produkte verantwortlich.

Ультраструктурные изменения нервных элементов у страдающих болезнью Крона

В. САБО и Э. ФЕХЕР

У пациентов, страдающих болезнью Крона, исследовали под электронным микроскопом нервные элементы стенки тонкой кишки и сравнивали результаты с контрольными. У страдающих болезнью Крона в подвздошной кишке можно было выявить лишь несколько синапсов. Число нервных волокон уменьшилось, так же как и число пузырьков в оставшихся нервных волокнах. Наблюдалась дегенерация некоторых нервных отростков. Число лизосом в нервных клетках возросло. В подслизистой ткани и в слизистой оболочке выявлялись воспалительные клетки, а также лимфатические, плазматические и тучные клетки, число их возросло. Можно предположить, что иммунологические клетки-эффекторы и их продукты ответственны за изменения, которые наступили в нервных элементах.

Motor Response to Electric Spatial Stimulation of Isolated Intact and Inflamed Human Appendix

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The smooth muscle responses to electric stimulation of intact, slightly or severely inflamed, isolated human appendix strips were studied. No changes were noted in the motility of the not inflamed and slightly inflamed appendices, (simple appendicitis), the preparations responded to nervous stimulation with contractions of the same size. The smooth muscle contractions were blocked by atropine, and enhanced by physostigmine, which proves the cholinergic nature of the innervation.

The severe inflammation (acute phlegmonous appendicitis) reduced also the contraction and relaxation of the appendix strips. With the advancement of the inflammatory process, the decreased motility of the appendix can play an *in vivo* role in the rapid progress of the process.

Introduction

It is known from animal experiments that, based on the motility responses to the electric stimulation of the nervous elements of smooth muscle preparations gained from the gastrointestinal tract, the neurotransmission relations of the organs can be mapped [3, 7, 11].

Recently, similar investigations were also made in surviving tissues obtained from human stomach, small intestine and colon [4, 8, 10].

The motility responses to the electric stimulation of human appendix of a complete wall thickness is reported here for the first time [1].

In this report, our findings with square-wave stimulation of appendices inflamed to different extent are reviewed.

Material and Method

The samples were collected from patients having undergone hemicolectomy or operated for the suspicion of appendicitis. Operations were performed at the 2nd Department of Surgery, under anaesthesia by the preoperative

i.m. administration of 1 mg atropine sulphate and 10 mg diazepam (Seduxen) and the i.v. administration of ethylbutylthiobarbital natrium (Inactin), and maintained by aspiration of 0.5–1% halothane. The relaxation of muscles was ensured by 1.5 mg/kg succinylcholine.

The longitudinal appendix strips (2.5 cm long, 0.3 cm wide, of a complete wall thickness) were placed immediately after removal to 4 °C oxygenated Tyrode solution and were stored at a temperature of 4 °C (in refrigerator). In the group of intact and differently inflamed appendix strips, there was the same proportion of preparations kept at 4 °C for a shorter or longer time. Each experiment was performed within a period of 24 hours, but the majority were made within 10 hours. During the experiments the appendix strips were suspended in an organ bath of 37 °C Tyrode solution by bubbling through oxygen, and prestretching of 5 mN was applied. The examinations were started after an incubation of one and a half hours at 37 °C.

Spatial electric stimulation was made with vertical platinum electrodes placed at a distance of 1 cm from each other parallel with the preparation, using a high-performance square-wave stimulator. The parameters of stimulation were as follows: tension 40 V, impulse width 0.1 ms, Hz frequencies 1.5 and 20. The stimulation of 1 Hz was maintained for 60, those of 5 and 20 Hz for 20 seconds. The individual impulse series were separated by intervals of 5 minutes.

The responses to spatial stimulation were registered by an isotonic relay on a compensograph (MTA KUTESZ).

Statistical analysis was performed by the one- and two-sample *t*-tests. The probability of $P > 0.05$ was considered significant. Reporting our results, the contractions and relaxations arising in the preparations during spatial stimulation were expressed in mN. The *in vitro* used pharmaca included atropine sulphate (Merck), bethanechol (SIGMA), physostigmine salicylate (PhHg).

Results

For judging how inflammation affects the motility of the appendix, intact and differently inflamed preparations were used. The intact, slightly and severely inflamed appendix strips responded with a frequency-dependent contraction to spatial stimulation (Fig. 1A). It is seen that, under identical conditions the intact (N) and slightly inflamed (S) appendix strips did not differ significantly in either the size or the nature of their contractions. The responses of the histologically verified phlegmonous appendices were, however, smaller. The difference proved also to be quantitatively significant (Fig. 2).

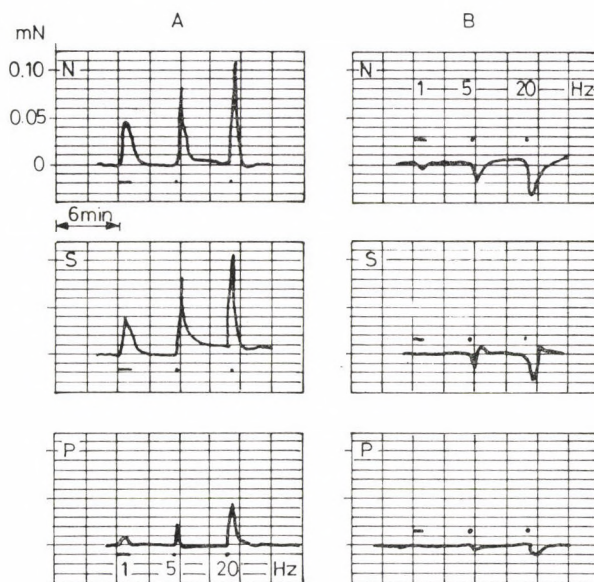


FIG. 1. Changes in motility of isolated longitudinal smooth muscle preparations of human appendix on electric spatial stimulation. Recordings from preparations A: in normal Tyrode solution; B: in the presence of $1 \mu\text{M}/\text{l}$ atropine sulphate. N: from an intact appendix; S: from a simple appendix; P: from a phlegmonous appendix. Stimulation parameters: 40 V, 0.1 ms; 1 Hz: 60s; 5.20; 20s

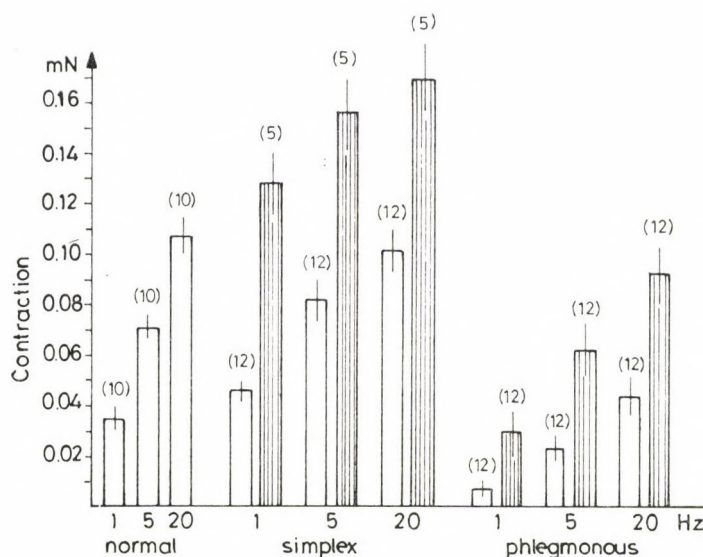


FIG. 2. The contraction of isolated longitudinal smooth muscle preparation of human appendix due to electric spatial stimulation. White columns: in normal Tyrode solution; Hatched columns: in the presence of $0.25 \mu\text{M}/\text{l}$ physostigmine ($\bar{x} \pm \text{SE}$). Over the columns in brackets the number of preparations are shown

Part B of Fig. 1 shows the registered responses to electric stimuli given to the incubating solution in the presence of atropine. In the intact (N) and slightly inflamed (S) appendices relaxations depending on the frequency of the stimulation was observed. In a part of both the intact, as well as slightly inflamed preparations also after-contractions arose (Fig. 1B, S). In the presence of atropine the response of the phlegmonous appendix to lower frequencies (1–5 Hz) was significantly smaller than in the slightly inflamed (Fig. 3) or intact preparations.

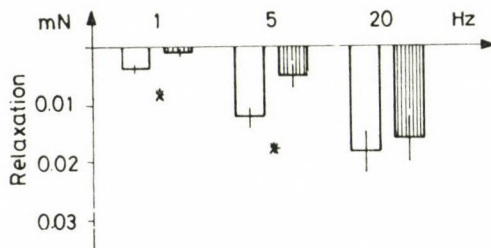


FIG. 3. The relaxations of isolated longitudinal smooth muscle preparations of human appendix due to electric spatial stimulation in the presence of $1 \mu\text{M}$ atropine sulphate. Responses of the preparations slightly inflamed (simple appendicitis) (white columns) and those obtained from phlegmonous appendix (hatched columns) ($\bar{x} \pm \text{SE}$) $P > 0.5$

It can be stated that with the advance of the inflammatory process, not only contractions but also relaxations decreased in our preparations. It is still undecided whether the reduced response can be primarily due to the decay of nervous elements or to the decreased smooth muscle contractility. Therefore, the effect of $2 \mu\text{M}$ bethanechol directly attacking the smooth muscle was studied in the simple and phlegmonous preparations. Considering the contraction elicited by a 20 Hz impulse to be 100%, the effect of bethanechol in case of simple appendices was found to be 117%, while in the phlegmonous ones to be 69% (12 preparations each). Consequently, the effect of the bethanechol directly affecting smooth muscle, was still more inhibited by the progression of the inflammation even in comparison to the responses elicited by nerve stimulation.

Discussion

The aetiology of acute appendicitis is not homogeneous and still obscure [5]. Besides the infectious factors, the obstruction of the lumen of the appendix—and thereby its motility disorder—can be of importance in giving rise to acute appendicitis [2].

By spatial electric stimulation, both the motility of the longitudinal appendix strips of complete wall thickness [1], as well as that of the longi-

tudinal muscles obtained from the appendix [6] can be studied well. These investigations have unanimously shown that acetylcholine plays an important role in the motility responses elicited by spatial stimulation of the human appendix.

In the present experiments the responses of the intact and inflamed appendix strips to square-wave stimulation were examined. It was established that the intact and slightly inflamed appendices did not differ in function. The size of the responses, the cholinergic nature of the contractions (their atropine-blocking and physostigmine-increasing effect) agreed concerning both in the weakly inflamed tissues and the control preparations. At the same time, the severe inflammation essentially reduced both contraction and relaxation. In the phlegmonous inflammation of the appendix the bethanechol directly affecting the smooth muscle was still less effective than electric stimulation. It seems probable that diffusion of bethanechol was made difficult as a result of wall thickening due to the inflammatory process, and also this factor played a role in reducing the effect. It can thus be stated that the smaller size of contractions elicited by nervous stimulation in the preparations obtained from the phlegmonous appendix cannot be attributed to the primary impairment of the nervous elements.

Our *in vitro* results may be the basis for the assumption that under *in vitro* conditions, in the case of phlegmonous appendicitis, the decreased peristalsis of the organ had also contributed to the rapid progression of the pathophysiological process.

In simple appendicitis, similar signs indicating the decrease of motility were not found. In our opinion, our results suggest that if the inflammation of the appendix becomes so severe that it results in reduced motility, a vicious circle occurs due to the stasis of the infected intestinal contents.

It is to be noted that markedly inhibited contractions could be elicited, in a similar way as in our experiments, by the spatial electric and bethanechol stimulation of isolated colonic smooth muscle preparations obtained from ulcerative colitis patients [9].

Acknowledgements

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References

1. Antal A, Bartho L, Szolcsányi J: Izolált humán appendix elektromos ingerléssel kiváltott neurogén simaizom-válaszai (Neurogenic smooth muscle responses of isolated human appendix elicited by electric stimulation). Kísérő Orvostud (submitted for publication)

2. Arnbjörnsson E, Bengmark S: Obstruction of the appendix lumen in relation to pathogenesis of acute appendicitis. *Acta Chir Scand* 149:789, 1983
3. Bartho L, Holzer P: Search for a physiological role of substance P in gastrointestinal motility. *Neuroscience* 16:1, 1985
4. Bennett A, Stockley H. J: The intrinsic innervation of the human alimentary tract and its relation to function. *Gut* 16:443, 1975
5. Dubez S: Akut appendicitis (Acute appendicitis) *Medicina*, Budapest 1988, p 170
6. Ekblad E, Arnbjörnsson E, Ekman R, Hakanson R, Sundler F: Neuropeptides in the human appendix. *Dig Dis Sci* 34:1217, 1989
7. Furness JB, Costa M: Types of nerves in the enteric nervous system. *Neuroscience* 5:1, 1980
8. Maggi CA, Patacchini R, Santicoli P, Giuliani S, Lippe ITh, Geppetti P, Del Bianco E, Selleri S, Meli A: The effect of omega conotoxin GVIA, a peptide modulator of N-type voltage sensitive calcium channels, on motor responses produced by activation of efferent and sensory nerves in mammalian smooth muscle. *Naunyn Schmiedeberg's Arch Pharmacol* 338:107, 1988
9. Snape WJ, Kao HW: Role of inflammatory mediators in colonic smooth muscle function in ulcerative colitis. *Dig Dis Sci* 33, Suppl 65, 1988
10. Stockley HJ, Bennett A: Relaxations mediated by adrenergic and nonadrenergic nerves in human isolated *Taenia coli*. *J Pharm Pharmacol* 29:533, 1977
11. Szolcsányi J, Bartho L: New type of nerve-mediated cholinergic contractions of the guinea-pig small intestine and its selective blockade by capsaicin. *Naunyn Schmiedeberg's Arch Pharmacol* 305:83, 1978

Auf die elektrische Raumreizung des intakten und entzündeten isolierten humanen Appendix gegebene motorische Antworten

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Die mit elektrischer Raumreizung auslösbaren Glattmuskelantworten wurden an intakten bzw. schwer entzündlichen, isolierten, humanen Appendixstreifen untersucht. Die entzündungsfreien und die eine milde Entzündung aufweisenden Appendixes (Appendicitis simplex) zeigten keine Motilitätsänderungen. Die Präparate antworteten auf die Nervenreizung mit Kontraktionen mit identischer Größe. Die Glattmuskellkontraktionen wurden durch Atropin blockiert und durch Physostigmin gesteigert, welche Umstände den Cholinergcharakter der Innervation bestätigen.

Durch schwere Entzündungen (Appendicitis acuta phlegmonosa) wurden auch die Kontraktion und die Relaxation der Appendixstreifen verringert. Die Motilitätsverringerng des Appendix kann mit der Fortschreitung des entzündlichen Prozesses in dem raschen Progredieren des Prozesses *in vivo* eine Rolle spielen.

Двигательные реакции интактного и воспаленного изолированного человеческого аппендикса на электрическое пространственное раздражение

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На интактных, слегка или сильно воспаленных изолированных человеческих аппендиксах изучали реакции гладких мышц, вызванные электрическим пространственным раздражением. В двигательной активности интактных или слегка воспаленных полос аппендикса (простой аппендицит) отклонений не наблюдали, на раздражение нерва препараты отвечали сокращениями одинаковой силы. Сокращения гладких мышц блокировались атропином, физостигмин же их усиливал, что доказывает холинергический характер иннервации.

Сильное воспаление (флегмонозный аппендицит) уменьшало силу сокращения и расслабления полосок аппендикса. Уменьшение двигательной активности аппендикса с прогрессированием воспалительного процесса *in vivo* может играть роль в быстром развитии процесса.

The potentials of CO₂ Laser in the Surgery of the Liver, Biliary Tract and Pancreas

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The Nd:YAG and CO₂ laser can be used with benefit in the surgery of the liver, biliary tract and pancreas. The Nd:YAG laser is most suitable for cutting parenchymatous organs, as e.g. the liver. In biliary surgery the CO₂ laser can be recommended. Based on their 12 cases, authors discuss the applicability of CO₂ laser.

Fiedler et al. [5] were the first to use CO₂ laser for liver resection.

In their experimental study, Meyer and Haverkamp [10] performed liver resection with a combination of CO₂ and Nd:YAG lasers. This combination was very effective from the point of view of cutting and haemostasis.

Subsequently, Sultan et al. [14] reported on combined laser operations performed in 15 patients.

Tranberg et al. [15] made a comparative study of the Cavitron ultrasonic aspirator (CUSA), the conventional finger blunt dissection technique and the liver resection technique using the noncontact Nd:YAG laser. They arrived at the conclusion that, although ensuring haemostasis, the noncontact Nd:YAG laser caused a considerable tissue damage (necrotic zone).

After developing the contact-sapphire probe Nd:YAG laser, it was proved to be very effective in both endoscopic surgery as well as open surgery [6]. Concerning liver resection it was also revealed that the contact-sapphire probe Nd:YAG laser is far better than the noncontact Nd:YAG laser.

The various surgical lasers proved to be very beneficial also in the surgery of the pancreas [7]. Partial pancreatic resections made by Nd:YAG laser were also reported [8]. Brechov et al. [1] published their 35 pancreatic operations performed by CO₂ laser in 1987: 28 were distal pancreatic resections, 2 local excisions and 5 total pancreatectomies. The mortality within 30 days was 7 out of 35.

Lasers are more extensively used also in biliary surgery. Davis [3] performed transduodenal sphincterotomy with CO₂ laser. In his opinion, CO₂ laser is very appropriate for this purpose, because there is no bleeding during transection of the sphincter as there is neither postoperative, or later scarring.

Skobelkin et al. [13] carried out 23 transduodenal sphincterotomies by using CO₂ laser and followed up their results with the endoscopic method. They also consider the absence of bleeding during transection of the sphincter an advantage as also that the laser unites the mucosae of the papilla and the duodenum and even after some years, a narrowing of only 20% will occur in the sphincters.

Skobelkin et al. [13] also apply extensively laser in cholecystectomies. They have found it extremely useful under inflammatory conditions, in biliary operations performed in cholecystitis. The tissues, otherwise with a frequent tendency to bleeding, can be separated practically without bleeding by this method.

Material and Methods

Our operations were performed by using a TUNGSRAM RT TLS₆₁ type CO₂ laser of a performance of 60 W. The manipulation arm of the device ends in an interchangeable sterilizable end-piece—this is held by the surgeon during operation. Accurate aiming is assisted by a parallel, well visible He-Ne laser beam. Starting of the advice is made by a pedal.

The manipulation arm consisting of several joints can be easily moved in any direction. This equipment has been used in the recent three years for performing approximately 500 operations.

Table 1 shows our cases with laser operations of the liver, pancreas and bile ducts.

TABLE 1
*The use of CO₂ laser in the surgery of the liver,
biliary tract and pancreas*

<i>Liver operations</i>			
No.	Diagnosis	Operation	No.
1.	Benign hepatic tumour	Liver resection	1
2.	Hepatic cyst	Excision + evaporation	1
<i>Biliary operations</i>			
1.	Cholelithiasis	Cholecystectomies	4
2.	Choledocholithiasis	Choledochostomies	3
3.	Pancreatic tumour (mechanical icterus)	Cholecystoduodenostomy	1
4.	Pancreatic tumour (mechanical icterus)	Cholecystojejunostomy	1
<i>Pancreatic operations</i>			
1.	Pancreatic cyst	Cystojejunostomy	1
Total			12

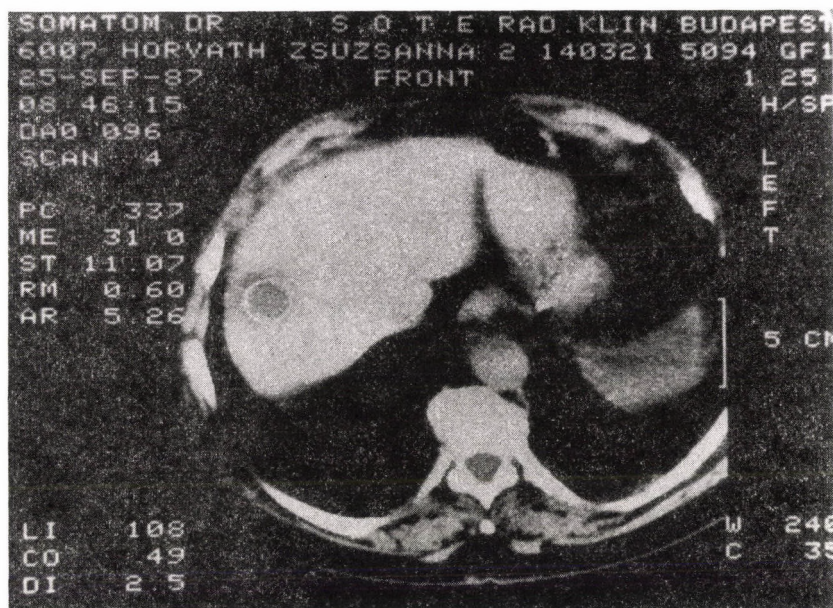


FIG. 1. CT scan of the cyst in the right hepatic lobe of a female patient, aged 61

There were two liver operations. A right lobe benign cyst of the size of an egg was resected and evaporated. Attempt was made to perform liver resection due to a benign liver tumour by using CO₂ laser. Figure 1 shows the CT scan of a liver cyst removed from the right hepatic lobe.

The number of biliary operations was 9. Three choledochostomies were performed by CO₂ laser. Figure 2 demonstrates the roentgenogram of a T-tube cholangiography after a choledochostomy by laser. Five cholecystectomies were carried out by laser, as well as two bilio-digestive anastomoses.

A cystojejunostomy for pancreatic cyst is also included in our material.

Discussion

After the initial great enthusiasm [5], it has turned out that CO₂ laser used alone is not suitable for liver resection. We had similar experience. The medium-sized and large vessels occurring in large number in the parenchymatous organ tend to bleed during laser transection—the CO₂ laser closes only the vessels of a diameter smaller than 0.5 mm during cutting. The outpouring blood absorbs the light and the blood starts to boil and this stops cutting. In liver resection the combined use of CO₂ and Nd:YAG [10] or still more the sapphire-probe Nd:YAG [6] laser are adaptable. CO₂ laser can be used for



FIG. 2. T-tube cholangiography of a 72-year-old female patient 12 days after choledochostomy

the excellent resection without bleeding of the extrahepatic part of a liver cyst on the diaphragmatic surface. The intrahepatic part of the cyst was also bloodlessly evaporated.

Based on literary evidence, both the CO₂ laser and the Nd:YAG laser can be recommended for pancreatic surgery [1, 7, 8]. In our own case, CO₂ laser was very useful for the anastomosing of a pseudocyst in the caudal part of the pancreas. A cystojejunostomy was performed with Roux-en-Y anastomosis including a small intestinal loop. The operation was almost bloodless, the patient healed uneventfully. The laser was applied for the opening of the cyst and the creation of the intestinal loop.

The laser knife can be used with benefit for performing choledochostomy. The bile in the choledochus protects the posterior wall of the biliary tract from injury. The choledochal wound edges do not bleed. The choledochus heals completely. Bile leakage was not observed in any of the cases (Fig. 2).

There is no need of placing supporting sutures for the opening of the choledochus. The lack of bleeding allows good visibility and unheeded work.

In cholecystectomies it was not found to be of particular advantage over the conventional operations. An inflamed gallbladder with a bleeding tendency can, however, be readily removed, with less or minimal bleeding with the CO₂ laser knife. This advantage was also noted by us on removing a subcutaneously inflamed gallbladder.

References

1. Brechov EI, Litvin GD, Kirpitchenov AG: Laser scalpel in pancreatic surgery. *Laser Optoelectronics in Medicine*, Laser 87, Springer Verlag, Munich 1987 p 177
2. Daikuzono N, Joffe SN: An artificial sapphir probe for contact photocoagulation and tissue vaporisation Med. Instrument 19:173–178, 1985
3. Davis R: Transduodenal sphincteroplasty using the CO₂ laser. *SGO*, 166:421–424, 1988
4. David CJ: Laser cholecystectomy. In, Joffe SN: *Laser in General Surgery*, Williams and Wilkins, London, Hong Kong 1989
5. Fiedler JP, Noeter RW, Polanyi TG et al: Laser surgery in exsanguinating liver injury. *Ann. Surgery* 181:74–80 1975
6. Joffe SN, Brackett KA, Sankar MY, Kaikuzono A: Resection of the liver with Nd:YAG laser. *Surg. Gynecol Obstet* 163:437–442, 1986
7. Joffe SN, Sankar MY: Lasers in hepato-biliary and pancreatic surgery. In: Shapsay SM, ed, *Endoscopic Laser Surgery Handbook*. Marcel Dekker, New York 1986
8. Joffe SN: Contact Nd:YAG laser surgery in gastroenterology. A preliminary report. *Lasers Surg Med* 6:155–159, 1986
9. Kouzu T, K Isone: Percutaneous treatment of gallstones In: Joffe SN, *Lasers in General Surgery*, Williams and Wilkins, London, Hong Kong 1989
10. Meyer MJ, Kaverkamp K: Experimental study of partial liver resection with a combined CO₂ and Nd:YAG laser. *Lasers Surg Med* 2:149–154, 1982
11. Orda R, Barak J, Orda S, Wiznitzer T: Partial distal pancreatectomy with a hand-held CO₂ laser *Arch Surg* 115:869–873, 1980
12. Schröder T, Rämör OJ: Lasers in pancreatic surgery In: Joffe SN, *Lasers in General Surgery*, Williams and Wilkins, London, Hong Kong p 96
13. Skobelkin OK, Brekhov KV, Bashilov VP: *Laser Surgical Units*, Medexport, Moscow 1985, pp 61–63
14. Sultan RA, Fallonk H, Lefebvre-Vilardebo H et al: A separate and combined use of Nd:YAG and carbon dioxide lasers in liver resections: a preliminary report. *Lasers Sci Med* 1:101–105, 1986
15. Tranberg KG, Rigotti P, Brackett KA et al: Liver resection. A comparison using the Nd:YAG laser, ultrasonic aspirator, or blunt dissection. *Am J Surg* 151:368–372, 1985

Möglichkeiten des CO₂-Laserstrahlas in der Chirurgie der Leber, der Gallenwege und des Pankreas

T. TÓTH und J. BÁTORFI

Die Laser Nd:YAG und CO₂ können in der Chirurgie der Leber, der Gallenwege und des Pankreas eine vorteilhafte Anwendung finden. Nd:YAG eignet sich sehr gut zur Inzision parenchymatöser Organe (z. B. Leber). In der Chirurgie der Gallenwege empfiehlt sich der Einsatz des CO₂-Lasers. Aufgrund der eigenen 12 Fällen finden die Anwendungsmöglichkeiten des CO₂-Lasers eine Besprechung.

Возможности CO₂-лазера в хирургии печени, желчных путей и поджелудочной железы

Т. ТОТ и Й. БАТОРФИ

Лазеры Nd: YAG и CO₂ имеют преимущества при операциях на печени, желчных путях и поджелудочной железе. Лазер Nd: YAG вполне годится для разрезания паренхиматозных органов, например печени. Для применения в хирургии желчных путей можно рекомендовать CO₂-лазер. На основании собственных 12 наблюдений авторы обсуждают возможность применения CO₂-лазера.

A Case of Multiple Cholangiogenic Liver Abscess Due to Residual Biliary Stone Cured by Percutaneous Drainage Controlled by CT and Endoscopic Papillotomy

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The case of a patient treated for multiple cholangiogenic liver abscess due to residual biliary stone after acute cholecystitis is reported. The multiple liver cyst was cured by percutaneous transhepatic double drainage controlled by CT as well as puncture and aimed local systemic antibiotic treatment. The residual gallbladder stone was removed by endoscopic papillotomy. A similar case has not been reported so far.

The diagnosis and therapy of bacterial liver abscesses are current and in many respects still unsolved problems of up-to-date surgery [2, 6, 7, 11]. Mortality could not so far been markedly improved by the classical surgical treatment in spite of all the advance in surgical techniques. The poor results of the treatment of liver abscesses have directed attention to applying new methods in the therapy of this rare but prognostically very severe disease.

The invasive radiological methods have been acknowledged in several branches of surgery, mainly as a surgical alternative of high-risk patients, or as a supplementary intervention for the higher risk reoperation. There are still controversies about what role percutaneous transhepatic interventions controlled by sonography (US) and computed tomography (CT) play in the treatment of liver abscesses [14, 15, 29].

The reservations of surgeons concerning the doubtful opportunities and results of aimed percutaneous transhepatic drainage (PTD) or puncture (PTP) in the treatment of liver abscesses, can be ascribed to several causes. The pyogenic liver abscess is the so-called „secondary disease”. In 85–90% of the cases it is consequential to a not primary hepatic process (biliary disorder of any origin, intraoperative or postoperative infection, inflammatory small intestinal or colonic processes, etc.). The chance of cure without curing the underlying disease resulting the abscess is minimal [8, 25]. The other, most important argument against PTD and/or PTP—mainly in the multiple multi-

locular abscesses—is that the drainage of one or several larger abscess cavities cannot ensure the free emptying of pus and the complete healing of the process [3, 11].

Of the invasive interventions, an accepted method is endoscopic papillotomy (EPT) for removing residual biliary stones, since it implies and essentially smaller strain than does reoperation [32].

In our study the case of a patient treated because of a cholangiogenic multiple liver abscess, who could be cured without surgical exposure by CT-controlled PTD and PTP as well as EPT. This two invasive methods helped in achieving a complete and final recovery. A similar case has not been encountered in the literature.

Case Report

A.V., a male patient, aged 50, was admitted to the Vishnevskii Institute of Surgery in Moscow on 14 January 1986.

History: In 1983 necrectomy and abdominal irrigation drainage were performed because of acute necrotizing pancreatitis. After a complaint-free period of two years, his typical cholelithiatic complaints under the right costal arch, radiating into his back started in August 1985. Due to the increased complaints, he was operated on in another institute in September 1985. On operation suppurative cholecystitis and choledocholithiasis were found. Cholectectomy, stone removal by choledochotomy as well as drainage of the foramen of Winslow were carried out. The patient became afebrile postoperatively and his condition was satisfactory. However, a biliary fistula developed through the Winslow's drain from the 7th postoperative day. His compensated, good general condition began to deteriorate from the 60th day of the operation. He was admitted to the Institute on January, 16, 1986 because of septic fever up to 40 °C, blunt pain under the right costal arch, and an abrupt loss of weight of 10 kg, i.e. a progressively deteriorating state.

State on admission: Thin male patient of a poor general condition. His skin and visible mucosae were pale, his sclera subicteric. His tongue was dry and furred. Pulse: 100/min. Blood pressure: 120/80 mmHg. Temperature: 38.8 °C. Chest: No pathological change was revealed on physical examination above the heart and lungs, there was sluggish diaphragmatic movement on both sides. Cardiac dullness, on percussion no thoracic effusion could be found. *Abdomen*: Scars of upper median and right subcostal incisions. Four or 5 cm laterally to the subcostal incision, drainage with a separate outlet, where biliary discharge was emptying. The abdomen was diffusely tender, but physical signs indicative of peritonitis were absent. Hepatic dullness could be felt on percussion, the liver extended over the right costal arch with 8 cm, being moderately tender on palpation. Normal intestinal peristalsis was heard.

The spleen was enlarged, well palpable. *Rectal digital examination*: The Douglas space was not tender and convex. No pathological signs in the rectum up to a height accessible to manual examination. *Urgent laboratory test results*: Hb: 74 g/l, haemat.: 0.25 l/l, WBC: 7.6×10^9 /l, urine: neg., blood glucose: 130,7 mmol/l, BUN: 7.8 mmol/l, creatinine sed. rate: 178 μ mol/l, SGOT: 45 IU/l, AP: 710 IU/l, diastase sed.: 12 IU/l.

Abdominal US: In the right and left lobes of the liver, inhomogeneous cystose changes were noted, the largest reaching 6 cm in diameter.

Abdominal CT: The liver was enlarged, with destructive changes in four places in its projection. One in the left and three in the right lobes. The largest was 8 cm in diameter, its densitometric index was 18–24 Hounsfield unit (HU). In the hepatic porta, the shadow of the drain tube could be seen. The spleen was homogeneous, and markedly enlarged. No changes in the kidneys. The structure of the pancreas was slightly inhomogeneous, moderately enlarged in the head. On the border of the pancreatic head and the duodenum, round density produced by the stone, 6 cm in diameter, with a densitometric index of 126 HU. *Opinion*: Multiple cholangiogenic liver abscess. Residual stone in the region of the intrapancreatic choledochous duct. Chronic pancreatitis.

PTD was performed controlled by CT under local anaesthesia with the observance of sterility. The drains were introduced into the two largest abscesses on the border of segments III and VI–VII. On puncturing the abscesses, 40 ml pus was obtained for bacteriological cytological and gas chromatographic studies. The duration of the intervention was 25 minutes, without any signs of complication (Figs 1, 2, 3).

Bacteriology: In the examined material, *Citrobacter* was cultured (9×10^9 bacterium/ml), pathogen sensitive to: Klarofan, metronidazole, kanamycin. *Chromatographic study*: the presence of anaerobic bacteria could be not verified. *Cytology*: The specimen obtained by puncture could not be shown to contain tumorous cells, or any change specific for infection (like TBC, *Entamoeba histolytica*).

Following aimed parenteral and local antibiotic treatment the patient's general condition improved. Forty-eight hours after the intervention he became afebrile. After normalization of his haematological status, ERCP was carried out on the fourth day after PTD.

Endoscopic retrograde cholangiography: The instrument could be introduced unheeded into the duodenum. The plication was thickened on the descending branch of the duodenum. The inflamed papilla of Vater was located and cholangiography performed. The cholangiogram revealed the choledochus to be 25–18 mm in diameter, with a density produced by the stone in its projection. A papillotomy of 18–20 mm was performed and the stone, about 5–6 mm in diameter, was removed. There was no bleeding. The control cholan-

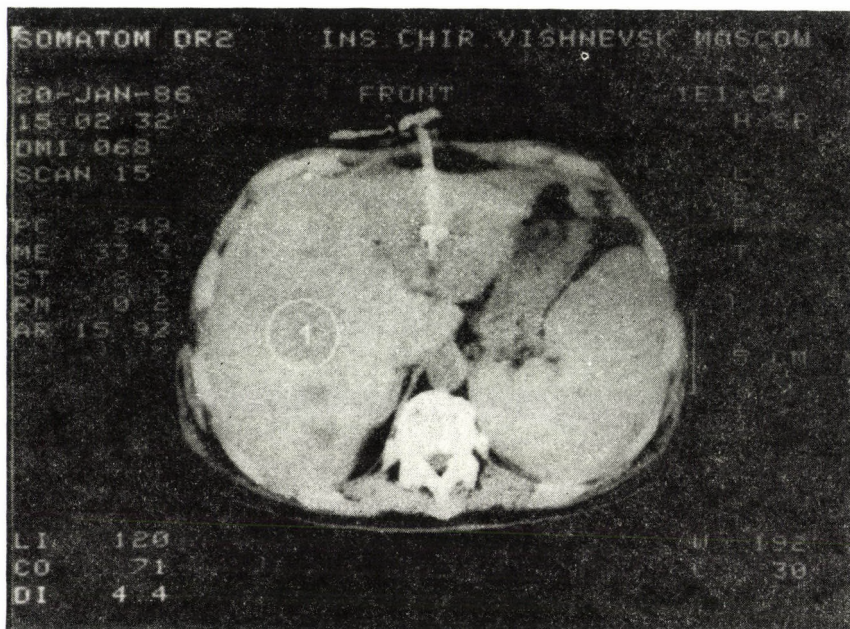


FIG. 1. CT scan of percutaneous transhepatic drain in the projection of segment III of the liver. On the border of segments VI-VII a nondrained abscess is seen

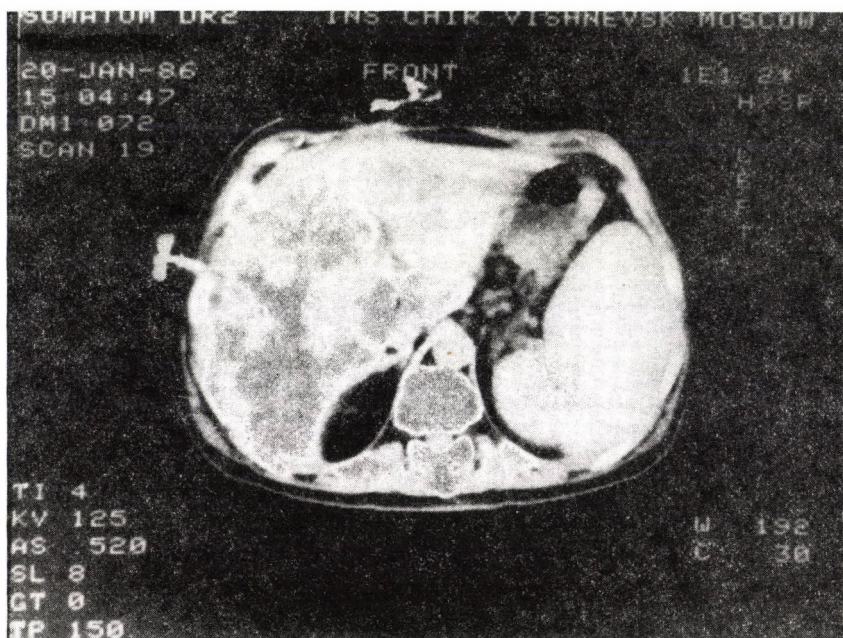


FIG. 2. CT scan of a drained abscess on the border of the hepatic segments VI-VII

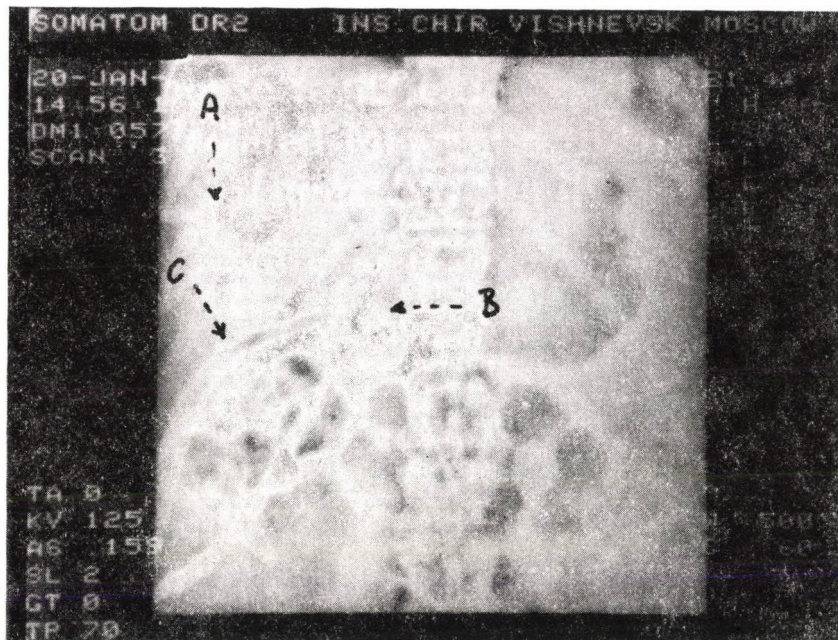


FIG. 3. The CT scan shows two percutaneous drains (A and B) as well as the shadow of the Winslow drain

giogram showed the contrast medium to be emptying somewhat slower, but there was no evidence of any organic obstacle (stone, stenosis).

By the seventh day following EST, emptying of bile through the Winslow drain stopped and the biliary fistula closed.

Ten days after CT-guided PTD, control examination was made. *Control abdominal CT*: The liver became considerably smaller. The two largest drained abscesses healed, the drains were removed. In segment VII a still not healed abscess was visible, of a diameter of 2.5 cm. Opinion: Regarding the improvement in the clinical picture, a repeated percutaneous intervention was not considered (still) to be justified due to the residual abscess. The parenteral antibiotic treatment applied so far was recommended to be continued (Fig. 4).

The patient's general state gradually improved, his subicterus ceased, his laboratory parameters normalized. After 11 days a repeat control examination was made. *Control abdominal CT*: The abscess in segment VII revealed by the previous examination could still be detected. The percutaneous puncture of the abscess guided by CT was performed. One gramme of Klarofan was administered into the abscess cavity. The control scan revealed no changes indicating abscess after three weeks following the first percutaneous intervention (Figs 5, 6).

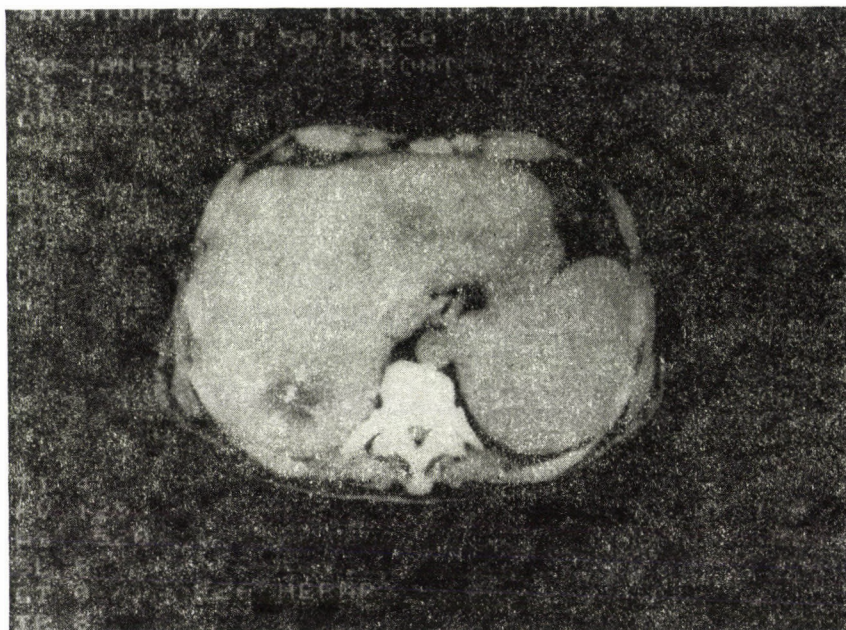


FIG. 4. Control CT scan from ten days later. The two large abscesses have healed, with the drains removed. The third 2 by 3 cm abscess is clearly seen in segment VII

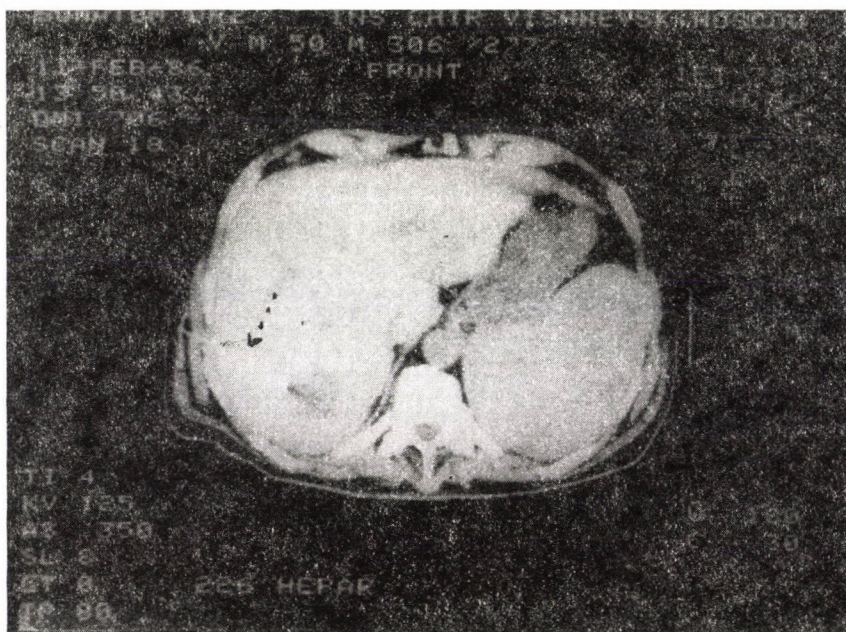


FIG. 5. Control CT scan eleven days later. The residual abscess was solved by puncture

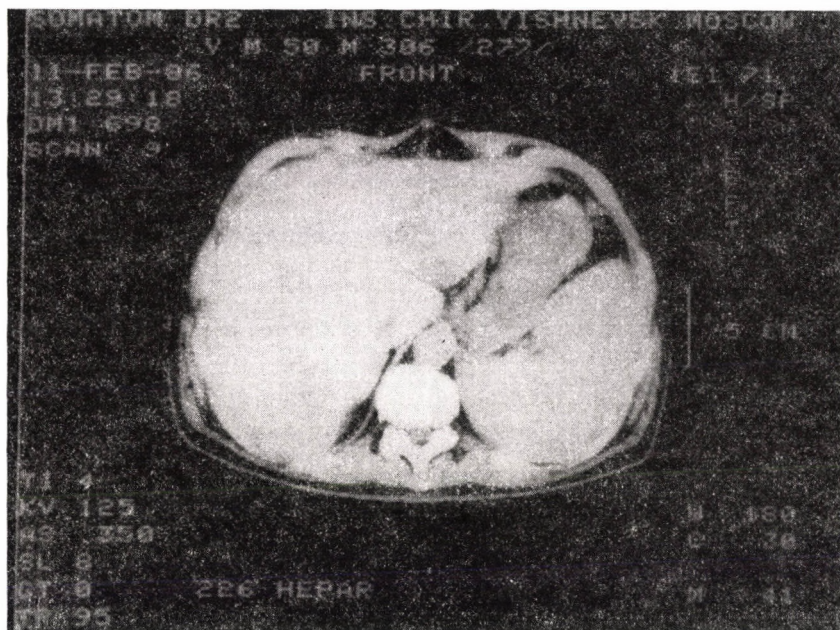


FIG. 6. Control scan after puncture. No change indicating abscess can be noted

Discussion

Up to the end of the 70s, the generally accepted principle was the conventional surgical exposure and administration of antibiotics in the therapy of liver abscesses [17, 26]. In solitary abscesses the wide exposure of the abscess cavity—possibly extraperitoneally—the incision of the suppurating focus, the emptying of the accumulated mass of pus and of the necrotic mass, the ensuring of the continuous and unheeded flow of the discharge were aimed at, to detoxify the patient and to reduce the perifocal edema. In the case of multiple abscesses, with a verifiable cholangiogenic origin, the ensuring of free bile flow was attempted.

To achieve an appropriate therapeutic level of the local antibiotic concentration to prevent the spread of the haematogen or lymphogen, local antibiotic perfusion of the liver was also performed with irrigation of the larger abscess cavities with antibiotic solutions, usually with the cannulation of the left gastro-epiploic vein or of the recanalized umbilical vein. In the case of liver abscess, liver resection was rarely made [12, 18, 23]. Mortality rate after the classical surgical treatment was 7–44%, with the number of postoperative complications between 25 and 52% [30]. The high lethality of the surgical intervention was most often due a diagnosis not formed early enough, to

repeatedly performing traumatizing interventions in the patient of a poor general condition and an upset metabolism. Other causes included the difficulties of establishing intraoperatively the exact localization of the abscesses —lacking the possibility of an intraoperative US examination—as well as the high number of postoperative surgical complications (recurrent abscesses in the abdominal cavity, wound infections, etc.) [2, 7]. Patients with liver abscess treated only by operation were hospitalized longer, with higher costs of treatment [24, 28].

The up-to-date imaging procedures (like CT and US) offered a possibility already for the preoperative and rapid detection of abscesses, their accurate localization, size, their proximity to vital organs and the establishment of the distance to the abdominal wall. It has become possible to recognize the hollow organs in the way of the percutaneous drain. In bacterial liver abscess, with the adequate personal and objective conditions given, regardless of the type of the abscess and of the underlying disease giving rise to the abscess, PTD and/or PTP controlled by CT, and/or US seems to be the method of choice, if there is no contraindication to the intervention or if the operation is not absolutely indicated [1, 5, 9, 20, 27, 33].

Percutaneous catheter drainage or puncture is contraindicated only by the presence of free abdominal fluid (due to rapidly developing diffuse suppurating peritonitis) or by an echinococcus cyst (due to the risk of anaphylactic shock and the dissemination of helminths) [33].

In the case of solitary, not large abscesses (of a diameter of less than 3–4 cm) even simple puncture may result complete healing. If necessary, it can be repeated or transformed into percutaneous drainage. In the case of solitary large abscesses (larger than 4–6 cm in diameter) or two or three abscesses, if the amount of pus is more than 5–100 ml, or of the discharge is thick and full of debris, closed drainage is recommended already as a first intervention [2, 8, 28]. In the case of large abscesses double drainage is performed to enable the continuous lavage of the abscess cavity with antibiotic or antiseptic solutions [33].

Multiple or multilocular abscesses are not considered to be contraindications of percutaneous abscess drainage. After drainage of two or three larger abscesses, aimed systemic or local antibiotic treatment is recommended. In the case of an unsatisfactory effect, the local perfusion of the liver can be carried out with aimed antibiotic treatment [5, 10, 27]. If at the time of the development or detection of the liver abscess the underlying disease still persists, this can be solved only by operation. PTD is then suitable for preparing surgery. By its slightly traumatizing use there is a possibility to release tension in the abscess, to gain time for the appropriate preparations for surgery and to improve the patient's general condition. Depending on the bacteriological result of pus, the elective operation can be performed in protection of the

aimed prophylactic antibiotic treatment and thus the number of postoperative complications can also be reduced [21, 23, 33].

Surgical exposure and drainage are indicated in all cases when an acute abdomen cannot be excluded and laparotomy is absolutely indicated (e.g. perforation of abscess, etc.), although, as mentioned earlier, by the time liver abscess was recognized and developed, the primary process had already healed. After a technically unsuccessful percutaneous abscess drainage, results can only be achieved by operation. If, following a successful PTD, the size of the abscess cavity does not change even after 2–3 weeks, surgical intervention is recommended for stopping the residual cavity [11].

The severe complications of PTD and/or PTP are rare. The most severe ones include after an inadequately performed drainage, thoracic empyema due to perforation of the diaphragm, or peritonitis due to pus running from the puncture track. Bleeding or perforation of a hollow organ rarely occurs. P. P. Mueller et al. [22] observed in their material of 388 cases of abdominal percutaneous drainage, 11 cases of perforation (5 gastric, 4 duodenal, two small intestinal) of which only two had to be operated. In the remaining cases, the abscesses responded to conservative treatment. In the case of PTD, the most frequent complication was the transitional feverish state, bacteraemia, in general, being also transitory [11].

Our case was found to be worth reporting because the multiple cholangiogenic liver abscess was treated by PTD or PTP guided by CT and aimed local systemic antibiotics, while the underlying disease leading to abscesses—residual biliary stone after acute cholecystectomy—was removed by EPT. These two invasive methods helped in achieving the complete and ultimate healing of the patient.

References

1. Allard JC, Kuligowska E: Percutaneous treatment of an intrahepatic abscess caused by a penetrating duodenal ulcer. *J Clin Gastroenterol* 9:603, 1987
2. Attar B, Levendoglu H, Cuassay NS: CT-guided percutaneous aspiration and catheter drainage of pyogenic liver abscesses. *Am J Gastroenterol* 7:550, 1986
3. Barnes PF, De Cock KM, Reynolds TN, Ralls PW: A comparison of amebic and pyogenic abscess of the liver. *Medicine, Baltimore* 6:472, 1987
4. Bergamini TM, Larson GM, Malangoni MA, Richardson JD: Liver abscess. Review of a 12 year experience. *Am J Surg* 10:596, 1987
5. Berger H, Pratschke E, Berr F, Fink U: Percutaneous drainage treatment of primary liver abscesses. *ROFO* 2:167, 1989
6. Bilfinger TV, Oldham KT, Lobe TE, Barron S, Hayden CK: Successful percutaneous drainage of pyogenic liver abscesses complicated by bronchobiliary fistula. *South Med J* 7:907, 1987
7. Buchman TG, Zuidema GD: The role of computerized tomographic scanning in the surgical management of pyogenic hepatic abscess. *Surg Gynecol Obstet* 1:1, 1981
8. Conter RL, Pitt HA, Tomkons RK, Longmire WP: Differentiation of pyogenic from amebic abscesses. *Surg Gynecol Obstet* 2:114, 1986
9. Dähnert W, Günthner RW, Börner N, Braun B, Gamstätter G, Rothmund M: Die percutane Drainage abdominalen Abscesse I. Technik und Ergebnisse. *Chirurg* 9:579, 1985

10. Dahnert W, Günthner RW, Börner N, Rothmund M: Die percutane Drainage abdominalen Abscesse II. Stellenwert im Vergleich zur septischen. *Chirurg* 9:584, 1985
11. Dietrick RB: Experience with liver abscess. *Am J Surg* 2:288, 1984
12. Galperin EI, Karagulyan CP, Mochalov AM: Opyt anatomicheskikh i atipicheskikh rezektsii pechenyi (Experience in anatomical and atypical resection of the liver). *Chirurgiya* 7:56, 1987
13. Gyorffy EJ, Frey CF, Silva J Jr, McGahan J: Pyogenic liver abscess. Diagnostic and therapeutic strategies. *Ann Surg* 6:699, 1987
14. Hau T, Hartmann E: Pathologie, Diagnose und Therapie der Leberabscesse. *Zentralbl Chir* 9:529, 1987
15. Heckemann R von, Krüger K, Wernecke K: Echomorphologie und Punktion-diagnostik von intraabdominellen Abscessen. *Fortschr Röntgenstr* 5:517, 1982
16. Jaques P, Mauro M, Safrit H, Yankaskas B, Piggott B: CT-features of intraabdominal abscesses: Prediction of successful percutaneous drainage. *Am J Roentgenol* 146:1041, 1986
17. Kandel G, Marcon NE: Pyogenic liver abscesses: New concepts of an old disease. *Am J Gastroenterol* 1:65, 1984
18. Kayabali I, Yilmaz S, Gurel M: Solitary pyogenic liver abscess: A statistical analysis of 117 cases. *Int Surg* 2:149, 1983
19. Kümmerle F, Thelen M: Interventionelle Radiologie und Chirurgie. *Dtsch med Wochenschr* 27:1047, 1986
20. Maxwell AJ, Mantora H: Fungal liver abscesses in acute leukemia—a report of two cases. *Clin Radiol* 1:197, 1988
21. Mechta RB, Parija SC, Chetty DV, Smile RR: Management of 240 cases of liver abscess. *Int Surg* 2:91, 1986
22. Mueller PP, Ferrucci JT Jr, Butch BJ, Simeone JF, Wittemberg J: Inadvertent percutaneous catheter gastroenterostomy during abscess drainage: Significance and management. *Am J Roentgenol* 8:387, 1985
23. Neoptolemos JP, MacPherson DS, Holm J, Fossard DP: Pyogenic liver abscess: a study of forty four cases in two centres. *Acta Chir Scand* 5:415, 1982
24. Pelissier G, Ranieri F: Ultrasound-guided puncture. A modern treatment of liver abscess 1:37, 1989
25. Rausch H, Gomez J, Hagenaukamp Ch: Computertomographisch gesteuerte Percutane Punction und Drainage von multiplen Leberabszessen, Fallbeschreibung. *Aktuell Chir* 6:248, 1985
26. Rothmund M: Intraabdominelle Abscesse - percutane oder chirurgische Drainage? *Dtsch med Wochenschr* 14:527, 1985
27. Rustgi AK, Richter JM: Pyogenic and amebic liver abscess. *Med Clin North Am* 4:847, 1989
28. Sheen IS, Chien CS, Lin DY, Liaw YF: Resolution of liver abscesses: comparison of pyogenic and amebic liver abscesses. *Am J Trop Med Hyg* 4:384, 1989
29. Sones PJ: Percutaneous drainage of abdominal abscesses. *Am J Roentgenol* 1:35, 1984
30. Sorrensen MR, Baekgaard N, Kirkegaard P: Pyogenic liver abscesses. A case report with a short review of current concepts of diagnosis and management. *Acta Chir Scand* 4:437, 1983
31. Sperling P, Wolff H, Luning M, Lorf T, Naundorf M: Behandlungsergebnisse pyogener Leberabscesse. *Zentralbl Chir* 9:548, 1987
32. Szántó I, Banai J, Bohár L, Rózsa I: Külső epesípoly esetében végzett endoscopy sphincterotomy (Endoscopic sphincterotomy in external biliary fistula). 35:66, 1982
33. Todua FI, Viljavin MJ: Invazivnye vmesatyelstva pad kontrolem komputernoy tomografii pri zbolepanyah gepatopankreatoduodenalnoy zony (Invasive interventions under controlled computer tomography in surgical diseases of the hepatopancreatoduodenal zone). *Chirurgiya* 10:27, 1986

**Mit, mit Computertomographie gesteuerter perkutaner Drainage
und endoskopischer Papillotomie geheilter Fall eines, einer sich nach
residualer Gallenweg-Steinkrankheit entwickelten multiplen,
cholangiogenen Leberabszesses**

T. FAZEKAS, F. I. TODUA, M. J. VILJEVIB und A. BÁLINT

Im dargestellten Fall handelt es sich um einen, nach akuter Cholezystitis zurückgebliebenen Gallenwegstein, wonach sich multiple, cholangiogene Leberabszesse entwickelten. Die multiplen Leberabszesse wurden mit Computertomographie gesteuerter, perkutaner transhepatischer Doppeldrainage sowie mit Punktion und gezielter lokaler bzw. systemischer antibiotischer Therapie geheilt. Der residuale Choledochusstein wurde mittels endoskopischer Papillotomie entfernt. Die Darstellung eines ähnlichen Falles war weder in der einheimischen, noch in der ausländischen Literatur vorzufinden.

**Случай излечения множественного холангиогенного абсцесса печени,
возникшего после резидуальной желчнокаменной болезни, с помощью
чрескожного дренирования, проводимого под контролем компьютерной,
томографии и эндоскопической папиллотомии**

Т. ФАЗЕКАШ, Ф. И. ТОДУШ, М. Й. ВИЛЬЕВИБ и А. БАЛИНТ

Авторы знакомят с историей болезни своего пациента, лечившегося по поводу множественного холангиогенного абсцесса печени, возникшего в связи с оставленным камнем желчных путей после острого холецистита. Множественный абсцесс печени был излечен с помощью контролировавшегося нутем компьютерной томографии двойного чрескожного транспатического дренирования, пункции, а также с помощью целенаправленного локального и системного лечения антибиотиками. Резидуальный камень желчных путей удалили посредством эндоскопической папиллотомии. Авторы не встречали описания подобного случая ни в венгерской, ни в имеющейся в их распоряжении международной литературе.

Gastrointestinal Angiodysplasia

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In the recent four years, 8 cases of gastrointestinal angiodysplasia (a.d.) were observed by the authors. Analysing the conclusions drawn from the patients course of disease, they found a.d. to be the cause of an unknown gastrointestinal bleeding. a.d. can be basically diagnosed by angiography. It is often associated with liver cirrhosis or arteriostenosis. The treatment of a.d. is surgical. The recurrence and repeated appearance of bleeding can be expected even after a thoroughly performed resection.

Among acute gastrointestinal bleedings, those of an unknown aetiology are also currently the most problematic. The use of up-to-date diagnostic procedures (like oesophago-gastro-duodenoscopy, colonoscopy, angiography) has considerably improved the ration of detecting the source of bleeding. The rate of gastrointestinal bleedings of unknown aetiology has decreased from 10–20% to some per cent [5a, b, 9]. It is essential that among bleedings of unknown origin, the gastrointestinal angiodysplasia (a.d.) is being increasingly diagnosed.

The aetiology of gastrointestinal a.d. is unknown. Similarly obscure is the aetiology of bleeding in a.d. It is undisputable that more and more information is available as a result of the clinicians increasing attention, and the increasing number of cases due to the improvement of diagnostic procedures. This latter statement applies basically to mesenteric angiography [6].

The first angiographic detection of colonic a.d. is linked with the name of Margulis [13], while selective angiography for the detection of bleeding deriving from a.d. to those of Baum [4] and Boley [5a, b]. These observations contributed to gastrointestinal a.d. having become the focus of interest in detecting the cause of gastrointestinal bleedings.

It is to be noted that in earlier years, a.d. was described mainly in the stomach and the small intestine. Recently, however, mainly a.d. of the caecum and the ascending colon has been reported [5a, b, 7, 9, 20].

Material and Method

The patient material was observed at the Clinic of Surgery, Semmelweis University School of Medicine between January 1, 1985 and 31 December, 1988. During this period the a.d. of 8 patients was detected. The a.d. of Patient 4 due to a massive gastrointestinal bleeding was detected only at autopsy.

The patients' mean age was 55 years (Table 1). In contrast with literary data, diverticula as associated diseases did not occur in our patients. In one patient aortic stenosis was detected. Three patients were found to show the symptoms of obliterative arteriosclerosis.

All a.d. patients were treated for gastrointestinal bleeding, being of different extent. The histories of bleeding ranged from some weeks up to a period of 5 years. In this latter patient operations had not earlier been made due to advanced age and cerebral vascular events. Upper panendoscopy, coloscopy, essentially without establishing a diagnosis were performed without exception in all a.d. patients. The patients were found to have gastrointestinal bleeding of unknown origin. Consequently, their treatment was prolonged and the blood requirement was considerable. The data in Table 1 are only estimates, based on retrospective processing. It can be rightfully presumed that the actual blood requirement exceeded the estimated value.

Concerning diagnosis, it can be stated that in our cases angiography led to diagnosis, with the exception of the female patient, aged 66, whose a.d. was unanimously verified only at autopsy. In Case 4 no angiography was made at all.

In concert with literary data, it occurred also in our material that only one a.d. was detected by the first angiography and the second angiography

TABLE I
The clinical characteristics

No.	Name	Age (years)	Sex	Site of a.d.	Occlusive vascular disease
1.	M.B.	66	female	desc. colon	aort. sten.
2.	Zs.J.	60	male	desc. colon	—
3.	K.J.	41	male	fl. lienalis	—
4.	T.J.	66	female	stomach	art. scl. o.
5.	M.F.	17	male	fl. lienalis	—
6.	K.M.	61	male	caecum	art. scl. o.
7.	J.K.	74	female	caecum, jejunum	art. scl. o.
8.	F.K.	40	female	asc. colon	—

performed due to recurring bleeding resulted in the detection of jejunal a.d. This patient is also discussed in detail for the conclusion to be drawn from her case.

J.K., female patient, aged 74, was treated at the 4th Department of Medicine, Janos Hospital. The history of her disease started in 1983 by the first less frequent, then increasingly intensive gastrointestinal bleeding, the cause of which could be revealed not even by detailed examinations, endoscopic and roentgenological studies. In 1986 she had a cerebrovascular episode associated with hemiplegia. Consequently, the planned laparotomy was not made. Gastrointestinal bleeding became more and more frequent. It is to be noted that the bleedings, although producing very severe anaemia requiring a blood replacement of considerable amount, did not cause circulatory failure or shock. In October 1988, she repeatedly became anaemic. At the 4th Department of Medicine, Janos Hospital, mesenteric angiography was indicated for detection of the source of bleeding. The examination was carried out at the X-ray Diagnostic Laboratory of the National Institute of Vascular Surgery (Dr. Simonfy).

During mesenteric angiography, in the region of the ileocolic artery, in a 5 cm region corresponding to the caecum, more intensive filling, and an irregular vascular structure were noted with the extravasation of the contrast medium (Fig. 1).

Following angiography, operation was indicated. During X-ray the a.d. and the mobilized caecum were well discernible, moreover blood was also observable in the lumen of the caecum. Right hemicolectomy was performed (Dr. Jakab). Scrutinizing the abdominal cavity, the stomach and the small intestine centimetre by centimetre, the X-ray did not reveal any change, there was no evidence of a.d.

On the preparation the ileocolic artery was cannulated and then methylene blue followed by contrast medium were injected: in the opened caecum, in a region, the size of a child's palm, the intensive permanent blue colour indicated the region of a.d. (Fig. 2). An angiogram was made of the preparation filled with contrast medium: the irregular submucous vascular structure was strikingly evident (Fig. 3).

Histological study of this region showed abnormally dilated vessels, veins and arterioles in the sections prepared from the blue-stained regions. The dilatation of the vessels could decisively be noted in the submucosa, in some regions, however, also in the mucosa. A thicker vascular lumen was noted protruding into the muscular layer.

The recovered patient discharged from hospital was brought by ambulance after one month to our department because of gastrointestinal bleeding. After blood replacement, urgent angiography was made. A new angiodysplasia was detected in the jejunum. At our request, the Seldinger catheter was left there, moreover, being pushed a little forward, the catheter sort of "pointing" to the 3 cm a.d.

of gastrointestinal a.d.

Predisposing factor	Nature, content of bleeding	Estimated blood requirement (litre)	Diagnostic procedure	Outcome
hepatic cirrhosis	recurrent for 1 year	14	angiography	+
alcoholic heapatop.	recurrent for more years	17	angiography	recovered
factor VII deficiency	15 months	5	angiography	recovered
hepatic cirrhosis	2 months	7	diagnosed at autopsy	+
—	acute	4.5	angiography	recovered
—	4 months	11	angiography	recovered
	5 years	8	repeat agniography	recovered
hepatic cirrhosis	2 years	3	laparotomy	+

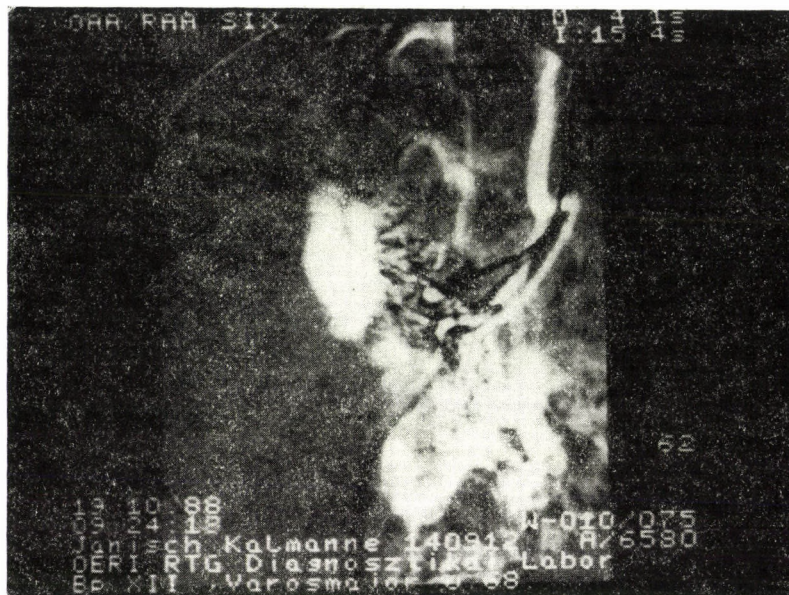


FIG. 1. Angiography of the superior mesenteric artery: in the region corresponding to the caecum, the end-branches of the ileocolic artery show a submucous irregular vascular pattern with a more intensive filling than the environment. Extravasation: contrast medium has entered the lumen of the caecum



FIG. 2. Blue-stained region, the size of a child's palm in the caecum. After filling with methylene blue (via the ileocolic artery)

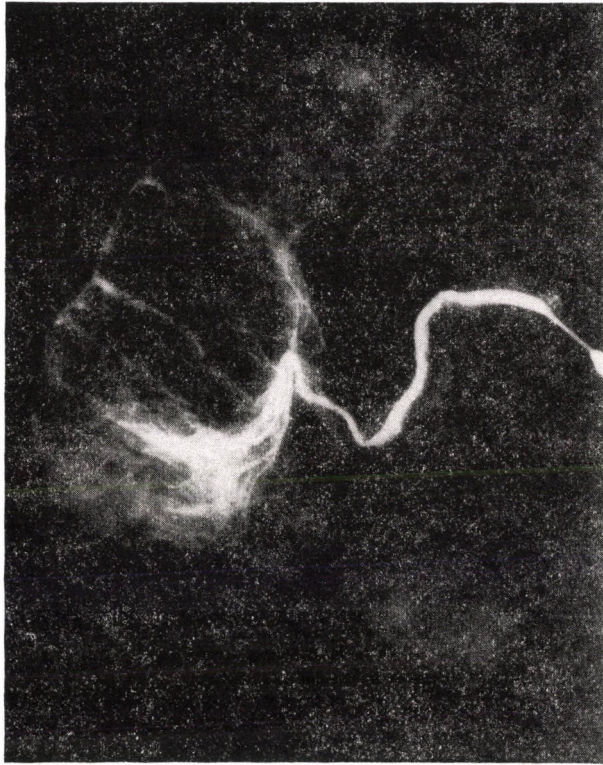


FIG. 3. Injection of contrast medium (UROMIRO) into the cannula introduced into the ileocolic artery. The picture of submucous a.d.

During operation indigo carmine was injected via the well palpable catheter, which stained permanently and segmentally the region of a.d., which was resected (Dr. Jakab) (Fig. 4).

Since the operation the patient has been free of complaints, her bleeding did not recur, she is under regular control.

A brief description of Patient 8 in Table 1, whose a.d. was detected after laparotomy is given below:

The 40-year-old female patient was admitted to our clinic due to massive gastrointestinal bleeding. During her previous check-ups hepatic cirrhosis had been verified also by liver biopsy due to her alcohol-dependence having persisted for 20 years, and varicosity of the oesophagus of 4th degree developed in the lower third of the oesophagus. Ensuring of a central vein then, anti-shock therapy were started in the patient being in a state preceding shock on admission. During the urgent oesophago-gastro-duodenoscopy, the bleeding was found not to be due to the rupture of oesophageal varices, therefore urgent colonoscopy was performed. As a result of the massive bleeding, the only diagnostic finding was that the source of bleeding was in the caecum. Based on vital indication, laparotomy was made: on the free surface of the caecum along the tenia libera, a vascular glomus, similar to spider's leg, the size of a infant's palm, was found the vascular dilatation in the middle of which could be emptied by pressure towards the lumen of the caecum. Right hemicolectomy was performed.

In the postoperative phase the patient's bleeding stopped, then, however, gradually hepatic failure developed and the patient was lost on the 5th postoperative day.



FIG. 4. A region stained with permanent blue indicates the jejunal a.d. Intravital intra-operative staining with indigo carmine. Injection into the Seldinger catheter retained in the femoral artery

Histology verified a.d., at autopsy no other a.d. was noted in the gastrointestinal region. There was unambiguous evidence of cirrhosis and portal hypertension, the oesophageal varices did not rupture.

During angiographies the most general finding was a serpiginous, submucous vascular network and draining vein. In three patients an irregular submucous vascular structure and tortuous vessels could be detected, with the extravasation of and entering of contrast medium in the form of "pools" into the intestine.

a.d.-s were found to be present in 7 patients in the colon, in one patient in the stomach. The previously reviewed patient had a.d. of the colon in addition to that in the jejunum (Table 2). In 6 patients one or two, in one patient several and in another patient 7 a.d.-s were observed. Following angiography, acute interventions were made in 3 patients, 4 patients were subjected to elective operation. During the operation the pathological vascular structure could be detected by X-ray, while in one patient it could be visualized by intraoperative staining. The interventions are shown in Table 3.

In one patient the ileocolic artery was cannulated then both stained and filled with contrast medium in her removed right colon.

Three of the eight patients were lost. This mortality rate was due to massive gastrointestinal bleeding and hepatic cirrhosis observed in all three patients.

TABLE 2
The clinical characteristics of gastrointestinal a.d.

<i>Localization</i>	
stomach	1
jejunum	1*
right colon	3*
flexura lienalis descendens colon	4
* a.d. occurred in one patient in the caecum and jejunum	
<i>No. of a.d.-s</i>	
1-5	6
6-10	1
over 10	1
<i>The size of a.d.-s</i>	
1-5 mm	3
6-10 mm	1
over 10 mm	4

TABLE 3
The treatment of a.d.

<i>Operation</i>	Acute: 3 Elective: 4
Right hemicolectomy	3
Left hemicolectomy	4
Ileal resection	1
<i>Complications</i>	
Subphrenic abscess	1
Wound suppuration	1
Respiratory failure	3
Recurrent bleeding	4
Secondary bleeding	2

Of the complications, respiratory insufficiency and the frequency of recurrent bleeding should be mentioned (Table 3).

In two patients secondary bleeding started in the postoperative period, the unambiguous cause of which could not be established. The secondary bleedings stopped in response to conservative treatment. In four patients repeated bleeding occurred, in one of them an additional angiodysplasia was found to be the cause, in another the factor-deficient state could be made responsible. The cause of the remaining two cases of recurrent bleeding could not be unanimously clarified.

Discussion

The arteriovenous malformations of the gastrointestinal tract were described in detail by Gentry (cit. De Diego [6]). Based on his angiographic studies and experience, a classification being also currently used was suggested by Moore [15] including the angiographic appearance, localization of a.d., age, moreover family history as well:

Type 1: Usually one a.d. on the right side of the colon in a patient of about 55 years.

Type 2: Visible small intestinal a.d. presumably of congenital origin, in a patient younger than 50 years.

Type 3: Multiple localization is associated with Rendu-Osler-Weber's syndrome (hereditary haemorrhagic telangiectasia).

According to Boley [5b], the degenerative vascular changes of the gastrointestinal tract, called by him the vascular dilatations of the gastrointestinal tract, correspond to Type 1 a.d. of Moore.

There are two theories concerning the development of a.d. According to Boley's hypothesis [5a, b], due to the repeated—intermittent—stenosis of submucous veins during muscle contraction and distensions, veins dilate and become tortuous. After some time minor small arteriovenous connections develop as a result of the loss of precapillary sphincter function (Fig. 5).

Others, however, assume that, due to intraluminal increase of pressure, ischaemia develops and this would lead to the development of the submucous arteriovenous fistula [4]. Greenstein [7], on the contrary, believes that the thinness of the right colonic wall promotes the development of a.d. [15]. This theory would explain the more and more frequent observation that the stenosis of the aortic valve is often associated with a.d. of the colon. The *pulsus parvus et tardus* in aortic stenosis affects the caecum which is supplied by the most distal branches of the superior mesenteric artery, as end-arteries by reduced perfusion pressure and the consequential mesenteric ischaemia [2, 3, 10, 11] also the occlusive arterial diseases are very frequently associated with a.d. [10, 11]. According to Boley [5b] and Groff [9], there is no logical, significant connection between the two diseases.

According to some observations, in chronic renal impairment and haemodialysis, a.d. is more likely to occur [5b]. a.d. associated with coagulopathy and thrombocytopathy has also been described, however, coagulopathy should rather be regarded as the consequence of prolonged bleeding and a risk factor [14, 20].

In our practice, although in a small number of patients, there was a strikingly more frequent occurrence of a.d. associated with liver cirrhosis. Portal hypertension promotes the possibility of development of arteriovenous

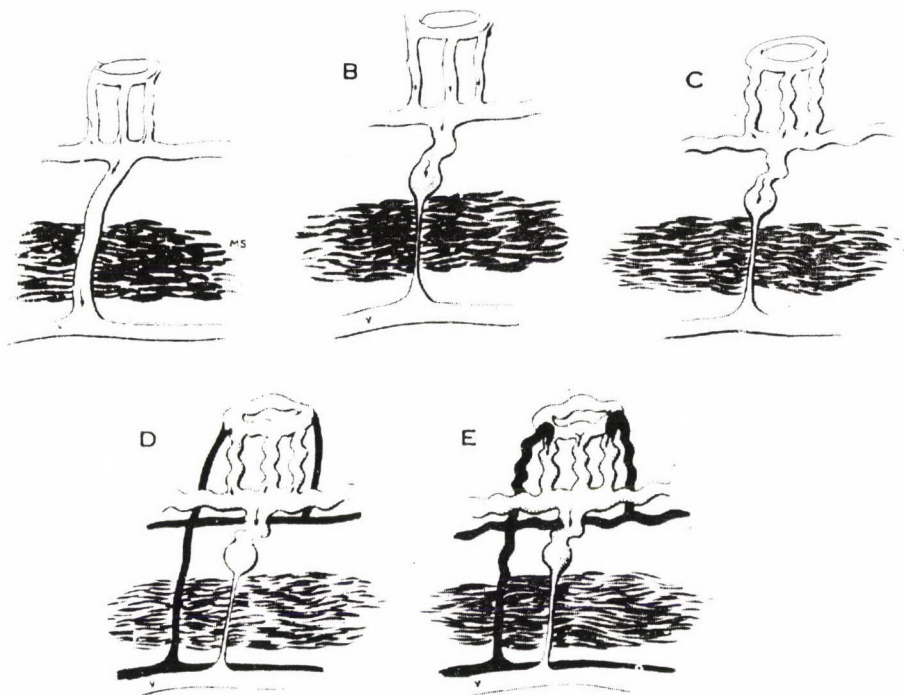


FIG. 5. Mechanism of development of a.d. (after Boley [5a]). A: normal state; B: compression of the efferent vein; C: submucous venous dilatation; D: onset of arteriovenous communication; E: submucous angiodysplasia with the loss of precapillary sphincter function

connections. This observation should be stressed because it is known that a.d. with diagnosed liver cirrhosis will be the least thought of by the physician as the source of bleeding. Therefore, we believe that with a known liver cirrhosis, if the oesophageal varices do not bleed and there is a negative coloscopic finding, angiography is indicated in haemorrhage.

The diagnosis of a.d. is largely based on angiography. Doubtlessly, there are several reports on the value of colonoscopy both in diagnosis as well as therapy with the use of electrocoagulation [10, 11, 12, 16, 17, 19]. It is generally believed that electrocoagulation is the treatment of choice for smaller than 1 cm changes. The larger a.d. should be cured by surgery.

As far as operation is concerned, it should be stressed that a.d. cannot be seen in the majority of cases, not even by X-ray. For a safer detection in our own case, the Seldinger catheter was retained after angiography during the operation. The angiodysplastic segment made visible by intravital staining could be easily removed.

The suggested intervention is by all means resection. The arterial injection with contrast medium of removed intestinal segment may reassuringly

clarify the submucous localization, moreover may provide clues to the accurate site of the histological section [1, 4, 5a, b, 18].

According to Meyer [14], following resection, recurrent bleeding can be reckoned with even with a positive angiographic or histological finding. This may be due to:

1. incomplete removal of a.d.;
2. that a second or additional a.d. was not detected by the preoperative mesenteric angiography and thus not removed by the operation;
3. that there was a new a.d. formation postoperatively.

Unfortunately, in cases associated with recurrent bleeding, the possibility may remain that the cause of bleeding has not been eliminated with 100% safety by angiography or surgery.

The following conclusions offered by our patient material can be drawn:

It seems that a.d. is more and more frequently diagnosed among gastrointestinal bleedings of an obscure aetiology.

a.d. is in an overwhelming majority the disease of an advanced age group age, localized most often in the colon (caecum and flexura lienalis coli). According to our observation it is mainly associated with liver cirrhosis and aortic stenosis.

The clinical picture is characterized by recurrent gastrointestinal bleeding of an unknown cause and origin. History ranges from a period of months to one even of years. Blood requirement is considerable. Although of a considerable degree, the bleedings do not give rise to circulatory failure or shock.

Angiography is the basic procedure for diagnosis.

The treatment of a.d. is by surgery, with resection being the accepted method of choice. In multiple a.d., multiple segmental resection should be considered.

The postoperative filling of the removed intestinal segment via the supplying artery is necessary, partly for proving the removal of a.d. and partly for selecting the site of histology.

Finally, the analysis of a patient material suffering from a.d. may call attention to an alertness by the physician, to the selection of the right diagnostic method in case of a gastrointestinal bleeding of unknown origin, the aim of which is to improve the results and to minimize the number of bleeding of unknown origin.

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References

1. Aldabagh SM, Trijillo YP, Taxy JB: Utility of specimen angiography in angiodysplasia of the colon. *Gastroenterology* 91:725–729, 1986
2. Balázs M, Szám I: Aortic stenosis, angiodysplasia of the caecum. *Acta Hepato-Gastroenterol* 26:508–512, 1979
3. Balázs M, Szám I, Büky P: Stenosis aortae-angiodysplasia coeci. *Orv Hetil* 121:287–289, 1980
4. Baum SMH, Nusbaum WS, Blakemore AK, Finkelstein AK: The preoperative radiographic demonstration of intraabdominal bleeding from undetermined sites by percutaneous selective celiac and superior Surgery 58:797–805, 1986
- 5a Boley SJ, Sammartano RJ, Adams A, Di Base S, Kleinhaus S, Sprayregen S: On the nature and etiology of vascular ectasias of the colon, degenerative lesions of aging. *Gastroenterology* 72:650–660, 1977
- 5b Boley SJ, Sammartano R, Brandt LJ, Sprayregen S: Vascular ectasias of the colon. *Surg Gynecol Obstet* 148:353–359, 1979
6. De Diego JA, Molina LM, Diez M, Delgado I, Moreno A, Solana M, Picardo 'A, Garrido R, Balibrea JL: Intestinal angiodysplasia: retrospective study of 18 cases. *Hepato-Gastroenterol* 35:255–259, 1988
7. Greenstein RJA, McElhinney D, Reuben D, Greenstein AJ: Colonic vascular ectasias and aortic stenosis: Coincidence or casual relationship? *Am J Surg* 151:347–351, 1986
8. Greiner JF, Gillet M, Dauchel J, Weil-Bousson M, Sava G, Camelot G, Marescaux Chovráth G: A propos d'un cas de telangiectasies colo-rectales diffuses. *Chirurgie* 103:747–759, 1977
9. Groff WL: Angiodysplasia of the colon. *Dis Colon and Rectum* 26:64–67, 1983
10. Heer M, Amman R, Bühler H: Die Klinische Bedeutung der Angiodysplasien im Kolon Schweiz Med Wochenschr 114:1416–1422, 1984
11. Heer M, Sulser H, Hany A: Angiodysplasia of the colon. An expression of occlusive vascular disease. *Hepato-Gastroenterol* 34:127–131, 1987
12. Howard OM, Buchanan JD, Hunt RH: Angiodysplasia of the colon. Experience of 26 cases. *Lancet* 16–19:2/8288, 1982
13. Margulis AR, Heinbecker P, Bernhardt R: Operative mesenteric arteriography in the search for the site of bleeding unexplained gastrointestinal hemorrhage. *Surgery* 48:534–539, 1960
14. Meyer TC, Troncale FJ, Galloway S, Sheanan D: Arteriovenous malformations of the bowel. An analysis of 22 cases and a review of the literature. *Medicine* 60:36–48, 1981
15. Moore JS, Thompson HW, Appelman HD, Foley D: Arteriovenous malformations of the gastrointestinal tract. *Arch Surg* 111:381–389, 1976
16. Niv Y, Bat L, Shemesh E, Wolfstein I: Bleeding of the angiodysplasia. *Isr J Med* 23:259, 1987
17. Ottenjann R, Weingart J, Kühner W, Frimberger E: Kolorektale Angiodysplasien (Vasculare Ektasien) Dtsch Med Wochenschr 109:1549–1552, 1984
18. Pounder ADJ, Rowland R, Pieterse AA: Angiodysplasias of the colon. *J Clin Pathol* 35:824–829, 1982
19. Stamm B, Heer M, Bühler H, Amman R: Mucosal biopsy of vascular ectasia (angiodysplasia) of the large bowel detected during routine colonoscopic examination. *Histopathology* 9:639–646, 1985
20. Smith G, Ellyson JH, Parks SN, Michols JG, Peters RS, Williams J, Bezmalinovic Z: Angiodysplasia of the colon. A review of 17 cases. *Arch Surg* 119:532–536, 1984

Gastrointestinale Angiodysplasie

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Im Verlauf der letzten vier Jahre wurde in 8 Fällen Nahrungskanal-Angiodysplasie beobachtet. Anhand der Analyse des Krankheitsverlaufes wird darauf hingewiesen, daß die Angiodysplasie unter Umständen auch eine Ursache einer unbekannten Nahrungskanalblutung sein kann. Die Angiodysplasie kann grundlegend mittels Angiographie diagnostiziert werden. Zur Grundkrankheit gesellt sich häufig Leberzirrhose oder Arterio-

stenose. Die Angiodysplasie erfordert eine chirurgische Behandlung. Mit dem Auftreten einer erneuten Angiodysplasie und mit einer erneuten Blutung kann auch nach einer unsichtig durchgeführten Resektion gerechnet werden.

Гастроинтестинальная ангиодисплазия

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За последние 4 года авторы наблюдали 8 случаев ангиодисплазии пищеварительного тракта. После анализа протекания этой патологии у больных они пришли к выводу, что причиной ангиодисплазии может быть неизвестное кровотечение в пищеварительном тракте. диагностировать ангиодисплазию можно главным образом с помощью ангиографии. Лечение заболевания хирургическое. Даже после тщательно выполненной резекции ангиодисплазия и кровотечение могут возникнуть заново.

Percutaneous Cholecysto-Lithotripsy

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Experience with the first 40 cases of percutaneous transhepatic cholecysto-lithotripsy in Hungary are reported. The indications and contraindications, results and complications of endoscopic gallstone removal performed with good results are analysed. The follow-up of patients after PTCL is considered important.

Cholecystectomy has been the dominant method of removing gallstones for decades. This exclusively surgical activity has been begun to be replaced by non-surgical methods like endoscopic lithotripsy [8–10, 12, 15, 26], extracorporeal shockwave lithotripsy [6, 13, 16–20] and local dissolution of gallstones [1, 13, 16–20]. There are two types of endoscopic percutaneous method, such as transhepatic [5, 12, 26] and subhepatic [2, 8, 9] penetration.

Patients and Method

In the period between October 11, 1989 and March 5, 1990, percutaneous gallstone removal was performed in 40 cholelithiatic patients. Of the patients 8 were men and 32 women. The youngest was 33, the oldest 70 years old, the mean age being 49 years. In 38 cases, the percutaneous channel was further introduced transhepatically into the gallbladder, while in two, the endoscope was directly introduced into the gallbladder, subhepatically. The technical performance of this intervention has been reported earlier [24]. We have acquired our practical skills during the removal of 2300 lithotripsies [22, 23].

Results

Thirty-nine patients had a history of some “cholecystitic” complaints, like a spastic pain under the right costal arch, or a blunt, uncertain abdominal pain and loss of appetite. Two patients had earlier been icteric, this having no laboratory evidence by the operation. One patient had a silent stone,

after the accidental detection of which she insisted on its being removed. In diagnosis, ultrasonography played the main role. In all 40 cases gallbladder stones were detected by ultrasonography. Thirteen gallbladders appeared to be closed by ultrasound and isotope studies (HIDA) as well as x-ray (oral cholecystography). In two of these cases preoperative diagnosis was empyema, which proved to be a false finding on intervention. Six preoperatively closed gallbladders were capable of good filling after endoscopic lithotripsy and stone removal. In judging the stones, no false-negative case occurred. Diagnostic ultrasonography can be applied with benefit in the puncture of the gallbladder. In cases where oral cholecystography revealed a well-filling gallbladder, direct puncture was performed following it on the image amplified monitor, omitting ultrasound guidance.

The gallbladder of all 40 patients could be penetrated. Comparing with the kidney, the wall of the gallbladder is more flexible, the whole organ is more mobile. This, however, did not cause major difficulties.

Among the stones, there were solitary ones, 1 cm in diameter, which were removed as a whole, there were large stones, which were crushed by ultrasound lithotripter (Storz), and the small pieces were removed partly by suction and partly by mechanical forceps. The gallbladder containing several hundreds of small stones was lavaged with isotonic sodium solution and so the concretions were washed out of them. Most stones were crushed mechanically and their pieces taken out one after the other. All stones could be removed.

	♂	♀	Σ
As a whole	1	3	4
Mechanical crushing	5	13	18
US lithotripsy	2	15	17
Total	8	31	39

A piece of stone, 5 mm in diameter, remained in one patient. Four patient had biliary colic after stone removal and one of them subicterus which stopped spontaneously. Results of histology of the biopsy taken from the mucosa of the gallbladder (39 cases):

1. Chronic fibrous cholecystitis	17 cases
2. Chronic ulcerative fibrous cholecystitis	2 cases
3. Chronic catarrhal cholecystitis	12 cases
4. Cholesterosis, chronic cholecystitis	3 cases
5. Fibrosis of the muscular tunic of the gallbladder	1 case

- | | |
|---|---------|
| 6. Absence of connective + muscle tissue epithelium and gland. The gallbladder was filled with "white" bile | 1 case |
| 7. Intact gallbladder mucosa | 1 case |
| 8. No biopsy was made | 2 cases |

Results of bile bacterium cultures removed by suction on puncture of the gallbladder:

No bacterium was cultured	35 cases
<i>E. coli</i>	2 cases
<i>Klebsiella</i>	2 cases
<i>Proteus mirabilis</i>	1 case

Change of laboratory blood tests due to percutaneous stone removal:

	Unchanged	Elevated
Leukocyte count	27	13
Erythrocyte sed. r.	28	12
Se biru	34	6
SGOT	38	2
SGPT	37	3
ALP	37	3
Se diast	40	—

Except for one case, the elevated values normalized within three weeks.

According to their chemical composition the stones included 27 cholesterin, 10 mixed cholesterin + bilirubin and 3 bilirubin + calcium calculi.

The average time of care from the day of stone removal was 6 days. The shortest postoperative hospitalization was 2 days, while the longest 15 days.

After stone removal elevation of temperature was observed in 6 patients, which stopped within days in protection of antibiotic administration. All patients were given antibiotics and Klion. Our patients were already walking on the first day after the intervention, they felt no pain at all. The drain introduced in front of the hepatic duct and the gallbladder orifice was removed on the 2nd postoperative day. Bile leakage was not observed in either of the cases. In two patients the gallbladder was drained, in these cases the drains had to be retained for a longer time and bile leakage was noted even one or two days after their removal, which ceased spontaneously.

The percutaneous site of penetration emptied discharge in one patient after some months. This was due to the erosion of the 10th rib, which was excochleated in another institute and small stone fragments were found in the simultaneously removed pericholecystitic gallbladder.

There was no severe complication.

Late results, like the experience with stone recurrence, recurrent complaints, repeated intervention and close follow-up can only be reported later.

PTCL is indicated in gallstones producing complaints if there is no contraindication. Silent gallstones are removed only if the patient is psychically disturbed by the awareness of having stones.

Contraindications:

Coagulation disorders

Internal liver diseases

Decompensated cardiac failure or metabolic disorders

Non-functioning cirrhotic gallbladder stone

Gallstone + cystic duct obstructing stone

Gallstone + choledochous duct stone

Gallstone + pancreatitis.

The smaller the stone, the shorter is the duration of removal (the shortest time was 10 minutes), and the more uneventful is postoperative convalescence.

The advantage of endoscopic percutaneous gallstone removal over explorative cholecystectomy is that stone removal incurs a lesser strain to the patients, after the intervention, they have no pain, the possibility of a wound healing disorder is minimal, there is no great scar as the one after explorative cholecystectomy, and no paraesthesia or weakness of the abdominal wall as neither herniation. The difficulties of reoperations after cholecystectomies and late operations cannot be compared with the advantage of PTCL, which can be performed several times without any special risk.

The advantage of endoscopic lithotripsy is proved by our three patients whose kidney and gallstones were removed by the percutaneous method within a week. Five days after kidney stone removal their gallbladder stones were also removed and they could be discharged after 5 days from our department. Two weeks later they were capable of work.

Discussion

The pioneers of percutaneous gallstone removal were the radiologists [8, 10], urologists [8, 26], surgeons [12, 26] in western countries, while general physicians in Japan [7]. It should be stressed that only those with a good command of bile surgery should enter upon the task of performing PTCL. Namely, it may occur that a complication develops during endoscopic operation which is immediately to be solved by exposure.

No severe complications were observed in the literature similar to our own practice.

No drainage is applied by Wenk [26] after the intervention. In our opinion, the drain introduced in front of the hepatic duct does not hinder recovery, however, it increases safety. The small amount of irrigating solution which up to the following day is leaking to the collecting sac, does not irritate the peritoneum but is designed for the good of the patient.

The exact indications have still not been clarified. There are authors in the international literature, who applied gallstone removal only in poor-risk cases [8, 10, 12]. In our opinion, percutaneous transhepatic cholecysto-lithotripsy can be applied for the stone removal of gallbladder containing bile and causing complaints regardless of age.

Those performing percutaneous subhepatic cholecysto-lithotripsy enter the gallbladder through the free abdominal cavity, via the fundus of the gallbladder [2, 8, 9]. We consider the transhepatic route via the liver bed of the gallbladder safer. This duct closes namely almost immediately after removal of the endoscope, and so there will be no bile leakage. Some surgeons seal the transhepatic duct [26] with a fibrin foam plug, which, in our opinion, is not necessary. True to say, there were no complications even after two accidental subhepatic penetrations, it is still better if the way of the bile is immediately blocked due to the flexibility of the hepatic tissue. This is an important point primarily in case of infected bile.

It is considered important to follow up patients postoperatively. In the case of cholesterol stones taking of chenodeoxycholic acid and ursodeoxycholic acid is recommended for prevention. After stone removal, the patients are followed up for 2–4 weeks (physical, US, laboratory), then they are controlled yearly. The recurrence of stone and the much debated question, whether accumulation of colorectal carcinomas following cholecystectomy [3, 4, 11, 14, 21, 25] can be observed after endoscopic gallstone removal (retained gallbladder) or not, can be answered only after some years.

Endoscopic gallstone removal is an important alternative therapy for gallbladder disease. Its place besides cholecystectomy, percutaneous lithotripsy and ESWL will be decided only in the future.

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References

1. Ellen MJ et al: Rapid dissolution of gallstones by methyl-tert-butyl ether—preliminary observations. *N Engl J Med* 312:217–219, 1985
2. Cope C: Percutaneous subhepatic cholecystostomy with removable anchor
3. Csonka Cs et al: A cholecystectomy lehetséges szerepe a colorectalis rák keletkezésében. (The possible role of cholecystectomy in the development of colorectal cancer). *Orv Hetil* 128:773–777, 1987
4. Editorial: Large-bowel Cancer after Cholecystectomy. *Lancet* 11:562–563, 1981
5. Eggermout A M, Lameris JS, Jeckel J: Ultrasound guided percutaneous transhepatic cholecystostomy for acute acalculous cholecystitis-arch. *Surgery* 120:1354–1356, 1985
6. Hood AK et al: Piezo-ceramic lithotripsy of gallbladder stones: initial experience in 38 patients. *Lancet* 1:1322, 1988
7. Inui K et al: Percutaneous cholecystoscopy *Endoscopy* 21:261–364, 1989
8. Kellett MJ, Wickham JEA, Russell RCG: Percutaneous cholecystolithotomy. *Brit Med J* 296:453–455, 1988
9. Kellett MJ, Russel RCG, Wickham JEA: Percutaneous cholecystolithotomy. *Endoscopy* 21:365–366, 1989
10. Kerlan RK, La Berge JM, Ring EJ: Percutaneous cholecystolithotomy: preliminary experience. *Radiology* 157:653–656, 1985
11. Linos DA et al: Cholecystectomy and carcinoma of the colon. *Lancet* 11:379–383, 1981
12. Min-Huo Hwang et al: Percutaneous transhepatic cholecystic ultrasonic lithotripsy. *Gastrointestinal Endoscopy* 33:301–303, 1987
13. Paumgartner G, Sauerbrich T: Heutiger Stand von Litholyse und Lithotripsie von Gallensteinen. *Chirurg* 59:190–196, 1988
14. Peters H, Keimes AM: Die Cholezystektomie als predisponierender Faktor in der Genese des Kolorektalen Karzinoms? *Dtsch Med Wochenschr* 104:1581–1583, 1979
15. Picus D et al: Percutaneous cholecystolithotomy: preliminary experience and technical considerations. *Radiology* 173:487–491, 1989
16. Sauerbruch T et al: Fragmentation of gallstones by extracorporeal shock waves. *N Engl J Med* 314:818–822, 1986
17. Schmassmann A, Zuber M, Ritz R: MTBE-Litholyse und extrakorporelle Stosswellenlithotripsie von Gallenblasensteinen. *Schweiz Med Wochenschr* 118:1297–1303, 1988
18. Sonnenberg E, Hofmann AF: Hrison in Gallstone Therapy 1988. *AJR* 150:43–46, 1988
19. Sonnenberg E et al: Gallstone dissolution with methyl-tert-butyl ether via percutaneous cholecystostomy: success and careats. *AJR* 146:865–867, 1986
20. Thistle JL et al: Dissolution of cholesterol gallbladder stones. *N Engl J Med* 320: 633–639, 1989
21. Tóth A et al: Összefüggés a vastagbél-daganatok gyakorisága, localisatiója és az epékövesség között (Correlation between the frequency of colonie tumours, their localization and between gallstone disease). *Magy Seb* 38:21–25, 1985
22. Tóth Cs et al: Primer percutan nephrolithotomia (Primary percutaneous nephrolithotomy). *Orv Hetil* 126:587–588, 1985
23. Tóth Cs: Endoszkópos vesekősebészet (Endoscopic kidney stone surgery). *Medicina*, Budapest 1987
24. Tóth Cs et al: Percutan transhepaticus cholecysto-lithotripsia (Percutaneous transhepatic cholecystolithotripsy). *Orv Hetil* 1990 (in press)
25. Weitz H et al: Cholezystektomie, Cholelithiasis und Dickdarmkarzinom. *Dtsch Med Wochenschr* 108:53–57, 1983
26. Wenk H et al: Percutaneous transhepatic cholecysto-lithotripsy (PTCL). *Endoscopy* 21:221–222, 1989

Perkutane Gallensteinentfernung

CS. TÓTH

Berichtet wird über die im Zusammenhang mit den ersten 40 einheimischen Fällen der perkutanen transhepatischen Cholezysto-Lithotripsie ermittelten Erfahrungen. Analysiert werden die Indikationen Kontraindikationen, Ergebnisse, Komplikationen und Vorteile der erfolgreich durchgeführten endoskopischen Gallensteinentfernung. Die Wichtigkeit der follow-up-Untersuchungen nach der PTCL wird betont.

Чрескожное удаление желчных камней

Ч. ТОТ

Автор обобщает опыт, полученный в связи с лечением первых 40 отечественных случаев чрескожной транспепатической холоцистолитотрипсии. Анализирует показания и противопоказания, результаты, осложнения и преимущества удачно выполненных операций по эндоскопическому удалению желчных камней. Считает важным отдаленное наблюдение за больными, перенесшими чрескожную транспепатическую холецистолитотрипсию.

Rupture of the Splenic Artery Aneurysm During Pregnancy

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The report deals with the rupture of a splenic artery aneurysm during pregnancy by reviewing the pathological course of a patient. Then the pathomechanism and differential diagnosis are discussed concerning the aneurysm of the ruptured splenic artery. It is stressed that the chances of survival of the patient and the fetus depend considerably on early detection and the rapid intervention, this being also interrelated with maternal and fetal mortality.

Aneurysm of the splenic artery is a rare alteration. It is twice as frequent in women than in men, and about half of the changes observed in women of fertile age were ruptured during pregnancy [1].

The disease was first described by Beaussier in 1770 as the autopsy finding of an elderly woman [18]. Kabay reported the splenic artery aneurysm of a 29-year-old male patient due to mycotic embolism [11]. Pongrácz and Fodor operated a ruptured splenic artery aneurysm perforating into the stomach in 1957 [21]. Mátyus reviewed a case of splenic artery aneurysm perforated into the gastrointestinal tract in 1959 [15]. His report is of particular importance because he could report on a successful operation and complete recovery. In 1961, Vidonyi and Molnár diagnosed and successfully operated an aneurysm in a female patient, aged 47 years [24]. In 1975, Szabó and Dzsinič have also published a case of successful outcome [22]. This year, Szentmiklósi and Maráz described the rupture and successful operation of the splenic artery aneurysm perforated into the pancreas [23].

Hoegler was the first to diagnose the rupture of the splenic artery aneurysm with physical examination in 1920 [10], and Evans documented it with arteriography in 1950 [7].

Bochor was the first to report the rupture of the splenic artery aneurysm in the Hungarian literature [3]. However, the ruptured splenic artery aneurysm in pregnant women has first been mentioned in the Hungarian literature by Mayer, who described the tragically ending aneurysm rupture of a 27-year-old woman in labour [16]. Gergely reported the rupture of the splenic artery aneurysm of a 24-year-old woman in the 3rd trimester [8]. Maka et al. reviewed the rupture of the splenic artery aneurysm in pregnancy of a 23-year-old

patient being the first survivor reported on in the Hungarian literature. She had a spontaneous abortion on the 2nd day of operation [14]. The first, really successful and unique report was published by Habony and Karácsony [9]. In their case the lives of both the mother and the fetus were saved.

Case Report

Her history in brief: E.K.M. 27-year-old woman, pregnant for the third time, was transferred by the ambulance after preliminary notification, in the 34th week of her pregnancy into our department on November 5, 1988. She had a history of two vaginal deliveries, and no artificial or spontaneous abortion as neither any other operation. The pregnant patient felt ill on the bus in the 34th week of her pregnancy. Her complaints included dizziness, sweating, nausea and weakness. She went home, but since she felt worse, the ambulance was called.

State on admission: The patient's skin and sclera were strikingly pale, her lips cyanotic. On admission her systolic blood pressure was 60 mm, Hg, the diastolic could not be taken, with easily obliterated pulse being weak and quick. She complained about strong, colicky gastric pain, her consciousness was gradually clouding and after some minutes she was inaccessible. Her abdomen was soft and palpable, her uterus was found to have a normal tone, her fundus could be palpated 5 cm supraumbilically. Internal examination: closed cervical orifice, intact cervix, escape of amniotic fluid, vaginal bleeding could not be observed. Fetal heart sound: could not be heard from the minute of admission.

She had no symptoms indicating bleeding in the abdominal cavity, but her gynaecological state did not account for the bleeding.

The previously obtained blood was immediately introduced into the cubital veins of both arms, and in agreement with the surgeon, explorative laparotomy was decided upon.

Following a lower median incision and the opening of the peritoneum, a large amount of blood was found in the abdominal cavity. The uterus was not injured, the adnexa being intact. Since the pregnant uterus in the 34th week filled the abdominal cavity and so prevented the finding of the source of bleeding, cesarean section was performed and a dead male fetus of 2350 g was delivered. After closure of the uterus in one layer, a large amount of blood was found to empty from the direction of the left hypochondrium. The surgeon found the spleen and liver to be intact. The retroperitoneum was imbibed with blood in the visible region with a livid discolouration. There was a massive haemorrhage all along the lesser curvature of the stomach, as well as along the descending colon. The mesenterium was also haemorrhagic.

Opening the peritoneum beside the descending colon, a considerable amount of haematoma was noted. Then the patient's heart stopped. Reanimation was immediately started, but it remained unsuccessful. The source of bleeding could not be detected intraoperatively.

Forensic autopsy revealed the rupture of the splenic artery aneurysm.

Coming back to, and reconstructing the events, the aneurysm must have ruptured on the bus. The retroperitoneum might have served as a partial tamponade for the bleeding for some time. It ruptured later from the tension of the amount of blood, triggering possibly a circulatory collapse, followed by shock and finally the patient's death due to bleeding to death.

Discussion

The pathomechanism of the disease is still obscure. It can occur due to:

- Congenital defect: as a result of some congenital abnormality of the arterial wall, or possibly due to some trauma—at the site of the subsequent aneurysm—the resistance of the layers of the vascular wall weakens. This can be noted mainly at vascular branching [12].

- Arteriosclerosis: It occurred in 20% in the patient material of Owens and Coffey, but the splenic artery aneurysm during pregnancy must have occurred due to sclerosis having existed already prior to pregnancy [19].

- Mycotic embolization: it is not probable during pregnancy.

- Pregnancy: it is not proved to be the cause, but haemodilution, tachycardia, the elevation of abdominal pressure, the expansion of the pregnant uterus as well as hormonal changes all promote the formation of aneurysm(s).

- Less frequently, pancreatitis or some inflammatory dissection may give rise to the disease.

Differential diagnostically, it may essentially have two forms: The first group includes the still intact splenic artery aneurysms. The clinical picture can be disturbed by other complaints due to pregnancy and the increased uterus. These may comprise from blunt epigastric pain to vague abdominal complaints, vomiting, diarrhoea, pains under the right or left costal arch, lumbar pain and loss of weight. Liver extending below the costal arch with several centimetres and an enlarged spleen are also palpable. The symptoms also depend on the size of the aneurysm. The larger aneurysms e.g. one of 17 cm in diameter, are naturally associated with more explicit and circumscribable symptoms than those of some millimetres, even if there are more of them [5]. If their wall is calcified, they produce a density on the roentgenogram, but even this is not regular [6]. A ring-like pattern is seen corresponding

to the calcification. Those containing no calcium cannot be visualized in the X-ray only by angiography or they can be diagnosed intraoperatively.

Concerning its differential diagnosis, the symptoms of renal cyst, tumour of the adrenal gland, pancreatic cyst, aortic aneurysm, echinococcus cyst, moreover those of a splenic infarction due to an embolism from the aneurysm can be similar.

The other group is constituted by the already ruptured aneurysms. They are difficult to diagnose preoperatively, since, in view of the symptoms, we may tend to consider acute abdomen. Partial detachment of the placenta can present similar symptoms, with the dominant ones of shock, supplemented by an increasing abdominal pain—mainly in the left upper quadrant—sometimes with a negative obstetric state or, as in our case, with an uterus of normal tone and a fetus having died intrauterinely [9].

The aneurysm of the intact splenic artery is bound to escape detection for a long time. The vigorous symptoms of the ruptured aneurysm may facilitate recognition—if we think about it—even if it has not been diagnosed preoperatively, since the solution is unambiguous—surgical—consisting essentially in a rapid arresting of bleeding. Its early detection is of decisive importance, as also the replacement of volume as soon as possible and the elapsing of the shortest possible time between then onset of symptoms and exploration.

Rupture of the splenic artery aneurysm is a rare diseases. Rupture incurs an especially great risk during pregnancy. Of 61 patients, the splenic artery aneurysm of only one was recognized by McFarlane and Throbjarnarson [17]. Gestation is of prime importance concerning rupture. According to Owens and Coffey, 12% of cases ruptured in the first six months, 69% in the last trimester, 13% during labour and only 6% in puerperium [20]. According to some literary data, like Buchet et al., up to 1984, 66 ruptures of splenic artery aneurysms during pregnancy were reported [4]. According to others [9], 81, and reviewing the literature, Lowry et al., found 7 patients up to 1986, when the lives of both the mother and the fetus could be saved [13].

It is, however, quite sure that it is about a rare and dangerous clinical picture with an extremely poor prognosis during pregnancy. Maternal mortality can be estimated at 80%, while the fetal approximately at 92.5% [2].

By reviewing the course of disease of our patient, we would have liked to call attention to the severity of the disease.

References

1. Barwin BN: Aneurysm of the splenic artery. *J Ir Med Assoc* 67:67, 1974
2. Baum SE: Aneurysm of the splenic artery with rupture during pregnancy. *Am Osteopath Assoc* 71:851, 1972
3. Bochkor A: Elvérzés a lépverőér tágulatából (Bleeding to death from the distension of the splenic artery). *Orv Hetil* 72:536, 1928

4. Buchet C, Simon P, Bertrand J, Lansac J: Spontaneous rupture of an aneurysm of the splenic artery in pregnancy. Apropos of a new case. *Gynecol Obstet Biol Reprod (Paris)* 13(2):157–163, 1984
5. Carlise B, Lawler M: Aneurysm of the splenic artery. Report of ten cases. *Am J Surg* 114:443, 1967
6. Culver GJ, Pirson H: Splenic artery aneurysm, report of 17 cases showing calcification on plain roentgenograms. *Radiology* 68:217, 1957
7. Evans RM: Early symptom of malignant hypertension. *Lancet* 11:846, 1954
8. Gergely M: Elvérzés a lépverőér aneurysmájából terhesség alatt (Bleeding to death from the aneurysm of the splenic artery during pregnancy). *Magy Nőorv Lapja* 30:182, 1967
9. Habony P, Karácsony T: Artéria linealis aneurysma rupturájának sikerrel műtött esete kihordott terhesség mellett (The successfully operated case of the rupture of the splenic artery aneurysm with a term pregnancy). *Magy Nőorv Lapja* 46:46–48, 1983
10. Höglér F: Ein Fall von Aneurysma der Aorta abdominalis in der Gegend des Tripus Halleri mit Verhalkungsherden in der Wand. *Arch Inn Med* 1:543, 1920
11. Kabay L: Adatok az ún. spontán hasüregi vérzések klinikájához és patológiájához (Data on the clinical aspects and pathology of the so-called spontaneous bleedings of the abdominal cavity). *Orv Hetil* 45:1462, 1951
12. Leger L: Deux cas de dilatation congenitale des canaux biliaris intrahepatique associée à une cirrhose du foie et à des malformations diverses. *J. Chir* 77:1953, 1959
13. Lowry-O-Dea-Gallagher-Mozenter: Splenic artery aneurysm rupture: the seventh instance of maternal and fetal survival. *Obstet Gynecol* 67(2):291–292, 1986
14. Maka Pchtel Bukovszky: Az artéria lienalis aneurizma terhesség alatti rupturája (Rupture of the splenic artery aneurysm during pregnancy). *Orv Hetil* 120:24, 1452, 1979
15. Mátyus L: Gyomor-béltraktusba perforált (rupturált) artéria lienális aneurizma. (Ruptured splenic artery aneurysm perforating into the gastrointestinal tract). *Orv Hetil* 105:1759, 1964
16. Mayer E: Artéria lienalis aneurysmájából elvérzés szülés után (Bleeding to death from the aneurysm of the splenic artery after delivery). *Orv Hetil* 72:538, 1928
17. McFarlane J, Thornbjär-Narson B: Rupture of splenic artery aneurysm during pregnancy. *Am J Obstet Gynecol* 95:1025, 1966
18. Owens JC, Coffey RJ: Rupture of splenic artery aneurysm and the pregnancy. *Int Abstract Surg* 97:313, 1953
19. Owens JC, Coffey RJ: Rupture of splenic artery aneurysm and the pregnancy. *Int Abstract Surg* 97:313, 1953
20. Owens JC, Coffey GJ: Rupture of splenic artery aneurysm and the pregnancy. *Int Abstract Surg* 97:313, 1953
21. Pongrácz F, Fodor I: Gyomorba perforált artéria lienalis aneurysma ritka esete (A rare case of splenic artery aneurysm perforating into the stomach). *Orv Hetil* 46:1280, 1957
22. Szabó I, Dzsinih Cs: A lépartéria-aneurysma (The splenic artery aneurysm). *Orv Hetil* 116:690, 1975
23. Szentmiklósi L, Maráz F: Artéria lienalis aneurysma operált esete (An operated case of splenic artery aneurysm). *Magy Seb* 28:392, 1975
24. Vidonyi M, Molnár J: Artéria lienális aneurysma operált esete (An operated case of splenic artery aneurysm). *Orv Hetil* 101:742, 1961

Ruptur des Arteria linealis Aneurysmas im Laufe der Schwangerschaft

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Aufgrund des Krankheitsverlaufes eines Patienten findet die während der Schwangerschaft aufgetretene Ruptur des Milzarterien-Aneurysmas eine Besprechung. Nach der Falldarstellung werden Pathomechanismus und Differentialdiagnostik vom Standpunkt des intakten und rupturierten Milzarterien-Aneurysmas ausführlich analysiert. Es wird

betont, daß die Lebensaussichten der Patientin und der Frucht in bedeutendem Maße von der Früherkennung und dem frühen Eingriff abhängen und auch die mütterliche und fötale Mortalität der and dieser Krankheit leidenden Personen damit zusammenhängen kann.

Разрыв аневризмы селезеночной артерии во время беременности

Р. ХУНКА, Т. ЧОРДАШ и З. ДОМАНЬ

Настоящая статья занимается случаем разрыва аневризмы селезеночной артерии в период беременности на основании ознакомления с историей болезни одной пациентки. Вслед за описанием данного случая обсуждаются вопросы патомеханизма и дифференциальной диагностики разрыва аневризмы селезеночной артерии. Авторы подчеркивают, что выживание больной и плода в значительной степени зависят от ранней диагностики и быстрого вмешательства, материнская и плодовая смертность тоже может быть связана с этой патологией.

Virus-host Studies in Human Seminal and Mouse Testicular Cells

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Virological studies were performed for male infertility and repeated abortions. It was found that in about 40% of infertile males infectious adeno- or herpes simplex virus is present in the semen, while the same viruses are present in 60% of the cells in a latent form. In the aborted fetuses the same viruses could be observed as in the father's cells. Due to semen added to tissue cultures the latent presence also of other viruses could be supposed. The affinity of adeno- and herpes viruses to urogenital organs was confirmed by animal experiments, where a new method was applied for in vivo infection. The close correlation between viruses and urogenital cells was similarly confirmed by infecting in vitro human seminal and testicular cells with adeno- and herpes simplex viruses absorbed by the cells, entering them, moreover replicating in the form of their components. Based on the results, it was assumed that chronic local urogenital infections, due to various viruses, may play a role in male infertility and in a part of repeated abortions by damaging their cells. Applying a Zovirax therapy, the seminal cells were stopped to be viral carriers and normal function was restored.

The cause of male infertility and chronic inflammation of the prostate has still not been clarified. There are data that semen can be carrier of cytomegalo-, hepatitis B and HI viruses [1, 7, 8]. According to animal experiments, cytomegalovirus can be present in the sperm and testicular cells for a longer time [1, 11]. Based on these data, it was studied whether infertile men as well as husbands whose wives had repeatedly aborted, carry adeno- or herpes simplex viruses with an affinity to the urogenital organs in their sperms testicular cells. Our human studies were confirmed by animal experiments by using a new method for the local infection of the testis.

Patient Material, Experimental Animals, Methods

The sperms of a total of 73 men were studied. Of them, 39 were referred to andrological examination because of infertility. In 10 cases examination was made for the repeated abortions of the wife, the sperms of 9 healthy men were in vitro examined with viruses added by us. There were 15 healthy male controls. The aborted fetuses were examined in 5 cases.

In the animal experiments, 30 CFLP adult male mice were intraperitoneally infected with adeno- and herpes simplex viruses, then after one, three and seven days it was looked of whether viruses had localized in the urogenital organs. The virus was directly injected into the testes of additional 30 mice. Our method of inoculation is new because, according to literary evidence, testicles can be infected only after opening the abdominal cavity [1]. We did not open it, because the testis can be palpated well and fixed with an adequate manipulation and the injection can be performed with a low percent of error. On injecting the virus into one testicle, the other testicle of the animal remained intact and served as control. Twenty white mice of the same weight and age were also used as controls, they were not injected or only physiological saline was injected into the testes. In herpesvirus infection, the animals were sacrificed one, in the case of infection with adenovirus 19 (oculogenital type), three days after injection. After opening the abdominal cavity, the testicles were removed and used for study purposes.

Reculturing of viruses was attempted from both human sperms and the testicles of experimental animals in human amniotic and human fetal primary fibroblast cultures and in a HEp-2 cell line. 0.1 ml of the freshly obtained semen, as well as the supernatant of the scrapings of the infected testicular cells of mice were transferred to the cell cultures. Changes in the cell cultures were studied by light microscopy.

The substances from both humans and experimental animals were studied also for the presence of viral antigens by the method of Coons and Kaplan modified by us [3]. The examination was made by a Zeiss-Fluoval microscope by using a magnification of 600.

For verifying that there was a possibility of testicular infection even without opening the abdominal cavity, i.e. that one of the testicles could be isolated from infection, in addition to viral infections, the inoculation was also performed with India ink, since its localization can be observed well.

Results

Due to human sperms, changes indicative of the presence of a cytopathogenic agent appeared in one part of the cultures after some days. Since sperm is, to some extent, also toxic for cells, more passages were made in additional cell cultures. Finally, by elimination of the toxic effect, the cytopathic effect was perceptible. After several passages, of the 64 seminal specimens studied by culture for infertility and abortion, cytopathogenic agents were obtained in 38%, while in 20% of the controls. Identifying the new, unknown agents (viruses) with a virus-neutralizing method, the following was observed: in the sperms studied for infertility latent and oncogenic adeno-

viruses, herpes simplex and cytomegaloviruses were present in almost the same proportions. In the sperms examined for repeated abortions, except for one case, all viruses were present, occasionally even two kinds of them. In the cells of the aborted fetuses—both in the fetal as well as amniotic cells—the same virus was present as in the husband's sperm.

In the sperm of the control males, only herpes simplex virus was found in a lower percentage. Otherwise, some changes could be noted due to sperms in the cell cultures, which indicated the presence of papova, rubella, morbilli, varicellazoster, etc. viruses.

Examining the presence of viral antigens (latent virus carriers) by the immunofluorescent method, it was found that the latent carrying of adeno- and herpes viruses in the sperm was over 60%, which is a higher rate than the culturability of infectious viruses. All abortus specimens could be found to be virus carriers both in their fetal as well as placental cells. Figure 1 shows virus carrying spermatic cells. Note that, among the numerous, greenish cells showing only autofluorescence, there are some, the head of which fluoresces in a bright yellow colour, indicating the presence of specific viral proteins, specifically binding the antiviral antibodies conjugated to fluorescein-isothiocyanate.

Viral antigen carrying in the control sperms occurred only sporadically. The healthy human spermatic cell, which had been matched in vitro with adeno- and herpes viruses, showed the following immunofluorescent results: after an incubation of 5 hours and one day, all types of both the herpes, as well as of the adenoviruses reacted with the spermatic cells, moreover, with testicular cells as well. As a result, in the case of herpesvirus, viral antigens could be shown to be present in the head of the spermatic cells and in the testicular cells, indicated by a bright fluorescence. Due to these viruses, the majority of these spermatic cells were damaged, so fluorescence was notable only in 10% of the cells. Of the various types of adenoviruses, those of a latent nature came to be less absorbed by the spermatic cells, while the oncogenic ones, as well as the so-called oculogenital type (type 19) reacted more vigorously with the cells—not only with the head, but also with the entire length of the spermatic cells. Adenoviruses were less intensively absorbed by the testicular cells. Characteristically, the spermatic cells were not damaged by adenoviruses, as opposed to the effect of herpesviruses.

In the experimental animals inoculated intraperitoneally, the localization of viruses in the genitals could not be adequately evaluated.

Following local viral infection of mouse testicle, the immunofluorescent study revealed both herpes- and adenoviruses to be absorbed by testicular and spermatic cells. One part of them entered their cells moreover their protein components even replicated. This is confirmed by the negative results of the animals, as well as the contralateral uninoculated testicle of the same animal,

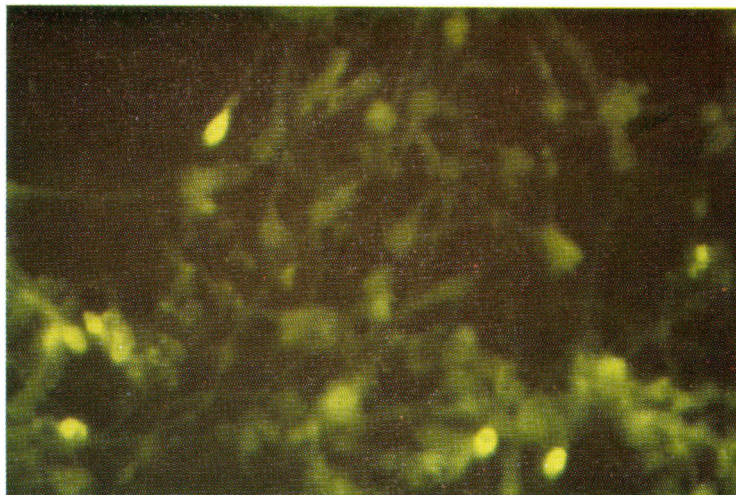


FIG. 1. There are some among the numerous greenish autofluorescent spermia the head of which fluoresces in a bright yellow colour, since they contain specific viral proteins which have bound the anti-viral antibodies conjugated with fluorescent stain

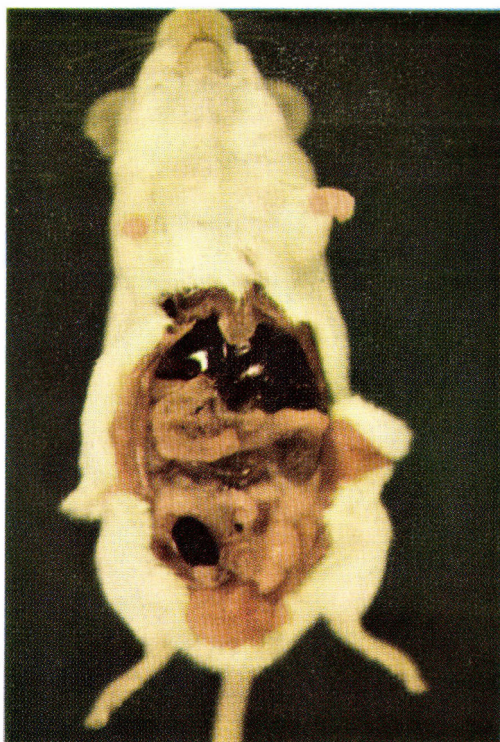


FIG. 2. One of the testicles of an animal inoculated in vivo by India ink and sacrificed after some days is full of India ink granules, but they did not pass on from there. The contralateral testicle is free of India ink

which also remained free of viral antigens. The fact, that the local infection of the testicle of one side remained isolated, was proved besides the studies, also by inoculation with India ink. This is shown in Fig. 2. It can be seen that the testicle of the animal sacrificed some days prior to in situ inoculation, is full India ink granules, but these granules could not pass on from it. The contralateral testicle is also free of India ink.

In addition attempts were made to culture viruses from the latent virus carrying testicular cells of the animals, however, no infectious viruses could be obtained. This allows the conclusion that genital infection with adeno- and herpesviruses does not generalize. It is capable of replicating as well as producing latent infection locally and in the surrounding tissue cells.

Discussion

The pathomechanism of a part of viral infections has still not been adequately clarified. Thus, it is known that if herpes simplex virus enters the organism through injured skin or mucosa, either in the oral or genital region, then the primary, manifested or latent, infection is often followed by recurrence. This is explained by the fact that at the site of entering, the virus multiplying in the epithelial cells, passes along the corresponding sensory nerve to the nerve cells, where it persists for a longer time, or for lifetime. Due to the environmental factors, or as a result of the changed internal milieu, the latent virus is activated and reaches the site of previous localization in the centrifugal direction. There it produces by multiplication the characteristic blistery changes. It is also known that if the fetus or the newborn is infected, then herpes sepsis develops with severe complications in most cases [10].

It is not known, however, what the further fate of herpesvirus will be, should it pass with semen or vaginal discharge into the genital organs of the partner. Based on the study of human materials as well as the results of animal experiments, in such cases the local, latent infection of the urogenital organs is produced by the virus. It may result in chronic prostatitis, orchitis, epididymitis, vaginitis, metritis, adnexitis, etc. According to our observations, the virus is not generalized, moreover infection may be localized to only one side. Such latently infected individuals may themselves be infecting sources for their partners. If the viruses damage the spermatogenic and testicular cells, the infection may also result in male infertility. Infertility can also occur by the formation of only a few or inadequately functioning spermatogenic cells due to the primary impairment of the testicular cells, as was verified also by animal experiments with cytomegaloviruses [1].

The importance of adenoviruses in the infection of the urogenital organs is not so well known because these viruses do not produce well perceptible

changes on the skin and mucosa. According to literary evidence, one type not infrequently infects the eyes and the urogenital organs at the same time [6]. Adenovirus has also been isolated in vaginal discharge [12], while one of the numerous human viruses is considered to be the pathogen of haemorrhagic cystitis [13]. It is also notable that successful culturing of adenoviruses was made from the urine of AIDS patients [4]. According to our earlier investigations, 6 to 8% of clinically symptom-free and colposcopically negative women may carry latent adenoviruses in their cervical cells, and almost the same ratio of symptom-free herpes simplex virus carrying was observed [10]. This symptom-free carrying of viruses in the genital organs may be of interest because they may potentially be oncogenic as well [2, 5, 9].

The affinity to urogenital organs of adeno- and herpes viruses and their participation in pathologic processes are supported also by our results according to which human semen can be in vitro infected with these viruses and this infection remains latent in the spermatic and testicular cells. Since there are increasing possibilities of getting infected with viruses, e.g. by frequent change of partners, their presence and role should be reckoned with considering their diagnosis and the adequate therapy used. Namely, according to our results, the viral infection of the urogenital organs can be one of the factors of male infertility and abortions. The importance of our studies also lies in the fact that after revealing the latent carrying of DNS-containing viruses, administering antiviral Zovirax treatment as well as immunostimulating Isoprinosin to the patients, the semen stopped to be a virus carrier and function was restored. In the long run, the stopping of the carrying of oncogenic viruses may perhaps even prevent the development of malignant diseases. It may also be an important issue that, beside adeno- and herpes viruses, changes indicating also the presence of other viruses in the tissue cultures due to spermatic cells may also appear. Namely, recently, it has been increasingly proved that several types of viruses in close correlation with each other may contribute to the development of malignant processes [5]. Therefore, we believe that the viral infection of urogenital organs, and its importance require further investigation.

References

1. Basker JF, Stanat SC, Eng-Shang Huang: Cytomegalovirus infection of murine testicular interstitial Leydig cell. *Infect Immunol* 40:726, 1983
2. Bernards R, Sehrier PI, Houweling A, Boss JL, van der Eb AJ, Zijlstra M, Melief JM: Tumorigenicity of cells transformed by adenovirus type 12 by evasion of T-cell immunity. *Nature* 305:776, 1983
3. Dán P, Geck P, Kulesár G, Nász I: Immunofluorescence studies on tissue cultures doubly infected with adeno- and herpesviruses. *Acta Microbiol Acad Sci Hung* 19:51, 1972
4. De Jong PJ, Valderrama G, Spigland I, Horwitz MS: Adenovirus isolates from urine of patients with acquired immunodeficiency syndrome. *Lancet* 1:1293, 1983

5. Everett RD, Dunlop M: Trans-activation of plasmid-borne promoters by adenovirus and several herpes group viruses. *Nucleic Acids Res* 12:5969, 1984
6. Harnett GB, Newnham WA: Isolation of adenovirus type 19 from the male and female genital tracts *Br J Vener Dis* 57:55, 1981
7. Hollós I, Kulcsár G, Ongrádi J, Nász I, László B: Hepatitisvírusok, vírushepatitisek (Hepatitisviruses, viral hepatitis). *Medicina*, Budapest 1986
8. Horváth A: AIDS. Szerzett immunhiány szindróma (AIDS. Acquired immunodeficiency syndrome). *Medicina*, Budapest 1987
9. Kulcsár G, Persistáló adeno- és herpes simplex vírusok a humán patológiában (Persisting adeno- and herpes simplex virus in human pathology). Thesis, Budapest 1975
10. Kulcsár G, Nász I, Dömötöri J, Dán P, Horváth J: A vírusok nőgyógyászati jelentősége (Magzatkárosító hatás, vírusok és danaganatok kapcsolata) (The gynaecological importance of viruses. Their fetus-damaging effect, interrelation of viruses and tumours). *Orvostud Aktuális Probl* 41:53, 1981
11. Lang DJ, Kummer JF: Cytomegalovirus in semen: Observations in selected populations. *J Infect Dis* 132:472, 1975
12. Laverty CR, Russel P, Black J, Kappagoda N, Benn V, Booth N: Adenovirus infection of the cervix. *Acta Cytol* 21:114, 1977
13. Numazaki Y, Shigeta S, Kumasaka T: Acute hemorrhagic cystitis in children. Isolation of adenovirus type 11. *New Engl J Med* 278:700, 1968

Virologische Untersuchung in menschlichen Samenzellen und Hodenzellen von Mäusen

S. CSATA UND GIZELLA KULCSÁR

Wegen männlicher Sterilität und sich wiederholenden Aborten wurden virologische Untersuchungen vorgenommen. Es wurde festgestellt, daß bei 40% der sterilen Männer in dem Sperma infizierende Adenoo oder Herpes simplex Viren vorzufinden sind, während in 60% der Zellen dieselben Viren in latenter Form anwesend sind. In den Aborten ließen sich dieselben Viren beobachten, wie in den väterlichen Zellen. In den Gewebekulturen konnte man unter Wirkung des Spermas *in vitro* auch auf die latente Anwesenheit sonstiger Viren folgern. Die Affinität der Adeno- und Herpes-Viren zu den urogenitalen Organen wurde auch in Tierexperimenten bestätigt, in denen zur *in vivo* Infektion eine neue Methode zur Anwendung kam. Ähnlicherweise wurde auch die enge Wechselwirkung zwischen den Viren und den urogenitalen Zellen nachgewiesen, so daß humane Samen- und Hodenzellen *in vitro* mit Adeno- und Herpes simplex-Viren infiziert wurden, die sich an die Zellen adsorbierten, in diese eindringen und sich in Form ihrer Komponenten sogar replizierten. Aufgrund der Ergebnisse wird die Ansicht vertreten, daß die durch die verschiedenen Viren verursachten, chronischen urogenitalen Lokalinfectionen — durch Schädigung der Zellen — in der männlichen Sterilität und in einem Teil der sich wiederholenden Aborten eine Rolle spielen können. Unter Wirkung der angewandten Zovirax-Kur wurden die Betroffenen von ihrem Leiden befreit — d. h., daß sie von hier an bereits keine Virenträger waren — und in den Samenzellen stellte sich die Normalfunktion wieder her.

Исследование вирусоносительства в человеческих сперматозоидах и клетках семенников мыши

Ш. ЧАТА И Г. КУЛЬЧАР

Выполнялись вирусологические исследования в связи с мужским бесплодием и повторными абортами. Установили, что примерно у 40% страдающих бесплодием мужчин в сперме обнаруживается заразный аденовирус или вирус простого герпеса, причем те же самые вирусы в латентной форме находятся в 60% клеток. В абортном материале обнаруживали те же вирусы, что и в клетках отца. В тканевых культурах *in vitro* при воздей-

ствии спермы можно было выявить латентное присутствие также и других вирусов. Аффинитет уrogenитальных органов к адено- и герпетическим вирусам подтвердилась также и в экспериментах на животных, в которых авторы применили новый метод для заражения *in vivo*. Подтвердили также тесное взаимодействие вирусов и уrogenитальных клеток, заражая в условиях *in vitro* челоовеческие сперматозоиды и клетки семенников аденовирусом и герпетическим вирусом, которые абсорбировались на клетках, проникали в форме их компонентов. На основании полученных результатов авторы полагают, что хроническая местная, уrogenитальная инфекция вызванная различными ивирусами, может играть роль в бесплодии в одной части повторных абортс путем повреждения клеток. После курса лечения зовираксом прекращалось вирусоносительство в семенниковых клетках и восстанавливалась их нормальная функция.

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CONTENTS

Sonographic scan of the normal and pathological endometrium. <i>K. Patai, Z. Harkányi, Zsuzsa Jakab and Z. Vigvári</i>	91
Effect of different intravenous nutrients on upper gastrointestinal secretion in rats. <i>E. Dárdai and J. E. Heavner</i>	101
Coronary artery revascularization after myocardial infarction. <i>F. Tarr, Gy. Lakos, I. Tomácsnyi, T. Sugár, L. Hajdu and T. Lónyay</i>	109
Treatment experiences with intracavitary ¹³⁷ Cs after-loading in a five-year patient material with uterine-cervical carcinoma. <i>S. Csömör, Z. Vigváry and L. Szanyi</i>	119
Intra-abdominal desmoids observed after total proctocolectomies. <i>K. Szilágyi, K. Kett and G. Hegedűs</i>	127
Follow-up of the effect of BCG in bladder tumour patients. <i>P. Tenke, S. Csata and Gizella Kulcsár</i>	131
Technique of extensive proximal selective vagotomy. <i>J. Bátorfi, M. Ihász, A. Bálint, K. Szabó, T. Fazekas and I. Koiss</i>	141
Effect of orchiopexy on human testicular ultrastructure. <i>Y. Martinova, D. Tzvetkov and M. Nikolovsky</i>	153
Our experiences with the management of pyogenic liver abscesses by percutaneous transhepatic puncture and permanent drainage guided by computed tomography. <i>M. Ihász, T. Fazekas, F. I. Todua, J. Bátorfy and M. Máté</i> ...	159
Pregnancy in women with chronic renal disease: A 14-year study. <i>A. Pajor, L. Lukácsi, L. Bakos, F. Lintner and B. Zsolnai</i>	175
Early complications of gastric resection. <i>M. Ihász, Z. Radnai, A. Bálint, F. Szalay, M. Máté, M. Bereczky and G. Pósfaí</i>	183
Book review	197

Sonographic Scan of the Normal and Pathological Endometrium

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(Received: February 14, 1991)

The cycle-dependent sonographic signs of the endometrium in healthy women, the morphological picture of the endometrium in the menopause as well as in tumorous changes are reviewed. The importance of sonography is pointed out in screening the pathological changes of the endometrium. The examination of the endometrium may provide useful supplementary data also to treating infertile patients. Transvaginal sonography may essentially enhance the precision of the method.

Pelvic sonographies are often performed as a routine. Therefore it is important for the examining physician to be aware of the sonographic anatomy of the pelvic organs and of the morphological changes of the uterus and the ovaries, associated with age or during the normal cycle. This knowledge is important for differentiating the pathological states from the normal physiological variations.

The currently available high-resolution realtime scanners enable the examination of the endometrium. Numerous papers deal with the cycle-dependent sonographic signs of the endometrium [4, 6, 7]. To our knowledge, no papers have so far been published in Hungary on the morphology of the endometrium, Hungarian authors have so far reported their findings concerning follicle monitoring [8, 10].

Our study aimed at investigating how the sonographic morphology of the normal endometrium changes during the cycle in healthy women. Examinations were performed in women in the menopause, and in some cases also in those suffering from endometrial tumour. Our experiences are reported and a short survey of the literature is given.

Patients

Our investigations were made with a Picker LSC 7000, high-resolution real-time scanner. 3.5 MHz convex and sector and 5 MHz convex transducers were used. The convex and sector transducers have advantages in examining the pelvic organs over linear ones. The endometrium of 20 young voluntary

women (aged 19–33) of normal cycle, being free of complaints were examined, who had not taken hormone preparations. In 5 cases examinations were carried out every third day during the cycle, from the end of their period up to the beginning of the subsequent period. In three women two, while in two women one cycle was monitored. In case of the other 15 women random examinations were made either in the proliferative or in the secretory phase. In this group one or two examinations were carried out in each person.

Ten complaint-free women in the menopause were examined. In some cases also the examination of a histologically verified endometrial adenocarcinoma and endometrial hyperplasia were performed.

The endometrium is lined with a unilayered high columnar epithelium, some cells of which have cilia. Underneath it, there is an extremely cell-rich tissue poor in fibres which is called stroma. From the epithelium tubular glands protrude into the stroma. The endometrium covers the smooth-muscle layer without submucosa.

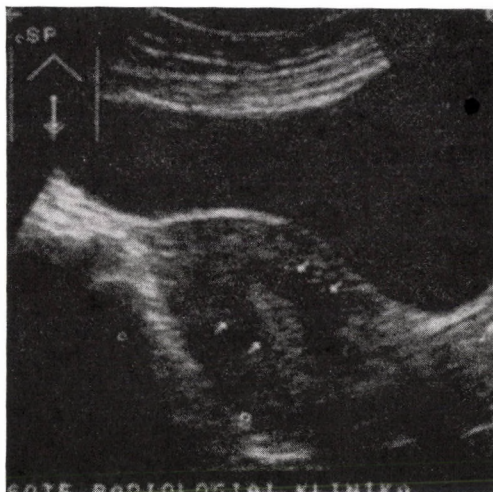
In the first half of the menstrual cycle the stroma of the endometrium thickens due to estrogen, the glands lengthen—this is called proliferative phase. In the second part of the cycle, due to progesterone associated with estrogen, proliferation of the glands continues, they become serpiginous, with glycogen appearing in their epithelium. The stroma becomes rich in interstitial fluid, its cells become swollen. This is the secretory phase of the endometrium, which enables the embedding of the ovum.

Results

In each case, transverse and longitudinal sections were made of the uterus. A well-filled bladder was an indispensable requirement. If the bladder was only partially filled, the patients were given fluid and one tablet of Furosemide, which soon made their examination possible. The thickness of the endometrium was measured on the longitudinal sections, its structure as well as its changes were studied. The thickness of the endometrium was measured from the external margins of the echo-poor ring marking the boundary of the myometrium and the endometrium. The actual endometrial thickness is the half of the value obtained (Scan 1).

In the early proliferative phase a thin linear echo can be seen in the centre of the uterus. In the later proliferative phase the central echo thickens, becomes markedly echodense in structure with a echo-poor halo around it. The echodense internal layer is the compact zone, the echo-poor halo may correspond to the stroma soaked with fluid and rich in vessels.

In the secretory phase the endometrium further thickenes, the superficial layers becoming more and more uneven, in accordance with further



SCAN 1. Longitudinal section of the uterus. The myometrial border is indicated by arrows

glandular proliferation, enhanced mucin production and hyperaemia (Scans 2, 3).

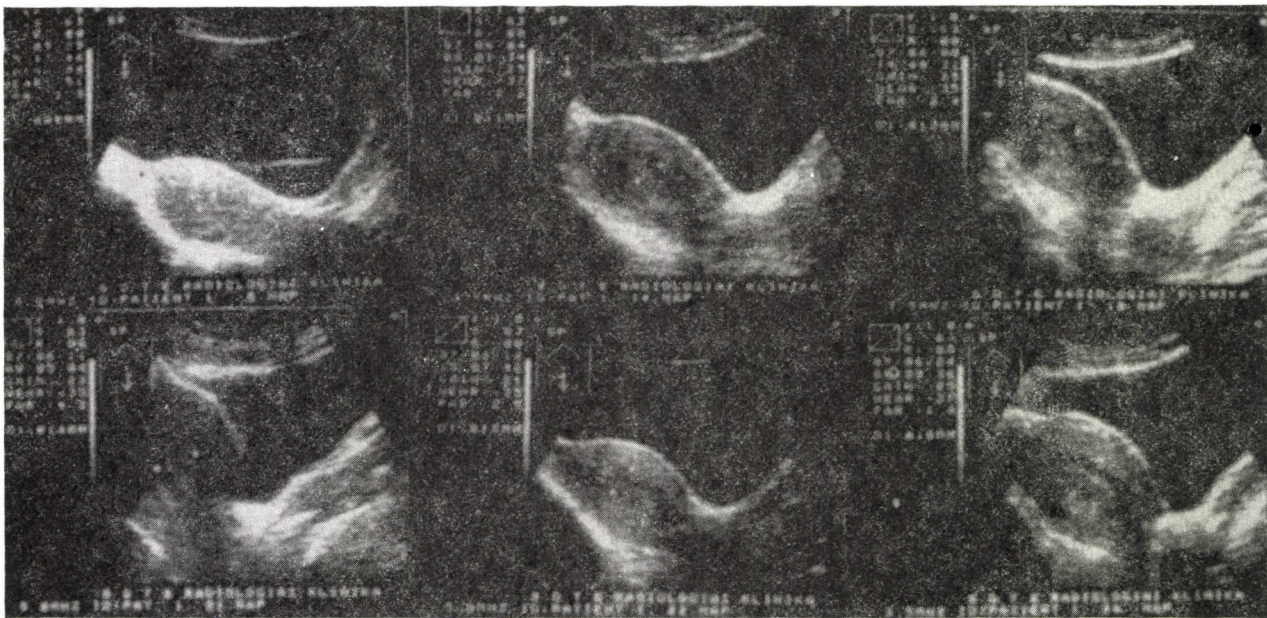
After menopause, the endometrium can be generally visualized as a thin, 2–3 mm echodense strip, corresponding to the atrophic state, the echo-poor ring becomes thinner or disappears altogether (Scan 4).

In adenocarcinoma the endometrium generally thickens, showing an irregular structure, the echo-poor ring is interrupted or disappears (Scans 5, 6).

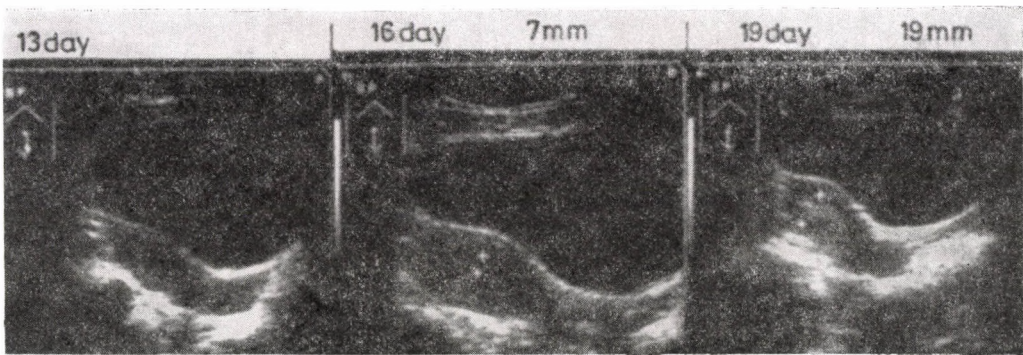
In 18 of the 20 healthy young women the characteristic change of the endometrium during the cycle could be noted.

Discussion

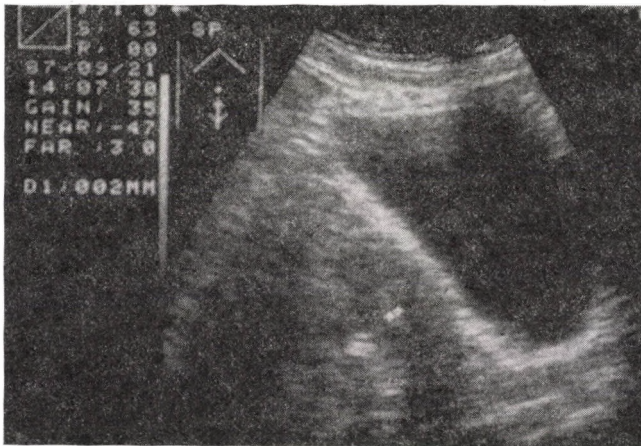
During the menstrual cycle, changes in the structure and size of the endometrium can be observed by sonography. Fleischer et al. [4] examined 38 patients, who were later subjected to hysterectomy. Their measurements were compared with the results of the pathological study. The endometrial thickness established by sonography in 33 cases precisely matched the results of the pathological study. According to their investigations, the thickness of the endometrium was 2–4 mm in the proliferative, 5–6 mm in the secretory phase, while in the postmenopause it was thinner, i.e. 2–3 mm. The echogenicity depends mostly on the number of glands, on their serpiginousness and on the amount of mucin produced. In a part of the cases an echo-poor ring was visible on the outer part of the endometrium [4, 6, 12].



SCAN 2. Cycle of a 28-year-old woman. On day 8, the endometrium can be visualized as a 8 mm echodense strip, on the 14th day, an echo-poor ring is developing, it becomes increasingly thicker, it is 18 mm on day 34. The last scan was taken on the day prior to her period

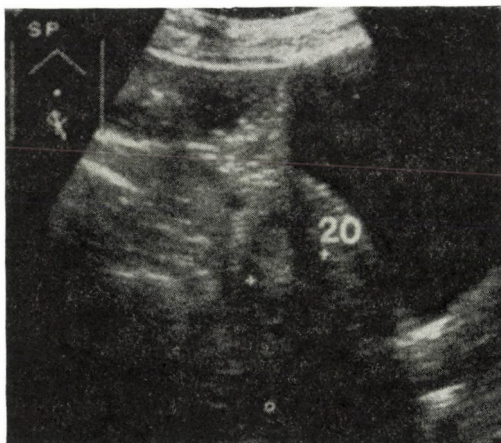


SCAN 3. The cycle of a woman, aged 21. On the 13th day, the endometrium cannot be differentiated from the myometrium, on day 16 it can be visualized, being 7 mm. The echo-poor ring can be seen clearly on the 19th day, the thickness of the endometrium being 19 mm



SCAN 4. Uterus of a 55-year-old woman having been in the menopause for 6 years. The endometrium can be visualized as a 2 mm echodense strip

Kurjak et al. [11] followed the cycle of 74 women, performing hormone examination at the same time. At the beginning of the proliferative phase the endometrium is thin and homogeneous in structure, appearing as a linear echo on the sonographic scan. After some days, the endometrium becomes thicker as a result of the proliferation of the glands and the swelling of the stroma. The fluid content of the cells on the superficial layer of the stroma increases, giving rise to an echo-poor ring. After ovulation the endometrium becomes thicker in the secretory phase, its surface becoming uneven. According to the authors' investigations, the changes of the endometrium comply



SCAN 5. Woman, aged 65. The endometrium has thickened, it is 20 mm, however with the echo-poor ring being clearly discernible. Pathological processing: superficial adenocarcinoma



SCAN 6. 42-year-old woman with a considerably thickened endometrium of inhomogeneous structure, almost filling the uterus. Histology: *in situ* carcinoma

with the hormone profile. No correlation was found between the thickness of the endometrium and the progesterone level [11].

The study of the endometrium in relation to infertility, has been neglected so far, researchers have focussed rather on the monitoring of follicle and the determination of the time of ovulation. In cases of infertility, it is worthwhile to follow the morphological changes of the endometrium during the cycle [2, 15].

With follicle monitoring, the biphasic cycle can be proven. The absence of typical morphological changes may draw attention to the disorder of the luteal phase.

Brandt et al. [2] examined 141 infertile patients. A part of them received ovulation induction treatment, while the other part were included in an *in vitro* fertilization programme (IVF). It was studied whether the typical transformation of the endometrium occurs in the two groups. According to their studies, normal endometrial morphology occurred in a smaller number in the IVF group. In the ovulation induction group, the typical transformation of the endometrium occurred due to treatment. No difference was found between the effects of ovulation induction drugs. The authors assume that in the IVF group the estrogen receptors of the endometrium have been destroyed due to chronic inflammations, and as a result, the sensitivity of the endometrium to the estrogen effect diminished, i.e. no transformation necessary to implantation has occurred. According to their experiences, this defect cannot be corrected even by ovulation inducing drugs [2, 14].

If the thickness of the endometrium differs from normal, some pathologic conditions should be considered. Thickening can be caused by several diseases, producing similar morphology on the sonographic scan. Adenocarcinoma, hyperplasia, adenomyosis, chronic endometritis and pyometra may give rise to the thickening and becoming irregular of the central echo [5, 6].

According to data in the literature, sonography can be used with benefit in assessing the myometrial invasion of detected endometrium adenocarcinomas. Treatment of the tumour largely depends on its stage. In deep myometrial invasion, there is already metastasis formation in 40% of the patients in the adjacent lymph nodes, thus preoperative irradiation is indicated. Fleischer et al. [5] carried out the examination of 20 histologically verified patients with endometrial adenocarcinoma prior to operation. In 16 patients the tumours displayed an echodense, while in 4 an echo-poor structure. In the latter, it was rather about a less differentiated tumour. According to their investigations, the presence of an echo-poor ring is characteristic of superficial invasion, deep invasion is associated with the interruption or disappearance of the ring. As to the extent of invasion, sonography corresponded to the results of pathologic work-up in 16 cases (80%). The examination can be disturbed by the tumour showing exophytic and polypoid extension towards the lumen, or if the lumen is filled with a large amount of blood or mucin. In such cases, the extent of invasion can be overestimated. Another disturbing factor can be the too thick abdominal wall, as well as a retroflected uterus [5].

For elimination of the disturbing factors, the use of intraluminal transducer is recommended. After dilatation of the cervix, the transducer is introduced into the uterine cavity, the examination is performed under total

anaesthesia. The method is also called hysterosonography. According to Becker's results, hysterosonography can help more accurately in determining tumour infiltration than percutaneous sonography, but it is also preferred to CT and MRI [1].

A less invasive method is the use of transvaginal transducer which is introduced into the vaginal fornix. The site of the carcinoma, the extent of the invasion and its spread to the cervix can be well visualized. With this method Nishi could precisely assess the extent of myometrial invasion in 11 out of 14 cases [13].

Transrectal and transurethral sonographies are rather suitable for studying cervical carcinomas and their invasion [16].

According to Chambers et al. [3] transabdominal sonography yielded negative results in 33% of the cases in histologically verified superficial endometrial tumours [3]. In the less advanced forms of hyperplasia and carcinomas the thickness of the endometrium revealed by sonography can also be quite normal.

Hricak et al. [9] determined the stage of endometrium carcinoma by MR examination. In assessing tumour stage, they found the accuracy of the examination to be 92%, this, however, cannot be considered specific, the carcinoma could not be safely differentiated from adenomatous hyperplasia or blood clot. The examination is not considered suitable for detection of lymph nodes, adnexal or peritoneal metastases. CT has not been found to be reliable for assessing myometrial invasion [9].

Sonography is non-specific as to endometrial diseases, therefore it cannot be looked upon as a safe method of detecting carcinomas. It cannot replace histological study.

It is important, however, to be familiar with the morphological picture of the normal endometrium, to be able to recognize the pathological state in patients referred to examination for various causes. If sonography is positive, gynaecological consultation is by all means recommended, or abrasion, depending on the results obtained. For the follow-up of the irradiation therapeutic results of endometrial carcinomas already documented by histological study it is considered a particularly useful method, especially in inoperable cases.

References

1. Becker H, Hoetzing H, Hautmann M: The determination of the extension of carcinomas of the endometrium by hysterosonography. *Proceedings of EURO-SON'87* 1987, p 188
2. Brandt TD, Lery EB: Endometrial echo and its significance in female infertility. *Radiology* 157:225, 1985
3. Chambers CB, Unis JS: Ultrasonographic evidence of uterine malignancy in the postmenopausal uterus *AM J Obstet Gynecol* 154:200, 1986

4. Fleischer AC: Sonographic depiction of thickness and texture changes that occur in the normal endometrium. *Proceedings of WFUMB '85* Pergamon Press 1985, p 281
5. Fleischer AC, Dudley BS, Entman SS: Myometrial invasion by endometrial carcinoma: Sonographic assessment. *Radiology* 162:307, 1987
6. Fleischer AC, Kalemeris GC: Sonographic depiction of normal and abnormal endometrium with histopathologic correlation. *J Ultrasound Med* 5:445, 1986
7. Hall DA, Hann LE, Ferrucci JT: Sonographic morphology of the normal menstrual cycle. *Radiology* 133:185, 1979
8. Hámori M, Németh J, Fedák L: Sonographic signs of ovulation. *Magy Nőorv L* 50:169, 1987
9. Hricak H, Stern JL, Fischer MR: Endometrial carcinoma staging by MR imaging. *Radiology* 162:297, 1987
10. Kolontáry L, Csongrády A, Török A: Sonographic follow-up of ovulation. *Magy Nőorv L* 50:50, 1987
11. Kurjak A, Jurkovic D, Funduk-Kurjak B: Demonstration of uterine endometrial changes during menstrual cycle. *Proceedings of WFUMB '85*. Pergamon Press 1985, p 224
12. McCarthy KA, Hall DA: Postmenopausal endometrium fluid collections. *J Ultrasound Med* 5:647, 1986
13. Nishi M, Akamatsu N, Masaoka H: The application of transvaginal scan for endometrial cancer. *Proceedings of EUROSON '87* 1988, p 189
14. Seelbach-Goebel B, Albert P, Feige A: Sonographical studies on the endometrium of IVF patients before and after follicular puncture. *Proceedings of EUROSON '87* 1987, p 160
15. Thickman D, Arger P, Tureck R: Sonographic assessment of the endometrium in patients undergoing in vitro fertilization. *J Ultrasound Med* 5:201, 1986
16. Ukita N, Akamatsu N, Kouchi T: Transurethral radial scan for estimating the extent of cervical cancer to urinary bladder. *Proceeding of EUROSON '87* 1987, p 191

Effect of Different Intravenous Nutrients on Upper Gastrointestinal Secretion in Rats

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Total parenteral nutrition has been advocated for nutritional support of patients with proximal small bowel fistula. Data on the direct effects of different nutrients on upper gastrointestinal secretion are controversial. Therefore, we examined the effects of glucose, amino acid, fat and mixed parenteral solutions on gastric juice secretion, hydrochloric acid and pepsin content, duodenal juice secretion, and pancreatic protein, amylase, bilirubin and bicarbonate content in thirty rats with chronic gastric and duodenal fistulas.

Gastric secretion was increased by glucose solution (D₁₀W) and by amino acid solution (5% AA) (13% and 12% increase respectively) but not to significant degree by fat emulsion (2% F). Both D₁₀W and 5% AA caused comparable increase in hydrochloric acid secretion (D₁₀W: +34%; 5% AA: +28%) and the pepsin secretion (D₁₀W: +37%). The single infusion of hypertonic glucose, amino acids and fat were associated with decreases in duodenal fistula volume ($p < 0.05$) or content output. Mixed nutrients decreased both gastric secretion (volume: -28%; HCl: -19%; pepsin: -65%) and duodenal juice volume ($p < 0.05$), protein and amylase content ($p < 0.05$). The elevated bilirubin in reduced volume of duodenal juice caused by mixed nutrients may be responsible for bile sludge formation. This study indicates that the use of parenteral nutrition can provide full nutritional support while decreases the fistula output.

Introduction

Total parenteral nutrition has been widely advocated for the nutritional support of patients with proximal small bowel fistula. This advocacy has been based on the expectation that intravenously administered nutrients will not stimulate the gastric, exocrin pancreatic and bile secretion as does enteral feeding [1, 13, 21]. The experimental data, however, concerning the upper gastrointestinal secretory response to different parenteral nutrients are contradictory.

Several authors have reported that intravenous amino acids and dextrose stimulate gastric acid secretion but fat infusion can inhibit this response [11, 17, 25]. Controversy also exists with regard to the pancreatic stimulatory effects of intravenously infused amino acids (5). Some investigators have demonstrated no exocrin pancreatic response to this component of parenteral nutrition, but Konturek et al. reported that both amino acids and fats stimulate canine pancreatic secretion [15].

Recent reports have documented an increased incidence of gallstones among both children and adults maintained on longterm parenteral nutrition [3, 16]. Animal data suggest that parenteral nutrition can produce extremely high level of bilirubin and calcium in bile with a consecutive sludge and stone formation [7, 18].

Material and methods

Thirty male Sprague—Dawley rats weighing 455 ± 22 g (mean \pm S.E.) were prepared with long-term gastric and duodenal fistulas. The animals were anaesthetized with halothane in oxygen. A midline abdominal incision was made and a polyethylene catheter (K-30 Pharmaseal, Toa Alta, Puerto Rico) was implanted into the stomach through a small incision made at the anterior surface of the greater curvature. Another catheter (K-31) was inserted through a prepyloric incision into the duodenum. The tip of the catheter was approximately at the orifice of the common bile duct. The other ends of the catheters were passed through a small cutaneous puncture made 2 cm lateral to the abdominal incision (Fig. 1). The left carotic artery and right external jugular vein were cannulated. The cannulas were exteriorized at the midscapular region. A specially constructed harness was fixed on the animals to protect the catheters. Animals were allowed to recover for seven days during which time they ate rodent laboratory chow diet (Harward Bioscience, South Natick, MA) ad libitum. The rats were fasted for 12 h after which residual gastric and duodenal contents were washed out by flushing lukewarm water through the gastric and duodenal catheter. The semirestrained rats were placed in a metabolic cage (Rodent Metabolic Cage, Harward Bioscience, South Natick,

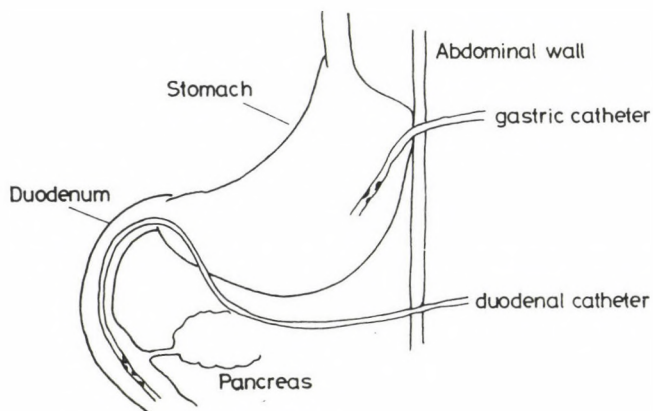


FIG. 1. Schematic illustration of gastric and duodenal catheter system for separate collection of digestive juices

MA) and the venous cannula was connected to infusion/withdrawal pump (Harward Apparatus, South Natick, MA) [22].

The rats were divided in two groups. Fifteen animals received intravenously, in random order, lactated Ringer's solution (LR), 10% dextrose in water with electrolytes (D₁₀W) and 5% amino acid solution (5% AA; Aminosyn, Abbott Laboratories, North Chicago IL) 45 ml of each for 12 h.

The other group of animals ($n = 15$) received the same amount of LR, 2% fat solution (2% F; Liposyn, Abbott Laboratories, North Chicago, IL) and D₁₀W + 5% AA + 2% F solution.

Gastric and duodenal secretion were collected by gravity for 12 h intervals and stored on ice to prevent digestion of enzymes. We measured the volume and hydrochloric acid and pepsin content of gastric drainage. Duodenal drainage volume and total protein, amylase, bilirubin and bicarbonate content were measured. Venous/arterial blood was sampled and glucose, glucagon, insulin, free fatty acid (FFA), creatinin and blood urea nitrogen (BUN) content were determined. Urine was collected and nitrogen excretion was measured.

Hydrochloric acid was titrated with 0.1 N sodium hydroxide. We used the method of Rick and Fritsch to measure pepsin [20]. Total protein content of duodenal juice was determined by spectrophotometry. Bicarbonate was measured by the Van Slyke method and recorded as concentration. Amylase, bilirubin, blood glucose, creatinin, BUN were determined by Beckman Astra 8 System Sample Assay Compartment. FFA was measured by colorimetric method [4]. Glucagon was measured by radioimmunoassay technique (Cambridge Medical Diagnostics Inc., Billerica MA). Insulin was measured by enzyme-immunological test (Boehringer Mannheim, GmbH, West Germany). Nitrogen excretion was determined by micro-Kjeldahl method.

We calculated the gastric and duodenal excretion for 12 h. The data gained under LR infusion served as control. (The mean values of the control period were arbitrarily assigned as a value of the 100 per cent). Then we determined the percentage of changes between the control data and gained ones under the infusion of different nutrients. We applied the paired t test to determine the significance of the differences between the percentage of changes in the control period and those under parenteral nutrition.

Results

Gastric juice secretion was higher during dextrose and amino acid infusion than during LR infusion. The hydrochloric acid concentration in gastric fluid increased by 34% during D₁₀W and by 28% during 5% AA infusions. The pepsin secretion increased by 37% during dextrose infusion. Marked

reduction in volume (28%), in hydrochloric acid secretion (19%) and significant decrease (65%; $p < 0.05$) in pepsin secretion occurred with the mixture of all nutrients (Fig. 2).

Each of the three different nutrients significantly decreased duodenal secretion. The lowest protein output occurred in response to dextrose and fat infusion (both were significant, $p < 0.05$). Reduced amylase output was

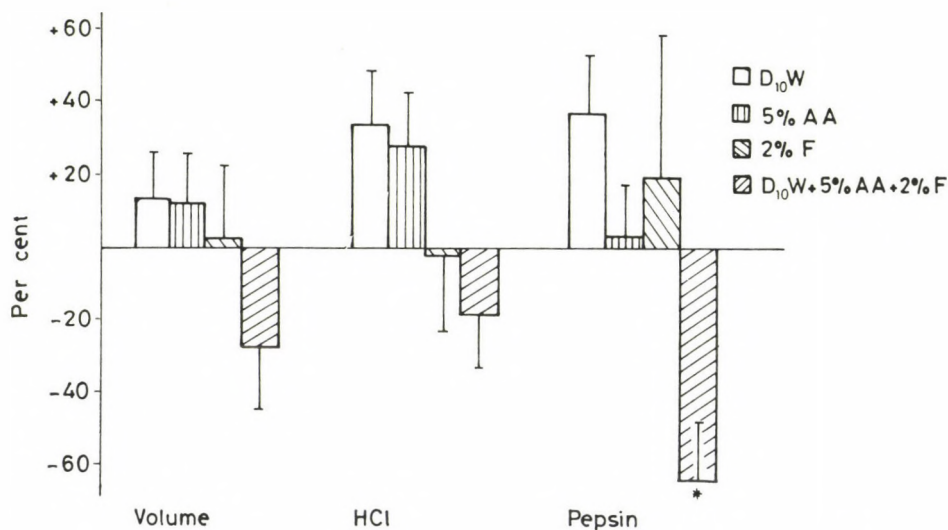


FIG. 2. Percentage of change in mean 12-h-gastric secretion under infusions of 10% dextrose (D₁₀W), 5% amino acids (5% AA), 2% fat (2% F) and mixed nutrient (D₁₀W + 5% AA + 2% F) solutions. (T = SEM; * $p < 0.05$)

obtained during the infusion of 5% AA and 2% F ($p < 0.05$). Amino acid infusion produced significant decrease in bilirubin and bicarbonate output. The concentration of bilirubin in duodenal juice elevated by 96%, the bicarbonate excretion by 104% during the infusion of mixture of all nutrients (Fig. 3).

Fasting blood sugar levels averaged 8.9 mmol/l. Significant decreases were observed during the dextrose-free infusions. There was no correlation between the pancreatic exocrine secretion and the plasma glucagon and insulin levels. Plasma FFA level decreased significantly during the infusion of mixed nutrients. BUN showed marked elevation during infusion of 5% AA (Table I).

Osmotic diuresis occurred during dextrose infusion with significant nitrogen excretion was elevated due to amino acid and mixed solution (Table II).

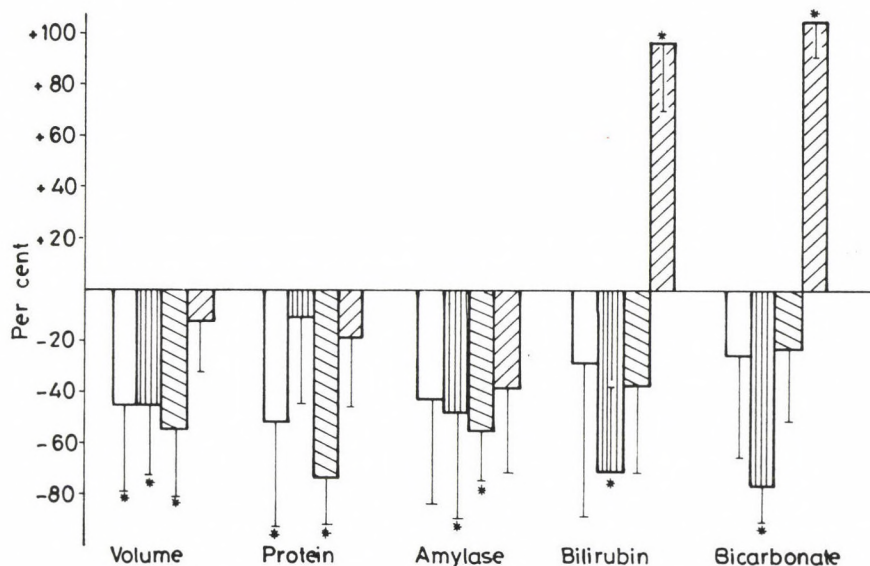


FIG. 3. Percentage of change in mean 12-h-duodenal fistula output under infusions of 10% dextrose, 5% amino acids, 2% fat and mixed nutrient solutions

TABLE I

Plasma glucose, glucagon, insulin, free fatty acid, creatinin and blood urea nitrogen values under infusions of different nutrients

	Control	LR	D ₁₀ W	5%AA	2%F	D ₁₀ W + 5%AA + 2%F
Glucose (mmol/l)	8.9 ± 0.43	6.8* ± 0.29	10.5 ± 1.36	6.8* ± 0.28	6.3* ± 0.36	8.3 ± 1.22
Glucagon (pg/ml)	617.6 ± 110.0	719.9 ± 177.1	694.9 ± 249.9	471.5 ± 144.5	1203.6 ± 307.6	1016.8 ± 224.8
Insulin (μU/ml)	49.4 ± 4.1	28.2 ± 4.8	21.3 ± 3.3	25.0 ± 2.6	34.5 ± 6.6	34.0 ± 4.0
FFA (maequ/l)	0.71 ± 0.05	0.65 ± 0.19	0.60 ± 0.14	0.70 ± 0.11	0.80 ± 0.13	0.30* ± 0.05
Creatinin (μmol/l)	57.5 ± 2.6	57.5 ± 2.6	53.0 ± 4.4	53.0 ± 2.6	61.8 ± 2.6	70.7 ± 7.7
BUN (mmol/l)	8.2 ± 0.43	8.1 ± 0.93	6.9 ± 1.2	10.2* ± 0.96	7.7 ± 1.14	11.9* ± 1.92

± SEM, * p < 0.05

(FFA = free fatty acid; BUN = blood urea nitrogen; LR = lactated Ringer's; D₁₀W = 10% dextrose; 5% AA = 5% amino acids; 2% F = 2% fat)

TABLE II
Urine output and nitrogen excretion

	LR	D ₁₀ W	5%AA	2%F	D ₁₀ W + 5%AA + 2F%
Urine (ml/12 h)	19.6 ± 2.4	24.8 ± 4.2	20.5 ± 2.6	18.9 ± 3.4	15.2 ± 2.2
N-excretion (mg/12 h)	1575.0 ± 145.0	1025.0 ± 104.0	1959.7 ± 188.0	1664.8 ± 160.5	2009.1 ± 307.0

± SEM, * $p < 0.05$

Discussion

Results of this study demonstrate that intravenous infusion of D₁₀W and 5% AA stimulates gastric juice, gastric acid and pepsin secretion in rats. These findings corroborate the report of Isenberg and Maxwell [11] who demonstrated stimulation of gastric acid secretion in man during infusion of amino acid with or without glucose. Human and animal observations indicate that intravenous infusion of fat markedly inhibited gastric acid secretion [17, 25]. In our study, fat alone has no inhibitory effect on gastric secretory response. The infusion of mixed parenteral nutrients is a potent inhibitor of gastric secretion. It appears that the major secretogouses contained in the parenteral nutrition are amino acids glucose. In parenterally fed rats, serum level of gastrin decreased [12]. The data of Friend et al. and those of Varner et al. show that this stimulation is not mediated by the release of gastrin [5, 25]. It is not known how parenteral nutrition exerted its inhibitory effect [9]. Possible mechanism would be a direct effect on parietal cells of indirectly by a neurohumoral pathway. There is need to determine wether the secretogogue effect of amino acid and dextrose occurs chemically when the fat emulsion is not used. (The clinical implication of the increased gastric secretion during intravenous amino acid and dextrose infusion makes it necessary to decide wether this secretogogue effect should be anticipated in cases when the fat emulsions are not used or no).

The different nutrients have marked inhibitory influence on pancreatic secretion in rats. It seems that concentrated glucose solution is the most effective inhibitor of pancreatic exocrine function in human and animals [10, 13, 14, 19, 21, 24]. Konturek et al. seriously challenged the concept that pancreatic rest could be maintained during parenteral nutrition, showing with their report that intravenous mixed amino acids and fat stimulated canine pancreatic secretion [15]. In our study the 5% amino acid solution decreased the pancreatic juice excretion and protein, amylase and bicarbonate output without exogenous hormonal stimulation. Recent clinical and animal inves-

tigations proved that combined mixed amino acids and hypertonic dextrose solutions decrease pancreatic exocrine function [1, 13, 14, 21, 23].

Felig reported that amino acids, when given intravenously, are potent stimulators of the endocrine pancreatic hormones [6]. Gimmon et al. suggested that the pancreatic A cells are more responsive to amino acids than to glucose [8]. Stimulation of pancreatic hormonal secretion did not occur in our rats during glucose and/or amino acid infusion. The complete hyperalimentation solution (synthetic amino acids, concentrated glucose and fat emulsion) has certainly influenced the plasma level of glucagon and insulin. This effect is likely due to fat in the solution.

The role of fat emulsions on pancreatic secretion is contradictory. Klein et al. reported that fat increases bicarbonate and amylase output in pancreatic fistula [14]. These data are supported by some previous canine investigations [15]. In other investigations, intravenous infusion of fat emulsions failed to evoke any significant stimulatory effect on pancreatic volume, protein or amylase secretion [1, 2, 5, 21]. Our study suggests that fat emulsion has a significant inhibitory effect on pancreatic exocrine function.

Several recent reports have documented an incidence of sludge and gallstone in man maintained on long-term total parenteral nutrition [3, 16]. Data of animal experiments suggest a significant elevation of both bilirubin and calcium in hepatic bile after parenteral nutrition [7, 18]. In reduced volume of duodenal juice we found significant elevation of bilirubin. The mechanism whereby concentration of bilirubin was increased in the bile of animals under mixed nutrient infusion remains unexplained. In this study the different nutrients alone had an inhibitory effect on bile secretion.

In summary our studies suggest that in the rats [1] both concentrated glucose solution and amino acid solutions given intravenously stimulate the gastric secretion; [2] mixed parenteral nutrients cause no increase in gastric juice volume, hydrochloric acid and pepsin secretion; [3] the single intravenous nutrients inhibit the pancreatic and bile secretion; [4] the total parenteral nutrition diminishes the pancreatic juice volume, protein and amylase secretion, however it causes an increase in the level of pancreatic bicarbonate and bile secretion.

We conclude that total parenteral nutrition has a direct inhibitory effect on upper gastrointestinal secretion. It is advocated in treatment of high output small bowel fistulas with respect to the ability to decrease to fistula output.

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References

1. Bivins BA, Bell RM, Rapp RP, Toedebusch WH: Pancreatic exocrine response to parenteral nutrition. *JPEN* 8:34-36, 1984
2. Edelman K, Valenzuela JE: Effect of intravenous lipid on human pancreatic secretion. *Gastroenterology* 85:1063-1066, 1983
3. Enzenauer RW, Montrey JS, Barcia PJ, Woods J: Total parenteral nutrition cholestasis: A cause of mechanical biliary obstruction. *Pediatrics* 76:905-908, 1985
4. Falholt K, Lund B, Falholt B: An easy colorimetric micromethod for routine determination of free fatty acids in plasma. *Clin Chim Acta* 46:105-111, 1973
5. Friend GM, Ogden WD, Rhea A, Greeley G, Thompson JC: Pancreatic protein secretion and gastrointestinal hormone release in response to parenteral amino acids and lipid in dogs. *Surgery* 92:902-905, 1982
6. Felig P: Parenteral nutrition: substrate and secretagogue. *New Engl J Med* 287:982-983, 1972
7. Gimmon Z, Kelley RE, Simko V, Fischer JE: Total parenteral nutrition solution increase lithogenicity of the bile in the rat. *JPEN* 4:587-590, 1980
8. Gimmon Z, Murphy RF, Chen M, Nachbauer CA, Fischer JE, Joffe SN: The effect of parenteral and enteral nutrition on portal and systemic immunoreactivities of gastrin, glucagon and vasoactive intestinal polypeptide (VIP). *Ann Surg* 196:571-575, 1982
9. Greenberg GR, Wolman SL, Christofides ND, Bloom SR, Jeejeebhoy KN: Effect of total parenteral nutrition on gut hormone release in humans. *Gastroenterology* 80:988-993, 1981
10. Hamilton RF, Davis WC, Stephenson DV, Magee DF: Effect of parenteral hyperalimentation on upper gastrointestinal tract secretions. *Arch Surg* 102:348-352, 1971
11. Isenberg JI, Maxwell V: Intravenous infusion of amino acids stimulates gastric acid secretion in man. *New Engl J Med* 298:27-29, 1978
12. Johnson LR, Copeland EM, Dudrick SJ, Lichtenberger LM, Castro GA: Structural and hormonal alterations in the gastrointestinal tract of parenterally fed rats. *Gastroenterology* 68:1177-1183, 1975
13. Kelly GA, Nahrwold DL: Pancreatic secretion in response to an elemental diet and intravenous hyperalimentation. *Surg Gynecol Obstet* 143:87-91, 1976
14. Klein E, Shnebaum S, Ben-Ari G, Dreiling DA: Effect of total parenteral nutrition on exocrine pancreatic secretion. *Am J Gastroenterology* 78:31-33, 1983
15. Konturek SJ, Tasler J, Cieszkowski M, Javorek J: Intravenous amino acids and fat stimulate pancreatic secretion. *Am J Physiol* 236:E678-E684, 1979
16. Messing B, Aprahamian M, Rauture M, Bories C, Bismalli A, Stock-Damge S: Gallstone formation during total adreneral nutrition: A prospective study in man. *Gastroenterology* 86:1183-1188, 1984
17. Levine GM, Mullen JL, O'Neill F: Effect of total parenteral nutrition on gastric acid secretion. *Dig Diseases Sci* 25:284-288, 1980
18. Muller EL, Grace PA, Pitt HA: The effect of parenteral nutrition on biliary calcium and bilirubin. *J Surg Res* 40:55-62, 1986
19. Nakajima S, Magee DF: Inhibition of exocrine pancreatic secretion by glucagon and D-glucose given intravenously. *Can J Physiol Pharmacol* 48:299-305, 1970
20. Rick W, Fritsch W: Pepsin. in Bergmeyer HU: *Methods of Enzymatic Analysis*, 2nd Ed., Verlag Chemie Berlin 1974, pp 1046-1057
21. Stabile BE, Borzatta M, Stubbs RS: Pancreatic secretory responses to intravenous hyperalimentation and intraduodenal elemental and full liquid diets. *JPEN* 8:377-380, 1984
22. Steiger E, Vars HM, Dudrick SJ: A technique for long-term intravenous feeding in unrestrained rats. *Arch Surg* 104:330-332, 1972
23. Stubbs RS, Stabile BE: Inhibition of CCK-OP-stimulated pancreatic enzyme secretion by parenteral and enteral amino acids. *Gastroenterology* 80:1325, 1983
24. Towne JB, Hamilton RF, Stephenson DV: Mechanism of hyperalimentation in the suppression of upper gastrointestinal secretions. *Am J Surg* 126:714-716, 1973
25. Varner AA, Isenberg JI, Elashoff JD, Lamers CBH, Maxwell V, Shulkes AS: Effect of intravenous lipid on gastric acid secretion stimulated by intravenous amino acids. *Gastroenterology* 79:873-876, 1980

Coronary Artery Revascularization after Myocardial Infarction

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Authors report on the revascularization resulted by noninvasive and invasive interferences carried out 6–9 months after surgery and on the improvement of functional status of 56 postinfarction patients with recurrent angina pectoris. They conclude that recoronarography performed in 12 patients revealed diminished patency rate as compared to the estimated rate, especially in those cases, where complete revascularization was considered to have been carried out. Ejection fraction, wall motion score by ventriculography and echocardiography did not seem to improve significantly. However Dipyridamol Thallium scintigraphy showed marked improvement in perfusion in all cases. NYHA functional status noticeably improved in the re-examined patients.

In Hungary — on the contrary to data obtained from the western world — the prevalence of ischemic heart disease and myocardial infarction steadily increases year by year [1, 2, 3, 15, 8, 26].

A possible explanation may come from the ineffectivity of preventive medicine, of certain social circumstances as well as of difficulties in eliminating the effects of classical risk factors.

An equally important additional phenomenon seems to be the totally inappropriate practice of treating the symptomatic patient with ischemic heart disease with highly effective antianginal drugs *prior to* establishing correct diagnosis.

Certainly leads this kind of practice in vast majority of patients, to spectacular improvement, moreover gives completely asymptomatic condition with no complaints whatsoever.

The described strategy might be taken as *iatrogenia*, since treatment is being carried out without diagnosis produced by a complete scale of investigational procedures eventually on such patients, who might be good candidates for percutaneous transluminal coronary angioplasty (PTCA) or coronary artery revascularization.

In the meantime, pathology of coronary stenoses proceeds to critical narrowing and finally myocardial infarction occurs seemingly all of a sudden [14, 17, 7].

Patients after myocardial infarction of different extent repeatedly becoming symptomatic often are subjected to noninvasive and invasive diag-

nostic investigations. Unfortunately, the obtained data are only partially informative concerning global ischemic reserve capacity of the myocardium during revascularization.

It is well known, that this is the reason why the incidence of perioperative complications is higher in patients with postinfarction angina, than in patients operated on with chronic, stable angina pectoris. Late results are also in question after surgery in patients with postinfarction angina pectoris [7, 12, 20, 11, 9, 4].

In this paper we describe the strategy followed at surgery, certain details of myocardium protection as well as conclusions drawn by results of tread-mill test, echocardiography, Dipyridamol Thallium scintigraphy and reangiography carried out 6-9 months after surgery.

Patients and method

Between October 1, 1988 and March 31, 1989 77 coronary revascularizations were carried out in the Postgraduate Medical School Budapest. Out of the 77 patients 56 had a history of previous myocardial infarction (MI) suffered 1-5 years earlier (79%).

Table I shows the patients' age, sex distribution, MI localization and NYHA functional state.

TABLE I
Preoperative clinical data

N°	Sex		Age	Preop MI			NYHA stage		
	F	M		ant	ant-lat	post	II.	III.	IV.
56	7	49	38-67 mean: 52.5	31	20	5	21	33	2

N°: number of patients, Preop MI: preoperative myocardial infarction, ant: anterior, ant-lat: anterolateral, post: posterior NYHA: New York Heart Association

On Table II. risk factors and associated diseases are shown. Table III. contains the extent of diseased coronary arteries, preoperative diskynetic score, relevant echocardiographic findings and preoperative ejection fractions (EF).

35 patients appeared to have stable angina pectoris (AP), 19 unstable AP, and 2 patients had Prinzmetal AP with paroxysmal nocturnal dyspnoe.

Details of extracorporeal circulation technique and special features of intraoperative myocardial protection have been discussed elsewhere [21, 23].

TABLE II
Risk factors, associated diseases

Hypertension	12/56	(20%)	Hypertension, diabetes
Obesity	23/56	(40%)	mellitus, obesity
Smoking	51/56	(90%)	together:
Diabetes mellitus	12/56	(20%)	
Hyperlipidemia	20/56	(32%)	6/56 (10.5%)
Sedentary life	9/56	(17%)	

TABLE III

Extent of IHD	Diskynetic score ESP/EDP (%) RAO		Preop EF (%) mean			Echocardiography finding		
						hypokynesis	akynesis	paradox
1 vessel disease	8/56	24–32	28	41–44	42.5	5/8	2/8	1/8
double vessel d.	38/56	21–30	25	35–45	40	31/38	5/38	2/38
triple vessel d.	8/56	18–24	21	29–38	34.5	3/8	4/8	1/8
LM stenosis	4/56	16–25	20	29–36	32.5	1/4	1/4	2/4

IHD: ischemic heart disease, ESP: endsystolic perimeter, EDP: enddiastolic perimeter, RAO: right anterior oblique plane, preop: preoperative, EF: ejection fraction, LM: left main stenosis

Here emphasis is made on steps entirely different to those used during surgery in noninfarcted patients' revascularizations.

Generally, prior to surgery beta blocking agents are not withdrawn, unchanged dose is given. Attention is paid to adequate information about the nature of surgery to be given to the patient, as well as to avoid anxiety generated by stress. These measures may jointly help to eliminate sympathetic overfunction resulting in blood pressure elevation.

When aortic cross clamp time is anticipated to be longer than 50 min total perfusion is employed. (Both vena cavae are snared: according to the results of our previous experiments—e.g.: with single venous cannula—with a flow of 2.5–3 l/m², a 500–700 ml of systemic warm blood enters the left heart in every minute, continuously warming up the otherwise unevenly cooled myocardium. This phenomenon can be avoided by total perfusion [25, 16].)

Core temperature is reduced to 26 °C. A St. Thomas like cardioplegic solution is administered into the aortic root in an amount of 500 ml, cooled to 4 °C at a pressure of 60 mmHg. Concomitantly, another 500 ml is given through the coronary sinus retrogradely at a pressure of 25 mmHg. Right ventricle is protected against overdistension by local compression. Slush is poured into the pericardial sac for topical cooling. Phrenic nerves are protected

with a Bonchek pad. Endocavital cooling of the left ventricle is achieved with a balloon left ventricular vent. Interventricular septal temperature is measured with a needle thermistor. (Yellow Springs Instr. Co.)

The techniques used for revascularization of the myocardium are described elsewhere [24].

As a special consideration, the left internal mammary artery graft is always applied—within reach—to salvage the most jeopardized myocardial region. Semivital areas shown on the angiogram or on the Thallium scan.)

The proximal anastomoses of the vein grafts are individually sutured to the ascending aorta with a separately applied side clamp. Simultaneously left atrial pressure is monitored, and the deflated balloon left heart vent is withdrawn to the left atrium. The load of the “empty beating heart” can be easily changed by the actual changing in stroke volume while attempts are being made weaning the patient from extracorporeal circulation. Stable stroke work thus gradually is established, so less is the danger of left ventricular overdistension.

Results

Every patient received the left IMA and 2–3 vein grafts each. The average grafts per patients were 3.9.

Early mortality (48 h after surgery) resulted 2 patients' death (3.2%). 1 patient died of acute anterolateral myocardial infarction or evidenced by ECG and myocardial specific enzyme elevation.

The other cause of death appeared to be acute left ventricular failure not responding to maximal positive inotropic support. (Autopsy revealed patent saphenous grafts and IMA anastomosis. Failure of adequate myocardial protection?)

Out of 54 patients 18 showed low cardiac output syndrome characterized by elevated left atrial pressure and “fixed”, relatively low systemic pressure (58–70 mmHg) lasting for 7 days as an average, and treated with moderately high dose of positive inotropic agent (Dobutamine, 5 μ g/kg/min.).

Six patients out of 54 suffered perioperative myocardial infarction of different extent (10.1%).

Reconstruction of the sternum had to be carried out because of instability in 1 patient 10 days after heart surgery [22].

At discharge from the hospital (14th day after surgery generally) 6 patients complained of effort AP, which was successfully eliminated by increased dose of Metoprolol tartarate (Betalloc) 25 mg q.d.s.

Other 5 patients' exertional capacity have remained somewhat limited for the end of the individually designed mobilization programme. None of

them belonged to the perioperatively infarcted group. Finally, at discharge from the hospital 5 patients (20%) produced angina-like symptoms during exercise. 43 patients were found to be asymptomatic and in NYHA class I.

Investigations indicative for late results (tread mill test, echocardiography, Dipyridamol Thallium scan re-angiography) could be performed in 12 patients 6 to 9 months after surgery (20% follow-up rate).

On admission 8 patients were found to be in NYHA class I., 4 patients in class II. with a medication of Metoprolol 25 mg b.d. and Isosorbide dinitrate 2.6 mg b.d. in the lesser group.

After omitting beta blocking agent patients were subjected to tread mill test based on the Bruce protocol. The improvement of exercise capacity seemed to be plus 30–35 watts—as an average—compared to the preoperative one without ECG changes. In 8 patients the tread mill test had to be stopped before the planned submaximal stress because of exertional dyspnoe, but not angina pectoris.

Echocardiography did not show significant changes in left ventricular dimensions compared to the preoperative images. Diskynetic score and ejection fraction calculated by this means also did not change essentially.

In 11 patients Dipyridamol Thallium scintigraphy showed marked improvement in perfusion even in those 4 patients where recoronarography revealed vein graft occlusion but widely opened IMA graft.

Recoronarography of the 12 patients with IMA and 2–3 vein grafts each, showed 4 vein graft occlusions. Three of them happened to be sequential feeding diskynetic area. One proximal IMA stenosis was found. (Harvesting failure, originally might be present?)

Table IV and V show preoperative and reinvestigation data of diskynetic score and of EF. No significant changes could be noted. However, in case of patient number 8. beside the widely opened IMA graft, both vein grafts were occluded, while Thallium scan proved significantly increased perfusion.

Discussion

Is there a place for bypass surgery in patients with reduced left ventricular functions after MI becoming symptomatic again?

Symptomatology of these patient due to limited activity and highly, effective antianginal drugs is very much mitigated.

Coronarography reveals surgically approachable coronary stenoses, which obviously challenge the surgeon, but a great many risk factors influencing perioperative morbidity and mortality, late results are to be taken into consideration before surgery is decided. According to Kirklin these incremental risk factors are: number of stenotic coronary branches, left main stenosis,

TABLE IV

Ejection fraction found preoperatively and at reinvestigation (12 pts)

Pts	Sex	Preop	Reinvest
		EF (%)	
1.	M	39	41
2.	M	35	34
3.	M	45	68
4.	M	52	50
5.	M	54	57
6.	F	39	41
7.	M	40	45
8.*	M	42	50
9.	M	40	61
10.	M	45	55
11.	M	39	51
12.	M	45	54

M: male, F: female, Preop: preoperative, Reinvest: reinvestigation, EF: ejection fraction, *: see Discussion

TABLE V

Clinical data, surgical solution of reinvestigated patients

Extent of IHD	N°	Mode of revasc	Diskynetic score	
			preop	postop
(mean, %)				
Double vessel				
Disease	3/12	LIMA + 2 vein grafts	25	24
Triple vessel				
Disease	7/12	LIMA + 3 vein grafts	21	22
LM stenosis	2/12	LIMA + 2 vein grafts	20	21

IHD: ischemic heart disease, revasc: revascularization, preop: preoperative, postop: postoperative, LIMA: left internal mammary artery, LM: left main stenosis

severity of AP, unstable AP, diminished left ventricular diastolic function, number and extent of previous MI, circumferential fiber shortening of the myocardium. These factors normally are considered preoperatively.

Intraoperative factors, which largely influence outcome are: aortic cross clamp time, intraoperative myocardial protection, number of grafts, use of IMA.

It is not easy to select those factors which surely exclude the benefits of surgery. Decision making on the surgeon's side is very much influenced

by the awareness of the not very good late results and limited improvement in quality of life [13, 5, 19, 18, 10, 6].

Considering the described facts a different surgical strategy and technique is employed during revascularization of postinfarction patients, than what is used in noninfarcted patients.

We advocate total perfusion completed with endocavital cooling on the left ventricle [23, 16].

Thus semivital area of the left ventricle perhaps can be more efficiently cooled and protected against rewarming [16].

The use of IMA seems to be imperative.

It is to repeat, that Thallium scan proves high IMA mediated flow in every case even in those where vein grafts were occluded.

It is noteworthy, that in the 4 cases with vein graft occlusion 3 of them were sequentials leading to the marginal branches of the circumflex artery in patients with a posterior localized MI. No technical difficulties were noted during surgery. (In all cases 90 degree end anastomosis and 75 degree side to side one were performed and the proximal end was positioned via the transverse sinus.)

Supposedly the vascular resistance of the coronary branches feeding the scar scattered myocardium cannot be calculated according to their diameter. Therefore it is difficult to decide the sequence of the anastomosis. (N.b.: the sequence of the end and side to side anastomosis normally is designed according to the recipient vessel's diameter and flow capacity respectively, keeping in mind the principle: resistance is inversely proportional to diameter.)

Based on these uncertainties, sequential vein grafts are not to be constructed in postinfarction patients least in scar spotted zones.

Employment of high flow producing IMA is very much recommended. Thallium scan clearly proved increased perfusion of the myocardium, though functional parameters have not improved substantially.

Late results of revascularization procedures in patients with postinfarction angina pectoris seem to be inferior to those of patients with no previous MI.

Therefore heart surgeons wish patient with AP to have correct diagnosis as early as possible.

Consequently the most appropriate therapeutic approach can be selected matching with the actual pathology in the hope to prevent irreversible changes to happen in the myocardium.

References

1. Antalóczy Z, Kárpáti P: Myocardialis infarctus, Medicina, Budapest, 1978
2. Árvay A., Békássy Zs, Porubszky I. et al.: Az iszkémiás szívbetegek kezelésének korai eredményei. I. Koszorúérszűkület (Early result in the treatment of ischemic heart diseases I. Coronary stenosis) Orv Hetil 117:2870, 1976

3. Árvay A: Az angina pectoris sebészi kezelése (Surgical treatment of angina pectoris) *Orv Hetil* 129:1191, 1988
4. Ashburn WL, Braunwald E, Simon AL, Peterson KL, Gault JH: Myocardial perfusion imaging with radioactive-labeled particles injected directly into the coronary circulation of patients with coronary artery disease. *Circulation* 44:351, 1971
5. Baumgartner WA, Borkon AM, Zibulewsky J, Watkins L Jr, Gardner TJ, Bulkley BH, Achuff SC, Baughman KL, Traill TA, Gott VL, Reitz BA: Operative intervention for postinfarction angina. *Ann Thorac Surg* 38:265-267, 1984
6. Berg RH, Engelman RM, Rouson JA, Lemeskow S: Postinfarction angina: An expanding subject of patients undergoing coronary artery bypass. *J Thorac Cardiovas Surg* 90:532-540, 1985
7. Bosch X, Theroux P, Waters DD, Pelletier GB, Roy D: Early postinfarction ischemia: clinical, angiographic and prognostic significance. *Circulation* 75:988-995, 1987
8. Campbell J, King SB III, Douglas JS Jr, Bradford JM: Prevalence and distribution of disease in patients catheterized for suspected coronary artery disease. In King SB III, Douglas JS Jr (eds) *Coronary Arteriography and angioplasty*. New York McGraw-Hill Book Co, Inc 1985, p 359
9. Friesinger GC, Page EE, Ross RS: Prognostic significance of coronary arteriography. *Trans Assoc Am Physicians* 83:78, 1970
10. Gardner TJ, Stuart RS, Greene PS, Baumgartner WA: The risk of coronary bypass surgery for patients with postinfarction angina. *Circulation* 79/6:79-90, 1989
11. Jones EL, Waites TF, Craver JM, Bradford JM, Douglas JS, Spencer BK, Done DK, Dorney ER, Clements SD, Thompkins T, Hatcher CR: Coronary bypass for relief of persistent pain following acute myocardial infarction. *Ann Thorac Surg* 32:33-34, 1981
12. Kesler KA, Naunheim KS, Kanter KR, Fiore AC, McBride LR, Pennington DG, Barner HH, Kaiser GC, Willman VL: Coronary bypass for recent infarction: Predictors of mortality. (Abstract) *Circulation (Suppl)* 76:487, 1987
13. Kouchoukos NT, Murphy S, Philpott T, Pelate C, Marshall WG Jr: Coronary artery bypass grafting for postinfarction angina pectoris. *Circulation (Suppl)* 79:69-71, 1989
14. Major L, Molnár F, Komáromy K, Berentey E: Coronarographiasalt betegek súlyossági összetételének változása egy évtized alatt (Changes in severity distribution of our coronarographised patients during one decade) Magyar Kardiológus Társaság tudományos ülése, Balatonfüred (Scientific Meeting of the Hungarian Cardiological Society Balatonfüred) 1988
15. National Center Health Statistics 1986 Summary: National Hospital Discharge Survey. Advance Data From Vital and Health Statistics. No 145 US Dpt of Health and Human Services. Publication Mc (PHE) Public Health Service Hyattsville, Mc, 1987 87-1250,
16. Papp L: Az ép és károsodott keringésű szív véráramlás eloszlásának vizsgálata állatkísérletekben és emberi szív-műtétben cardioteletermographiával (Study of blood flow patterns in hearts of intact and insufficient circulation in animal experiments and in human cardiac operations by cardioteletermography) Doktori értekezés (Doctoral theses) Budapest 1988
17. Muhlbaier DH, Oldham HN, Hlatky MA, Mark DB, Reves JG, Califf RM: The changing survival benefits of coronary revascularization over time. *Circulation (Suppl V)* 76:V13-V21, 1987
18. Rankin JS, Newton JR Jr, Califf RM, Jones RH, Wechsler AS, Oldham HN Jr, Wolfe WG, Lowe JE: Clinical characteristics and current management of medically refractory unstable angina. *Ann Thorac Surg* 200:457-465, 1984
19. Singh AK, Rivera R, Cooper GN Jr, Karlson KE: Early myocardial revascularization for postinfarction angina: Results and long-term follow-up. *J Thorac Cardiovas Surg* 6:1121, 1985
20. Stuart RS, Baumgartner WA, Soule L, Borkon AM, Gardner TJ, Gott VL, Watkins L Jr, Reitz BA: Predictors of perioperative mortality in patients with unstable post-infarction angina (Abstract) *Circulation (Suppl IV)* 78:488, 1987
21. Tarr F, Tomácsnyi I., Lónyai T, Lakos Gy, Sugár T: Az intraoperatív szívizomvédelem néhány sajátossága gyakorlatunkban (Some features of intraoperative heart muscle protection in our practice) Magyar Kardiológus Társaság Tudományos ülése (Scientific Meeting of the Hungarian Cardiological Society) Balatonfüred, 1984

22. Tarr F, Lónyai T, Lakos Gy, Tomcsányi I: Nyitott szív műtétek utáni sternum szétválás kezelése (Treatment of sternal diastasis following open heart surgery) *Magy Seb* 36:153–158, 1983
23. Tarr F, Lakos Gy, Tomcsányi I, Sugár T, Hajdu L, Lónyai T: Az endocavitalis hűtés jelentősége intraoperatív szívizomvédelemben (The role of endocavital cooling in intraoperative heart muscle protection) *Orv Hetil* 130/1:13–16, 1989
24. Tarr F, Lakos Gy, Tomcsányi I, Sugár T, Hajdu L, Lónyai T: Teljes revascularizációra való törekvés az a. mammaria internák felhasználásával (An attempt to reach complete revascularization by using the internal thoracic arteries) *Magy Seb* 43:159–165, 1990
25. Tarr F, Tomcsányi I, Lónyai T, Lakos Gy, Sugár T, Hajdu L: Endocavital Seeling in intra-operative myocardial protection during extra-corporeal circulation. *The J Cardiovasc Surg* May–June 3:289–293, 1990
26. Varnauskas E: The European Coronary Surgery Study Group: Survival, myocardial infarction and employment status in a prospective randomized study of coronary bypass surgery. *Circulation (Suppl. V)* 72:V90–V101, 1985

Treatment Experiences with Intracavitary ^{137}Cs After-loading in a Five-year Patient Material with Uterine-Cervical Carcinoma

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Between 1979 and 1983 a total of 106 patients with carcinoma of the cervix and 53 with that of the uterine body were treated. The irradiation treatment of the patients was carried out by after-loading, with Curiatron equipment using ^{137}Cs . Since no reports have so far been published in Hungary on a patient material treated by the above method and with caesium isotope, it seems worthwhile to review the material. Our report is concerned with parameters which enable the assessment of the after-loading method. In cervical carcinoma a five-year survival rate of 59.4% was found, with the same in uterine carcinoma being 69.8%. It should be noted that data referred to all stages in the given tumour. The tumour-free state of the surgical preparations was also examined, and finally, postirradiation complications are also reviewed. Based on our results, the intracavitary Cs^{137} after-loading is considered by us to be one of the safely and efficiently used procedures in the irradiation treatment of cervical uterine carcinoma.

Material and method

The CGR MeV Curiatron after-loading equipment using ^{137}Cs radiation sources was set in operation in 1978. The characteristics of the equipment and the essence of the method have already been reported elsewhere [9]. In the present study the results of treatment in the period between January 1979 and December 31, 1983 are reported. The material includes 106 cervical and 53 uterine carcinoma patients. Figure 1 shows the stage distribution of the patients with uterine carcinoma. Here, 51 patients were considered operable and after-loading treatment was administered preoperatively, while in 55 cases, from the outset only curative irradiation was found to be justified. Figure 2, similarly demonstrates the stage distribution of the uterine carcinoma patients. A total of 32 patients were irradiated preoperatively, while 21 were irradiated curatively.

Our treatment method is similar to the method used in Paris. In cervical carcinoma, preoperatively a focal dose of 35 Gy was applied on point "A", then irradiation treatment was followed by operation in 4–5 weeks. In case

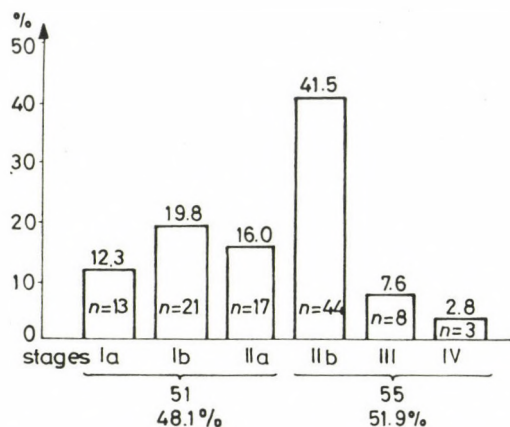


FIG. 1. Distribution of stages in cervical cancer

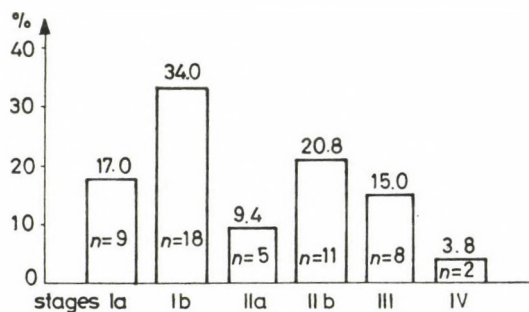


FIG. 2. Distribution of stages in uterine cancer

of a tumour-specimen, a regular cytological, gynaecological control was agreed upon. In the opposite case cavital treatment was completed by a stump dose of 30 Gy, then a focal dose of 50 Gy was used for external (Telecaesium) irradiation in a daily dose of 1.7–2 Gy fractions.

In stages I/B–I/A, intracavitary irradiation treatment was administered interval of ten days. After operation point “B” was additionally irradiated with a 50–60 Gy focal dose from an external irradiation source.

In patients in stage II/B the two intracavitary irradiations (with a total dose of 60–65 Gy on point “A”) were followed by an external one with a dose of 55–60 Gy.

In patients in stage II or II/B an applied scheme is used, or first a dose of 30 Gy from an external irradiation source is used on a large lower abdominal region, followed by the intracavitary irradiation (35 Gy on point “A”). Finally, point “B” is completed with an additional treatment up to a dose of 50–60 Gy by using Telecaesium treatment.

In patients with uterine carcinoma, orientation about the parameters of the uterus is made by atraumatic hystero-graphy applying gray-scale echography and a child's Foley catheter, then a myometrial dose of about 45 Gy is given by using subsequently introduced radiation sources of different lengths (activity) in applicators introduced into the corpus in accordance with its parameters. Postoperatively, if the specimen has remained tumorous, stump (30 Gy) and external Telecaesium irradiations are performed.

Discussion

The efficiency of a treatment method is best reflected in the case of oncological patients by their survival statistics.

Table I shows the survival data of cervical carcinoma patients in years, in the separate stages, in collated stages, in both percentage and absolute numbers as well. It seems to be a matter of course—and this is primarily not

TABLE I

Stage		Survival in uterine cancer (years)					
		0.5	1	2	3	4	5
I	e/n	34/34	33/34	33/34	33/34	33/34	33/34
	%	100.0	97.1	97.1	97.1	97.1	97.1
II	e/n	57/61	9/31	42/61	38/61	35/61	29/61
	%	93.2	80.3	68.8	63.3	57.3	47.5
III	e/n	6/8	4/8	2/8	1/8	1/8	1/8
	%	75.0	50.01	25.0	12.5	12.5	12.5
IV	e/n.	2/3	1/3	0/3	0/3	0/3	0/3
	%	66.7	33.3	0.0	0.0	0.0	0.0
I-IV	e/n	99/106	87/106	77/106	72/106	69/106	63/106
	%	93/4	82.1	72.6	67.9	65.1	59/4

the merit of ^{137}Cs after-loading—that the best results can be found in the earlier stages (97.1% survival rate). From stage II onwards, there is a great decline in survival rates, amounting to 47.5% for five years. The trend of deaths suggests that stage II can be regarded as a sort of turning point, and here prevention, cancer screening and the importance of early diagnosis should be repeatedly stressed. As a literary comparison, the paper of A. C. Voss et al. [10] should be pointed out, who made irradiation by radium brachytherapy, i.e. not by after-loading. Their survival results were worse in stage I, while better than those with ^{137}Cs after-loading in stage II. The data of our

TABLE II

Stage		Survival in cervical cancer (years)					
		0.5	1	2	3	4	5
I	e/n %	27/27 100.0	26/27 96.3	25/27 92.6	24/27 88.9	24/27 88.9	24/27 88.9
II	e/n %	15/16 93.8	13/16 81.2	13/16 81.2	12/16 75.0	12/16 75.0	11/16 68.8
III	e/n %	6/8 75.0	3/8 37.5	2/8 25.0	2/8 25.0	2/8 25.0	2/8 25.0
IV	e/n %	2/2 100.0	2/2 100.0	0/2 0.0	0/2 0.0	0/2 0.0	0/2 0.0
I-IV	e/n %	50/53 94.3	44/53 83.0	40/53 75.5	38/53 71.7	38/53 71.7	37/53 69.8

uterine cancer patients are shown in Table II, given in detail similarly to cervical cancer. Although the number of cases is not high, they still reveal that the 88.9% survival rate achieved in stage I was worse than in the case of uterine cancer (97.10%). It seems that in uterine cancer, at least in stage I, the effect of after-loading is weaker than in cervical cancer. On the contrary, however, the results of the five-year survival in stage II are more favourable in cervical cancer (68.8% and 47.5%, respectively). This can obviously be attributed to the fact that, because of the larger number of tumour-positive surgical specimens, postoperative irradiation of the stump and external irradiation have been made more frequently, the patients have received gestagen treatment more often, i.e. their treatment has been more radical in its entirety. This, however, raises the question whether a more radical treatment should be administered in stage I, even in case of histologically tumour-negative surgical specimens. A special evaluation of the more advanced cases demonstrated in the two tables is not justified because of the scarce number of cases.

As mentioned earlier, in stages I/A-II/A of uterine cancer, 51 patients received intracavitary ^{137}Cs after-loading, similarly to the 32 patients in stages I/A-II/A of uterine cancer. The study of the number of cases in which the surgical specimens have turned tumour negative was considered as the justification for irradiation. It is possible that in some per cent of the cases even diagnostic abrasion may sometimes in toto remove the tumour in the initial phase [3], however, it practically occurs only in endometrium carcinoma. In uterine carcinoma no operation was made in 55 patients because of the stage, so here there were no surgical specimens either, nevertheless, 32 specimens became tumour-free in 51 operable cases (62.7%) as opposed to the

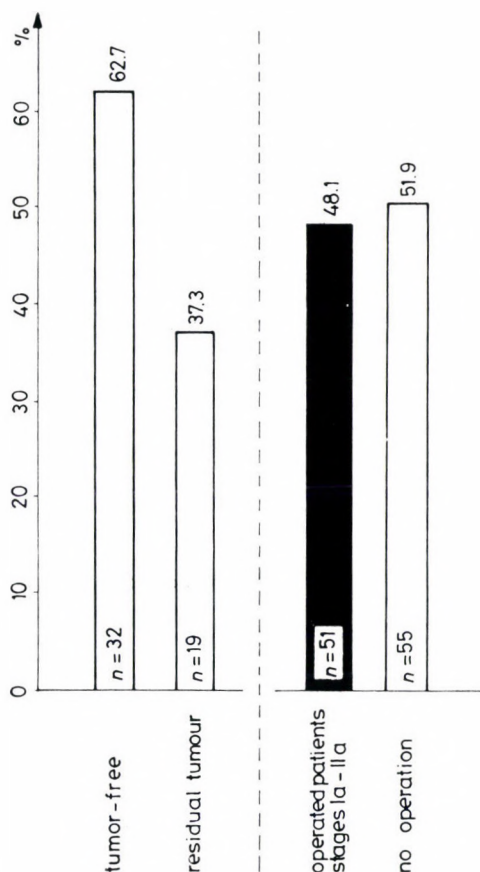


FIG. 3. Tumour-free state of surgical specimens in cervical cancer

19 cases where residual tumours were found by the pathologist even despite preoperative irradiation. Similarly, in uterine cancer (Fig. 4) 21 only irradiated patients were excluded from the analysis, and 12 out of 32 operable cases proved to be free of tumour (37.5%) as compared to the 20 residual tumours. In our opinion this favourable trend in the histological findings of the surgical specimens can be attributed to the intracavitary ^{137}Cs method.

Finally, one other question to be reviewed here is the occurrence of complications associated with irradiation (Figs 5 and 6). As seen, in cervical cancer no complications associated with irradiation occurred in a total of 101 patients (935.3%), while the same figure was 41 (77.3%) in uterine cancer. In the latter, primarily rectal complications developed in 16% of the cases. Considering the already cited paper of Voss et al., they described a 16.4% frequency rate of complications after radium brachytherapy.

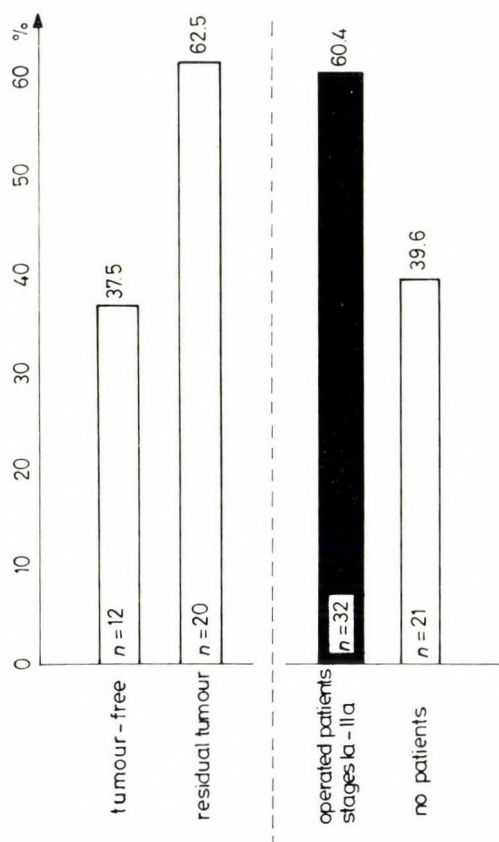
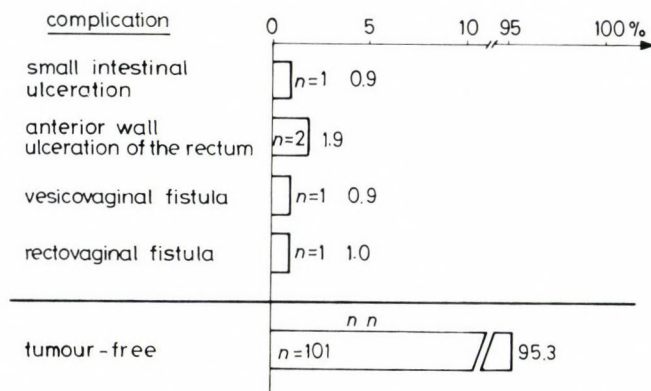


FIG. 4. Tumour-free state of surgical specimens in uterine cancer

FIG. 5. The frequency of various complications after ^{137}Cs after-loading irradiation in cervical cancer patients

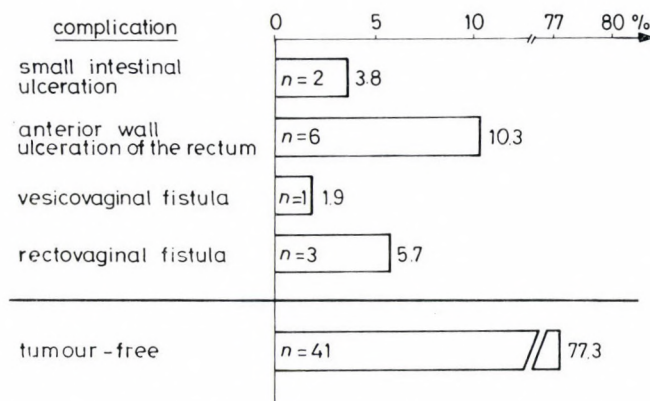


FIG. 6. The frequency of various complications after Cs^{137} after-loading irradiation in uterine cancer patients

Curietron after-loading equipments are applied by several institutes abroad. Henschke et al. [4] drew attention already in 1964 to the advantages of after-loading. The applicator containing the isotope ^{137}Cs and introduced by Henschke, ensures the distribution of the appropriate superficial dose, since after-loading brachytherapy is aimed at the concentration of the desired radiation dose in the "target" region, being only minimal on other points. Several experts concerned with the issue acknowledge that the ^{137}Cs radiation sources have been gaining ground in therapy [3]. Chassagne et al. [2] emphasize, in addition the possibility of elimination of the radiation exposure of therapists. Several authors have pointed out that ^{137}Cs after-loading brachytherapy is favourable concerning irradiation complications and this can be ascribed to optimization of dosage [1, 8]. In agreement with all opinions and critical comments made so far, Leung [7] emphasizes, the expensiveness of the procedure. Since the equipment itself is expensive and not available to all institutes, there are understandably controversial views concerning after-loading in gynaecological brachytherapy. We mention on the basis of personal experience that in the Radiumhemmet in Stockholm—although using Caesium—Heyman's packing seems to dominate, while in Göteborg the after-loading method is preferred. Among Hungarian authors, the pioneering study of Lehoczky et al. [6] should be mentioned, where they drew attention, as early as in 1972, to the potentialities inherent in the method.

In summary, although the after-loading method has been adopted by practice, primarily as a procedure ensuring the radiation protection of the staff, the favourable survival results based on our own material and experiences, the histologically verifiable cancerocidal effect on tumour, as well as the small number of associated complications, have all proved that intracavitary ^{137}Cs after-loading is one of the adequate and well-applicable procedures in the combined treatment of cervical and uterine cancers.

Acknowledgements

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References

1. Anderson LL: Physical optimization of afterloading techniques. *Strahlentherapie* 161/5:264, 1985
2. Chassagne D, Delovche G, Rocoplan JA, Pieque B, Gest J: Description et premieres essais du Curietron. *J Radiol Electrol* 50:910, 1969
3. Csömör S Jr, Hunka R: A Méhtestrák kezelésével szerzett tapasztalataink (our experiences obtained on treating uterine cancer). *Magy Nőorv L* 42:607, 1979
4. Henschke UK, Hilaris BS, Mahan CD: Remote after-loading with intracavitary applicators. *Radiology* 83:344, 1984
5. Jones WK: Gynecological cancer treatment with the Curietron. *Austral Radiol* XIII/3:253, 1979
6. Lehoczky Gy, Tordy B: After-loading kezelésről (After-loading treatment). *Magy Nőorv L* 35:205, 1972
7. Leung PMK: Experience with after-loading technique in intracavitary therapy. *Int Rad Oncol Biol Phys* 10:157, 1984
8. Vayrynen T, Kiviniitty K, Kaupilla A: CRE calculations for different combined radiation treatment schemes of uterine cervical carcinoma. *Strahlentherapie* 157:396, 1981
9. Vigváry Z, Csömör S, Fehér L, Hintalan A: Klinikai tapasztalataink a Curietron típusú after-loading berendezéssel nőgyógyászati daganatos beteganyagunkon. (Our clinical experience with Curietron after-loading equipment in gynaecological tumour patients) *Magy Nőorv L* 48:349, 1985
10. Voss AC, Decker K, Brandt H, Koch HL: Die Kombinierte Behandlung des Zervixkarzinoms. *Strahlentherapie* 157/9:557, 1981

Intra-abdominal Desmoids Observed after Total Proctocolectomies

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Two cases of mesenteric desmoids observed after colectomy are reviewed. In one of them the familial polyposis had been known, in the other familial history could not be proved. Fibrous change prevented making of the planned Kock reservoir.

Familial colonic polyposis is a disease of autosomal dominant inheritance [1, 9]. The genetic abnormality is associated with chromosome 5 [2, 12].

If this is associated with ossification disorder in the skull and mandible, dental abnormalities appear, epidermoid cysts can be noted, and there is on increased proneness to fibrosis, desmoids formation, and malignant diseases, Gardner's syndrome can be considered [3, 4, 5, 8, 10, 11].

All symptoms cannot be observed in each case. In 1986 Thomas reported 87 cases where all symptoms were present, in additional 79 cases, one or two main symptoms were absent. Genetic studies considered these, on the basis of familial occurrence as Gardner's syndrome [7].

In 1962 it was described by Schiffman that the clinical picture is often associated with retroperitoneal and mesenteric fibrous proliferation [6]. In our department, recently two such patients were observed, who had previously undergone total proctocolectomy, and the second operation revealed abdominal wall and mesenteric fibromatosis.

Case Reports

Case I. V. I. female patient, aged 47 years. She had a history of medicinal treatment for thyroid enlargement from 1961. In 1973 she was operated because of rectal papilloma. In 1978 melaena developed, followed after one year by colonic polyposis. Total colectomy and ileorectostomy were performed. In 1978 she felt a hard mode in the scar of the abdominal wall, which was not painful, but was growing gradually. She was admitted this year for creation of a permanent ileostomy. Sonography and CT performed preoperatively disclosed a pelvic tumour, it was primarily considered to be gynaecological in

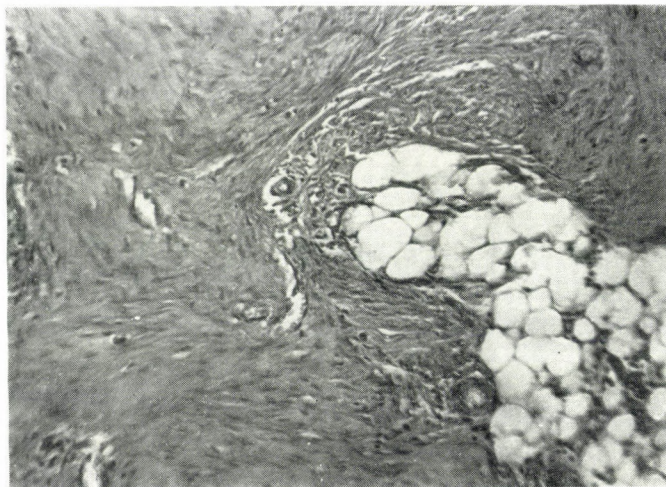


FIG. 1. The moderately cell-rich, fibromatous tumour infiltrates the adipose tissue

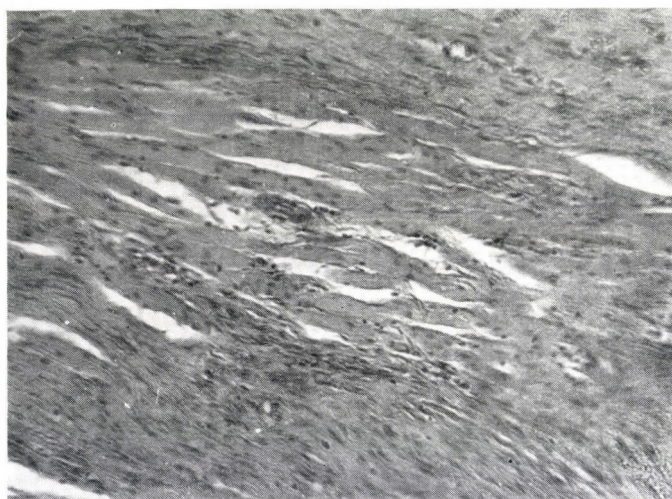


FIG. 2. Note the infiltration by the tumour tissue of the striated muscle of the abdominal wall, too, in the form of irregular bands. The picture illustrates clearly why is it so difficult to excise the tumour completely

origin. On exploration a compact, hard mesenterium of nodular surface was detected. Biopsy was performed from this as well as from abdominal wall the tumour displaying the same structure on the cut surface. The microscopic picture was the same in both biopsy specimens, consisting of a compact, fascicular fibrous tissue poor in cells, with adope tissue and striated muscle on its edges and internally. The microscopic picture was suggestive of desmoids fibromatosis (Figs 1,2).

Case 2. Male patient, aged 43 years. In 1983 he underwent total proctocolectomy because of degeneration of his familial colonic polyposis having been known and controlled for years. After two years of being complaint-free, abdominal cramps and passage disorders appeared. He was referred to us for establishment of a permanent ileostomy. On exploration, a shortened mesenterium with rigid infiltration was found, a hard tumours formation, 2–3 cm in diameter in the musculus rectus abdominis. At surgery, injury of the small intestine occurred which was sutured. On the eighth day after operation paralytic ileus developed. Operation was performed, revealing feculent peritonitis. The patient died on the evening of the operation.

Histological study of the parts of tissue excised from the mesenterium and abdominal wall, respectively revealed desmoids fibromatosis.

Discussion

Abdominal wall and extra-abdominal desmoids are well known clinical pictures. The intra-abdominal form, associated in one of our cases with a known, while in the other with a verifiable familial colonic polyposis, is primarily a partial phenomenon of Gardner's syndrome. The fibroblastic increase of activity present from the onset in this disease is enhanced by the operations and traumas.

Although in patients having undergone colectomy for carcinoma underlying familial colonic polyposis, local tumour recurrences, should also be reckoned with. Intra-abdominal desmoids, first of all in the mesenterium or retroperitoneum may also pose a differential diagnostic problem. These may diminish, or eventually frustrate the possibilities of later corrective operations.

References

1. Lokhart-Mummery HE: Intestinal polyposis: the present position. *Proc R Soc Med* 60:381, 1967
2. Nakamura Y, Lathrop M, Leppert M, Dobbs M, Wasmouth J, Wolf E, Carlson M, Fujimoto E, Krapchor K, Sears T, Woodward, S, Hughes J, Burt R, Gardner I, Lalouel M, White R: Localization of genetic defects in familial adenomatous polyposis within a small region of chromosome 5. *Am J Hum Genet* 43:638, 1988
3. Mayler EW, Gardner EJ, Richards RC: Desmoid tumours and mesenteric fibromatosis in Gardner's syndrome. Report of Kindred 109. *Arch Surg* 114:1181, 1979
4. Piffer S: Gardner's syndrome and thyroid cancer. A case report and review of the literature. *Acta Oncol* 27/4:413, 1988
5. Richards RC, Rogers SW, Gardner EJ: Spontaneous mesenteric fibromatosis in Gardner's syndrome. *Cancer* 47:597, 1981
6. Shiffman MA, Beach L: Familial multiple polyposis associated with soft-tissue and hard-tissue tumors. *JAMA* Feb 17:514, 1962
7. Thomas KE, Watne AL, Jonson JC et al: Natural history of Gardner's syndrome. *Am J Surg* 115:218, 1968

8. Traboulsi ET, Maumenee IH, Krush AJ, Giardiello FM, Leven TS, Hamilton SR: Pigmented ocular fundus lesions in the inherited gastrointestinal polyposis syndromes and in hereditary nonpolyposis colorectal cancer. *Ophthalmology* 95:964, 1988
9. Ujszászi L, Nagy Gy, Prónay G: Genetikai tényezők a vastagbélrákban (Genetic factors in cancer of the colon). *Az orvostudomány aktuális problémái* (Current problems of medicine) 191:207, 1986
10. Vaquero G, Lis F, de: Síndrome de Gardner asociado a un carcinoma de mama. *Rev Esp Enf Ap Digest* 74:4, 1988
11. Vereckei L, Gál I, Dobi S, Krajczár G, Arany L: Gardner szindróma (Gardner's syndrome). *Orv Hetil* 121/7:401, 1980
12. Woodward SR: RFLP analysis in familial polyposis and Gardner syndrome. In: *Basic and Clinical Perspectives of Colorectal Polyps and Cancer*. Alan R Liss Inc London, 1988, pp 305

Follow-up of the Effect of BCG in Bladder Tumour Patients

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The intravesical BCG effect in 38 patients with superficial bladder tumour after TUR was followed by the lymphocyte transformation test (LTT) and the staphylococcus phagocytosis test of *in vitro* washed leukocytes. The results have confirmed the immunostimulating and hence anti-tumour effect of intravesical BCG. The beginning and the duration of the stimulation effect were defined and the necessity of maintenance treatment was verified. Authors consider monitoring of the cellular immune response suitable for the continuous follow-up of the BCG effect. Comparing the tolerable side-effects with their favourable therapeutic results, BCG is considered to be suitable for the prevention of recurrences in treating superficial bladder tumours.

While diagnosed, 70 to 80% of bladder tumours are still in the superficial stage [23]. According to literary data, within one year after surgical removal of the tumour the ratio of recurrences is 50–70%, the recurrences being notable in grade in 20–28%, while in stage in 7–25% of the cases [11, 12]. That is why it is necessary to apply a possibly effective therapy following the surgical removal of the visible tumour.

In addition to local chemotherapy having been used since 1961, as a result of the tumour-immunological researches of the 70s, intravesical BCG treatment has been extensively employed in the last two decades [19]. It is true that BCG treatment has already been known for a decade, several questions, among them first of all its mechanism of action has still not been completely clarified. According to some authors, intravesical BCG exerts a favourable effect through the intact or injured bladder mucosa [2], while according to others through the interaction with fibronectin [25, 26]. As a distant effect, it increases interferon and interleukin production, i.e. the anti-tumour mechanisms by activation of macrophages, T-lymphocytes and K-(killer)cells [2, 21].

Nor it is appropriately known when, beside the local effect of BCG, its immunostimulating effect appears, for how long it lasts and, as a consequence, at what intervals it is indicated or else contraindicated to be applied. To follow these parameters, the reactivation of the T-lymphocytes and the phagocytotic ability of leukocytes of tumour patients were investigated *in vitro*.

Patients and method

In the period from January 1989 to April 1990, intravesical BCG was administered to 38 patients with superficial uroepithelial carcinoma (T_a, T₁) according to the scheme of Morales [19] (Table I). For treatment, 20 mg/ml lypophilic Pasteur's BCG vaccine having been put at our disposal by the BCG laboratory of the National Institute for Public Health was used, the unit live bacterial count being 2.4×10^6 ml.

TABLE I
The most important data of our 38 patients

No. of patients	Males: 24	Females: 14	Total: 38
Superficial bladder tumour	Primary 29 Single 28	Recurrent 9 Multiple 10	
Follow-up time (months)	6-18	Mean	12
Stage/grade	T _a G ₁ 18 G ₂ 8	T ₁ G ₁ 5 G ₂ 3	

The immune effect was measured by the phagocytosing ability of *in vitro* washed leukocytes as well as the lymphocyte transformation test (LTT) indicating cellular immunoreactivity. Blood coagulation was inhibited by pure heparin, to prevent the culturability of lymphocytes by the preservative. On using LTT, one part of the lymphocytes were cultured without antigen (control), which remained unchanged until the end of culturing in healthy individuals.

To the other part of T-lymphocytes Difco-P Phytohaemagglutinin (PHA) was given, which is a non-specific, but vigorously mitogenic substance.

On evaluation, the ratio of cells transformed into blast was compared to the intact T-lymphocytes, while on examining phagocytosis, it was assessed what percentage of leukocytes was capable of phagocytosing the bacteria. and, on the other hand, how many bacteria one cell is able to ingest.

In addition, T-lymphocytes were in some cases treated also directly *in vitro* with BCG.

The examination was made prior to administering BCG, during the treatment and at weekly then, in general, at monthly intervals. Every three months cytoscopic and random bioptic controls were performed, in addition to the chest X-rays and laboratory tests. Average follow-up time was one year.

Results

Depending on the tumour stage, the stimulability of T-lymphocytes as compared to the controls (mean 65–85%) in the patients with superficial bladder tumour was found to be reduced (46–60%). Following BCG treatment, this value—being the expression of the cellular immune response—approached the normal value (Fig. 1).

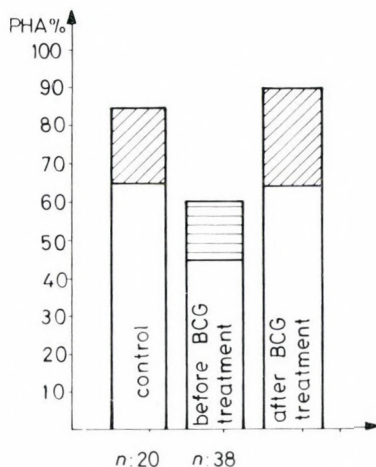


FIG. 1. Change in the stimulability with PHA of lymphocytes due to BCG treatment

During the follow-up study, it was observed that the favourable immunoreactivity following administration of BCG decreased after some months (on average: 3.5 months), then by repeated administration (1×120 mg), the stimulability of T-lymphocytes again increased (Fig. 2).

In other cases morphological and functional impairment of the cells could be noted. In this patient group side-effects occurred at a higher rate. In such cases BCG was not administered. Complications arising during treatment are shown in Table II, the light microscopic picture of cells produced due to PHA and BCG in Fig. 3a–b, while the impaired cells in Fig. 4.

It is notable that in patients, who did not show an adequate immune response to repeated BCG administration, recurrences occurred more often (Table III).

The bacterium phagocytosing ability of the same patients was, similarly to the LTT test, diminished (30–35%) as compared to the control (70–75%). However, after treatment this value approached the normal value with lymphoblast transformation (Fig. 5).

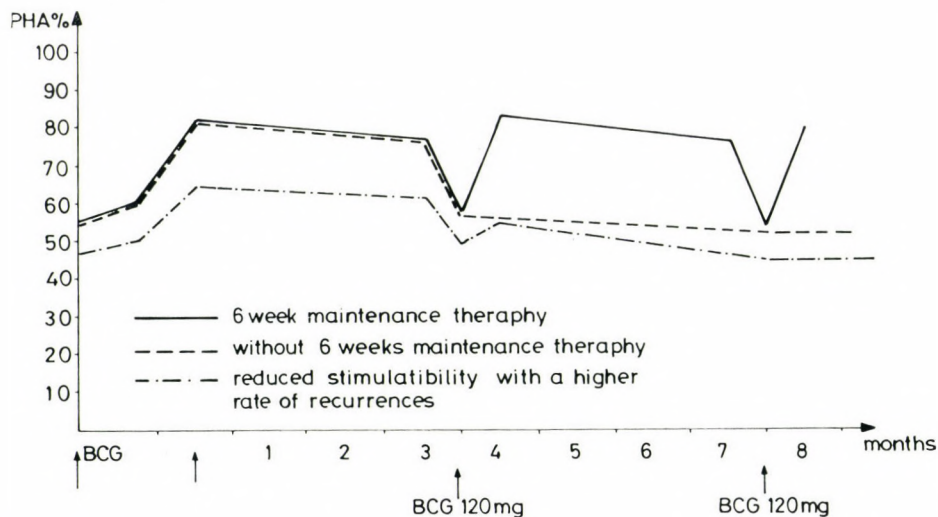


FIG. 2. Change in the stimulability of PHA of lymphocytes during BCG treatment and subsequently in the function of time

TABLE II

Distribution of side-effects in 38 patients with bladder tumour treated with intravesical BCG

Frequent micturition	23
Haematuria	14
Dysuria	12
Fever	10
Articular pain	6
Flu-like	6
Pyuria	7
Suspension of treatment because of severe symptoms	3

Discussion

It is known from the literature that stimulation of the weakened immune system in tumourous diseases favourably influences the disease [3, 7, 29]. Besides levamisole [6], haemocyanin [14, 15] and interferon [8, 24], undoubtedly BCG has recently come to the fore as a non-specific stimulant in relation to bladder tumours [18, 33]. Results obtained so far reflect that, in superficial bladder tumours, postoperative intravesical BCG treatment causes a more complete remission in a higher percentage of cases, even despite the more serious side-effects, than do Adriamycin, thiotepa, Epodyl, Doxorubicin and mitomycin-C [17, 22, 31, 32].

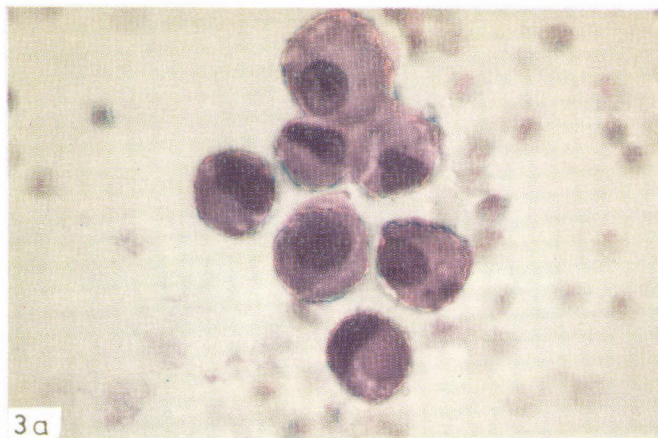


FIG. 3a. Note the giant blast cells, arising due to BCG treatment

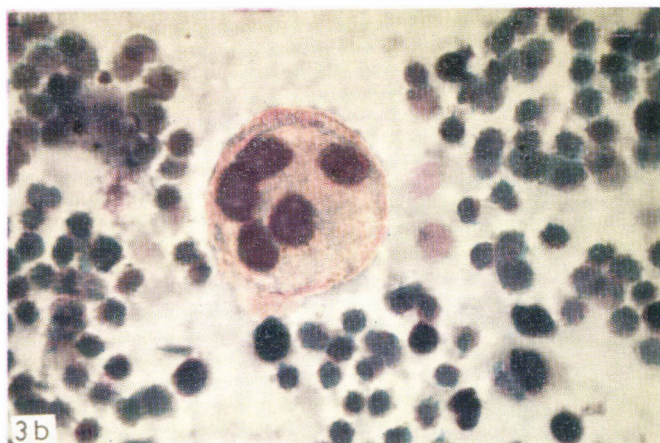


FIG. 3b. Among the small lymphocytes, polynuclear blast cells can be seen

Although recently a considerable amount of experience has accumulated concerning intravesical BCG treatment (the strain to be selected, treatment protocol, dosage, etc.), its mechanism of action is still debated. A great part of authors agree that BCG, as a non-specific immunomodulator, has a local and general effect [2, 7, 33].

The studies with monoclonal antibodies of the diffuse mucosal inflammation arising after BCG treatment, as well as of the suburothelial granulomas appearing later have verified, as opposed to the advocates of the theory of

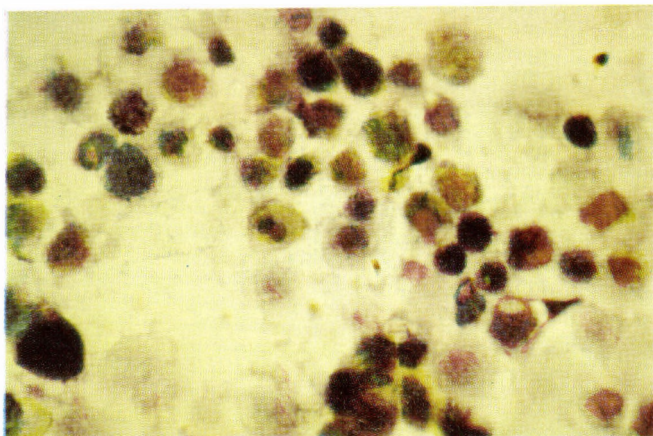


FIG. 4. Light microscopically lymphocytes with fragmented nucleus are noted produced by BCG overdosage

TABLE III

*Survey of results obtained with intravesical BCG treatment after TUR
(mean follow-up time: 1 year)*

Total number of patients: 38	
Recurrence within one year	Free of recurrences
12 (31%)	26 (69%)
9 (75%)	
Reduced PHA stimulability	

cell-detachment after simple inflammation, the local immunostimulating effect of BCG. Besides the quantitative difference, an essential qualitative difference was also found in the immunohistochemical picture of the non-specific or cytostatic cystitis [10, 27].

Following treatment, mostly lymphocytes (T-helper) suppressor (1 : 2–2 : 1) and plasma cells were found to be present in the mucosa and the submucosa, but also polynuclear giant cells, histiocytes and neutrophils, appeared. It is notable that these changes, supposed to be related with the effectivity of BCG, were observed permanently if the patients received a maintenance therapy every three months after the 6-week treatment [2, 3, 34]. Others, however, question the necessity of maintenance therapy [1, 4, 13].

The immune response of the host organism is elicited by the circulating macrophages. The macrophages, besides their anti-tumour cell-destructive ability, activate cytotoxic lymphocytes, and K-cells through the growth of interferon and interleukin production.

There have been scarce reports on the changes in peripheral blood. Similarly to the animal experiments of Schellhamer, after BCG therapy Winters found a significantly higher anti-BCG antibody titre in the blood, and found their changes to be more sensitive indicators than the PPD (Purified Protein

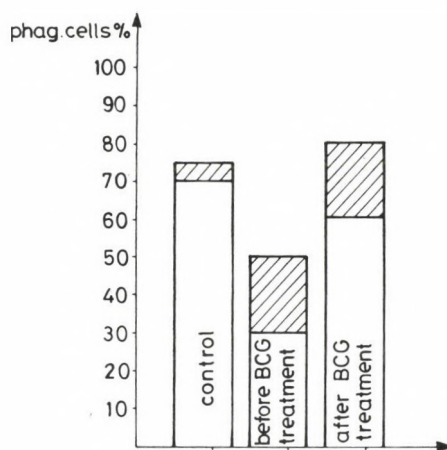


FIG. 5. Change of the phagocytosing ability of polymorphonuclear cells due to BCG treatment

Derivative) skin test [35]. The applicability of PPD skin test was also questioned by others [9]. In 1987 Nissenkorn determined the monocyte activation of peripheral blood after BCG treatment. He found that in patients where the activation of monocyte was of a smaller extent, there were more recurrences. In 1987 he treated human monocytes with BCG. As a result of treatment, the isolated monocyte cytolytic factor elicited a considerably anti-tumour effect against the bladder tumour cells [35]. Ruitenbergh verified in animal experiments the macrophage and lymphocyte function-stimulating effect of BCG preparations. The maximal lymphocyte stimulation after BCG administration was found by him to be 14 to 21 days [30].

Our results have confirmed the observations according to which, in addition to its local effect, intravesical BCG has an immunomodulator effect as well.

The effect in the immune system becomes evident immediately after starting treatment, increasing abruptly from the 2nd–3rd weeks onwards and lasting for some months (on average 3–4 months).

On repeated administration of BCG (120 mg) the decreasing immune response can again increase. That is why maintenance therapy is considered necessary.

In addition to the generally favourable stimulating effect, BCG occasionally produces the morphological and functional impairment of the immune cells. Therefore, in such cases, it is not recommended to administer BCG for the risk of more severe side-effects.

In cases where the patient's immune cells cannot be mobilized even on repeated BCG treatment, there is a greater risk of recurrence, and it may be an alerting sign for changing therapeutic strategy.

Finally, it can be stated that the study of cellular immune response is suitable for following the efficiency of BCG therapy and for the selection of the maintenance therapy.

References

1. Badalament RA, Herr HW, Wong GY: A prospectiv randomized trial of maintenance versus non-maintenance intravesical BCG therapy of superficial bladder cancer. *J Clin Oncol* 5/3:441, 1986
2. Böhle A et al: Effect of local BCG therapy in patients with bladder carcinoma on function of mononuclear cells. *Int Soc Urol Rep.* (Churchill Livingstone, Edinburgh, London, Mellbourne, New York) 10:83, 1990
3. Catalona WJ: Immunotherapy of genitourinary cancer. In: Javadpour IV (ed): *Recent Advances in Urologic Cancer.* Springer Verlag, London 1982, p 280
4. Catalona WJ et al: Risk of benefits of repeated courses of intravesical BCG therapy for superficial bladder cancer. *J Urol* 137:220, 1987
5. Catalona WJ, Tarpley JL, Chretien PB: Lymphocyta stimulation in urologic cancer patients. *J Urol* 112:373, 1974
6. Csapó Z et al: Urothelium dysplaziák diagnosztikája, prognosztikai és terápiás következményei hólyagtumoros betegekben (Diagnosis, prognostic and therapeutic consequences of urothelial dysplasia in bladder tumour patients). *OrvHetil* 125: 1875, 1984
7. Eric O et al: Role of immunotherapy in prevention of recurrence and invasion of urothelial bladder tumours, A review. *World J Urol* 3:76, 1985
8. Fontana G, Sesia G, Albadio F: Pilot study on the effects of peritumoral and intranodal injection of low doses of interferon-gamma in patients with recurrent superficial bladder carcinoma. *Int Soc Urol Rep.* (Churchill Livingstone, Edinburgh, London, Mellbourne, New York) 16:145, 1990
9. Gögös O, Safak M, Küpel S: Five-year follow-up bladder tumours treated with BCG. *Int Soc Urol Rep.* (Churchill Livingstone, Edinburgh, London, Mellbourne, New York) 16:37, 1990
10. Guinon P, Show M, Ray V: Histopathology of BCG and thiotepa treated bladders. *Urol Res* 14: 211, 1986
11. Haff EO et al: Two courses of intravesical BCG for transitional cell carcinoma of the bladder. *J Urol* 136:820, 1986
12. Herr H: Effect of intravesical BCG for carcinoma in situ of the bladder. *Cancer* 51:1323, 1983
13. Hudson MA, Ratliff TL: Single course v.s. maintenance BCG therapy for superficial bladder tumor. A prospective randomized trial. *J Urol* 138:299, 1987
14. Jurincic C, Stöcker W, Markl J: Immunotherapy with Keyhole-limpet haemocyanin (KLH) as prophylaxis against superficial bladder tumour recurrence. *Int Soc Urol Rep.* (Churchill Livingstone, Edingburgh, London, Mellbourne, New York) 15:139, 1990
15. Klippel KF, Paulini C: The effect of keyhole limpet hemocyanin (KLH) on the bladder cancer. *Immunology and immunotherapy* 3:65, 1977

16. McLaughlin AP: Immunkompetenz bei urologischen Krebserkrankungen. *Akt Urol* 6:215, 1975
17. Martinez-Pimeiro JA: BCG versus Doxorubicin v. thiotepa instillation for primary superficial bladder cancer. Interim report of a randomized prospective study. *SIU Immunother Urol Tumours* 8:59, 1990
18. Morales A: Long-term results and complications of intracavitary BCG therapy for bladder tumours. *J Urol* 132: 457, 1984
19. Morales A: Long-term results on complications of intracavitary BCG therapy for bladder cancer *J Urol* 132: 675, 1984
20. Nakamura I: Monocyte cytolytic factor in promoting monocyte-mediated lysis of bladder cancer cells by BCG. *J Urol* 138:867, 1987
21. Nissenkorn J, Lavie G, Keisar H: Value of monocyte activation in patients with superficial transitional cell carcinoma of bladder treated with BCG. *Eur Urol* 13:246, 1987
22. Netto NR, Ancone ID: BCG immunotherapy in bladder cancer. *Int Soc Urol Rep* (Churchill, Livingstone, Edinburgh, London, Melbourne, New York) 1:12, 1990
23. Otto U, Huland H, Klosterhelfen H: Rezidiv Prophylax oder lacklicher Harnblasenkarzinome. Thieme Verlag, Stuttgart, New York 1984, p 1
24. Ratliff TL, Kadman D, Shapiro A: Inhibition of mouse bladder tumour proliferation gamma and its synergism with interferon beta. *Cancer Res* 44:4377, 1987
25. Ratliff TL, Kavaoussi L, Catalona WJ: Role of fibronectin in intravesical BCG therapy for superficial bladder cancer. *J Urol* 139:410, 1988
26. Ratliff TL, Palmer JO, McGarr JA: Intravesical BCG therapy for murine bladder tumours: initiation of the response by fibronectin mediated attachment of BCG. *Cancer Res* 47:1762, 1987
27. Riedasch G: Local immune response in experimental and clinical urinary tract infection. *Dial Transplant* 10:644, 1981
28. Romics I: Diagnosztikus és terápiás lehetőségek hólyag és prostata daganatos betegek immunstatusa alapján (Diagnostic and therapeutic possibilities on the basis of the immune status of bladder and prostatic tumour patients). Thesis, Budapest 1984
29. Romics I: Urológiai daganatok immunológiai változásai (Immunological changes of urological tumours). *Orvosképzés* 60:45, 1985
30. Ruitenberg EJ, Jong WH de, Dreeftenberg JG: BCG preparations, cultured homogeneously dispersed or as a surface pellicle elicit different immunopotentiating effects but have similar antitumor activity in murine fibrosarcoma. *Cancer Immunol Immunother* 11:45, 1981
31. Rübber H, Graf C, Dobberstein R: Prospektiv randomized study. Adjuvant therapy after complete resection of superficial bladder cancer, mitomycin-C v.s. BCG Connaught v.s. TUR alone. *Int Soc Urol Rep* (Churchill, Livingstone, Edinburgh, London, Melbourne, New York) 3:37, 1990
32. Solway MS: BCG for tretment of the bladder in patients WHO failed Thiotepa and/or Mitomycin-C. *J Urol* 137:871, 1987
33. Samodai L et al: A BCG immunoterápia és eredményei a hólyagdaganatok kezelésében (BCG immunotherapy and its results in the management of bladder tumours). *Orv Hetil* 131:1677, 1990
34. Winkler H et al: The significance of tumour histology in the results of treatment with intravesical BCG for superficial bladder cancer. *Int Soc Urol Rep* (Churchill, Livingstone, Edinburgh, London, Melbourne, New York) 6:45, 1990
35. Winter WD, Lamm DL: Antibody responses to BCG during immunotherapy in bladder cancer patients. *Cancer Res* 41:2672, 1981

Technique of Extensive Proximal Selective Vagotomy

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Based on the experience of 727 operations, the technique of proximal selective vagotomy used by the authors is reviewed in stages. They consider pyloroplasty justified to perform only in complicated cases (bleeding, perforation, stenosis) for preventing complications. Based on their results (mortality rate: 0.68%, recurrences: 6.3%, excellent or good results: 90%), they argue for the operation.

In the surgical management of duodenal ulcer and its complications (bleeding, perforation, stenosis), proximal selective vagotomy (PSV) has been a more and more extensively used and accepted operation. Its main advantage, as opposed to traditional (resection) operations, lies in its low mortality and morbidity, as well as the good functional results.

Several synonyms are used in the literature for the operation:

1. Proximal selective vagotomy
2. Selective proximal vagotomy
3. Superselective vagotomy
4. Ultrasensitive vagotomy
5. Highly selective vagotomy
6. Parietal cell vagotomy
7. Acid-fundic selective vagotomy
8. Secretory selective vagotomy
9. Selective gastric vagotomy
10. Partial gastric vagotomy
11. Acid-secreting vagotomy.

The essence of the operative technique was developed in the course of dog experiments by Griffith and Harkins [10]. The operation was carried out in humans, in combination with pyloroplasty first by Holle and Hart [12]. PSV without pyloroplasty was introduced into clinical practice by Burge [cit. 7] five years later, in the non-stenosed forms of duodenal ulcer. In the subsequent period, the number of reports on PSV has increased and it has become a generally used operation.

In Hungary, Berger [5] was the first to report on PSV. Gergely [8] published well-grounded observations on the necessity of a change in views. In 1982, the Surgical World Congress in Stockholm persistently advocated this surgical solution in the management of peptic ulcers.

In spite of all these, PVS has not gained full recognition, and the number of resections performed in ulcerous diseases has multiply exceeded that of organ-preserving vagotomies. The analysis of the causes of this phenomenon would be out of the scope of this report, however, the lack of mastering the surgical technique would be most probably one of them, as well as its possibly incorrect use and its consequential incomparability to resections. These thoughts have prompted us to report on this operative technique based on the experience of more than 700 proximal selective vagotomies performed by us.

Several surgeons have contributed to improving the operative technique [1, 7, 9, 14, 15, 17, 18]. The so-called extensive PSV worked out by Johnston and Wilkinson [15], then modified by Kuzin et al. [17] differs from the classical PSV in our performing, besides skeletization of the lesser curvature, also that of the greater one. Our team has made the operation easier and more effective by further modifications based on the practice of performing 727 operations up to that time.

In order to have a better insight, the operation has been divided into stages.

Stage I. Positioning the Patient on the Operating Table, the Role of the Boas' Probe

The appropriate positioning of the patient on the operating table largely facilitates dissection to be made on the oesophagus and its region. Care should be taken that elevation should be in the height of the xiphoid process, as well as the operating table should be slightly tilted towards the foot (anti-Trendelenburg position). Thus both the small intestines as well as the transverse colon are removed from the surgical area according to the gravitational force. A Boas probe, 1.5 cm in diameter, is introduced into the stomach of the already anaesthetized patient, through which the contents of the stomach is aspirated. Subsequently, with the abdomen being open, the Boas probe is introduced through the pylorus into the duodenum. A probe placed like that, flexibly stretches out the stomach, revealing the greater curvature in a shoe-tree-like manner, making thereby easier the dissection on the lesser curvature. Alongside this, the assistant can pull the stomach downwards together with the Boas probe without any difficulty, to facilitate denervation in the higher segments and around the oesophagus (Fig. 1). The Boas probe may play a role in establishing the fact of stenosis, i.e. the necessity of performing pyloroplasty as well.

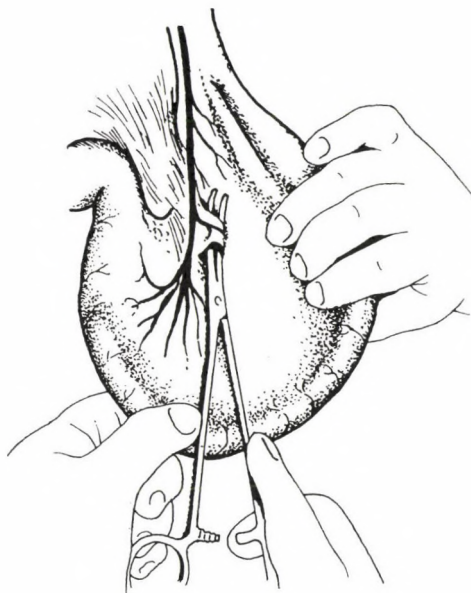


FIG. 1. Stomach stretched by using the Boas probe. Latarjet nerve of the anterior wall and its craw-foot-like branching. Starting of denervation on the anterior wall of the stomach

According to our experience, if the probe can be introduced unheeded under the ulcerous part, organic stenosis can be excluded. In perforation, if suturing is made above the Boas probe, there is no risk of stenosis due to suturing.

Stage II. Laparotomy, Obligatory Revision of the Abdominal Cavity, Operative Plan

The operation was performed from upper median laparotomy by passing round to the left (sometimes to the right) the xiphoid process. Carrying the incision below the navel is justified only in obese patients. Special instruments for exploration are not used. Transection of the ligament teres hepatis is not by all means necessary: the pylorus can mostly be explored also without it, in case of need a plastic operation can be made. Laparotomy is followed by the obligatory revision of the abdominal cavity: all abdominal organs are inspected, searching for an associated disease, the detection of which may have surgical or other therapeutical consequences. After the obligatory inspection of the abdominal cavity the diagnosis is made more accurate and this is the time for the final decision to be made concerning the operation. It may occur in a previously operated abdomen (e.g. suturing because of perforation and peritonitis) that the gastrohepatic ligament has adhered to the inferior

surface of the liver, being unfit for fine dissection. In this case, as a matter of course, PSV should not always be performed. PSV is also contraindicated in stages III and IV of a stenosed duodenal ulcer, too, when it is pointless to perform an organ-preserving operation because of the marked ectasia, the definitive impairment of the stomach musculature.

Stage III. Isolation of the Vagal Trunk

After introduction of the Boas probe as described above, with the stomach being pulled down, the intra-abdominal segment of the oesophagus is exposed by spatulas and the peritoneum is cut transversely in the phrenico-oesophageal junction. The anterior and posterior vagal trunks are located and isolated, suturing them by supporting sutures (Fig. 2). This procedure, mainly if the surgeon is not experienced enough, will prevent him from accidentally transecting the trunci on exposure of the periesophageal region on termination of the operation, which, remaining undetected, may result in gastric stasis in PSV without pyloroplasty as well as in a failure of the opera-

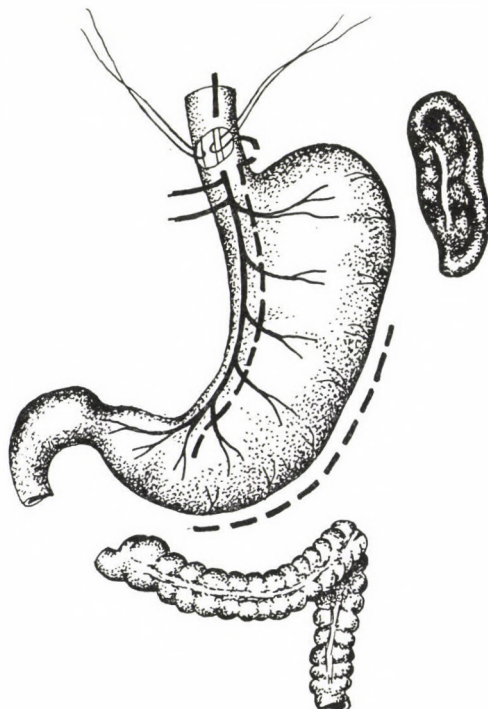


FIG. 2. Isolation of the vagus trunks. The line of skeletization of the greater and lesser curvatures as well as of the periesophageal region

tion. In addition, it is easier to locate and dissect the nerves running from the vagal trunks to the gastric wall by pulling the vagal trunks to the right and the sutures reperitonizing the lesser curvature to the left.

Stage IV. Skeletization of the Greater Curvature of the Stomach

Skeletization of the greater curvature, i.e. the detachment of the gastro-colic ligament from the stomach has two advantages:

1. Thus the stomach can be "leafed through" in upward direction, and identification of the posterior Latarjet nerve, and dissection in the posterior

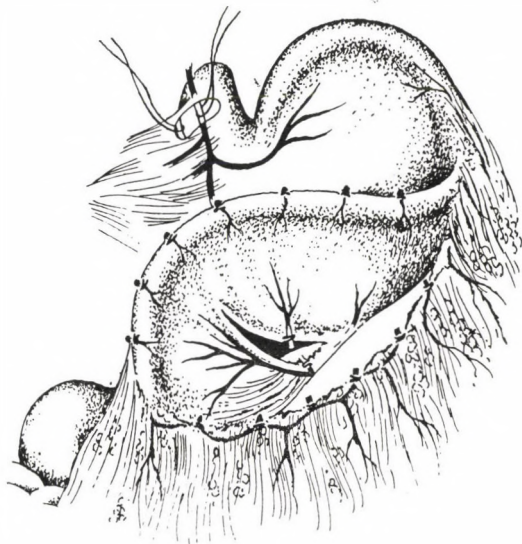


FIG. 3. The stomach leafed through upwards. The posterior Latarjet nerve. The beginning of denervation on the posterior wall of the stomach

wall of the stomach can be made under inspection of the naked eye (Fig. 3). The posterior Latarjet branch is, namely, not always in the projection of the inferior one, and if we try to find it blindly from the front by "piercing through" the lesser curvature, it may be easily injured and destroyed.

2. This procedure results in further decrease in acid secretion. According to Brizzi's observation [6], the stomach is supplied by parasympathetic fibres also along the greater curvature. This observation has also been confirmed by intraoperative pH measurements: after skeletization of the larger curvature, no pH values below 4 along the greater curvature can be found.

Skeletization of the greater curvature is commenced in the projection of the anterior Latarjet nerve and is carried at a length of about 12–15 cm up-

wards (Fig. 2), quite up to the line of origin of the short gastric arteries. This is the region where the vascular (and nerve) structures running to the stomach are becoming reduced in number. It is not necessary to preserve the left gastroepiploic artery, moreover it is recommended to transect it between ligations. By leafing through the stomach in upward direction the omental bursa is exposed. Here, fibrous adhesions are often found (perigastritis) which can be transected without ligation, they do not contain any vessels. So the posterior Latarjet branch can be easily brought into the visual field, and the ulcers of the posterior wall can be identified (Fig. 3).

**Stage V. The Substantial Part of the Operation:
Denervation of the Acid-producing Region of the Stomach
Retroperitonization of the Lesser Curvature**

PSV is based on the physiological observation that the acid-producing regions (parietal cells) are situated only in the proximal two-thirds of the stomach, in the region of the corpus and fundus. There is no direct acid production in the antrum: the antral "G" cells exert their effect via the gastrin hormone produced by them. Denervation should, as a result, be only confined to the region of the corpus and fundus. Preservation of the innervation of the antrum and the pylorus is of great importance in ensuring the adequate emptying of the stomach: the preserved "atropyloric pump"—the pylorus opening at the end of the constricting antral peristalsis—enables PSV to be performed without pyloroplasty. In complicated cases of duodenal ulcer, where pyloroplasty is inevitable for prevention of the complication, the preserved antropyloric mechanism ensures the regular evacuation of the stomach through the well-fashioned orifice.

Denervation of the acid-producing region consists in the transection of the delicate nerve branches bifurcating into the region of the corpus and fundus from the anterior and posterior Latarjet nerve. Since these small structures cannot be separated from the also delicate vascular structures running along them, denervation of the corpus-fundus means, at the same time, its complete skeletization, denervation and devascularization, too. This way, the proximal two-thirds of the lesser curvature of the stomach are completely denuded. This is made in three steps, since also the lesser curvature consists of three "layers".

1. In our practice, denervation of the acid-producing region in the leafed through state of the stomach is begun on its posterior wall (Fig. 3). One should be aware that the gastric ligament sort of "rides" the lesser curvature and the feet (i.e. the vascular and nerve structures) running to the posterior and anterior wall of the stomach anchor the gastric ligament to the lesser curvature.

In view of this, it is not recommended to pierce the gastric ligament through right at the beginning of skeletization, because the Latarjet nerve attached to (or running on) the lesser curvature by anchoring, may become injured. It is advisable to transect the anchoring structures on the posterior, then on the anterior wall separately, by viewing the posterior and anterior Latarjet nerve at the same time at a distance of half to 1 cm in the direction of the stomach. Transection is made between fine ligatures, taking care not to tug the suture, since the thin vessels may easily get torn, haematoma may arise in the gastric ligament, which makes orientation difficult. Here, therefore, it is particularly important to apply the principal of "local knotting". The keeping of a distance of 0.5 to 1 cm is important for other reasons as well: should a minor vessel be torn or the ligature be detached, there is still room for arresting bleeding without the risk of injury of the Latarjet nerve.

The posterior Latarjet branch and its "crowfoot"-like division in the antral region is easy to identify, with the stomach kept upwards. *The nerve running to the region of the antrum, being continuous to the Latarjet nerve should be preserved*, as well as all the others leading to the pylorus with this "crow-foot" like branching. The branches of this division returning to the stomach are transected and all the structures lying above them, i.e. the vessels and nerve running in the posterior ligament of the gastrohepatic ligament, and the anchors indicated by the posterior "riding foot". With adequate exposure even the cardia can be reached.

2. By leafing back of the stomach, *the same is carried out also on the anterior wall proceeding bottom up* (Fig. 1). In such a way the anterior plate (anterior "riding feet") of the gastrohepatic ligament is transected together with the structures contained in them, with careful controlling of the Latarjet nerve.

3. The third layer is known under the name "intermediary layer". This loose connective tissue layer is situated between the anterior and posterior layers, with structures leading directly to the edge of the gastrohepatic ligament. Transection of this intermediary layer does not cause any difficulty, since by transecting the posterior and anterior layers (by eliminating the anchors), the Latarjet nerves become removed from the lesser curvature.

Reperitonization of the lesser curvature implies the invagination into the stomach of the lesser curvature detached from the gastrohepatic ligament, skeletized and hence deprived of its serosal lining, in a way that the anterior wall covered with intact serose is joined by seromuscular sutures to the posterior wall of intact serosal lining (Fig. 4). This has two: (i) With the reperitonizing sutures, the lesser curvature can be pulled downwards and so dissection in the upper segments becomes easier, and (ii) it prevents the complication known as ischaemic necrosis of the lesser curvature. Should this still happen,

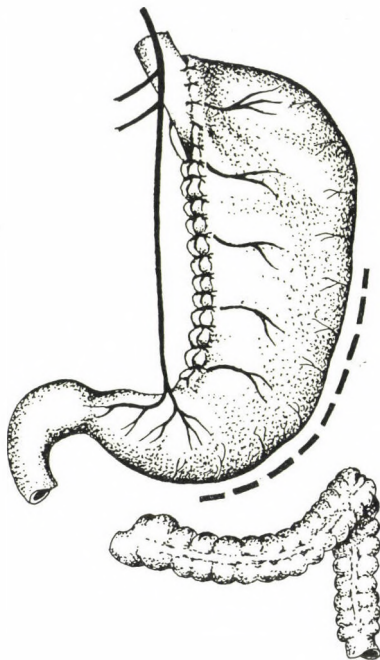


FIG. 4. Reperitonization and fundoplication of the lesser curvature

perforation or mural necrosis occur into the closed lumen of the stomach, which so cannot give rise to peritonitis. Experiences at home and abroad concerning ischaemic necrosis of the lesser curvature have been reported elsewhere [2].

Stage VI. Circular Denervation of the Lower Segment of the Oesophagus, Fundoplication According to the Modified Procedure of Nissen-Rosetti

Denervation of the lower oesophageal 4–5 cm long segment (Fig. 2) and fundoplication according to the modified procedure of Nissen-Rosetti are integral parts of the operation. Circular skeletization of the abdominal segment of the oesophagus is important because small nerve branches can detach from the vagal trunks at this height reaching the fundus (the acid-producing region) of the stomach proceeding among the longitudinal muscle fibres of the oesophagus. The nerve branch named “ramus criminalis”, which occasionally branches off high from the anterior vagal trunk and runs to the fundus, and which, being not transected, may even ruin the operation itself, can be located only with the circular denervation of the oesophagus up to this height [7, 17]. Fundoplication is actually the continuation of the reperitonization of the lesser curvature to the oesophagus. In addition to protecting and covering the denuded oesophagus, it acts as an “anti-reflux” operation, because it prevents

gastro-oesophageal regurgitation. The modified procedure of Nissen-Rosetti is preferred: this eliminates the so-called telescope-phenomenon, i.e. the downward-upward movement of the oesophagus in the invaginated fundus, making permanent the physiological His' angle. It should be noted here that the stomach can be pulled and kept to the right by the subdiaphragmatic isolation of vagal trunks described in stage III of the operation and by passing through them a supporting suture, while to the left by applying reperitonizing sutures, and hence the tissues stretching between the threads can be better viewed and the direction of skeletization of the lesser curvature can be better determined. Tearing of the hepatic branches of the vagus nerve is a risk of isolating the vagus trunks, the prevention of which is the essential part of selective and proximal selective vagotomy.

Stage VII. Pyloroplasty

Pyloroplasty (ppl.) is justified to perform if it is inevitable in preventing some complications (haemorrhage, perforation, stenosis). Results are namely better if PSV is made without ppl.: the pyloric function is preserved and no duodenogastric biliary reflux has to be reckoned with.

In haemorrhage, the operation is to be started by arresting bleeding. The bleeding ulcer is located from a longitudinal antroduodenotomy. If it is on the anterior wall, after its excision in a laurel-leaf form, a Heinecke-Mikulitz ppl. is made. If it involves the posterior wall, bleeding is arrested conventionally by supporting sutures (Fig. 5), which is followed by ppl. In case of a deep, postbulbar ulcer, longitudinal duodenotomy not reaching the pylorus can be made with its longitudinal or transversal closure as required by the situation. Thus pyloric function can be preserved [11, 16, 17, 18].

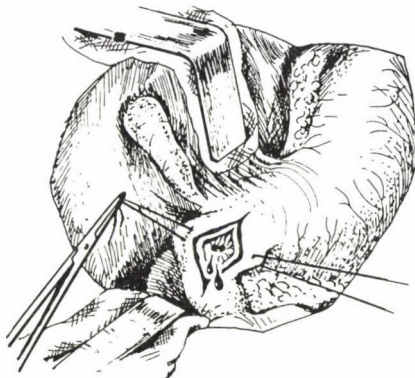


FIG. 5. Localization of a bleeding ulcer of the posterior wall from longitudinal antroduodenotomy

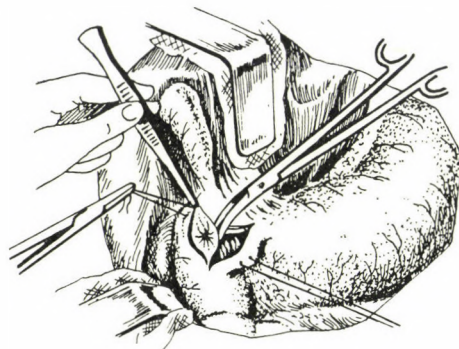


FIG. 6. Laurel-leaf-shaped excision of the perforated ulcer

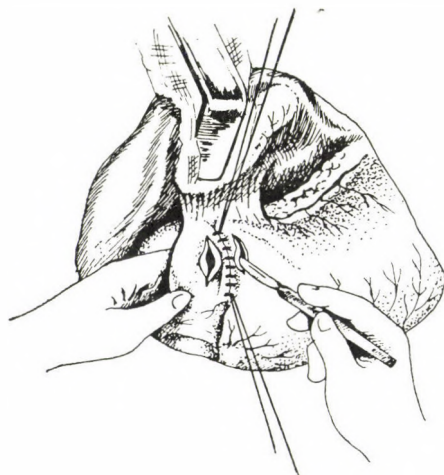


FIG. 7. Jaboulay's pyloroplasty (antroduodenostomy)

Under limited conditions, PSV can be performed also in perforation [4]. In such a case the operation is commenced with management of the perforation orifice. If there is no stenosis and the perforation orifice can be easily sutured, then traditional sutures are applied, with a row of sutures in two layers. In stenosis, or if suturing is not safe because of an oedematous or sometimes callous environment, the perforation orifice is excised in the form of a laurel-leaf and the resulting defect is closed with sutures placed in the already intact wall by the Heinecke-Mikulitz ppl. (Fig. 6).

According to our experiences, the best results in stenosis can be obtained by Jaboulay's ppl. (Fig. 7). Ignoring the ulcer attached to its scarred, shrunk environment (hepatoduodenal ligament, pancreas) and penetrating into it, a

new two-inch broad gastric outlet is fashioned in between the antrum covered with intact serose and the pars descendens duodeni mobilized according to Koch (antroduodenostomy).

Stage VIII. Intraoperative pH-measurement

The importance of intraoperative pH-assessment has been reported separately [13]. Intraoperative control examination can be of great help in mastering a correct surgical methodology and in reducing the number of recurrences. After an adequate practice, however, the operation can also be performed without intraoperative pH-measurement.

Stage IX. Reconstruction of the Gastrocolic Ligament Revision before Closure. Drainage, Nasogastric Probe

The gastrocolic ligament transected during skeletization of the greater curvature is reconstructed, the ligament is sutured back to the greater curvature of the stomach. Drain is retained only after perforation. The introduction of a nasogastric probe is unnecessary after PSV without pyloroplasty, no retention occurs in the denervated-devascularized stomach. In cases with pyloroplasty, it is by all means recommended to ease tension in the suture line. The operation is terminated by the layerwise closure of the laparotomy wound.

The patients are mobilized on the first postoperative day and they are given tea already 24 h following the operation.

In the recent ten years (1989–1989), using the above technique, a total of 727 PSVs have been performed. The distribution of our operations according to indication in function of mortality and recurrences is summarized in (Table I). In concert with data in the literature, the mortality rate (0.68%) not even

TABLE I
Distribution according to indication of patients operated by PSV
Mortality, recurrences
No. of cases: 727

Indication	No. of cases	Deaths	Recurrences
Chronic duodenal ulcer	450	2	27
Stenosing duodenal ulcer	134	1	17
Perforation	75	1	—
Haemorrhage	45	1	6
Ventricular or double ulcer	23	—	1
TOTAL	72	5(0.68%)	46(6.3%)

reaching 1% has proved the low risk of the operation, which is, at the same time, its greatest advantage as opposed to traditional operations. The recurrence rate of 6.3% is an acceptable incidence rate, which can be ascribed to the standardized technique detailed above. The detailed clinical results are going to be reported and evaluated in a separate paper.

Follow-up of the operated patients, as revealed by our five-year follow-up examination, showed almost in 90% (excellent and good) results according to groups I to II of Visick's classification [3].

References

1. Amstrup E, Jensen H: Selective vagotomy of the parietal cell mass preserving innervation of the undrained antrum. *Gastroenterology* 59:522-527, 1970
2. Bátorfi J, Ihász M, Balogh I, Kiss S, Horkai F, Bálint A: A proximális selectiv vagotomia speciális szövődménye: a kiscsőbületi ischaemiás necrosis. (Special complication of proximal selective vagotomy). *Magy Seb* 35:251-259, 1982
3. Bátorfi J, Szabó K, Fazekas T, Kiss S, Pintér L: A perforált duodenális fekély gyógyítása proximális selectiv vagotomiával (Management of perforated duodenal ulcer by proximal selective vagotomy). *Magy Seb* 41:9-16, 1988
4. Bátorfi J, Balogh I, Török A, Irházi Gy, Bálint A, Pintér L: A proximális selectiv vagotomia 5 éves eredményei (Five-year results of proximal selective vagotomy). *Orv Hetil* 128/51:2673-2675, 1987
5. Berger R: Selectiv proximális vagotomiadrainage műtét nélkül (Selective proximal vagotomy without drainage operation). *Magy Seb* 28:285, 1974
6. Brizzi E, Serantoni C, Ciani PA, Orlandini E, Pernice L: The distribution of the vagus nerves in the Chirurg. *Gastroenterol* 7:17, 1973
7. Civalero LA: Selective proximal vagotomy in duodenal ulcer. *Acta Chir Scand Suppl* 491, 1979
8. Gergely M, Assela Abebe J, Csonka Cs: Szemléletváltozás szükségessége a fekélybetegség sebészeti kezelésében (kezdeti tapasztalataink szuperszelektív vagotomiával) (The necessity of a change in views in the surgical management of ulcer (initial experiences by superselective vagotomy)). *Orv Hetil* 123/28: 1715-1719, 1982
9. Grassi G: The technique of proximal selective vagotomy. *Chirurg Gastroenterol* 5:399-405, 1971
10. Griffith CA, Harkins HN: Partial gastric vagotomy: an experimental study. *Gastroenterology* 32:96102, 1957
11. Hedenstedt S, Lundquist G: Selective proximal vagotomy (SPV) as an emergency and definitive operation for massive ulcerous bleeding. *Acta Chir Scand* 144:241-248, 1978
12. Holle F, Hart W: Neue Wege der Chirurgie des Gastroduodenal Ulcus. *Med Klin* 62: 441, 1967
13. Ihász M, Bátorfi J, Szabó K, Fazekas T, Horkai F, Bálint A, Kiss S: A vagotomia teljességének intraoperatív meghatározása (Intraoperative assessment of the completeness of vagotomy). *Magy Seb* 36:19-23, 1983
14. Inberg KR: Proximal selective vagotomy. *Chir Gastroenterol* 3:475-480, 1969
15. Johnston D, Wilkinson A: Highly selective vagotomy without a drainage procedure in the treatment of duodenal ulcer. *Br J Surg* 57: 289, 1970
16. Johnston D Lyndon PJ, Smith RB, Humphrey CS: Highly selective vagotomy without a drainage procedure in the treatment of haemorrhage perforation, and pyloric stenosis due to peptic ulcer. *Br J Surg* 60:790-797, 1973
17. Kuzin MI, Postolov PM, Kuzin NM: Technika rozhilennoy selektivnoy proksimalnoy vagotomii. *Chirurgiya* 2:3-9, 1980
18. Pencürev JM, Grinberg AA: Vagotómia. *Medicina*, Moscow, 1979

Effect of Orchiopexy on Human Testicular Ultrastructure

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The effect of orchiopexy performed before puberty on the testicular ultrastructure in sexually mature infertile men have been levels, as well as an analysis of permogram and karyotype was carried out. It was found an elevation of FSH and LH, while T levels were decreased. Disturbances in the ultrastructure of all testicular cell types-germ, Sertoli and Leydig cells are related with the smooth and rough endoplasmic reticulum and mitochondria as well. It is concluded that the application of orchiopexy in 8–10 years old cryptorchid boys have no curative effect on the descended testes.

Cryptorchism, a congenital anomaly carries a high risk of infertility in adulthood even if unilateral [6, 8]. The alterations in cryptorchid testis are concerned not only the seminiferous tubules but the interstitial Leydig cells as well [4, 5]. Application of different medical treatment (hormonal therapy or surgical operation) puts forward the problem of assessment their efficiency. In the literature many dogmatic statements exist about cryptorchidism and its treatment, reflecting subjective opinions more than scientific data [6]. Medical treatment by means of classic orchiopexy is always recommended if the testis is located in the inguinal canal. The operations seem to be clinically successful, but subsequent morphological studies of the operated testes are scarce [1, 3].

The aim of the present work was to study the effect of orchiopexy performed before puberty on testicular ultrastructure in sexually mature patients and to compare it with their endocrinological state.

Material and methods

The testicular material was obtained by the method of Vilar [14] from 3 healthy men who had normospermia and 6 men aged 19–26 years who had aspermia and sterility. The sterile men have suffered from unilateral undescended testes and orchiopexy has been performed before puberty (8–10 years). The specimens were fixed in phosphate-buffered 2.5% glutaraldehyde and

TABLE I

		Testosterone ng/ml	FSH mU/ml	LH mU/ml
Control (average)		476.5	10.31	7.61
Patients	Age	Age of operation		
1. A.R.	10	364	39.5	16.7
2. S.G.	9	93	50.4	19.5
3. D.V.	10	125	65	24.8
4. A.F.	10	320	17.3	13.8
5. E.A.	8	236	19.1	17.2
6. V.P.	9	258	23.2	18.3

postfixed in 2% OsO₄. The samples were embedded in Durcupan, semithin sections were stained with toluidine blue/borax, while ultrathin sections were contrasted according Reynolds [9]. The observations were carried out with Opton 109 electron microscope.

The results on FSH, LH and testosterone levels are summarized in table I.

The analysis of spermogram showed azoospermia, reduced ejaculate volume (average 2.2 ml), with normal pH and viscosity. Cytogenetic study indicated normal karyotype in all patients.

A semithin sections reveals longitudinal and cross sections of the seminiferous tubules, lined by an epithelium that comprised two categories of cells the germ and Sertoli cells. The lamina propria was considerably thickened. The germ cells present did not include all maturational types. In some tubules there were Sertoli cells only or Sertoli cells and spermatogonia, while in others the spermatogenesis proceeded as far as the primary spermatocytes and spermatids. The interstitial space was composed of Leydig cells, fibroblasts, macrophages and mast cells.

Germ cells. Among persisting spermatogonia a pale type. A cells were predominant whereas a dark type A and type B were rarely seen. The primary and secondary spermatocytes did not differ from normal ones. The spermatids in Golgi, cap and maturation phase were to be seen in some tubules, but very often immature spermatide were situated in the lumen without any contact with Sertoli cells (Fig. 1). Degenerating germ cells were encountered in large numbers within the seminiferous tubules (Fig. 2).

Sertoli cells. If the tubules consisted of Sertoli cells only or Sertoli and spermatogonia, the Sertoli cells appeared as oval cells with non-lobulated nuclei. Their typical inclusions and junctional specializations were absent and Sertoli cells were similar to immature Sa-Sb type described by Hadziselimovic [4]. If however a primary spermatocytes were present in the tubules, the

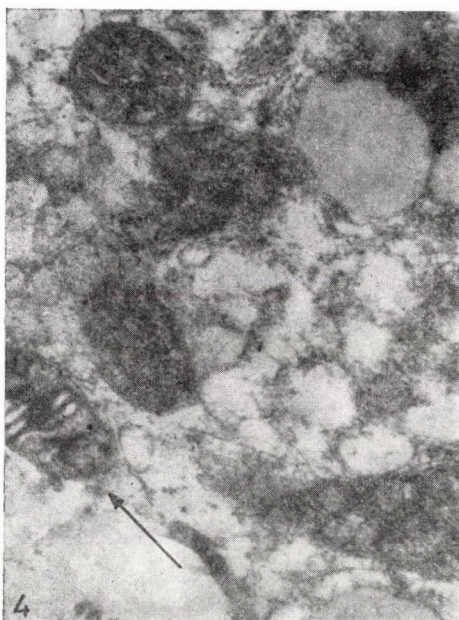
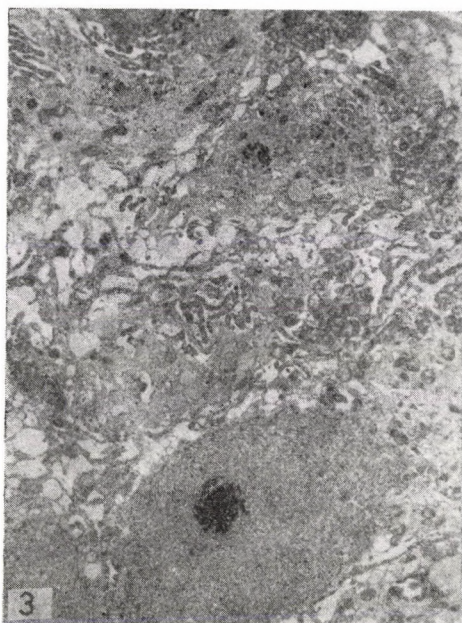
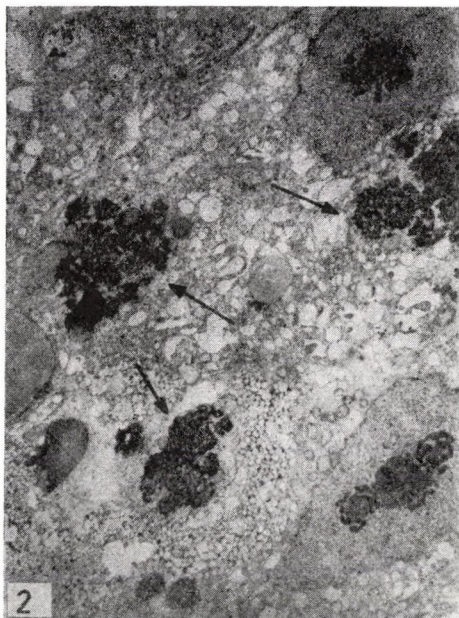
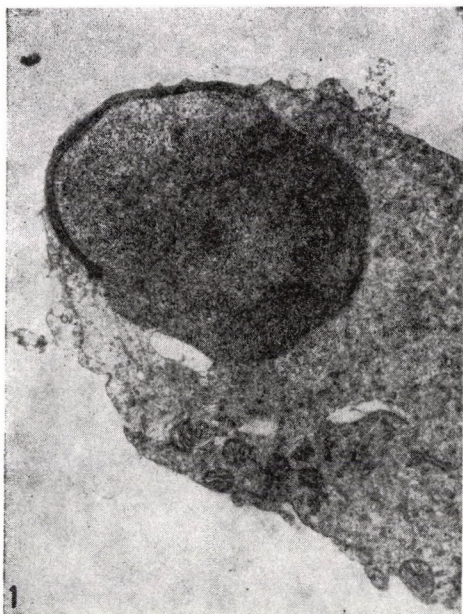


FIG. 1. Spermatid in cap phase without any contact with Sertoli cells. $\times 7000$

FIG. 2. Pyknotic nuclei of the degenerating germ cells (arrows). Sertoli cell cytoplasm is vacuolized. $\times 3000$

FIG. 3. Sertoli cell cytoplasm with dilatation and hypertrophy of SER and RER. $\times 3000$

FIG. 4. Network appearance of Leydig cell cytoplasm and degenerating mitochondria (arrow). $\times 30\,000$

Sertoli cells appeared as mature ones. The nucleus was lobulated and nucleolus was composed by three parts: pars amorpha, granularis and fibrilaris. The cytoplasm was damaged in different degree even in the same biopsy. A dilatation and hypertrophy of smooth and rough endoplasmic reticulum, disruption of the outer or inner mitochondrial membrane and crista swelling were often visible (Fig. 3). Various shaped osmiophilic inclusions either solitary or in membrane-limited complexes and lipid droplets were found in the basal cytoplasm. Abundance of tonofilaments was seen peripherally in the cytoplasm, as well as dilatation of the extracellular space between adjacent Sertoli cells.

Leydig cells. Apart from well preserved Leydig cells, there were many of them with atypical morphology: the nucleus was strongly lobulated with dense karyoplasm. In addition the cytoplasm was heavily vacuolized with a network appearance. The mitochondria were found to consist of roughly granulated matrix with closely outlined cristae displaying signs of pigment (myelin) degeneration (Fig. 4).

Discussion

The results presented suggest that the spermatogenesis in orchioepexian testis is damaged in all patients. In general, the morphology of the testis is similar to the cryptorchid ones [7]. In all patients the majority of seminiferous tubules consists of wide destructive zones. In addition, the seminiferous tubules of Sertoli-cell only syndrome patients do not contain germ cells. As is known, subjects with Sertoli-cell-only syndrome display elevated FSH level. This elevation has been attributed to disturbance of the FSH feedback mechanism, which in turn, has been explained up to now by deficient production of an inhibiting factor, reflecting the damage to the germinal epithelium [10]. In our cases an elevation in FSH levels could be established in all the patients with azoospermia. It was shown, that seminal fluid of azoospermic patients contained no inhibin [12].

The ultrastructural alterations of Leydig cells concern the smooth endoplasmic reticulum which became vacuolized and mitochondria which show myelin degeneration. As it is accepted the cholesterol is synthesized in the smooth ER, while mitochondria exhibit the side-chain cleavage enzymes which convert cholesterol to pregnenolone [10], and the smooth ER is responsible for the transformation of pregnenolone to testosterone [2]. Probably the alterations in Leydig cell ultrastructure in our patients resulted in a suppression of testosterone synthesis, confirmed by radioimmunoassay.

The results from this study indicate that the application of orchioepexy in 8–10 years old cryptorchid boys has no curative effect on the descendent testes. Our results put forward again the problem about the suitable time of

the orchiopexy. According to Gaudio et al. [3] the operation should be carried out at the age of two: Sizonenco et al. [13] recommended that surgery should be performed between 5 and 7 years of age, if the medical treatment has failed; while Scorer, one of the foremost experts on cryptorchidism wrote already in 1967 that the best moment for such an operation is the first year.

References

1. Alpert PE, Klein SR: Spermatogenesis in the unilateral cryptorchid testis after orchiopexy. *J Urol* 129:301, 1983
2. Christensen AK: Leydig cells. In: Hamilton DW, Greep RO (eds). *Male reproductive system. Handbook of Physiology Sect. 5p7*
3. Gaudio E, Paggiarino D, Caprino F: Structural and ultrastructural modifications of cryptorchid human testes. *J Urol* 131:292, 1984
4. Hadziselimovic F: Cryptorchidism. Ultrastructure of normal and cryptorchid testis development. *Adv Anat Embryol Cell Biol* 53:1, 1977
5. Hedinger Chr: Histological data in cryptorchidism. In: (ed) Job JC: *Cryptorchidism. Diagnosis and Treatment Vol 6*, Karger, Basel 1979
6. Job JC: Introductory remarks. In: Job JC (ed), *Cryptorchidism. Diagnosis and Treatment. Karger, Basel, Vol 6*, 1979
7. Kancheva LS, Martinova YS, Zvetkov DP: Nuclear ultrastructure of the spermatogenic cells in man under normal conditions and in fertility. *CR Acad Bulg Sci* 36:1127, 1983
8. Papp Gy, Lantos J, Molnár J: Orchidopexie und Fertilität. *Z Urol Nephrol* 74:541–545, 1981
9. Reynolds ES: The use of lead citrate at high pH as an electron opaque stain in electron microscopy. *J Cell Biol* 17:208, 1963
10. Schulze C: Sertoli cells and Leydig cells in man. *Adv Anat Embryol Cell Biol* 88:1, 1984
11. Scorer CG: Early operation for the undescended testis. *Br J Surg* 54:694, 1967
12. Scott RS, Burger HG: Inhibin is absent from azoospermic semen of infertile men. *Nature* 285: 246, 1980
13. Sizonenco PC, Schindler AM, Cuendet A: Clinical evaluation and a management of testicular disorders before puberty. In: Burger H, De Kretser D (eds) *The Testis*, Raven Press 303, 1981
14. Vilar O: Testicular Biopsy. *Int Congr of Andrology Barcelona* 1976

Our Experiences with the Management of Pyogenic Liver Abscesses by Percutaneous Transhepatic Puncture and Permanent Drainage Guided by Computed Tomography

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Thirty-three patients with pyogenic liver abscess were treated by percutaneous transhepatic puncture or permanent drainage between the period of 1, January 1985 and 31, December 1990. The closed puncture or drainage resulted in the complete recovery of 26 patients ($26/33 = 78.8\%$). Surgical intervention was made 6 ± 5 days following closed drainage in 7 cases ($7/33 = 21.2\%$). After percutaneous intervention complications ensued in four patients ($4/33 = 12.1\%$). one patient died ($1/33 = 3\%$). Solitary abscess occurred in 24, while multiple in 9 patients. Based on the authors' experiences, they consider the closed percutaneous puncture, or drainage guided by computed tomography—provided that proper skills and facilities are available—them does not enable in all cases the precise preoperative diagnosis even despite its richness of detail. In order to reduce uncertainties and to establish an accurate diagnosis, Herbert et al. [13], McCorreel et al. [6] and Perera et al. [22] proposed three criteria to be met before establishing the diagnosis of pyogenic liver abscess. According to the authors the conditions for accepting these criteria can be summarized as follows:

1. On the US examination of the liver, echo-free or echo-poor regions can be seen with increased background echoes. CT verifies an inhomogeneous, circumscribed or irregular-shaped, blurred focus of finely deformed contours being hypodense in contrast with the environment. On administration of contrast medium, the change is surrounded by a hyperdense border, and other causes for the above change can be excluded.

2. Verification of the presence of pus (by percutaneous puncture or surgery) from the liver biopsy.

3. The negative result of serological tests characteristic of amoebic infection. CT and US examinations have opened up new vistas not only in establishing diagnosis but also in the management of the disease. The closed percutaneous an effective method in the management of liver abscesses.

Liver abscesses belong to the rare changes. The incidence rate of recognized cases in the countries of temperate climate is 0.001–0.008 [5, 20]. In autopsy materials it occurs at a rate of 0.32–1.0% [18]. The prognosis of pyogenic liver abscesses is currently very serious. The mortality rate is 95–100% without treatment, while it is about 30% with up-to-date surgical therapy [22, 28]. According to Gerzof et al. [10], in 601 patients collected by

23 authors, the average mortality rate was 26% (156/601). The lethality in solitary abscesses ranged between 0 and 58%, while in multiple abscesses between 29 and 95%. The prognosis of pyogenic liver abscesses is defined, besides the underlying disease, primarily by rapid and accurate diagnosis and an immediately started complex therapy. Diagnostic errors at the onset of the disease reach 50 to 60% [6, 28]. In the recent decades, the extensive use of up-to-date imaging procedures—the 3rd generation axial tomography (CT) and of the high-resolution real-time sonographic (US) equipments—have offered a new possibility for the rapid and accurate diagnosis of the disease. The visual information obtained by puncture or drainage guided by CT or US has gained ground nowadays in the treatment of pyogenic liver abscesses [30]. In the present paper the experiences with percutaneous transhepatic puncture and drainage guided by CT in 33 patients are reported. In establishing an accurate diagnosis of the abscesses, the internationally accepted protocol detailed above was followed. Since amoebic liver abscess occurred only sporadically in the population attended by the two Institutes, no serological tests were performed for the exclusion of amoebic infection.

Material and method

In the 3rd Department of Surgery, Semmelweis University School of Medicine and in the A. V. Vishnevskii Surgical Institute in Moscow, a total of 33 patients were treated by percutaneous transhepatic puncture or drainage for liver abscess during the period of January 1, 1990 to December 31, 1990. The male: female ratio was 13 to 20. Average age was 47 years, the youngest patient being 17, the oldest 76 years old.

The studies were carried out in both institutes by Somatom a DR-2 Siemens third-generation computerized axial tomograph. Bacteriological and cytological (and if possible gas-chromatographic) studies of the discharge obtained by percutaneous transhepatic puncture were performed for the isolation of aerobic and anaerobic bacteria and for the exclusion of tumour.

The technique of percutaneous transhepatic puncture or drainage applied by us is as follows.

1. After the precise localization of the abscess detected by CT or US, the site of introduction of the puncturing needle, its direction and the depth of puncture are defined with the help of metal "marker" needles placed on the skin (Figs 1, 2).

2. Puncture is made under sterile conditions in local anaesthesia, after an incision of 0.5 to 1.0 cm by using a Chiba or modified Chiba needle (diameter: 0.3 to 0.7 mm). In case of successful puncture, attempts are made to

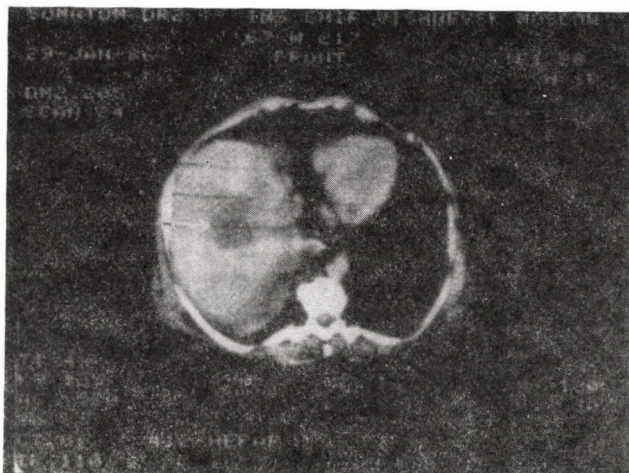


FIG. 1. Tomogram with the densities of the three "marker" metal needles placed on the skin

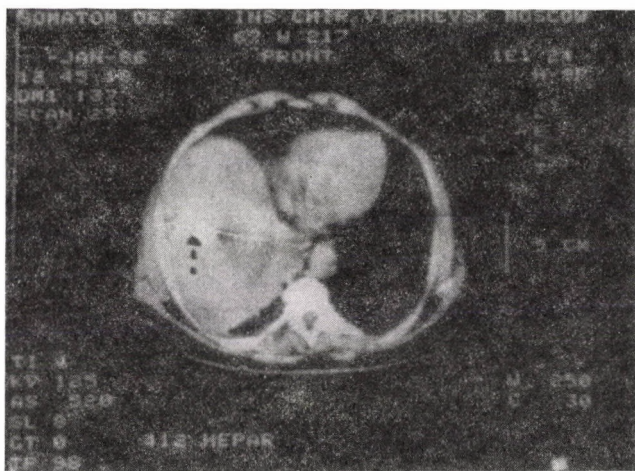


FIG. 2. Puncture of a solitary abscess in segment VII of the liver (tomogram of the same patient)

completely aspirate pus and the above-mentioned examinations are made from the discharge. In case of a minor solitary abscess ($0 < 3-4$ cm), the cavity is filled, after complete aspiration of the discharge with an antiseptic solution (Betadin) or a broad-spectrum antibiotic also affecting anaerobes (third-generation cephalosporin derivative, aminoglycoside antibiotic, etc.).

In case of a large abscess ($0 > 5-6$ cm) double drainage was performed (Figs 3, 4, 5).

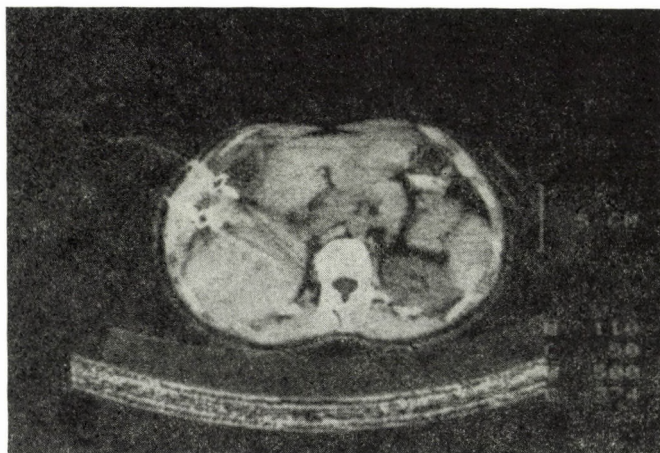


FIG. 3. Dual drainage of an abscess, 11×6 cm in size, in hepatic segments V, VI and VII (tomogram)

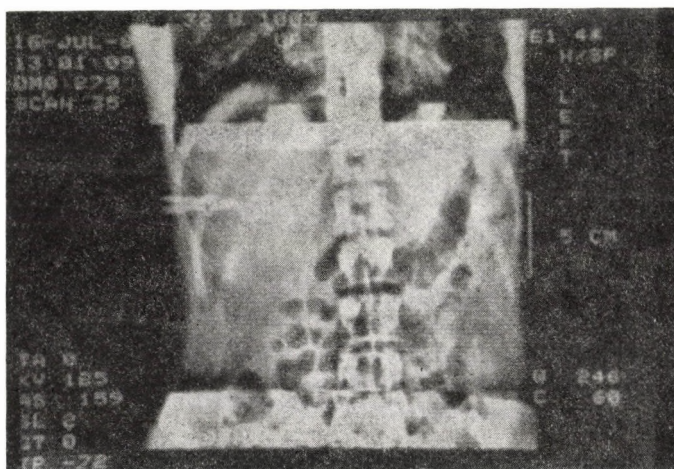


FIG. 4. The position of drains on a tomogram

For permanent drainage a basket-tipped stilet catheter (diameter: 3 mm) is used. Introduction is made by Seldinger's method. After removal of the guiding trocar, the tip of the catheter with a basket regains its original basket form thereby fixing the catheter tip in the abscess cavity.

In case of multiple abscesses, the two or three largest abscesses are drained simultaneously (Figs 6, 7).

3. The catheter is sutured to the skin. The patient receives parenterally a broad-spectrum antibiotic from the start of the intervention, which is modified in view of the results of the bacteriological studies.

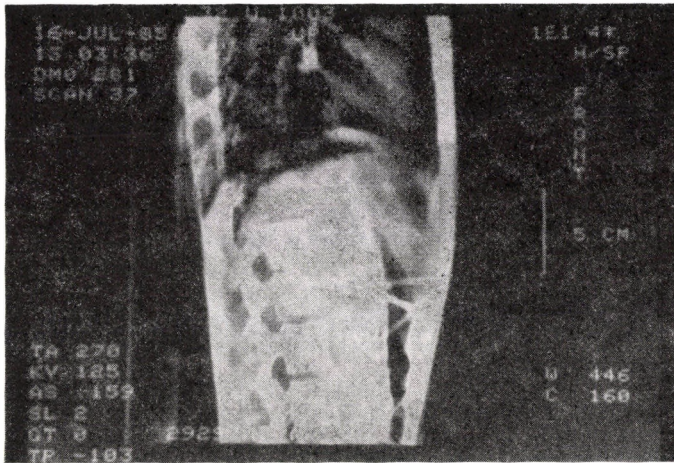


FIG. 5. Localization of drain tubes in a lateral view tomogram

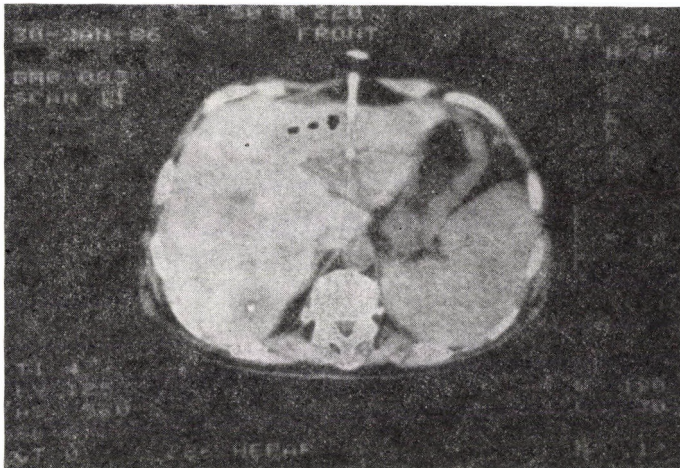


FIG. 6. Tomogram of a multiple cholangiogenic liver abscess. One of the large abscesses in segment IV is drained

4. The abscess cavity is lavaged continuously (dual drainage) with an antiseptic or antibiotic solution. Control study is performed depending on the clinical picture by US or CT. In case of need, puncture of the residual or recurrent abscess is repeated (Figs 8, 9, 10).

The drain tubes are held in place, depending on the change of the clinical picture as well as on the character of the discharge, for 12 to 14 days. Aimed antibiotic treatment is continued for additional 7 to 10 days after complete afebrility and a clinically symptom-free state. Healing of the abscess is followed up by CT or US. Temporarily, the patients are controlled by US every three to six months.

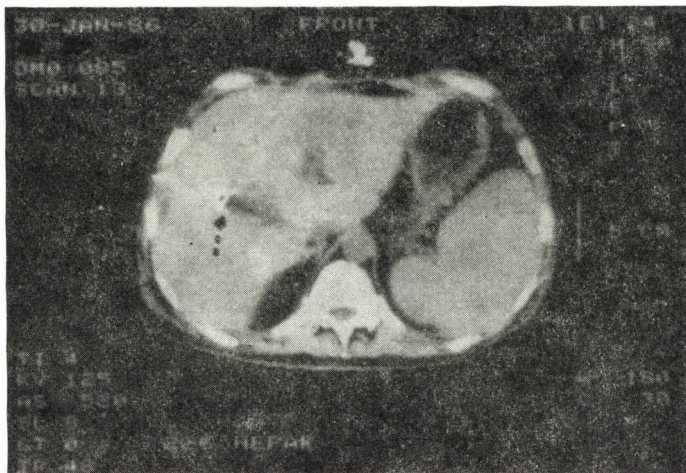


FIG. 7. Catheter introduced into another abscess in segment VII. (Drainage of the two largest abscesses were performed simultaneously)

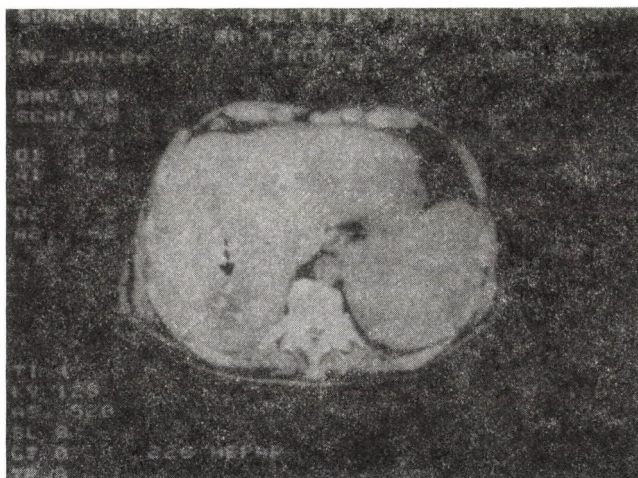


FIG. 8. A small abscess still not integrated into segment V

Results

Percutaneous transhepatic puncture or drainage guided by CT was made in 33 patients in a total of 40 cases. Solitary abscess occurred in 72.7% (24/33), multiple abscess in 22.3% (9/33) of the patients. The underlying diseases leading to the development of abscesses as well as the aetiological factors are shown in (Table I).

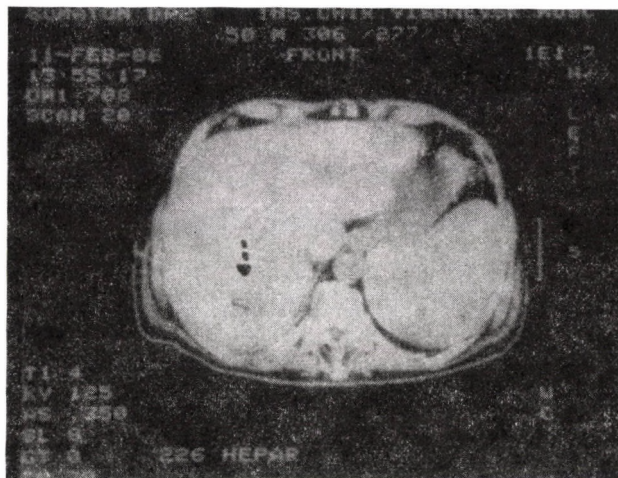


FIG. 9. Control tomogram taken 11 days later. The two large abscesses have healed, the drain tubes were removed. The small, not yet healed abscess in segment V has been aspirated by puncture

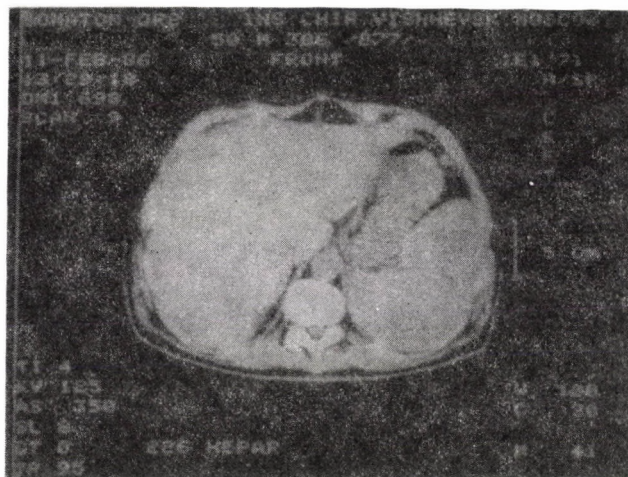


FIG. 10. Removal of drain tubes without any sign of the presence of abscess after puncture. The patient has recovered, regular tomogram

More than two-thirds of the abscesses were cholangiogenic ($22/33 = 6.9\%$). In three cases the abscesses were due to portal bacteriaemia ($3/33 = 9\%$), in one case to sepsis following extraction of carious teeth. "Cryptogenic" abscesses of unknown origin were found in six cases ($6/33 = 18.2\%$). In 40% of the patients ($13/33 = 39.4\%$) underlying or accompanying diseases (tumour: 3,

TABLE I
Aetiological factors and way of development of abscesses
 (n = 33)

Way of development	Underlying disease	Absolute no. of patients	%	Total (%)
Biliary duct	Cholelithiasis	5	15.2	69.8
	Choledocholithiasis	8	24.2	
	Iatrogenic bile duct stenosis	1	3.0	
	Stricture of papilla of Vater	2	6.1	
	Chronic pancreatitis	2	6.1	
	Tumour of pancreatic head	1	3.0	
	Liver cyst suppuration	2	6.1	
	Suppuration after liver resection	2	6.1	
TOTAL		23	79.8	
Portal vein	Colonic diverticulitis	1	3.0	9.0
	Perforated appendicitis	1	3.0	
	Septic abortion	1	3.0	
TOTAL		3	9.0	
Hepatic artery	Sepsis (extraction of carious teeth)	1	3.0	3.0
Unknown	Unknown	6	18.2	18.2
TOTAL		33	100.0	100.0

diabetes mellitus 8, change requiring steroid treatment: 2) with a disposition to development of abscess were also present.

Bacteriological and cytological studies of the discharge obtained by puncture were carried out on each occasion (Table II).

One pathogen was identified in one-third of the cases ($10/33 = 30.3\%$). Two bacteria were identified also in 10 cases. In seven instances ($7/33 = 21.2\%$) three, while in three cases ($3/33 = 9\%$) four different bacteria were isolated (Table III).

Haemoculturing was made in 14 cases ($14/33 = 42.4\%$). Positive results were obtained in eight cases ($8/33 = 57.1\%$). Pathogens cultured from the abscess and the blood corresponded with each other. In two cases two bacteria were isolated from the haemoculture, i.e. *E. coli*, *Pseudomonas aeruginosa* as well as *Staphylococcus aureus*.

TABLE II
Results of bacteriology and cytology
($n = 33$)

No. of isolated bacteria	Patients	
	Absolute no.	%
One bacterium	10	30.3
Two bacteria	10	30.3
Three bacteria	7	21.2
Four bacteria	2	6.1
Negative culture	3	9.1
One bacterium + tumour cells	1	3.0
TOTAL	33	100.0

TABLE III
Types and the number of occurrence of bacteria

Types of bacteria		Absolute number of occurrences
Gram-negative	<i>Escherichia coli</i>	15
	<i>Pseudomonas aeruginosa</i>	13
	<i>Proteus mirabilis</i>	8
	<i>Proteus morgani</i>	1
	<i>Enterobacter</i>	3
	<i>Bacteroides</i>	2
	Not classifiable accurately	2
Gram-positive	<i>Staphylococcus aureus</i>	5
	<i>Staphylococcus epidermis</i>	1
	<i>Streptococcus alpha-haemolyticus</i>	2
	<i>Enterococcus</i>	5
	<i>Streptococcus faecalis</i>	5
	<i>Peptostreptococcus</i>	5
	Not classifiable accurately	2

Puncture and drainage guided by CT were successful in 23 patients ($23/33 = 67.9\%$). Septic fever disappeared 24–48 h after the intervention, the clinical picture improved and CT or US studies verified the diminishing of the abscess(es). Nineteen patients of those treated by closed therapeutic puncture or drainage had solitary, while 5 multiple abscesses. The total number of interventions was 24 (Table IV).

Following a technically successful drainage, one patient died of symptoms of hepatic coma ($91/33 = 3\%$). The nursing time of patients treated by drainage

TABLE IV
Types of interventions and abscesses, complications and mortality
 (n = 33)

Type of intervention	Patient Abs.	no. %	Type of abscess Solitary Multiple		Complication	Mortality
Therapeutic drainage	13	39.4	8	5	4	1
Therapeutic puncture	11	33.3	11	—	—	—
Preparatory or diagnostic puncture or drainage	9	27.3	5	4	—	—
TOTAL	33	100.0	24	9	4(12.1%)	1(3%)

TABLE V
Causes, types and distribution of operations

Cause of operation	Type	Distribution Absolute no.	%
Tumour cells at cytology	Lobectomy of left side	1	3.0
Persisting abscess cavity	Atypical wedge-resection	2	6.1
Multiple abscess	External decompression + local liver perfusion		
	via recanalized umbilical vein	1	
	via portal vein	3	18.2
	via hepatic artery	2	
Peritonitis after percutaneous drainage	Abdominal drainage + peritoneal lavage	1	3.0
TOTAL		10	30.3

was between 84 ± 45.8 days, the average diameter of the abscesses was 9.5 ± 3.7 cm. The nursing time of patients treated by puncture was 22.5 ± 9.3 days, the average diameter of the abscesses was 3.9 ± 2.6 cm.

Following 40 invasive interventions in 33 patients, complications arose as a result of puncture in four cases: in one of them permanent biliary fistula, in two slipping out of the drain tubes, while in another purulent peritonitis after drainage.

For failure of closed percutaneous puncture or drainage (or complication due to invasive intervention) 10 patients had to be operated ($10/33 = 30.3\%$) (Table V).

In one case the cytological examination of the discharge verified tumour cells, the patient recovered after lobectomy of the left side. In two patients, following successful drainage, the abscess cavity persisted even after 10–11 days following the intervention. After detoxication, the operation—extirpation of the thick-walled abscess by atypical wedge-resection—was performed at an elected time. In six patients the operative solution was aimed antibiotic perfusion because of the multiple abscesses: in one case via the recanalized umbilical vein, in three, via the portal vein, and in the other two cases through the hepatic artery. In one case, after introduction of the percutaneous drain tube purulent peritonitis developed. At surgery, purulent peritonitis was due to discharge escaping from the puncture track in the left paracolic region. Drainage of the abdominal cavity and peritoneal lavage were performed. The percutaneously introduced drain tubes, being in good position, were not removed. The patient recovered after wound suppuration.

A patient with multiple abscesses (not listed in the above table), recovered after the combination of two invasive interventions. The two largest of the cholangiogenic abscesses due to residual biliary stone were drained. After stopping of the septic state, the biliary stone maintaining the abscess was removed by endoscopic papillotomy. The residual small abscess was eliminated by percutaneous puncture. Healing was uneventful [8] (Figs 6, 7, 8, 9).

Discussion

The aetiological factors playing a role in the development of pyogenic liver abscesses have by now changed considerably. According to Ochsner et al. [20], about 45% of the abscesses were due to portal bacteraemia still up to 1938. Within this pylephlebitis due to acute appendicitis had a share of 77%. As a result of a “more aggressive” surgical treatment, by 1945 this ratio decreased to 12%, while from the 60s onwards, to 0.005% [27].

Abscesses developing after pylephlebitis due to acute appendicitis are mostly multiple ones and in about one-third of the cases—also in case of other abdominal abscesses of different origin—the pathogen is *E. coli* occurring most often in combination with anaerobic bacteria [25]. Presently, the frequency of pyogenic liver abscesses due to portal bacteraemia is estimated at 18% [3, 18]. In most cases acute inflammatory changes of the gastrointestinal tract (acute diverticulitis, acute necrotizing pancreatitis, etc.), as well as intra- or postoperative infections may lead to liver abscess, particularly if other factors disposing to abscess formation (like diabetes mellitus, acute or chronic hepatitis, diseases requiring immunosuppressive treatment, etc.) promote this [14]. Liver abscess is nowadays cholangiogenic in origin. Its ratio has been assumed to be 50–70% [16, 18]. As a result of systemic bacteraemia,

the ratio of pyogenic liver abscesses arising through the hepatic artery has decreased from the 70ties to 1–3% [18].

The essence of the complex treatment of liver abscesses is the elimination of the abscess and a systemic (in multiple abscesses, isolated perfusion of the liver) and prolonged antibiotic treatment [7, 8]. Up to the end of the 70s the generally accepted principle had been the surgical exploration of the abscess [12, 17]. In solitary abscesses the extensive exposure of the abscess cavity, the emptying of pus and of the necrotic tissues and the ensuring of the free flow of the discharge were aimed at. In multiple abscesses, with the cholangiogenic origin verified, attempts were made to ensure bile flow by biliodigestive anastomosis (surgical drainage relieving the bile tract, etc.) combined with local antibiotic perfusion of the liver.

The earlier view of Rubin et al. [24] that "prolonged antibiotic treatment and aggressive surgical drainage are the cornerstone of effective treatment . . .", is subject to controversy. The mortality rate is 7–44%, with the number of postoperative complications reaching 25–52% [4, 27]. The causes of the high morbidity and lethality of surgical interventions include late diagnosis, the traumatizing intervention on the patient otherwise also of a bad general condition, the difficulties in the exact localization and intraoperative detection of the abscesses (in lack of US), and postoperative surgical complications (recurrent intraabdominal abscesses, wound suppuration) [23].

With the extensive use of up-to-date diagnostic imaging procedures and the possibility of radiological interventions the range of surgical indication has changed considerably. Currently, the classical surgical exploration and drainage are considered justified only if there is an absolute indication, also otherwise, of acute abdomen (diverticulitis causing peritonitis, abscess perforation, etc.) [23]. Operation is also justified if closed percutaneous aspiration has failed. If, after a successful percutaneous intervention, 48–72 h later, the clinical picture has still not improved, or the abscess has not diminished after 2–3 weeks, surgical intervention is indicated. If the abscess is connected via a fistula with some kind of hollow organ, surgery is indicated only with the fistula becoming chronic, with a wide duct, and without any hope of spontaneous closure [19, 21, 28]. If the abscess is blocked by an obstacle to bile flow, in elected cases, this obstacle can be solved by endoscopic papillotomy as also illustrated by the case mentioned in our material. If the obstacle to bile flow cannot be solved endoscopically, operation is recommended to be performed at the chosen time. In this case percutaneous transhepatic puncture or drainage may play a role in preparing the operation [8, 28]. In some 30% of the cases, elective surgical drainage may become necessary [23].

Currently, first of all closed percutaneous transhepatic puncture or permanent drainage guided by CT or US are recommended for the management of liver abscess [1, 9, 10, 11, 14]. The treatment by percutaneous puncture and

aspiration of pus of pyogenic abscesses is known. McFadzean et al. [15] were the first to report on the curing of 14 patients with liver abscess. Pus was aspirated from the abscess, then the cavity was filled with penicillin and streptomycin. Their patients recovered. However, closed percutaneous puncture and drainage guided by CT and US have been extensively used only from the 80ties onwards. The intervention has dual advantage: it is of diagnostic value and of therapeutic effect. If pus can be obtained from the change, it may confirm and make more precise the diagnosis. It becomes possible to carry out an accurate bacteriological examination, to establish the sensitivity of bacteria to antibiotics and to administer aimed antibiotic treatment. The toxic effect of purulent focus(foci) as well as the possibility of the haematogenic dissemination of bacteria decrease [10, 11, 13, 22]. In case of a solitary small abscess, even a single puncture may lead to complete recovery. If needed, it can be repeated or transformed into percutaneous drainage. In solitary large abscesses ($0 < 5-6$ cm), if the obtained discharge is thick, fragmented or is more than 100 ml, a permanent drainage is indicated already on the first intervention [25]. In large abscesses, it is appropriate to use a dual drainage, to enable the continuous antibiotic or antiseptic lavage of the abscess cavity [8, 28]. Multiple or multilocular abscesses do not mean a contradiction either. If there are two or more abscesses, their drainage or the locally and parenterally administered aimed antibiotic treatment are the recommended procedures [28].

The absolute contraindications to percutaneous catheter drainage are free abdominal fluid and *Echinococcus* infection. Haemophilia of various origins can be considered only a relative contraindication [28]. In our material no tendency to bleeding of an extent to contraindicate percutaneous intervention was observed.

The complications of percutaneous transhepatic puncture guided by CT are rare. The most serious are chest empyema developing after an intervention performed with inadequate technique following a diaphragmatic injury, or peritonitis due to pyorrhoea from the puncture track. Bleeding and bile flow infrequently occur, which heal as a result of conservative treatment. Perforation of a hollow organ also occurs rarely. In the collected material of Mueller et al. [19] it occurs at a rate of 2.8%. In two cases the small intestine, in four, the duodenum, while in five the stomach was injured, but surgical intervention had to be made only in two of them. The most frequent complication was the febrile state after the intervention, which is supposed to be due to bacteraemia, but which is only transitory. Therefore, this intervention is performed under antibiotic protection. A technical complication of minor importance, characteristic first of all of the initial period could be the premature slipping out of the catheter.

Based on our own experiences and the literature, in our opinion, percutaneous, transhepatic puncture and drainage guided by CT open up new vistas

in the therapy of bacterial liver abscesses. By using it, there is a possibility for the rapid and accurate diagnosis of the abscesses and, in possession of the adequate experience—partly as an alternative to surgical intervention—it may lead to complete recovery even when performed in itself.

References

- Berger H, Pratschke E, Berr F, Fink U: Percutaneous drainage treatment of primary liver abscesses. *ROFO* 150:167, 1989
- Besnier JP, Hasenpouth A, Janoudet D: Les abcès du foie d'origine appendiculaire une complication toujours actuelle. *Fra J Chir* 118:493, 1981
- Conter RL, Pitt HA, Tomkins RK, Longmire WP: Differentiation of pyogenic from amebic hepatic abscesses. *Surg Gynecol Obstet* 162:114, 1986
- Dietrick RB: Experience with liver abscess. *Am J Surg* 147:288, 1984
- Fagniez PL, Villet R, Thomsen C, Hannoun S, Julien M, Germain A: Absces du foie a pyogenes: une etude de vingt cas operes. *Chirurgie* 108:37, 1982
- Fazekas T, Horváth Gy, Szabó K, Bátorfi J: Komputertomográfiával vezérelt, célzott percutan transhepatikus punkcióval diagnosztizált pyogen májtályog (Pyogenic liver abscess diagnosed by aimed percutaneous transhepatic puncture guided by CT). *Magy Seb* 42:151, 1989
- Fazekas T, Todua FI, Viljavín JM, Bátorfi J: Perforált, akut appendicitis után kialakult multiplex májtályog komputertomográfiával vezérelt drénézással gyógyított esete (A case of multiple liver abscess due to perforated acute appendicitis, cured by drainage guided by CT). *Magy Seb* 42:329, 1989
- Fazekas T, Todua FI, Viljavín JM, Bálint A: Rezidualis epeút-kövesség után kialakult multiplex cholangiogen májtályog komputertomográfiával vezérelt drénézással és endoszkopos papillotomiával gyógyított esete (A case of cholangiogenic liver abscess due to residual bile calculus, cured by percutaneous drainage guided by CT and by endoscopic papillotomy). *Magy Seb* 43:356, 1990
- Ferrucci JT, Sonnenberg E: Intraabdominal abscess. Radiological diagnosis and treatment *JAMA* 246:2728, 1981
- Gerzof SG, Johnson WC, Robbins AH, Nabseth DC: Intrahepatic pyogenic abscesses: treatment by percutaneous drainage. *Am J Surg* 149:487, 1985
- Greenwood LH, Collins TL, Yrizarry JM: Percutaneous management of multiple liver abscesses *Am J Radiol* 139:390, 1982
- Henry A, Pitt: Surgical management of hepatic abscesses. *World J Surg* 14:498, 1990
- Herbert DA, Fogel DA, Rothman J, Wilson S, Simons F, Ruskin J: Pyogenic liver abscesses: Successful non surgical therapy. *Lancet* 1:134, 1982
- Mandel SR, Boyd D, Jaques PF, Mandel W, Staab EV: Drainage of hepatic intra-abdominal and mediastinal abscesses guided by computerized axial tomography. *Am J Surg* 145:120, 1983
- Mc Fadzean AJS, Chang KPS, Wong CC: Solitary pyogenic abscess of the liver treated by closed aspiration and antibiotics. *Br J Surg* 41:141, 1953
- Meier R, Vogtlin J, Gyr K: Diagnose der Leberabscesse. *Dtsch Med Wochenschr* 113:62, 1987
- Meier R, Vogtlin J, Gyr K: Therapie der Leberabscesse. *Dtsch Med Wochenschr* 113:64, 1987
- Miedema BW, Dieën P: The diagnosis and treatment of pyogenic liver abscesses. *Ann Surg* 200:328, 1984
- Mueller PP, Ferrucci JT, Butch RJ, Simeone JF, Wittenberg J: Inadvertent percutaneous catheter gastroenterostomy during abscess drainage: Significance and management. *Am J Roentgenol* 145:387, 1985
- Ochsner A, De Bakey M, Murray S: Pyogenic abscess of the liver. An analysis of 47 cases with review of the literature. *Am J Surg* 40:292, 1938
- Peretz TY, Ben YR, Lebensart P, Finkelstein R, Biran S, Durst AL, Krausz MN: Hepatic intraarterial antibiotic therapy for resistant hepatic abscesses. *Int Surg* 74:171, 1989

22. Perera MR, Krik A, Noone P: Presentation diagnosis and management of liver abscess. *Lancet* 2:629, 1980
23. Rothmund M. Intraabdominelle Abszesse percutane oder chirurgische Drainage? *Dtsch Med Wochenschr* 110:527, 1985
24. Rubin RH, Swatz MN, Malt R.: Hepatic abscess: changes in clinical bacteriologic and therapeutic aspects. *Am J Med* 57:601, 1974
25. Sheinfeld AM, Steiner AE, Rivkin LB: Transcutaneous drainage of Abscesses of the liver guided by computed tomography scan. *Surg Gynecol Obstet* 155:662, 1982
26. Sones PJ: Percutaneous drainage of abdominal abscesses. *Am J Roentgenol* 142:35, 1984
27. Sorensen MR, Baekgaard N, Kirkegaard P: Pyogenic liver abscesses. A case report with a short review of current concepts of diagnosis and management. *Acta Chir Scand* 149:437, 1983
28. Todue FI, Pomelov VS, Visnevski VA, Vilyavin MJ, Lulinski DM: Diagnostika i leschenie abscessov pecheni s ispolzovaniem kompyuternoy tomografii. *Vest Hir* 7:39, 1988
29. VanDer SP, Peters O, Claes H, Devis G: Percutaneous catheter drainage of solitary pyogenic liver abscess. *Act Clin Belg* 39:363, 1984
30. Wong KP: Percutaneous drainage of pyogenic liver abscesses. *World J Surg* 14:492, 1990

Pregnancy in women with chronic renal disease: A 14-year study

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Between 1975 and 1988 authors encountered 44 pregnancies in 26 women who had had chronic renal disease and unimpaired renal function before the conception. Complications during pregnancy and the outcome of pregnancy were studied. There were 5 spontaneous abortions between the 11th and 20th weeks of gestation, 1 therapeutic abortion, 3 stillbirths at weeks 28, 32 and 33, 6 neonatal deaths at age of 26 to 35 weeks, 11 preterm newborns, 35 live births, 9 infants with intrauterine growth retardation including 4 preterm newborns and 1 fetal malformation and 2 cases with premature rupture of the fetal membranes. The pregnancies were complicated with anaemia in 23 cases, with urinary tract infection in 19, with hypertension in 16, with proteinuria in 12 and with edema in 11 cases. Increase in the serum creatinine value during pregnancy was found in 6 cases. These data indicate that the pregnancy in patients with chronic renal disease who had normal renal function before the planned conception, is accompanied with increased risk for both the mother and child.

Pregnancy in women with chronic renal disease is accompanied by and increase in the perinatal fetal morbidity and mortality and by the development of maternal complications [9, 11, 12, 17]. Some authors consider the occurrence of pregnancy in patients with renal disease hazardous [5, 14], others believe that the outcome of pregnancy is mostly determined by the development of renal failure and hypertension irrespective of the histological type of renal disease [1, 10, 11, 13].

This study was aimed at evaluating the fetal or obstetrical and maternal complications in the pregnant women with history of chronic renal disease.

Patients and methods

44 pregnancies were managed in 26 patients with chronic renal disease at the 2nd Department of Obstetrics and Gynecology, Semmelweis University Medical School between 1975 and 1988. Medical records of the patients were reviewed and the data gained were analyzed from the point of view of maternal complications during pregnancy and delivery as well as of pregnancy outcome. Evaluated were the pregnancies of patients which had conceived subsequent

to the diagnosis of renal disease. Patients who had had spontaneous and therapeutic abortions after the renal disease and had not delivered were excluded from the study.

Diagnosis of the renal disease was based on the medical history of the patients, and on clinical, laboratory, roentgenological and ultrasound findings, and in some cases on the histological examination.

Numbers of the patients and pregnancies in term of the renal diseases are summarized in Table I. Four patients had chronic glomerulonephritis. One of

TABLE I
Complications during pregnancy and delivery in patients with renal disease

Renal disease	Patients	Pregnancies*	Serum creatinine more than 1.0 mg/dl	Hypertension	Edema	Proteinuria	Anemia	Urinary tract infection			Cesarean section	
								B	P	E		
CGN	4	5		(3)	5	5	3		1			
RTR	1**	1	1		1	1	1	1				
PRD	2	3	1					1				
CPN	3	6		(2)	3		4	4	1	1	1	
CPN + MNE	5	7	1		3	2	1	5		2	2	4
CPN + UTM	7	11	3	(1)	3	4	3	9	5	1	4	3
MNE	3	3			1			2				
UTM	2	2						1	1			1
Total	26	38	6	(6)	16	12	12	23	8	4	7	8
Percentage		100	15.8	(15.8)	42.1	28.9	31.6	60.5	50.0			21.0

* = pregnancies ended in abortions are excluded

** = this patient is identical with one of the patients with CGN

Abbreviations

CGN = chronic glomerular nephritis, CPN = chronic pyelonephritis, RTR = renal transplant recipient, PRD = polycystic renal degeneration, UTM = urinary tract malformation, MNE = monolateral nephrectomy, B = bacteriuria, P = pyuria, E = exacerbation of the pyelonephritis, () = number and percentage, respectively, of patients who were hypertensive before the pregnancy

these underwent hemodialysis and bilateral nephrectomy and subsequently received a living renal allograft from her mother. This patient was kept on continuous treatment with prednisolone, 150 mg per day, and azathioprine, 100 mg per day. One year following the transplantation she became pregnant. Two patients had polycystic renal degeneration revealed some years before the conception. 15 women suffered from chronic infectious pyelonephritis of 1 to 10 years' duration. Before pregnancy, 5 of them underwent monolateral ne-

phrectomy due to nephrolithiasis or nephritis aposthematosa. Of the 15 women 7 had urinary tract infection: 1 patient had bladder extrophy surgically corrected by removing urinary bladder and implanting ureters into the colon; 1 had bilateral vesicoureteral reflux; 2 had monolateral renal agenesis; 1 had monolateral hypoplastic kidney; 1 had a congenital horseshoe-kidney surgically corrected by monolateral nephrectomy; and 1 had ureteral stenosis in the monolateral hypoplastic kidney. Three patients were without evident predisposing factors to pyelonephritis. Two women had renal malformations (monolateral dystopic kidney and monolateral renal agenesis, respectively) without any sign of complication, furthermore, 3 patients with history of the monolateral nephrectomy due to nephrolithiasis and tuberculosis, showed no sign of the complications before the conception.

Before pregnancy 4 women (2 with chronic glomerulonephritis and 2 with chronic pyelonephritis) had a history of hypertension (blood pressure over 140/90 mm mercury). None of all women reported here started the pregnancy with a serum creatinine concentration above 1.0 mg/dl (88 μ mol/l). Before the planned pregnancy all patients were subject to clinical and laboratory studies so that the desired pregnancy could or could not be medically advised.

All pregnant patients were managed with iron and folic acid, furthermore, all who had the signs of any urinary tract infection received antibiotics. When preterm labor presented, the patient was treated with tocolytics unless she had fever.

Preterm delivery was defined as that occurring before the 36th week of gestation; stillbirth as the death of a viable fetus after the 26th week; intra-uterine growth retardation as an infant whose birth weight was more than 2 SD below the mean; edema as a weight gain more than 14 kg during pregnancy; proteinuria as the presence of protein in the urine; anemia as a hemoglobin level lower than 110 g/l.

Results

Maternal complication in pregnancy (Table I)

Hypertension was present before pregnancy in 3 patients with chronic glomerulonephritis and in 3 ones with chronic pyelonephritis, and it worsened in all these cases. Seven patients (1 with chronic glomerulonephritis, 1 with renal transplant, 4 with chronic pyelonephritis and 1 with monolateral nephrectomy) became hypertensive during the pregnancy. Since some of these patients had more than one pregnancies, hypertension was noted in 16 out of 38 pregnancies ending in delivery (42.1%). The hypertension during pregnancy proved to be severe (blood pressure more than 180/100 mm mercury) in 4 cases

(10.5%). In all five pregnancies of patients with chronic glomerulonephritis the hypertension was present. Of 24 pregnancies of 15 women with chronic pyelonephritis the hypertension developed in 9 cases (37.5%). The hypertension in pregnancy was easily controlled by antihypertensive drugs except for two patients with chronic glomerulonephritis. Edema was noted in 11 pregnancies (28.9). In two of them it was, however, of severe grade. Proteinuria was present in 12 pregnancies (31.6%). The serum creatinine level rose over 1.0 mg/dl in the second half of pregnancy in 6 pregnancies of 4 patients (15.8%). It was 1.3 mg/dl in the patient with renal transplant, 2.1 mg/dl in a patient with chronic pyelonephritis complicated with monolateral nephrectomy, 1.5 mg/dl in a patient with chronic pyelonephritis complicated with urinary tract malformation, and 1.2 mg/dl in the 1st pregnancy and 1.1 mg/dl in the 2nd pregnancy of another patient with chronic pyelonephritis complicated with urinary tract malformation. Out of these 5 pregnancies the 1st one ended in preterm stillbirth, the 2nd one in a surviving term newborn with intrauterine growth retardation, the 3rd one in a surviving term newborn, the 4th and 5th ones in preterm newborns with neonatal death due to respiratory distress.

Anemia was noted in 23 pregnancies (60.5%). In 2 of them (5.3%) the hemoglobin concentration ranged between 81 and 99 g/l. One of these pregnancies ended in stillbirth and the other in preterm delivery.

Urinary tract infection occurred in 19 pregnancies (50.0%): asymptomatic bacteriuria was found in 8, pyuria in 4, and clinical exacerbation of the pyelonephritis in 7 cases. Among the latter pregnancies 2 ended in neonatal death of preterm infants, 1 in preterm stillbirth, and 1 in term newborn with intrauterine growth retardation. Four of the pregnancies, in which an exacerbation was seen were coupled with hypertension in otherwise normotensive patients. Among the 4 pregnant patients who had pyuria in pregnancy, 3 complications took place: one ended in preterm delivery, the other was complicated by intrauterine growth retardation and in the third one hypertension presented. Ten fetal or obstetrical complications (stillbirth, preterm labor, neonatal death, intrauterine growth retardation) and 7 complications with hypertension were documented in the group of the pregnancies with urinary tract infection.

Outcome of pregnancy (Table II)

Five pregnancies ended in spontaneous abortions between 11 and 20 weeks of gestation (11.3%): 1 was in a patient with chronic pyelonephritis, 2 occurred in a patient with chronic glomerulonephritis, and 2 were in another patient with chronic glomerulonephritis who later underwent renal transplantation. There was one therapeutic abortion performed in the latter patient due to renal failure before the hemodialysis therapy.

TABLE II
Outcome of pregnancy in patients with renal disease

Renal disease	Pregnancies	Live birth	Still-birth	Neo-nata death	Prematurity		Abor-tion	Intrauterine growth retardation	Fetal malforma-tion	Premature rupture of membrane
					2 500 g	36 wk				
CGN	10	5			1	1	5*	1		1
RTR	1		1		1	1		1		
PRD	3	3			1	1				
CPN	7	5	1	2	4	4	1**	1		1
CPN + MNE	7	7		1	2	1		4		
CPN + UTM	11	10	1	3	5	4		1	1	
MNE	3	3								
UTM	2	2						1		
Total	44	35	3	6	14	12	6	9	1	2
Percentage	100	79.5	6.8	13.6	31.8	27.2	13.6	20.4	2.3	4.6

* = 4 spontaneous and 1 elective abortions

** = spontaneous abortion

wk = weeks of gestation

There were 35 live births (79.5%), 12 of them occurred before the 36th week of gestation (27.2%). Birth weight of 14 newborns out of 35 was less than 2 500 g (31.8%). There were 3 stillbirths (6.8%) in the 28, 32 and 33 weeks of gestation, 1 in the patient with renal transplant and 2 in patients with chronic pyelonephritis. There were 6 neonatal deaths (13.6%) among the infants born to the mothers with chronic pyelonephritis, between 26 and 35 weeks of gestation. Out of them 2 infants had intrauterine growth retardation and birth weights of 600 g and 1 000 g, respectively, furthermore, 2 of them had birth weights of 1 500 and 2 050 g and were born in seriously hypoxic state. Premature rupture of fetal membranes occurred in 2 pregnancies (4.6%) and it was associated with preterm delivery only in one case, just concerning the infant born to the mother with congenital bladder extrophy. Intrauterine growth retardation was seen in 9 cases (20.4%): 1 in a preterm newborn with stillbirth, 2 in preterm newborns with neonatal death, 1 in a term infant with malformation, and 1 in a preterm and 4 in term newborns.

Caesarean section was performed in 8 pregnancies at 37 and 40 weeks of gestation (21.0%).

Discussion

Using retrospective data this study has documented a series of pregnancies in the patients with history of chronic renal disease. In contrast to other

studies [10–12, 17] the particular aspects of the present series are the high proportion of patients with chronic pyelonephritis and the unimpaired renal function before the conception.

In the present series, deterioration of mild grade in the renal function was found in 15.8% during pregnancy. In most women the worsening of the renal function was shown to reverse after the delivery [11]. Approximately in one third of the cases the pregnancy can, however, accelerate the progression of renal disease [10, 17]. Correlation was found between the elevated serum creatinine values before as well as during pregnancy and the increase in frequency of both fetal and maternal complications [1]. Hypertension has been found to occur in 20.5 to 25% during pregnancy in the patients with chronic renal disease and with well-preserved or slightly impaired renal function [1, 11, 17]. In contrast, it was 56 to 64.7% in pregnancies of the women with marked renal failure [9, 10]. In the series presented here hypertension was noted in 15.8% before the conception and in 42.1% during the pregnancy despite the low frequency of impairing renal function.

Edema was found in 28.9% of the pregnancies and proteinuria presented in 31.6% in the above series. Proteinuria was reported to be present among pregnant women with chronic renal disease in even higher percentage in connection with mostly glomerular diseases and marked renal failure [10, 11].

Recurrent urinary tract infection during pregnancy has been noted in 50% of the patients with elevated serum creatinine value and in 23% of those with chronic renal disease and with lower serum creatinine value [1]. In the present study its incidence amounted to 50.0%. It is noteworthy that these patients when having more severe infection were afflicted also by hypertension and anemia as well as fetal complications.

There are several mechanisms in the patients with chronic renal disease which can result in anemia during pregnancy [2, 3]. Sometimes profound anemia can also be noted in the pregnant women with renal insufficiency [9]. According to the present study anemia is the complication occurring most often during pregnancy in the women with chronic renal disease. This is of clinical importance because the anemia itself in pregnancy has been shown to be associated with an increased incidence of maternal and fetal morbidity and mortality [6, 7].

It has been shown that also in the women with renal transplant hypertension and the renal failure are the crucial predictors of pregnancy outcome [12], and 71% of the pregnancies in these women result in live birth of full-term infants [15]. In our study the pregnancy of the woman with renal transplant ended in stillbirth of a preterm infant. There are some factors in pregnancy such as the development of hypertension and the elevation of serum creatinine value and the immunosuppressive treatment [16] which all may have contributed to the severe fetal growth retardation that finally resulted in

stillbirth. Although it has recently been reported that the perinatal complication in the renal transplant recipients is rare except for the preterm labor [8].

The perinatal loss has been reported to significantly increase in the women with chronic renal disease [1, 9, 14, 17]. The neonatal death rate has been found to range between 4.9 and 6.6% [10, 11]. In the series presented above the latter one amounted to 13.6%. The stillbirth rate has been registered as 5.8 and 6.6% [10, 11] but we found it to be 6.8%. In women with chronic renal disease the prematurity rate has ranged from 11.0 to 60.8% [1, 9, 10, 11, 17] and the rate of intrauterine growth retardation has been noted to be between 5.9 and 33.0% [10, 11, 17]. In the present study preterm infants were born in 27.2% and small for-gestational-age infants were seen in 20.4%. The wide scatter of the literature data referring to the fetal complications can be explained by the various types and severity of the chronic renal diseases as well as by the divergent obstetrical or neonatal care that made great strides during the past one or two decades, from the period of which the majority of the data were collected by the authors quoted. In this respect it is noteworthy to consider that the rate of Caesarean section, being 40.0% in the survey by Imbasciati et al [10], and being 21.0% in the present study, furthermore the rate of fetal loss, being 13.2% in the former and 31.7% in our studies, show an inversed proportion suggesting that the fetal loss might be reduced by increasing the rate of Caesarean section in the high-risk cases even at the preterm gestational age. In any case, of clinical importance is the high incidence of low birth weight which principally predicts the neonatal morbidity and mortality and may have long-term health consequences, too [4]. In the above study, out of 9 cases with—perinatal loss the hypertension was present in 6, the anemia in 8, and the urinary tract infection in 8 pregnancies. These data point to that the maternal complications mentioned mostly determine the fetal outcome.

In conclusion, the present results indicate that the pregnancy of women with history of chronic renal disease is at high risk even in case that the renal function has been unimpaired before the conception.

References

1. Bear RA: Pregnancy in patients with renal disease. *Obstet Gynecol* 48:13, 1976
2. Bitron JD, Miller JB, Golomb HM: Megaloblastic anemia during pregnancy. *J Reprod Med* 19:186, 1977
3. Catchatourian R, Fried W: Hyporegenerative anemia in pregnancy. *J Reprod Med* 19:177, 1977
4. McCormick MC: The contribution of low birth weight to infant mortality and childhood morbidity. *N Eng J Med* 312:82, 1985
5. Fairly KF, Whitworth JA, Kincaid-Smith P: Glomerulonephritis and pregnancy. In: ed. Kincaid-Smith P, Methew TH, Becker EL, *Glomerulonephritis*, Vol 2, John Wiley, New York, 1973, p. 997
6. Garn SM, Ridella SA, Petzold AS, Falkner F: Maternal hematologic levels and pregnancy outcomes. *Semin Perinatol* 5:155, 1981

7. Göltner E: Hamatologische Erkrankungen in der Schwangerschaft. *Gynäkologe* 12:52 1979
8. Hadi HA, Stafford CR, Williamson JR, Fadel HE, Devoe LD: Pregnancy outcome in renal transplant recipients: Experience of the Medical College of Georgia and review of the literature. *South Med J* 79:959, 1986
9. Hou SH, Grossmann SD, Madias NE: Pregnancy in women with renal disease and moderate renal insufficiency. *Am J Med* 78:185, 1985
10. Imbasciati E, Pardi G, Capetti P, Ambroso G, Bozetti P, Pagliari B, Ponticelli C: Pregnancy in women with chronic renal failure. *Am J Nephrol* 6:193, 1986
11. Katz AI, Davidson JM, Hayslett JP, Singson E, Lindheimer MD: Pregnancy in women with kidney disease. *Kidney Int* 18:192, 1980
12. Klockars M, Saarikoski S, Ikonen E, Kuhlback B: Pregnancy in patients with renal disease. *Acta Med Scand* 207:207, 1980
13. Lindheimer MD, Katz AI: *Kidney Function and Disease in Pregnancy*, Febiger, Philadelphia, 1977, p. 146
14. Mackay EV: Pregnancy and renal disease: a ten-year study. *Aust NZ J Obstet Gynaecol* 3:21, 1963
15. Rudolph JE, Schweizer RT, Bartus SA: Pregnancy in renal transplant patients: A review. *Transplant* 29:26, 1979
16. Scott JR: Fetal growth retardation associated with immunosuppressive drugs. *Am J Obstet Gynecol* 128:668, 1977
17. Surian M, Imbasciati E, Cosci P, Banti G, Barbiano di Belgiojoso G, Brancaccio D, Minetti L, Ponticelli C: Glomerular disease and pregnancy. A study of 123 pregnancies in patients with primary and secondary glomerular disease. *Nephron* 36:101, 1984

Early Complications of Gastric Resection

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Analyzing the patient material of 506 patients with gastric resection, authors deal with the early complication of resection, its diagnosis and treatment. They review the complications, their frequency and mortality in their own material. After operations made for tumour, complications occurred more frequently than after interventions because of ulcer. Total mortality was 10.2%. In order to reduce mortality they call attention to the possible prevention of complications and their careful management.

Billroth resection has been dating back to 100 years. Its extensive use has started by the introduction of the surgical treatment of ulcer (1855) this period mainly involving the first decades of our century. This implied, at the same time, the rapid spread and turbulent progress of gastric surgery. The technique of the operations has been perfected during the past decades, thus with its use—where indication was correct—increasingly better results could be achieved. Clinical experiences, however, have also verified that, despite the improvement of the operative technique, also resection has its non-desirable early and late complications. Several reports at home and abroad have dealt with the complications in recent years. Undoubtedly, the number of resections, mainly in the past decade, has decreased not only at home but also all over the world partly due to the extensive use of H_2 receptor antagonists, and partly to that of various types of vagotomy introduced for the surgical treatment of duodenal ulcer. It probably accounts for the fact that reports on the complications of resection are scarce not only in Hungarian but also in international literature, despite its currently being a frequent surgical intervention. Contrary to general experience, in our material the number of gastric operations has markedly increased in the past years, which probably can be attributed to one of the profiles of our clinic (Fig. 1).

In view of the above, by analysing the 10-year material (1980–1989) of the 3rd Department of Surgery, Semmelweis University Medical School, we have dealt with the early complications of this operation.

Indications of the operation of the given period are shown in Table I.

The total mortality for the 506 cases was 10.2%. The mortality of the diseases calling for surgery are in the medium range of mortality statistics

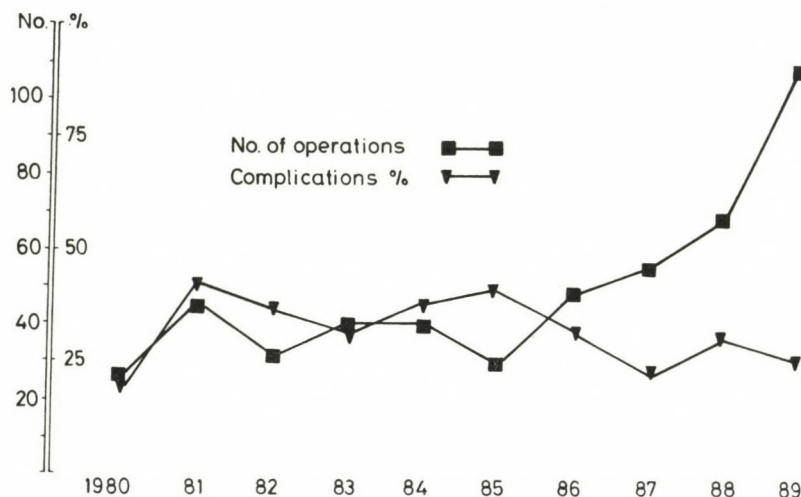


FIG. 1. The number and complication of gastric operations (1980-1989)

known from the literature (Table I) [18]. There were no deaths after the 139 operations performed due to ventricular and duodenal ulcers. This can by all means be ascribed to the relatively low number of cases, because the mortality of resections for ulcer is also currently between 2 and 4% [2, 9, 18].

The distribution of gastric operations and the mortality of the various types of intervention are shown in Table II.

By early postoperative complications we mean those occurring after resections of various types and extensions. These, too, can be divided into two groups: the general or indirect complications (such as pneumonia, thrombosis, etc.), which can arise after each kind of operation, as well as the direct or

TABLE I
Analysis of gastric operations (1980-1989)
($n = 506$)

	No. of cases	Deaths
Tumour	218 43.0%	28 12.8%
ventr. 68 (13%)	139 27.5%	—
Ulcér duod. 71 (14%)		
Perforation	112 22.2%	17 15.2%
Bleeding	37 7.3%	7 19.0%
TOTAL	506	52
Overall mortality:	10.2%	

TABLE II
Distribution of gastric operations (1980–1989)

Type of operation	No. of cases	Mortality
Billroth II	179 35.4%	17 9.5%
Billroth I	77 15.1%	1 1.3%
Subtotal resection	27 5.3%	1 3.7%
Gastrectomy	31 6.1%	4 12.9%
Suture	112 22.2%	17 15.2%
Ulcer ligation	10 2.0%	3 30.0%
GEA	23 4.5%	6 26.6%
Gastrotomy	2	—
Jejunostomy	1	1
Exploratory laparotomy	44 8.7%	8 18.2%
TOTAL	506	52

“surgical” complications connected with the gastric operation. This latter can be further divided into two groups: to early and late complications. Now we wish to deal with the general complications in detail.

Figure 2 analyzes the complications. It shows the frequency of “surgical” complications to be 18.3%, while that of “non-surgical” ones to be 19.3%.

The “surgical” complications occurring, in general, in the early post-operative stage are demonstrated in Table III.

These complications, in some per cent, can be ascribed to the inappropriate operative technique, but other factors are at least as much important, like the nature of the associated disease, its complications, the magnitude of the intervention, the general state, age, etc. The sooner the complication is detected, the more effective the treatment is going to be. This applies also to the determination of the necessity of reoperation and of the date of the intervention. Both require careful consideration and considerable surgical expertise.

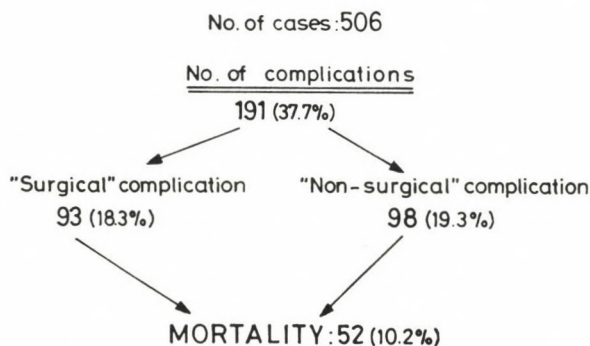


FIG. 2. Analysis of surgical complications (1980–1989)

TABLE III

Early complications of gastric operations (resections)

-
1. Wound suppuration, disruption
 2. Duodenal stump insufficiency: early, late (2–3%)
 3. Fistula formation
 4. Postoperative bleeding (1%)
intra gastric, intraabdominal
 5. Postoperative pancreatitis, pancreas necrosis (1%)
 6. Anastomosis insufficiency (1–2%)
 7. Postoperative obstructive jaundice (0.5%)
primary, secondary
 8. Postoperative passage disorder (2%)
 9. Retrograde intussusception
 10. Torsion of the gastroenteroanastomosis
 11. Postoperative enteritis necrotisans
-

TABLE IV

Analysis of "surgical" complications

No. of cases: 93	No.	%
Wound suppuration, disruption	28	30.0
Passage disorder	28	30.0
Anastomosis insufficiency	15	16.1
Duodenal stump insufficiency	10	10.7
Intraabdominal abscess	3	3.2
Postoperative pancreatitis	3	3.2
Pancreas fistula	2	2.1
Suture insufficiency (perforation)	2	2.1
Postoperative bleeding	2	2.1
TOTAL	93	

In our own material, the "surgical" complications and their frequency were demonstrated in Table IV.

Analysis of lethal complications is shown in Table V.

1. *Disorders of wound healing, disruption.* The suppuration of laparotomy wounds, has not changed considerably even despite the spread of up-to-date instruments, in the past decades. Its frequency rate is 10 to 20%. After resection made for ulcer it is 9–13%, while after those for carcinoma it is 20–25%. [1]. The majority of infections arise intraoperatively, when due to carelessness, the contents of the gastrointestinal tract gets onto the abdominal wound. Several factors predisposing to wound infection are also known which are as

TABLE V
Analysis of lethal complication
 (n = 52)

* Cardiorespiratory insufficiency	27
* Duodenal stump insufficiency	5
* Hepatorenal insufficiency	3
* Renal insufficiency	3
* Infarction or pulmonary embolism	3
* Pneumonia	3
* Anastomosis insufficiency	3
* ARDS	1
* Suture insufficiency (perforation)	2
* Postoperative pancreatitis	2
TOTAL	52

follows: haematoma, local circulatory disorder because of the too tight sutures, destruction of the wound edges (rough use of retractors), hypoproteinaemia, diabetes, obesity, etc. The severity of infection may range from the emptying of a moderate seroma to a severe necrosis involving all layers of the abdominal wall. Infection accompanied by the known local symptoms generally develops already in the first postoperative week. These local symptoms may also be absent if the infection is superficial or the patient has been given antibiotics. Exploration should be made only to the level of infection. A more extensive exposure is necessary only in case of necrosis, or if a blind pouch (or pouches) occurs. In the former case necrectomy, in the latter one relieving incisions and insertion of drain tubes are required. In case of a spreading infiltration an aimed systemic antibiotic therapy is necessary.

Disruption can be partial, subcutaneous, when continuity of the skin is retained, and it can be complete when it involves all layers of the abdominal wall, with the prolapse of the abdominal organs, primarily of the small intestines and the omentum. Dysjunction of the wound edges occurs in general between the 5th and 14th postoperative days. Disruption due to a technical error in closure of the abdominal wall is relatively rare. Of greater importance are the following: hypoproteinaemia, cachexia, anaemia, metabolic diseases, lack of factor XIII, infections, steroid or cytostatic treatment, abrupt increase in intraabdominal pressure (coughing). Disunion of the wound edges often occurs with profuse emptying of a serosanguineous discharge often following a coughing fit or vomiting. What to do depends on the degree of disruption. In case of a complete disunion of the wound edges, the abdominal wall should be closed immediately. This can be made layerwise or in one layer, with sutures placed through all layers. The row of sutures should also be ensured by retention sutures. With partial disruption and the abdominal cavity being closed

towards the outside world—due to adherence of the intestines and the omentum—the wide straps placed over a sterile dressing to secure it and the use of an abdominal bandage may suffice. If prolapse of the abdominal organs does not occur, healing by second intention can be ensured. A similar procedure is followed if continuity of the skin is preserved. In case disruption can be attributed to any of the above causes and it can be corrected, it should be replaced along with the administration of a broad-spectrum antibiotic.

In our material wound suppuration and disruption concurred in 30%, most often following resections due to carcinoma.

2. Duodenal stump-insufficiency. This is one of the most frequent local complications, making up, age-dependently, 20–25% of deaths occurring in the early postoperative stage [3, 15, 16]. Its frequency is 2–3% [17]. In our material it was 10.7% (10 cases) (Table IV). Its distribution according to the types of operation: in 4 cases after Billroth II resection (because of 2 tumours, 2 ventricular ulcers), in 4 patients after subtotal resection (due to tumour) and in two cases following total gastrectomy (for tumour). The average age of the deceased was 58.5 years (between 50 and 80 years). Suture insufficiency of the stump followed in general on the 3rd to 10th day, most often on day 9. Therefore, it is advisable to remove the drain tube inserted intraoperatively always beside the stump, only on the 9th to 10th day after the operation. In our own cases these dates were as follows: 4th postoperative day: 3–, on the 6th day: 2–, on the 8th day in 4 cases. The earlier stump insufficiency occurs, and of the greater extent the insufficiency is, the higher is mortality. Naturally, it may occur also at a later phase even one year after the operation [18].

Stump insufficiency occurs most often after the operation of deep-seated duodenal ulcers of the posterior wall, penetrating into the pancreas, mainly in cases where the surgeon attempts to remove these ulcers “at all costs”. It cannot be ignored that stump insufficiency can occur also with an intact duodenum. The stump orifice can generally be attributed to technical, mechanical processes, those connected with blood supply as well as to pathophysiological ones. Among the technical and mechanical causes, the shortening due to the scarring of the anterior wall of the duodenum, penetration, the size of the ulcer, the localization of the bile duct and the pancreatic duct, the stretching of the row of sutures supporting the stump and the obstacle to flow in the afferent loop are to be pointed out. A disorder of blood supply, occasionally partial necrosis should be reckoned with in each case if the upper horizontal segment of the duodenum is excessively mobilized, since the rectal arteries are end-arteries. Of importance are the following pathophysiological processes: anaemia, hypoproteinaemia, stasis, hypernatraemia, abscess formation, antidiigestive processes due to the injury of the pancreas. By all means, the concurrence of several factors is necessary for the development of stump insufficiency. A high percentage of stump insufficiencies occurring in the early

postoperative phase heal only in response to conservative therapy. Relaparotomy is justified only with the insufficiency being evident during the first days after the operation. This calls for the following to do: the escaped faecal contents is aspirated, the abdominal cavity is lavaged by physiological saline or an antiseptic solution. With dehiscence being insignificant, or if it cannot be brought into the visual field, it should be covered with a wide part of the omentum, its environment being drained. With the insufficiency being considerable, the end of the stump being oedematous, it is useless to insert sutures, they will not be durable. The best solution if a Foley of Petzer's catheter is introduced into the duodenum, which is fixed with purse string sutures and covered with the omentum in a way to keep it isolated from the abdominal cavity. The catheter is brought out in a separate orifice. Drain tubes are inserted into the subphrenic and subhepatic spaces. There are authors who perform Roux'anastomosis for the management of stump insufficiency even in the early stage, claiming good results [4].

Late stump insufficiency may, in general, develop in the 2nd postoperative week being already of "fistulous nature", therefore, it is advisable to just wait and see.

Prevention, symptoms and management of stump insufficiency—to avoid repetition—are not dealt with in detail. We refer, here, to Szabó's [17] and our own relevant papers [6].

3. Both the early as well as the late *stump insufficiency* may lead to fistula formation, the spontaneous healing of which can be reckoned with even months later. Therefore, here, too, the wait-and-see attitude is advisable to adopt, with the known active conservative therapy which has been recently completed with somatostatin (Stilamine 250) treatment. Results have been surprisingly favourable. Discharge diminishes considerably within some days, then the fistula closes. The relatively early operation is justified only if the electrolyte or protein loss due to the large amount of duodenal discharge cannot be replaced or is difficult to replace. Indication for an early operation can also be a flow obstacle in the afferent loop, or development of the so-called "lip-fistula" (*Lippenfistel*). Final decision should depend on the flow possibilities of the duodenum. This can be revealed by fistulography. In all other cases, prolonged conservative therapy is to be preferred. Operation can be considered only after several weeks or months of unsuccessful conservative treatment, when the outer fistula is transformed into an internal one with the help of a Roux' loop. The same surgical solution can be used for the elimination of persisting fistulas. Direct fistulotomy is often followed by the recurrence of the fistula. Experience has verified that any of the operative procedures for closure of the fistula are relatively rarely successful.

4. *Postoperative bleeding* can be intragastric or intraabdominal. The latter is caused by insufficient vascular ligation, or by the neglecting of the tran-

sected, however, during the operation not bleeding—occasionally coagulated—vessel. It can arise in the gastric artery, the omental vessels, injuries of the spleen, liver or pancreas, but most often in the gastrocolic ligament. Symptoms of haemorrhagic shock do not, or arise only slowly in a bleeding from a minor vessel, while they appear rapidly in one from a larger vessel. This, however, may cause misunderstanding, since the patient is in a postoperative condition, and, mainly in cases, when there is no fresh, red blood flow even through the drain tube closed by clot formation. If there is the least suspicion of an intra-abdominal bleeding, arising generally during the first 24 h, mainly if symptoms of shock are also present, relaparotomy should be immediately performed.

In establishing the diagnosis, beside clinical symptoms, also the tympanic resonance produced by the effusion of blood in the abdominal cavity as well as sonography may be of help.

It is more difficult to decide on operative reintervention if it is about an intragastric bleeding. This occurs also mostly in the first 24 hours if bleeding occurs in the region of the anastomosis. Later it may arise in a residual ulcer, or stress ulcer as well as in haemorrhagic gastritis [7, 8]. It should be mentioned that this kind of postoperative bleeding occurs more frequently if operation has been performed for some kind of complication (haemorrhage, perforation) [10]. Under normal conditions, after resection, in the first 24 h 100 to 300 ml of gradually clearing blood may empty via a nasogastric probe. The intensity of bleeding cannot be assessed exclusively on the basis of the aspirated amount of blood because of the temporary clogging of the nasogastric tube and the escaping of blood into the small intestine. Changes in central venous pressure, pulse rate, haemoglobin and haematocrit values should also be considered. Possible coagulation disorders should also be excluded. Acute gastroscopy has been gaining ground in assessing the site of bleeding, and, in some cases, in its ultimate management. If this is not possible, or it fails to occur and—despite the applied conservative therapy—800 to 1000 ml fresh blood escapes via the nasogastric tube within a matter of some hours, reoperation should be made. By no means should the development of haemorrhagic shock be permitted. Surgical solution depends on the cause of bleeding. Exploration is made through the original laparotomy incision. Gastronomy is to be performed 3 to 5 cm above, parallel to the anastomosis. The anastomosis is not opened directly, but it is carefully checked reversing it through the gastronomy. The bleeding vessel is sutured. Direct opening of the anastomosis is not advisable since repeated suturing of the oedematous tissues is difficult and unsafe. If there is no bleeding source at the site of bleeding, then the gastric stump should be thoroughly explored. If no erosion or ulcer to be managed by saturating are found, it is advisable to suture the whole anastomosis by running sutures without narrowing the lumen.

In case of erosion it is appropriate to perform truncal vagotomy. If the source of bleeding cannot be detected either in the anastomosis or the gastric stump and fresh blood is emptying from the afferent loop, then a residual, deep-seating duodenal ulcer or a introverted duodenal stump should be considered as the source of bleeding. Then exploration from a longitudinal incision in the intact duodenum may clarify the origins of bleeding. Bleeding is reduced by ligation, then the duodenum is closed by knotted sutures in two layers. In our material postoperative bleeding requiring reintervention occurred in two cases (Table IV), both intraabdominally.

5. *Postoperative pancreatitis, pancreas necrosis* arises due to the ligation of the normal or aberrant duct of the gland and/or to the injury of its substance, mainly after the removal "at all costs" of the ulcer penetrating into the pancreas. In such a case it is advisable to perform palliative resection by Billroth II reconstruction, or to make some form of vagotomy. Acute afferent loop syndrome and ligation of the lineal artery can also be inducing causes. An improper surgical technique can also in itself cause without injury postoperative pancreatitis! The clinical symptoms appear largely on the 2nd–4th day of the postoperative phase. In general, they are of a mild or moderate course, and heal spontaneously as a result of conservative treatment which corresponds to the non-postoperative pancreatitis treatment. In severe cases the known complications (including cyst, fistula, abscess, etc.) may develop. In this case, the mortality rate is 5–7%. In pancreas necrosis it is practically 100%. For the management of these complications also the surgical and other interventions used for the treatment of complications following pancreatitis also due to other causes should be performed. In our material, irrespective of mild pancreas irritation, severe pancreatitis occurred in 3 patients with pancreatic fistula formation in two of them (Tables IV, V). Two of them died. Death in one of them was due to complete pancreas necrosis, while in the other to multilocular bleeding.

6. *Anastomosis insufficiency.* It may occur in both forms of reconstruction, but undoubtedly, it is more frequent after Billroth I reconstruction. It can most often be ascribed to the inadequate suturing technique (too close or too sparse stitches, too strong knotting, incomplete closure of the corners). Following Billroth I reconstruction, tension in the row of sutures can also produce insufficiency. In the same case, another causal factor can be the disorder in the blood supply of the stump because of the excessive mobilization of the upper segment of the duodenum. After Billroth II reconstruction suture insufficiency occurs more rarely. It arises primarily after subtotal resection in the lesser curvature of the stump, also as a result of disorder of the blood supply. Sometimes, mural ischaemia can still be recognized intraoperatively and insufficiency can be prevented by placing an additional row of sutures. The known symptoms of suture insufficiency appear, in general on the 5th

to 9th day. By this time, due to adhesion, diffuse peritonitis does occur any more, however, abscess can develop, moreover, it is very likely to occur, first of all proximal to the anastomosis. This abscess appears often in the form of the "suppuration of the abdominal wall". Whether the subphrenic or subhepatic abscess due to insufficiency is diagnosed this way or any other ways, wide exposure and drainage of the abscess are necessary along with continuous decompression of the gastric stump and administration of the known other conservative therapies (like fluid-electrolyte replacement, transfusion, protein, antibiotics, etc.).

If diagnosis of the insufficiency is uncertain, however, also for its localization, sonography, CT or X-ray study with Gastrografen, occasionally Gastrografen test can be considered [11, 12]. This latter is mainly to be preferred if the patient cannot be transported in order to perform the X-ray examination. Its essence is as follows: The orally administered Gastrografen (100 ml) enters the pancreas through the insufficient anastomosis, it becomes absorbed and enters the blood, is excreted through the kidneys and can be precipitated with hydrochloric acid in the urine. The well-known methylene blue test can also be applied. The insufficiency being insignificant, spontaneous closure is likely to occur with the above therapy within 8 to 10 days.

The form accompanied by diffuse peritonitis develops as early the 1st to 3rd postoperative day, and is of fulminant course. The inflammatory process spreads rapidly, because the adhesions around the anastomosis have still not developed and drainage has still not been made or it is in the improper place. The dramatic clinical picture makes diagnosis almost unambiguous including an abrupt and strong abdominal pain, muscular defence, shivers, tachycardia then paralytic ileus with the consequential marked changes in laboratory values. Relaparotomy is justified. Here, the solution also depends on the possibilities: the abdominal cavity is thoroughly lavaged, the atomic small intestinal loops are relieved of tension. In a fortunate case closure of the orifice can be by sutures, but it is more appropriate and safe to cover it with a part of the omentum. After gastroduodenostomy, if insufficiency is considerable and circumstances allow, conversion by Billroth II operation can be considered. The operative site as well as the subphrenic space and the Douglas space should be drained. In our material the anastomosis insufficiency—in contrast with data in the literature [18]—occurred at a surprisingly high rate, i.e. 16.1% (Table IV). Three of the patients died (Table V), all three being over 60 years of age.

7. *Postoperative obstructive jaundice* is relatively rare, although an incidence rate of even 20 to 30% has been reported [5, 13]. In the early phase it usually occurs if resection of a deep-seated, penetrating ulcer is attempted at all costs. It can be due to obstruction of the papilla of Vater caused either by a deep-reaching, invaginated stump edge or its oedema, primarily after

introversion of an atypical stump. An essentially more dangerous case is the obstruction of the bile duct when it is ligated. Ligation of the proper hepatic artery may also produce jaundice. Another cause can be the partial kinking of the supra- or retroduodenal part of the of the bile duct due to manipulation during operation. Sometimes, oedema itself can cause a transitory jaundice. Non-obstructive jaundice may be induced by intraoperative hypoxia of the liver, hepatic lesion due to drug (such as noxa due to halothane and ethanol), or transfusion of incompatible blood. If the patient has received transfusion, haemolysis following transfusion should by all means be excluded differentially! In diagnosing occlusion due to obstruction, percutaneous transhepatic cholangiography (PTC) is of decisive importance. In a "high risk" patient a polyvinyl drain can be introduced through the puncturing cannula for decompression, however, relaparotomy, as soon as possible should be performed for ensuring bile flow. If the patient's general condition is good and obstruction of the bile duct has been documented, immediate reoperation should follow. Solution depends on the cause of obstruction: in case of obstruction of the papilla of Vater, or in that of the partial kinking of the bile duct, obstruction can be possibly eliminated by removing the sutures placed into the introverted stump. Insertion of the Kehr tube can also be considered. On ligation of the bile duct ligation should be removed. If the former intervention cannot safely eliminate obstruction, there is indication for performing a choledochojejunostomy. If postoperative jaundice is also associated with peritonitis, there is a high probability of early suture insufficiency where peritonitis has been due to resorption of the bile. Immediate reoperation is called for in this case as well. If jaundice has been due to ligation of the proper hepatic artery with an already persisting lobar liver necrosis, after removal of the ligation the necrotic region should also be resected. If jaundice develops with the symptoms of hepatic coma, then complete liver necrosis due to the ligation of the proper hepatic artery should be considered. Immediate surgery would also be indicated in this case, however, the patient's rapidly deteriorating condition makes this impossible.

Late (secondary) obstruction of the bile duct is caused by scarring in the retroduodenal region—in the environment of the bile duct—after healing of the suture insufficiency of the duodenal stump or of the postoperative pancreatitis. Clinically, the symptoms of cholangitis are dominant. PTC plays a decisive role in establishing diagnosis. Unheeded bile flow can be ensured only by an additional operation, by choledochojejunostomy. In our material, obstructive jaundice occurred in neither the early nor in the late postoperative stage.

8. *Postoperative passage disorder* may occur in both forms of Billroth resection, but, as it is known, it is more frequent after Billroth I. It may develop in the early postoperative stage, but it is also known as a late complica-

tion. The transitory passage disorder after operation is known as a functional phenomenon. If, however, it still persists on the 5th–6th day after stopping of peristaltic atomy, a mechanical passage disorder should be contemplated. This can be attributed to narrowing of the anastomosis, primarily after Billroth I operation, where the duodenal lumen is decisive as to the diameter of the anastomosis. In both types of reconstruction passage disorder can be caused by a mucosal oedema of lesser or greater extent, haematoma, the so-called “calcar”- or less frequently abscess formation and pancreatitis. After Billroth II resection, partial or complete kinking of the afferent and efferent loop can be considered, the jejunal segment impacted between the afferent and efferent loops and the strangulation by the mesocolon of the ileal loops entering the supramesocolic space as a result of the defective stitching of the mesocolon, or the loosening of some sutures. Similarly, after Billroth II resection, a passage disorder due to retrograde intussusception or gastroenteroanastomotic torsion should also—though rarely—be considered.

Passage disorder is usually associated with atomy. Early atomy is solved without difficulty by the continuous aspiration of the gastric stump, by carefully maintaining the fluid and electrolyte balance and by administering antiphlogistics probably stimulating peristaltic movement. This treatment is also necessary if there has been a persisting atomy for a longer time, because it can also be caused by a mechanical obstruction the spontaneous disappearance of which can be expected (oedema, haematoma). Should this fail, however, the above therapy cannot be omitted in this case either. If the passage disorder persists even after the 2nd–3rd postoperative weeks, relaparotomy should be considered. Gastroscopy performed prior to it and/or X-rays may provide useful information on the cause of the passage disorder, but the former may also serve a useful therapeutic purpose, e.g. a nasogastric tube can be introduced with the instrument into the efferent loop. After revision first of all the patency of the anastomosis should be checked, e.g. by passing through the nasogastric tube. If the gastroduodenostoma (Billroth I) has considerably narrowed or is not patent, resection or antecolic GEA by Braun anastomosis can be contemplated. After Billroth II resection, if partial kinking or obstruction of some of the loops occur and it cannot be solved, enteroenteroanastomosis is the most simple solution. The strangulation by the mesocolon of the ileal loop entering through the mesocolonic orifice the supramesocolic space can be sufficiently solved by the additional stitching reconstruction of the mesocolon, if there is no intestinal necrosis. After Billroth II resection, complete obstruction of the anastomosis is more than just an error in operative technique! In this case it is more advisable to prefer antecolic GEA instead of Braun anastomosis. These reoperations, similarly to the other operations performed in the early postoperative phase after gastric operations, require a full-fledged surgeon of great expertise.

In our material passage disorder occurs at a frequency of 30% (28 cases) (Table IV). This high figure was the result of our considering all cases where there was a marked atony (600–1000 ml) after the 5th day of the postoperative stage. In 22 of them, passage disorder stopped between the 8th–12th postoperative days in response to the known conservative therapy. In two cases it stopped only on the 14th and 16th day, respectively. Three patients had to be reoperated. In two of them passage disorder was caused by the abscess around the gastroduodenostomy. The anastomoses were patent, during operation, even to the Boas probe. Macroscopically, no suture insufficiency was detected. In one case the inappropriate “stapling” (Billroth II) of the colon was the cause of ileus without intestinal necrosis.

9–10. *Retrograde intussusception and torsion of the gastroentero-entero-anastomosis* (after Billroth II) are extremely rare complications. They are relatively more frequent after the simple GEA than following Billroth II resection. Gastroscopy and/or X-ray study may also be of considerable help, mainly in the former case, in forming a diagnosis. If intussusception does not disappear spontaneously as a result of the continuous draining of the stomach, reoperation should be made. Disinvagination may also be considered as a solution, if the involved intestinal segment is intact. If the invaginated intestinal segment is nonviable, it should be resected. Endoscopy of the intussusception can also be attempted.

Concerning prognosis, torsion of the gastroenteroanastomosis is essentially less favourable. The amount of gastric retention, the disorder of intestinal blood supply and the severity of necrosis of the afferent and efferent loops depend on the degree of torsion. The abdominal pains with an abrupt onset, presenting in spasms, which cannot or can hardly be influenced by medication, should be looked upon as alarming signs. In this case operation should be immediately performed, which, however, is generally delayed, because we do not have sufficient experience in recognizing this rare complication. Mortality is practically 100% [11]. In our materials these two rare complications did not occur.

11. *Postoperative enteritis necrotisans* is also a rare but dangerous complication of gastric operations. Its aetiology is obscure. The aetiological role of a circulatory disorder, the immune or autoimmune mechanism, the change in flora due to antibiotic therapy as also that of the weakening of general resistance can be taken into consideration [14]. The clinical picture is dramatic: in general, 48 h after operation abruptly high fever, peritonitis, paralytic ileus develop associated with septic shock, accompanied by bloody, stenchy diarrhoea, acidosis, somnolence, renal insufficiency and jaundice. If intraoperative drainage is performed in the abdominal cavity, a characteristic sweet and foul-smelling discharge empties through it. After elimination of shock, if possible, reoperation should be made to remove the necrosed in-

testinal segment. Its mortality is practically 100%. In our material this complication did not occur.

Undoubtedly, gastric resection is a routine operation with a history dating back to several years. In everyday practice sometimes it may superficially appear as if the complications of this operation occurred rarely. On the contrary, the data of our material as also those of the cited authors, confirm that the complications of the operation cannot be ignored and further decrease of mortality can be achieved only by the possible prevention and thorough treatment of these complications. This is what we wished to call attention to.

References

1. Becker HD, Herfath CH, Lierse W, Schreiber HW: Surgery of Stomach. Springer Verlag, Berlin 1986
2. Daham K, Rehner M: Der Billroth Imagen. Ferdinand Enke Verlag, Stuttgart 1984
3. Dimakahos PB: Die Relaparotomie in Rahmen Wichtiger frühpostoperativer Komplikationen nach Mageneingriffen. *Helv Chir Ac* 37:547, 1970
4. Dinstl K, Fritsch A, Hill H: Zur Versorgung des nicht verschlissbaren Duodenalstumpfes und sekundärer Duodenaldefecte. *Acta Chir Austr* 1:15, 1975
5. Häring R, Semsch B, Vosberg W: Erkennung der Nahtinsuffizienz- Klinik, Labor-, Röntgen-, Spezialuntersuchungen. *Langenbecks Arch Chir* 358:265, 1982
6. Ihász M, Réfi M, Bátorfi J, Jakab F, Regös J: Duodenumcsont-*insufficiencia* gyakorisága a klinika 12 éves anyagában (The frequency of duodenal stump insufficiency in the 12-year material of the clinic). *Magy Seb* 26:9, 1976
7. Kollig G, Encke A: Die postoperative Blutung in der Magen Chirurgie. *Langenbecks Arch Chir* 318:281, 1967
8. Koster KH, Fischermann K: Gastrointestinal hemorrhage following gastric surgery. *Acta Chir Scand (Suppl)* 343:177, 1965
9. Kothe W, Mlynec HJ, Schenker U, Albert H, Hartig W: Therapie des Gastroduodenalulcus. *Zentralbl Chir* 100:1473, 1975
10. Langer G, Stauck R: Frühe postoperativ Rezidivblutung. In: Häring (ed): Das komplizierte Gastroduodenale Ulcus, Thieme, Stuttgart New York 1978
11. McCraw L, McLeod R, McDonald W, Stevenson HE: A rapid bedside test for intestinal perforation. *JAMA* 191:939, 1965
12. Riedel P, Dinstl K, Keminger K, Lechner G, Schissel N: Die diagnostische Wertigkeit des Gastrografintests bei der Diagnose von Anastomosendehiszenzen des Intestinaltrakts. In: Pichlmayer R (ed): Postoperative Komplikationen. Springer, Berlin, Heidelberg, New York 1976
13. Schriefers KH, Wenn B: Über den Icterus nach operativen Eingriffen. *Dtsch Med Wochenschr* 92:540, 1967
14. Schwartz SI, Lilliehei RC, Shires GT, Spencer FC, Storer EH: Principles of Surgery. McGraw-Hill Book Company 1974
15. Stengel BF, Close AS, Thomas WD: The influence of prophylactic drainage on the results of duodenal stump perforation. *Surg Gynecol Obstet* 117:623, 1963
16. Stücker FJ, Larena A, Hoffmann K, Zumbotel V.: Frühe und späte Reintervention nach Resektion wegen Gastro-Duodenal-Ulcus. *Der Chirurg* 44:7, 1973
17. Szabó L: A duodenumcsont zárásának nehézségeiről (The difficulties in closure of the duodenal stump). *Magy Seb* 20:43, 1967
18. Waheed A, Phil JH, Hiram CP. Leaks and obstruction after gastric resection. *Am J Surg* 152:301, 1986

Book review

J. HUREAU, J. PRADEL: Tomography of the Trunk.
Normal and Pathoanatomy

Piccin, Padua 1990, 487 pp., 1090 Figures

The French surgeon-anatomist and radiologist co-authors present in twelve main chapters the computed tomography of the trunk by an excellent and expressive description of the normal and pathoanatomical changes. The core of the book is an atlas. The trunk can be studied in 103 sections from the upper aperture of the chest to the perineum. The authors also present 335 normal and pathological CT scans. An anatomical picture corresponding to each section is available for orientation, so that the 5—sometimes even 17—CT scans can easily be assessed, clearly revealing the pathological changes. The book's prime concern was to offer a morphological survey, without aiming at a complete coverage of the pathology of the trunk. The material was a random selection, and by using the index, the reader is offered valuable documentary information. The precise correspondence between the spinal segments and the visceral anatomy visible on the CT has not always been possible (the difference being sometimes of the size of a vertebral body).

Since various projection of the object are reflected on the screen, this can be manifold even in case of a given organ. It should also be borne in mind that the range of densities appearing in radiological imaging will by no means provide histological diagnosis. Chapter 1 gives a clear outline of the technical information.

With the help of the tomodensitometric possibilities of CT, the subsequent chapters consider more in detail the normal and pathological anatomy of the individual body regions, such as the changes of the mediastinum, the lung segments the hilar vessels, the diaphragm and of the abdominal wall, each separately. The gluteal region, being almost inaccessible to clinical examination can be particularly well visualized by CT.

● The retroperitoneal space is difficult to expose surgically, while having an important role in pathological processes. With the help of CT this region is easily accessible.

● CT offers valuable information in examining the abdominal lymph nodes.

● In possession of CT, the interpretation of liver segmentation has become part of up-to-date knowledge.

● The residual cavities arising during the various operations (e.g. pneumonectomy, splenectomy, nephrectomy, etc.) modify the anatomy, and therefore the examining physician should be familiar with the situation to be able to form a correct diagnosis.

● The final chapter deals with the examination of the aorta and its changes.

Although book does not consider all problems associated with CT, it provides a very good synthesis of the currently available, practical knowledge.

Orientation is easy and fast by studying the anatomical segments in the atlas part and the anatomical terms in the Appendix.

In addition to the morphological interpretations, the clinical comments enable the reader to attempt himself to establish a diagnosis in some cases.

The explanatory drawings assist in memorizing the individual situations and in safe orientation. The excellent quality of photos of the anatomical sections should also be emphasized.

The book clearly systematizes the up-to-date knowledge on CT.

András Bécsi

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CONTENTS

Endothelin-induced long-lasting mesenteric vasoconstriction: a hypothetical mechanism of non-occlusive intestinal infarction. <i>I. Dóbi, Violetta Kékesi, M. Tóth and S. Juhász-Nagy</i>	199
CO ₂ laser in septic surgery. <i>T. Tóth and Gy. Benedek</i>	209
Surgical treatment of the hip in cerebral palsy. <i>T. Vizkelety, A. Rényi-Vámos and Gy. Szóke</i>	215
Experience with Solcotrans® orthopaedic in hip arthroplasty. <i>Anikó Faluhelyi and J. Koczor</i>	225
Successful treatment of erectile dysfunction with Fortisex coated tablets. <i>Gy. Papp and Zs. Kopa</i>	229
Concomitant incidence of fertility chance reducing varicocele and chromosome aberration. <i>J. Béres and Gy. Papp</i>	233
Dopamine-induces aggravation of myocardial ischaemia in the paced heart: cardio-surgical perspectives. <i>A. Kollár, Violetta Kékesi and A. Juhász-Nagy</i>	237
Comparison of histological effect of electrocoagulation and Nd-YAG laser coagulation in intact and tumorous rat tissue. <i>Z. Szemes and I. Számadó</i>	245
Assessment of the efficiency of endovesical laser treatment of urinary bladder tumors on the basis of polyamine content measured in the eluent. <i>Z. Szemes, B. Schumann, R. Kovács and E. Rimanóczy</i>	253
Magnesium transport in human pregnancy (Magnesium content of human gestation tissues and tissue fluids). <i>L. Lukácsi, F. Lintner, B. Zsolnai and J. Somogyi</i>	263
Biological valve prosthesis replacement—experiences and considerations. <i>Z. Szabó, E. Bodor, T. György, E. Moravcsik, L. Papp, Z. Szabolcs and E. Bartha</i>	269
Book review	277

Endothelin-induced Long-lasting Mesenteric Vasoconstriction: A Hypothetical Mechanism of Non-occlusive Intestinal Infarction

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(Received: Juni 5, 1991)

The *in vivo* mesenteric vascular effect of the novel, endothelium-derived endogenous polypeptide, endothelin-1 (ET-1) was examined in experiments performed on pentobarbital-anesthetized dogs. Blood supply to a segment of the small bowel was measured simultaneously with an electromagnetic flow probe and computer-assisted thermography which senses flow-dependent infrared irradiation. It was found that close mesenteric arterial injections of ET-1 produced long-lasting flow decreases of considerable magnitude: the single dose of 1 nmol reduced blood flow by nearly 90 percent, and even the minimal single amount of 1 pmol produced statistically significant vasoconstriction. The thermographic analysis proved the homogenous character of these reactions. Unlike vascular responses elicited by most of the known vasoconstrictive agents, the ET-1-induced spastic effects were maintained without a continuous exposure (drug infusion). All features that characterize the spastic ET-1 action qualify the peptide for a hypothetical candidate of mediating the nonocclusive mesenteric ischemic syndrome.

Over the past 15–20 years many concepts have been evolved for explaining the development of non-occlusive mesenteric infarction [for reference see (15)]. It has become increasingly clear that [repetitive or prolonged periods of ischemia may elicit irreversible] intestinal damages in patients having a patent mesenteric vasculature—provided that the spastic stimulus is sufficient to elicit marked flow reductions lasting for considerable periods of time. However, the identity of endogenous factors mediating spastic reactions of such strength and duration is still obscure. Along the development of substantial evidence for vasoactive factors that are released from the endothelial cells in response to variety of physiological stimuli, new possibilities are also emerging regarding the above pathological phenomenon. Among the most intriguing of these observations are the recent reports (most of them describing isolated vessel reactions) on the novel vasoconstrictor peptide endothelin-1 (ET-1) of extreme potency. This raises the prospect that this agent acts not only as a physiological regulator but also exerts its effect by enhancing the vascular tone to pathologically important levels. In answering the related questions, however, isolated vessels cannot be substituted for the vasculature of whole organs. The aim of this study was, therefore, to determine whether the

in vivo administration of ET-1 is capable of increasing mesenteric vascular tone and reducing local blood flow to pathological ranges in preparations which possess the multiple (physiologic) control mechanisms.

Methods

Mongrel dogs of either sex, weighing 7–12.5 kg and fasted overnight were anaesthetized with pentobarbital sodium (30–35 mg.kg⁻¹ i. v.); subsequent small doses (15–30 mg) were given as needed. After tracheal intubation the abdomen was opened in the midline, a suitable segment of the small intestine was exteriorized, and the branch of the superior mesenteric artery supplying this segment was prepared free for application of an electromagnetic flow probe (Statham SP 2201) of appropriate size. Phasic and mean (electronically integrated) flows were continuously recorded together with the arterial pressure (Statham gauge) on a Hellige multichannel recorder. A small side branch of the mesenteric artery was also prepared just proximal to the flow probe and cannulated with a fine (o. d. 0.8 mm) polyethylene tubing for intraarterial administration of drugs.

In each experiment computer-assisted telethermography of the mesentery was performed according to the technique developed in our laboratory and fully described elsewhere [13]. Briefly, thermograms were taken with the aid of an AGA 750 Thermovision camera which senses the infrared rays in the 2 to 5.6 μ m wavelength range. These rays projected by a rotating prism on an indium-antimonide crystal cooled with liquid N₂ to -196 °C are converted continuously to electric signals. Next, the signals are transmitted to the monitoring unit of the device working on the principle of a closed colour television chain (where they can be photographed) and/or to the computing unit, where the signals are converted from analogue to digital, classified and evaluated by a special program. Knowing the total extension of the thermographic image and the distribution of the respective temperature ranges (colours), the ratios of these ranges to the whole image can be described and the mean temperature characterizing the rate of blood flow can be calculated. In this study the sensitivity of detection was chosen so that each colour represented a 0.2 °C step, the whole scale thus being 2.0 °C. In the thermographic images the warm and cold ranges are represented by white-red and blue-green colours, respectively. A very close parallelism has recently been demonstrated between mesenteric blood flow changes and changes in mean temperature calculated over the mesenteric area [4, 5].

At the termination of the experiment Evans-blue (\simeq 20 ml) was injected into the mesenteric artery to delineate the bowel segment served by the vessel under study. On the average, the segment weighed 149.7 ± 18.4 g.

Drugs were injected intraarterially. Endothelin-1 (human, porcine; synthetic [pfs]) was purchased from Sigma and dissolved in physiologic saline. The peptide was employed in a dose range of 1–1000 pmol, the main aim being to ascertain the dose which reduced the segmental blood flow to about one-tenth of its original level. In all cases except two, the animals were subjected to asphyxia of 3 min duration by clamping the tracheal tube in the control state, and this procedure was repeated in the course of each experiment after a 300 pmol dose.

Statistically evaluated numerical data are given as mean \pm SEM. The significance of results was calculated by using Student's *t*-test for paired data.

Results

ET-1 produced in the mesentery a slowly developing intense vasoconstriction which was often preceded by a short-lived (< 15 sec) slight dilator response. We found that the close arterial injection of the peptide in the single dose as low as 1 pmol invariably reduced mesenteric blood flow by an average value of $10.5 \pm 2.7\%$ ($p < 0.02$). Since the resting level of total blood flow in the bowel segments amounted to 168 ± 17 ml/min in our experiments, this (threshold) concentration of ET-1 was roughly identical with a concentration of 6 fmol/ml* (≈ 0.00001 $\mu\text{g/ml}$) in the arterial blood. It was the 1 nmol dose of ET-1 which permanently decreased the mesenteric blood supply to about one-tenth of its initial value (Fig 1). Since the agent was locally administered,

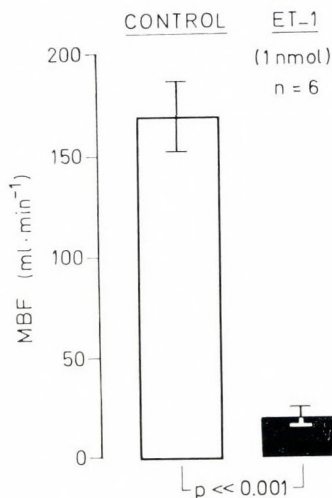


FIG. 1. Profound vasoconstriction induced by intraarterial endothelin (ET-1). Mean values \pm SEM. MBF mesenteric blood flow

* femtomol, 10^{-15} mol

the concomitant change of mean blood pressure even at the highest dose was slight or minimal (-6 ± 4 mmHg), and not statistically significant ($p > 0.1$).

Direct thermographic recordings of the ET-1 action revealed similar pictures which were, however, far more complex in details than could be estimated from the single parameter of blood flow record (Fig 2). As shown, ET-1 induced a dose-dependent profound cooling of the mesenteric segment. This thermographic effect reflecting the vasoconstriction-dependent decrease of heat

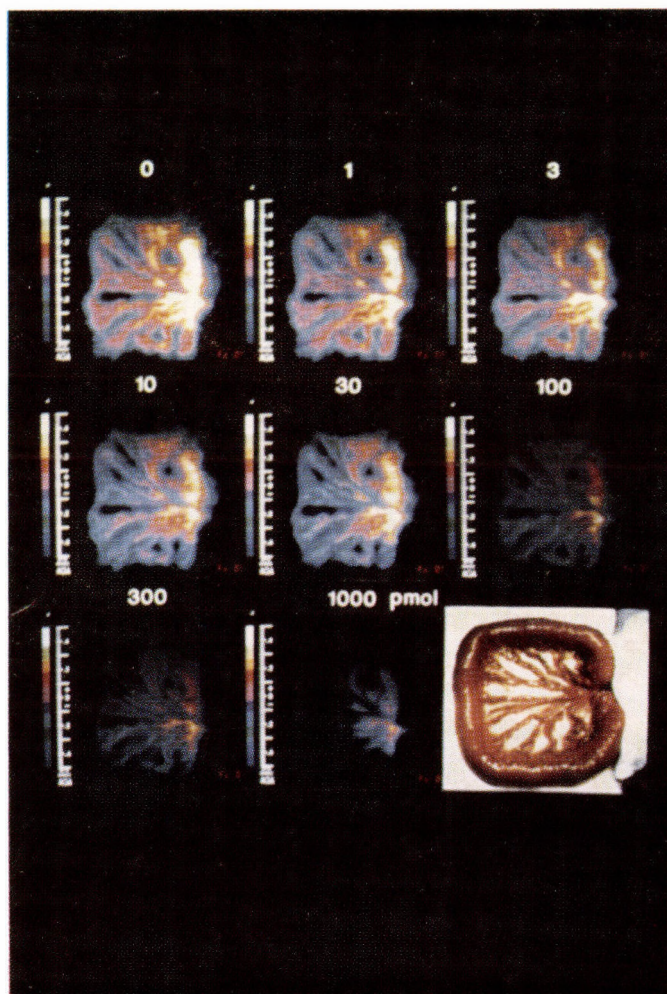


FIG. 2. Representative thermograms indicating progressive cooling of the mesentery after increasing doses of ET-1. The colour scale in each thermogram (left) shows 0.2°C temperature steps (from above downwards: cooling). Note the final disappearance of measurable heat emission from the major part of the image at the given temperature range. Computer-evaluated mean temperature decreased by $0.96 \pm 0.1^{\circ}\text{C}$ from control (0) to final stage (1000 pmol)

emitted from the mesenteric area, was usually uniform, i.e. it was evenly distributed over the whole affected surface. In some cases, after the administration of smaller doses the fairly homogenous thermographic image tended to show a characteristic mixed pattern of cooler and warmer subsegments (indicating moderately different local sensitivities of the vessels), but the intermingled nature of the response disappeared after injecting higher ET-1 doses (Fig 3). The original fine texture of the images was invariably preserved, except after employing higher doses (≥ 300 pmol, Fig 3).

Fig 4 depicts the typical time course of ET-1 action: the long duration of the vasoconstrictor effect is indicated by the fact that the near-maximal spastic response was maintained even at the 25–30th minute of the long lasting flow reduction, while the level of blood flow was still less than 25 percent of the control at the 60th, and only slightly more than 50 percent at the 150th minute. Another feature of the stability of the ET-1-induced vasoconstrictor response was revealed by its resistance against vasorelaxant drug actions: large doses of the extremely potent mesenteric vasodilator drug papaverine

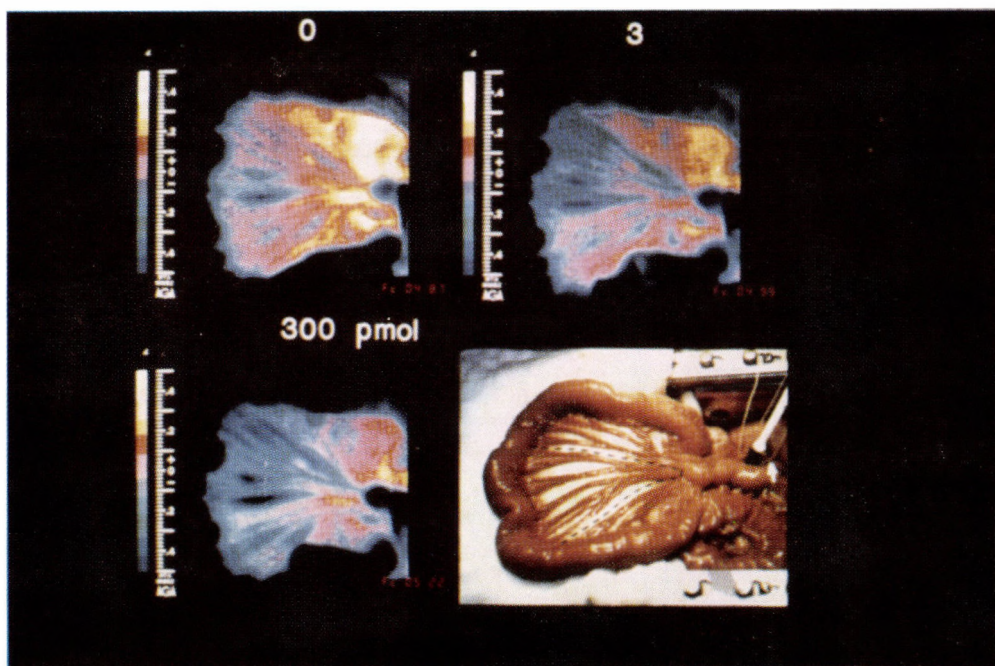


FIG. 3. Moderate inhomogeneity of thermographic responses after a small (3 pmol) but not after a large (300 pmol) ET-1 dose. Highly sensitive area is indicated by dashed black lines on the photo. (Note the mirror image of the mesentery on thermograms as compared to the photographic picture.) White arrowhead denotes the site of the intra-arterial cannula proximal to the flow probe. Computed temperature changes amounted to $-0.21 \Delta^{\circ}\text{C}$ (3 pmol) and $-0.41 \Delta^{\circ}\text{C}$ (300 pmol)

were able to offset the stabilized spastic reaction only for a short-limited period of time, after which the local vascular tone returned to its established high level (Fig 5).

The vasoconstrictor action of ET-1 could tentatively be explained either by an extremely powerful potentiation of the sympathetic drive to the mesenteric arteries or the inhibition of metabolic stimuli affecting the same vessels. We therefore examined whether the ET-1 action interfered with the vascular responses elicited by subjecting the animals to a strong asphyxic stimulus which simultaneously activates both types of mechanisms (Fig 6). Comparison of the characteristic phases of these responses in the control state and after administering ET-1 in a dose of 300 pmol (which considerably reduced but did not minimized mesenteric flow), revealed that ET-1 inhibited rather than potentiated the vasoconstrictor response accompanying the central sympath-

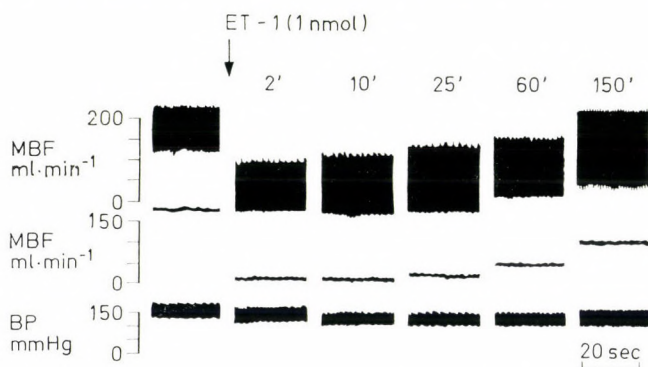


FIG. 4. Time course of the ET-1 action (representative tracings). From above downwards in each block: phasic and mean mesenteric blood flow (MBF), arterial blood pressure (BP)

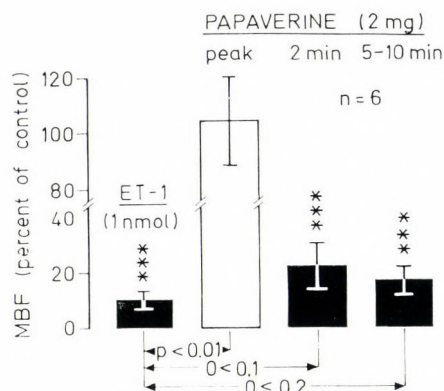


FIG. 5. Transitory character of papaverine-induced vasorelaxation in the mesenteric vascular bed precontracted by ET-1. *** $p < 0.001$

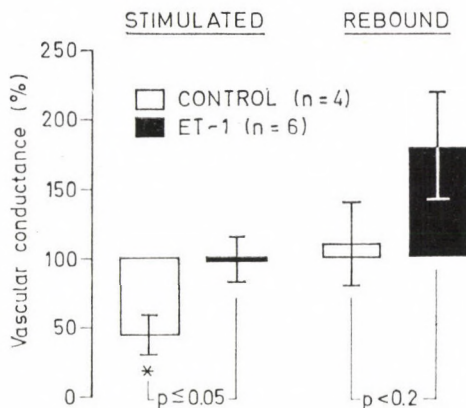


FIG. 6. Characteristic changes in the biphasic asphyxic response: final stage of the 3 min asphyxic stimulation (left pair of columns) and postasphyxic rebound (right pair of columns). The responses represent calculated relative vascular conductance changes from the preasphyxic level which was only $42 \pm 5\%$ of the untreated control after the 300 pmol ET-1 dose. * $p < 0.05$

etic excitation and tended to unmask a postasphyxic vasodilator rebound. However, the latter phenomenon was not statistically significant. Accordingly, these tests did not substantiated any explanation based on indirect mechanisms of mesenteric ET-1 actions.

Discussion

The evidence is now overwhelming that endothelial cells release at least a dozen kinds of major vasoactive factors. These substances either relax (EDRF-nitric oxide, hyperpolarizing factor, prostacyclin, adenosine etc) or contract (endoperoxides, angiotensions, thromboxane A_2 , prostaglandin $F_{2\alpha}$ etc.) the vascular smooth muscle. The picture that is beginning to emerge suggests that the vascular tone is influenced parallelly by two independent (though interacting) regulatory systems: the network of vegetative (mainly sympathetic) nervous elements which transmits signals from the central nervous system (i) and the local paracrine system of endothelial cells which transmits signals in response to chemical and physical changes occurring in the proximity of the vessels (ii). In general terms of control theory both systems may be regarded complete "reflex arches" containing sensory-transduction and effector components [11].

The list of transmitter substances acting at the effector arm of the *local* regulatory arch (ii) has recently been supplemented by the discovery of the peptides endothelins, the most powerful constrictor agents known to physio-

logical sciences. The novel vasoconstrictor peptide ET-1 was isolated and sequenced in 1988 by Yanagisawa and his co-workers [19] from the cultured supernatant of porcine aortic endothelial cells. Its molecular weight was estimated to be 2492 from the sequence data [19]. A sequence homologous to ET-1 was not detected until now in the mammalian body. However, the snake venom sarafotoxin S6_B shows a surprisingly homologous structure [17].

ET-1 in adequate doses was found to increase blood pressure [19]. Regarding its direct action on the vascular wall, a great body of evidence indicates that it contracts the isolated strip of all kinds of vessels so far studied [14] and reduces flow in perfused isolated organs including the heart [1, 12] and the mesentery [8]. Recently there have been other sparse reports on the blood flow decreasing ET-1 action in the intestinal circulation [6, 9]. However, the precise, fully characterized action of the peptide on the *in situ* mesenteric vascular bed of the intact organism remained unknown. As far as we know, the present work is the first attempt to connect ET-1 action with surgical research.

A major finding of our study has been the experimental proof of the outstanding mesenteric vasoconstrictor potency of ET-1 under *in vivo* conditions. More importantly, our measurements showed the unequivocal maintenance of this spastic reaction after employing a single dose. In previous studies, including ours [2, 3] various agents such as catecholamines or angiotensin II, have been postulated to be candidates for eliciting mesenteric vasospasm. Indeed, it is reasonable to assume that these agents may play a decisive role in the pathological events under the conditions of a continuous exposure. However, when their administration or release is discontinued, in most cases the mesenteric vasoconstriction induced by these agents is fully recovered by 3–10 min. Compared with these agents, ET-1 produced not only strong but also long-lasting spastic effects.

Although ET-1 is capable of inducing vasospasm in larger (conductive) arteries [14, 19], its action seems to affect mainly the small resistance vessels such as those of the coronary circulation [7, 10]. This type of response presupposes a fairly uniform and profound involvement of the whole organ. Since our present thermographic evidence also indicated in the mesentery widespread, evenly distributed flow reduction of great magnitude which is more likely to develop via a small than a large vessel reaction, the results of these investigations also seem to be consistent with the assumptions related to the coronary vessels [18].

We have tested two important aspects regarding the mechanism of action of ET-1. [1] Although strong vasodilator drug effects could temporarily inactivate the ET-1-induced spasm, it is highly improbable that the inhibition of physiologic vasodilator mechanisms are involved in the potentiation of the peptide action. [2] The same conclusion holds for the involvement of the local

adrenergic system: ET-1 action is independent of adrenergic activation. In this respect our results confirm recent observations indicating the inhibition by ET-1 of electrically stimulated overflow of noradrenaline in arterial preparations [16].

Taken together, a single stroke of ET-1 (the most potent vasoconstrictive substance so far discovered) is in itself sufficient to reduce dangerously the blood supply to the bowel wall. It is tempting to speculate that such a mechanism may be responsible for the still enigmatic pathomechanism of non-occlusive mesenteric infarctions. Interestingly, the stimuli that increase formation of mRNA for ET-1 (i.e. thrombin, catecholamines, increased shear stress) are all stimuli that may facilitate or precipitate the above pathologic event as well [14]. However, at this stage of our knowledge much more is known about the pharmacological effects of exogenously administered ET-1 than about the actions of the endogenous substance. This gap in our information constitutes the weak point of our hypothesis. In the future, advances of methodology probably will allow the direct measurement of ET-1 in the crucial clinical situations, thus making these assumptions a testable hypothesis.

References

1. Baydoun AR, Peers SH, Cirino G, Woodward B: Effects of endothelin-1 on rat isolated heart. *J Cardiovasc Pharmacol* 13 (Suppl 5): S193-S196, 1989
2. Dóbi I: Alterations of vascular reactivity in the mesenteric circulation. Thesis Budapest, 1990
3. Dóbi I, Kékési V: Factors influencing the vascular action of dopamine in the canine mesenteric bed. *Acta Chirurg Hung* 30:251-260, 1989
4. Dóbi I: Evaluation by thermography of vascular adaptation in the mesenteric bed: an experimental study. *J Cardiovasc Surg* 31:114-115, 1990
5. Dóbi, I, Juhász-Nagy A: Substitution by adenosine for glucagon as a surgical tool to detect mesenteric vascular adaptation. *J Vasc Surg* in press, 1991
6. Dohy Y, Luscher TF: Aging differentially affects direct and indirect actions of endothelin-1 in perfused mesenteric arteries of the rat. *Br J Pharmacol* 100:889-893, 1990
7. Fukuda K, Hori S, Kusuvara M, Satoh T, Kyotani S, Inoke S, Ohno H, Yamaguchi K, Handa S, Nakamura Y: Intracoronary endothelin-1 increases coronary retrograde pressure by constricting arterioles. *Cardiovasc Res* 24:987-992, 1990
8. Hiley CR, Douglas SA, Randall MD: Pressor effects of endothelin-1 and some analogs in the perfused superior mesenteric bed of the rat. *J Cardiovasc Pharmacol* 13 (Suppl 5): S197-S199, 1989
9. Hoffman A, Grossman E, Ohman KP, Marks E, Keiser RH: The initial vasodilation and the later vasoconstriction of endothelin-1 to specific vascular beds. *Am J Hypertension* 3:783-791, 1990
10. Larkin SV, Clarke JC, Keogh BE, Araujo L, Rhodes C, Davies GJ, Taylor KM, Maseri A: Intracoronary endothelin induces myocardial ischaemia by small vessel constriction in the dog. *Am J Cardiol* 64:956-958, 1989
11. Miller VM: Interactions between neural and endothelial mechanisms in control of vascular tone. *NIPS* 6:60-63, 1991
12. Neubauer S, Ertl G, Haas U, Pulzer F, Kochsiek K: Effects of endothelin-1 in isolated perfused rat heart. *J Cardiovasc Pharmacol* 16:1-8, 1990
13. Papp L, Álló G, Szabó Z, Juhász-Nagy A: Natural history of acute regional myocardial ischaemia revealed by infrared thermography in the canine heart. *Acta Morph Hung* 33:123-142, 1985

14. Proceedings of the First William Harvey Workshop on Endothelin. J Cardiovasc Pharmacol 13 (Suppl 5): S1-S231, 1989
15. Shepherd AP, Granger DN (eds): Physiology of the Intestinal Circulation Raven Press, New York 1984
16. Tabuchi Y, Higashimori M, Rahugi H, Nagano M, Higashimori K, Mikami H, Ogihara T: Effects of endothelin on neuroeffector junction in mesenteric arteries of hypertensive rats. Hypertension 15:739-743, 1990
17. Takasaki C, Tamiya N, Bdolah A, Wollberg Z, Kochva E: Sarafotoxin S6: several isotoxins from *Atractapis engadensis* (burrowing asp) venom that affect the heart. Toxicol 26:543-548, 1988
18. Tóth M, Tóth P, Kékesi V, Juhász-Nagy A: Endothelin does not interact with angiotensin II in the canine coronary vascular bed. J Mol Cell Cardiol in press, 1991
19. Yanagisawa M, Kurihara H, Kimura S, Tomobe Y, Kobayashi M, Mitsui Y, Yazaki Y, Goto K, Masaki T: A novel potent vasoconstrictor peptide produced by vascular endothelial cells. Nature 322:411-415, 1988

CO₂ Laser in Septic Surgery

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Authors have performed 29 septic operations by a TLS₆₁ 60 W CO₂ laser apparatus. In accordance with international experience, favorable results have been obtained in laser surgery of vascularized, hemophilic and bacterium penetrated alterations and infected wounds.

As suggested in the literature [1, 3, 10], CO₂ and Nd: YAG, as the most important surgical lasers, can be applied very effectively in the operation of various surgical alterations.

Skobelkin et al [9] reported on laser interventions in more than 300 septic patients.

Sohn [7] recommended CO₂ laser for the surgical treatment of perirectal abscesses and fissures. He operated sacral dermoid cysts by Nd: YAG laser.

Lanzafame et al [5] applied CO₂ laser for surgical excision of chronic breast abscesses: the infected segments were excised *en bloc* at 60 W output performance.

Kaplan [4] applied CO₂ laser for the excision of decubitus, burn injuries and necrotic areas, the advantage of the method being no or minimal bleeding during the procedure and the bactericide effect of laser along the line of incision.

Material and methods

Our interventions were performed by a 60 W TUNGSRAM TLS₆₁ CO₂ laser instrument allowing continuous and impulse modes of operation. Accurate aiming is allowed by the red light of a low performance (1 mW) helium-neon laser parallelized by the worklight of the CO₂ laser. The CO₂ laser beam is initiated by foot pedal. The weight of the apparatus is 220 kg. Four wheeled, the instrument is easy to roll to the operating table or from one room to the other. Before the start of operations, a sterile bag is pulled onto the manipulation arm of the machine, or the sterilizable handpiece is replaced before each operation (this is held by the surgeon).

Wearing protective goggles is mandatory for the members of the operating team and for everybody staying in the operating room during the procedure.

Major vessels and hollow organs behind the concerned areas (intestines, stomach, etc.) are protected by salted plates, metal probes or plates.

In the last 3 years, a total of 29 septic operations have been performed by CO₂ laser at our department. The diagnoses and the interventions are illustrated in Table 1.

Figures 1–3 show a septic finger granuloma and its surgical excision by laser knife.

TABLE 1

CO₂ laser operated septic cases at the 3rd Department of Surgery of Semmelweis Medical School

No.	Diagnosis	Type of intervention	No.
1.	Mammary fistula	Excision + primary suture	2
2.	Septic granuloma	Excision + primary suture	2
3.	Varicose crural ulcer	Debridement	2
		Sterilizing the ulcer base	1
4.	Postlaparotomic thread suppuration	Excision	4
5.	Tumor rec. (absced.)	Incision + drainage	2
6.	Sternal osteomyelitis	Sternal resection	1
7.	Finger osteomyelitis	Ablation	1
8.	Costal osteomyelitis	Costal resection	2
9.	Finger congelation	Ablation	6
10.	Pulmonary actinomycosis	Excision	1
11.	Abscessive pulmonary tumor	Cuneiform pulmonary resection	1
12.	Atheroma absced.	Excision + primary suture	2
13.	Status after tumor excision (supp.)	Excision + skin graft	1
14.	Subacute cholecystitis	Cholecystectomy	1
Total:			29

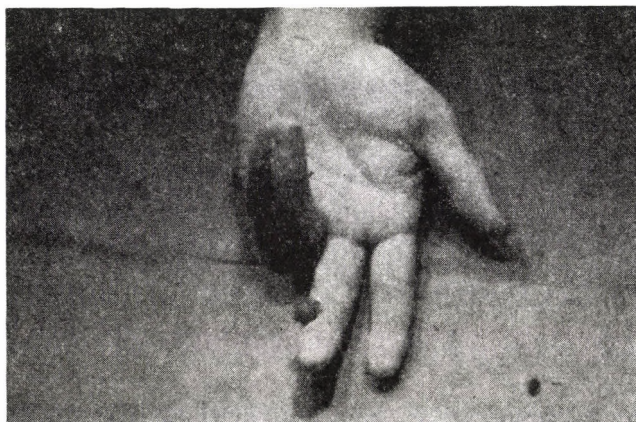


FIG. 1. Hemophillic, septic granuloma on a finger of a 52-year-old male patient



FIG. 2. Laser excision of a septic granuloma



FIG. 3. Primary sealing of the laser excision site

Figure 4 illustrates a suppurative wound after the excision of an infected tumor on the lower leg of a 60-year-old male patient. The tumor was a histologically verified melanoma. The suppurative wound was *en bloc* excised by laser knife, and the epithelial deficiency was covered by grafting a semi-thick lobe taken from the abdominal skin (Figure 5). The graft adhered well to the ray sterilized, non-bleeding base, and showed a good healing tendency.

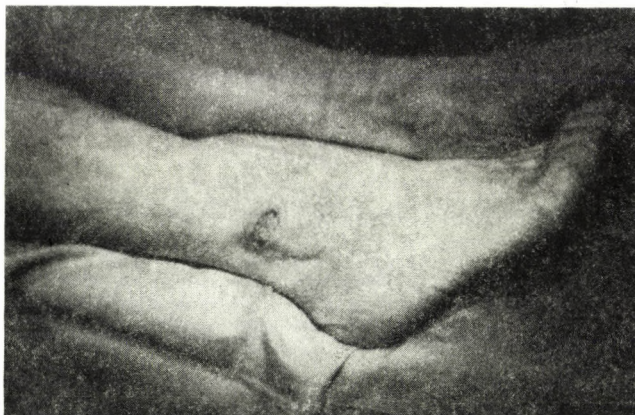


FIG. 4. Discharging dysrumped wound remained after the excision of a hazelnut-sized malignant melanoma on the lower leg of a 61-year-old male patient



FIG. 5. The discharging wound was widely excised down to its base by CO₂ laser knife, and the "sterilized" wound was covered by a semi-thick graft from the abdominal skin

Discussion

A major field of application of various surgical lasers is septic surgery, including the treatment of inflamed wounds, vascularized, hemophilic and bacterium infected areas.

The method of *Skobelkin et al* [9] is to excise minor abscesses, infected atheromas and furuncles *en bloc* by focused laser light and to ray sterilize the wound bases by defocused laser light. The wounds are closed in a primary way or above drain. This technique has decreased both the healing time and the hospitalization period. The authors report on p.p. wound healing in 93% of the cases.

We may report on a relatively smaller patient material; though we performed more than 400 laser operations, the number of septic cases was only 29. The CO₂ laser knife is apparently very useful in the excision of septic stitch abscesses and mammary fistulas. The intervention features minimal bleeding and fast wound healing. The skin can be covered either by primary suture or above the drain.

CO₂ laser is also suitable for cutting soft parts and even flat bones (e.g. sternum). Tubular bones are cut more slowly by CO₂ laser in the continuous mode, but the more recent TLS₆₂ laser is perhaps more useful in this respect (we still have no experience with this apparatus). TLS₆₂ is able to work even in the superpulsating mode (with 400 W performance at the peaks!).

Bacteria, viruses and fungi are destroyed along the incision line, and no hematomas remain in the wound hollow, which is important in the wound healing process.

References

1. Fidler JP, Law P, Millen BG et al: Comparison of carbon dioxide burns with other thermal knives. In: Proceedings of The First International Symposium on Laser Surgery, Israel, pp. 90–94, 1975
2. Hall RR: The healing of tissue incised by a carbon dioxide laser. *Br J Surg* 58(3):222–225, 1971
3. Herrera HR, Hinshaw JR, Lanzafame RJ: Application of the CO₂ laser in thoracic surgery. In: Proc of the 7th Congress of the International Society for Laser Surgery and Med. Laser. 1987, Munnich, pp. 172–175
4. Kaplau I: The CO₂ laser in clinical surgery: past present and future—state of the art. Proc. of the 7th Congress of the International Society for Laser Surgery and Medicine, Laser 87. Munnich, pp. 119–126, Springer
5. Lanzafame RJ, Herrera HR, Pennino RP and Winschaw JR: Breast surgery with laser. In: S. Joffe: Lasers in General Surgery, Williams and Wilkins, 1989, 22. 26
6. Hadden JE, Edlich RF, Custer JR et al: Resistance to infection of surgical wounds made by knife electrosurgery and laser. *Am J Surg* 122:532–535 1971
7. Sohn N: Anorectal disorders. In: S. Joffe: Lasers in General Surgery, Williams and Wilkins Pb. 1989, pp. 130
8. Mester F, Spiry T, Szende B: Effect of laser rays on wound healing. *Am J Surg* 122: 532–535 1971
9. Skobelkin OK, Tolstikh PI, Ryabov VI: Comparative assessment of conventional laser treatment for suppurative wounds, Laser 87, Munnich Proc of the 7th Congress of the International Society for Laser Surg. and Med., pp. 154–158, Springer
10. Stellar S, Meier R, Walia SA: Carbon dioxide laser debridement of decubitus ulcers. *Ann Surg* 179(2):230–237 1974

Surgical Treatment of the Hip in Cerebral Palsy

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Hips are affected generally in CP but in favourable cases we can prevent dislocation by adductor tenotomy performed in time (530 cases). Posterior transposition of the origins of the adductor muscles is performed if the patient walks with inwood rotated inferior extremities (105 cases).

In the treatment of real subluxation and valgus deformity the open tenotomy of adductor muscles and femur osteotomy with derotation and varisation were used (180 cases).

We accomplish open reduction in frank dislocation (35 cases). In such cases it is often necessary to shorten the femur. Also normal acetabulum is found in elder children.

The disturbance of the growth of the proximal femoral end and the increased coxa valga and antetorsion is quite frequent in cerebral palsy [6, 7, 9, 10] and it leads to subluxation or dislocation. The data on subluxation and dislocation are quite different and depend on the age in which the examinations were made and also on the extent and severeness of the paralysis [1, 2, 10].

Independently from the method of conservative treatment, in a significant part of the cases we have to perform operations. As a result of the operations performed in due time the development of motion may suddenly improve, the contractures, the dislocations, the deformities may be prevented or if they have already appeared they may be corrected. This is valid also for the operations around the hip. In the indication of the hip operations and the choice of the adequate methods the hip of CP patients has to be considered as a paralytic hip and one has to strive to eliminate the disturbance of muscular equilibrium and to correct the secondary deformities. If it is possible one can prevent with soft tissue operations performed in due time the development of more serious deformities that are difficult to be influenced or cannot be solved at all.

Materials and methods

The number of operations performed in CP patients gradually increased (Fig 1). In 1951–86 totally 3305 operations were made. From these 945 were hip operations (Table 1). We could not control all and therefore only a small

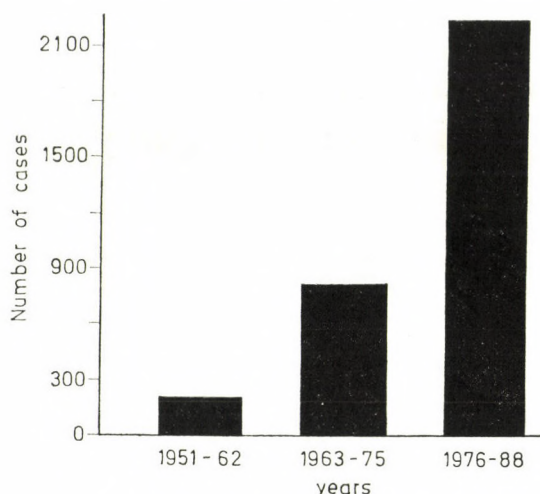


FIG. 1. Number of operations on the lower extremities in 3 different periods

TABLE I
Operations on hips in cerebral palsy

	1951-62	1963-75	1976-88	Total
Open adductor tenotomy (obturatorius resection)	20	150	360	530
Posterior transfer of the hip adductor origins			105	105
Stripping of the spine muscles		30	40	70
Varus derotation osteotomy		40	140	180
Open reduction		10	25	35
Chiari pelvic osteotomy			25	25
Total	20	230	695	945

part of the patients are presented for the different operations. The number of the patients, the sex distribution, the average age in the time of the operation, the results and the complications are given.

Open adductor tenotomy. We have performed open adductor tenotomy at each CP patient and the origins of the long adductor and of the gracilis were detached. In case of a very great tension of the short adductor a partial section of this was performed.

The number and result of the operations are demonstrated on Table 2. Postoperatively the patients got a plaster for 4 weeks in 40°-40° abduction. On the 10th day the patient was raised. The anterior branch of the obturator

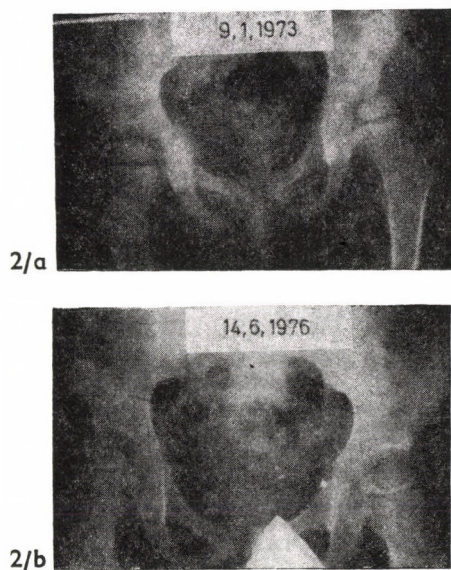


FIG. 2.a. Roentgenogram of a 3 years old child. Subluxation on the left side. b. 3 years after open adductor tenotomy. On the left side: normal relations, subluxation on the right side

TABLE 2
Open adductor tenotomy

1951-1980: 530 cases, 213 ♂, 317 ♀		
Average age at the time at the operation	4.3 years	
Average follow up time	9.2 years	
without subluxation	subluxation, coxa valga	
35%	65%	
	5 years later	
without dislocation tendency	75% improved	25% worsening

nerve was rarely sectioned (in 33 cases). The results were overwhelmingly favourable. Figure 2 shows the development of the left hip after adductor tenotomy, and that of the right hip without adductor tenotomy.

Posterior transposition of the adductor origins was performed in the 3rd period in 1976 to 1988. Generally it was made under 10 years of age because of walking with inward rotation and we have found improvement in each case.

Stripping of the spine muscles, if necessary together with the tenotomy of the iliopsoas, is performed more and more frequently. We think it advisable to make this operation also in 20° hip flexion contracture.

In coxa valga subluxans or dislocation, beside the elimination of the hip flexion contracture, the restoration of the normal hip relations is thought also to be important. The reduction and the femoral osteotomy are performed even than if the child cannot walk or walking cannot be expected; even in these cases a more symmetrical sitting is made possible, the care is enlightened and the chances of later hip pains diminished.

The results of 43 *varus derotation osteotomies* are assessed and demonstrated in Table 3. Varus derotation osteotomies were performed in cases where,

TABLE 3
Varus derotation femur osteotomy

33 patients	43 hips		
	11 ♂	22 ♀	
Average age at the time of the operation		7.3 years	
Average follow up time		3.3 years	
	preop.	op.	postop.
CD angle	158.9°	124.8°	138.5°
AC angle	31.2°		29.2°
CE angle	10.3°		13.8°

beside coxa valga and increased antetorsion, subluxation was also observed, expressed by the CE angle (Fig. 3). The osteotomy was made after an open adductor tenotomy in the level of the lower edge of the lesser trochanter and fixed with Sherman plate and screws. In each case plaster was also given, as we have observed that without this an adduction position will develop and the internal fixation may be insufficient. The antetorsion was corrected to 5°–8°, the neck shaft angle to 125°. The development of revalgization was connected with the adductor spasm and contracture, that remained after the operation. We have found complications in 10 cases, a part of these was the consequence of technical errors. The complications are demonstrated in details on Table 4.

The results of *open reduction* could be assessed in 23 cases. The operation was performed independently from the fact whether the patient could walk or not, or a walking could be expected or not in the future. In the later case our aim was the enlightening of the sitting, to reach symmetry and to enlighten the care. The detailed results are demonstrated on Table 5, the complications in Table 6. In 14 cases, after reaching the above mentioned goals, there

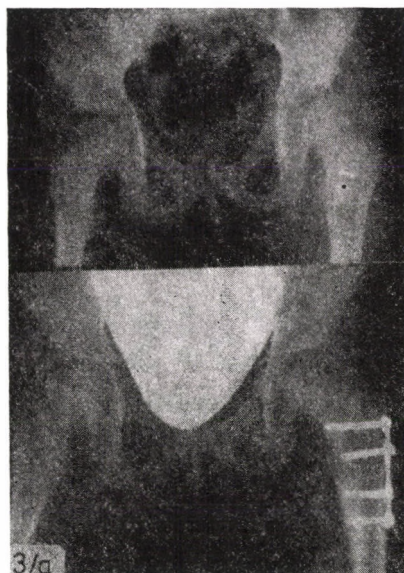


FIG. 3.a. Varus derotation osteotomy was performed for subluxation of the left hip.
b. 6 years later—adequate development of the hip

TABLE 4

Varus derotation femur osteotomy: 43 hips

Complications	
Redislocations	2
Extreme varus position	3
Extreme limb shortening	4
Total	9

TABLE 5

Open reduction + varus derotation femur osteotomy

	23 hips		
	19 patients	8 ♂	11 ♀
	preop.	op.	postop.
CD angle	158°	125°	135°
AC angle	33.5°		32.5°
CE angle	-32.4°		11.3°

TABLE 6

Open reduction + varus derotation femur osteotomy: 23 hips

Complications	
Redislocation	2
Femoral head necrosis	3
Total	5

TABLE 7

Open reduction + varus derotation femur osteotomy + Chiari pelvic osteotomy

	10 hips	3 ♂	7 ♀
Average age at the time of the operation			11.6 years
Average follow-up time			2.5 years
	preop.	op.	postop.
CD angle	151.2°	128°	135°
AC angle	35.2°		21.2°
CE angle	-20.5°		22.2°

was an expressed improvement, the parents were satisfied with the operation. More than one of the patients has begun to walk after the operation, the asymmetric position of the hips has ceased.

Open reduction is performed after open adductor tenotomy. The hip is exposed according to Watson Jones and the iliopsoas is always detached, exceptionally also the muscles originating from the superior and inferior iliac spine. The acetabulum was found generally well developed. An oblique osteotomy was performed at the level of the lesser trochanter. The CO angle was set to 125°, the antetorsion between 5°–10°. Depending on age a 10–20 millimeter

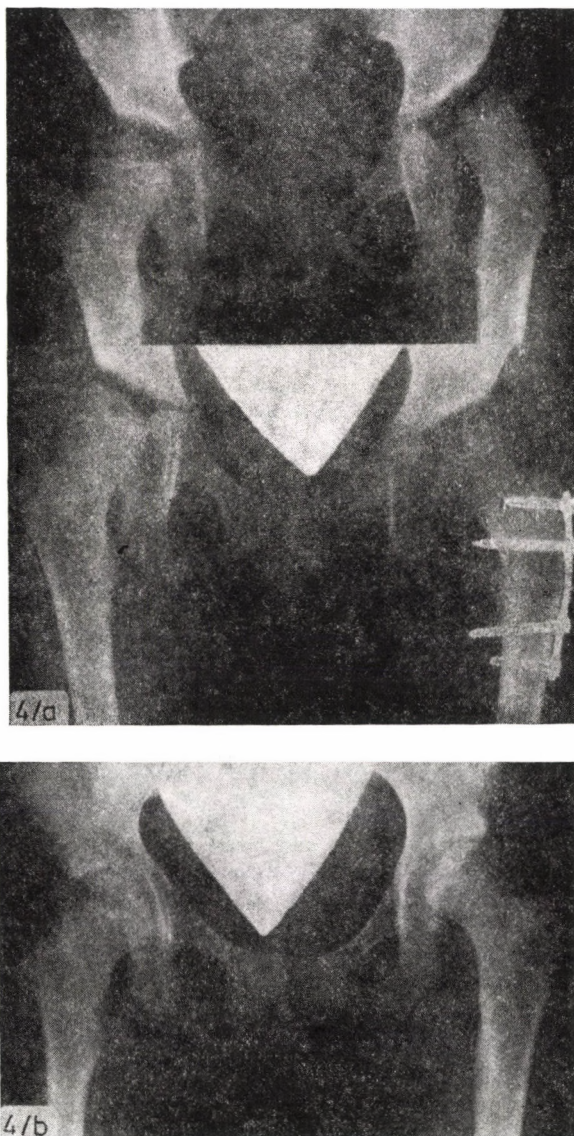


FIG. 4.a. Open adductor tenotomy, open reduction of the hip, varus derotation femoral osteotomy. b. Roentgenogram made 5 years later

abbreviation was also necessary. To reach a reduction without tension this was frequently more important than the varization (Fig. 4). Chiari's pelvic osteotomy was performed in 25 cases, the patient could be followed in 10 cases (Table 7, Fig. 5). In 1 case redislocation was observed and this has ment the failure of the operation.

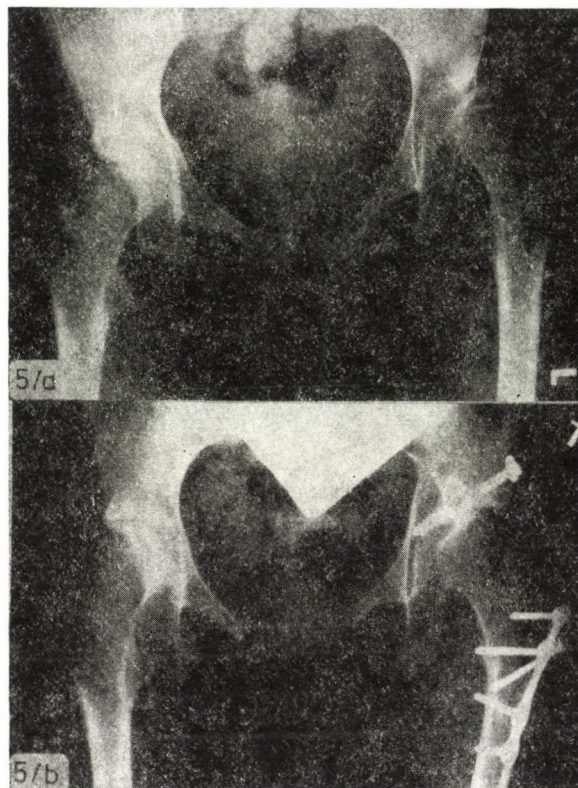


FIG. 5.a. Open reduction, varus derotation osteotomy and Chiari's osteotomy performed in a 14 years old child. b. 1 year postoperatively

Discussion

In Hungary generally Pető's conductive education is used for the conservative treatment of CP patients. Although this method is suitable for milder cases with more favourable prognosis [8, 11, 12] in a significant part even of these cases operation is needed.

In the last 40 years operations were performed more and more frequently in these children and also in those cases which were previously treated conservative. The unfavourable functional state of the hips, and the subluxation or luxation developing in a significant part of the cases are serious consequences of the disease [1, 3, 4, 5] and we have to strive for prevention, or if these lesions have already developed, to eliminate them. The open adductor tenotomy performed in due time influences favourably the development and function of the hips. These operations were made according to the suggestion of Sharrard and others [2, 9] after 2,5 years of age if the abduction was not more

than 30° . The results can be assessed also on basis of the Roentgenograms. The neck-shaft angle shows a favourable development, and especially after operations performed in younger age the dislocation tendency also improved. The effect that the gait of the preoperatively scissoring child improved also considerably is also not less important. To obtain a good result it is important to weight the measure of the adductor tenotomy. The long adductor and the gracilis were always detached. The section of the anterior branch of the obturator nerve in case of major spasm may be equally necessary. To this, however, the force of the abductors has to be measured exactly.

The retroposition of the origins of the hip abductors is a good alternative of the tenotomy. If the gait with inward rotation dominates, this operation is performed. We have obtained good results even in adolescence. It can be made in cases in which the inward rotation is caused by spasm and it appears first of all during gait and if in flexion the hip can be rotated outward.

Varus derotation osteotomy is performed in elder children (average age 7.3 years) in cases of subluxation, if the femoral head can be centralized in the acetabulum. Even after open adductor tenotomy such a muscular force is exerted on the femur that, after having experienced some complications in the past, the internal fixation is completed with plaster, to handicap excessive varization or the tear of the screws from the bone. Because of the frequent complications (21/cnt) this operation is chosen only in cases of subluxation, the valgity of the femoral neck in itself is not considered as an indication.

The open operative reduction together with open adductor tenotomy and varus derotation abbreviation osteotomy is without doubt a major intervention and we would perform it more willingly in children who will be able to walk afterwards. It is performed however also if we can secure the symmetrical position of the extremities and enlighten the care and hygienics. Except the 2 cases of redislocation we have obtained improvement. In cases with shallow acetabulum and if it is thought that these is a major danger of subluxation 2-3 months after the operative reduction Chiari's pelvic osteotomy is performed. This operation made in adolescence gives generally a good result.

Naturally it is more favourable if subluxation or luxation can be prevented and in this open adductor tenotomy performed in due time has a decisive role. If, however, subluxation or dislocation have already developed, with open reduction, femoral and Chiari's pelvic osteotomy it will be possible to treat the serious functional disturbance and deformity of the hips and to promote the gait and enlighten the care of the patient.

References

1. Baker LD, Dodelin R, Bassett FH: III. Pathological changes in the hip in cerebral palsy: incidence, pathogenesis and treatment. *J Bone Joint Surg* 44-A:1331-1342, 1960

2. Banks HH, Green WT: Adductor myotomy and obturator neurectomy for the correction of adduction contracture of the hip in cerebral palsy. *J Bone Joint Surg* 42-A:111-126, 1960
3. Feldkamp M, Infantile Zerebralparese in Bernbeck R, Dahmen G. ed: *Kinderorthopädie* Stuttgart, Thieme Verlag 409-436, 1976
4. Feldkamp M, Denker P: Importance of the iliopsoas muscle in soft-tissue surgery of hip deformities in cerebral palsy children, *Arch Orthop Trauma Surg* 108:225-230, 1989
5. Knupfer H: Besondere Gesichtspunkte bei operativer Behandlung spastischer Lähmungen. *Orthopädische Praxis* 21:22-45, 1985
6. Phelps WM: Prevention of acquired dislocation of the hip in cerebral palsy. *J Bone Joint Surg* 41-A:440-448, 1959
7. Pollock GA, Sharrard WJW: Orthopaedic Surgery in the treatment of cerebral palsy. In Ronald S, Illingworth RS, ed. *Recent advances in cerebral palsy* London, Churchill Ltd. 286, 1958
8. Robinson RO, McCarthy GT, Little TM: Conductive education at the Pető Institute, Budapest *BMJ* 299:1145-1148, 1989
9. Sharrard WJW: *Paediatric Orthopaedics and Fractures* Oxford, Blackwell Scientific Publications 1014-27, 1979
10. Tachdjian MO, Minear WL: Hip dislocation in cerebral palsy. *J Bone Joint Surg* 38-A:1358-1364, 1956
11. Thom H: Orthopädie in the Thom H. ed. *Die infantilen Zerebralparese*. Stuttgart, Thieme Verlag 221-236, 1982
12. Thom H: Die infantilen Zerebralparesen, operative Therapie, Grundlagen, Indikationen und Verfahren *Orthopädische Praxis* 22:487-497, 1986

Experience with Solcotrans® Orthopaedic in Hip Arthroplasty

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An uncontrolled study on 20 patients undergoing hip prosthetic surgery is reported. Solcotrans® Orthopaedic, a sterile, disposable device for the post-operative salvage and reinfusion of drained whole blood was used on all patients. 70% of patients did not require additional homologous blood and there was a saving of 76% in homologous blood usage.

The device is safe and simple to use and no clinically significant adverse effects were observed. Its use is recommended in patients undergoing hip prosthetic surgery in the absence of joint infection or malignancy.

There are many reasons for a resurgence of worldwide interest in autologous blood transfusion in the past twenty years. Among these must be included shortage of bank blood due either to a shortfall in donors or increased demands with increasing complexity of surgical procedures; concern regarding transmission of disease viruses, primarily Non A, Non B hepatitis virus and HIV; risk of alloimmunization; haemolytic reactions and an awareness of the quality of salvaged autologous blood with modern devices.

Two main groups of product are available for salvaging intraoperatively or post-operatively shed blood. These are cell processing machines whereby mainly red cells are administered, and combined salvage and reinfusion devices through which whole blood is reinfused. Cell processing machines involve a high initial cost, a software cost and the need for a technician to operate the device. Solcotrans® Orthopaedic, a sterile, disposable device for the salvage and reinfusion of whole blood, is of relatively cheap cost and requires no technician for usage.

Blood draining from the joint space following hip or knee arthroplasty is defibrinogenated and therefore slow to clot. Experience in U.S.A.^{1, 2, 3} and U.K.^{4, 5, 6} have indicated that this whole blood is sterile, safe to reinfuse and creates a 70–80% saving in homologous blood requirements. We decided to evaluate this product in our orthopaedic unit.

Study

The Solcotrans® unit consists of a sterile, disposable semirigid transparent polycarbonate shell within which is a plastic blood-compatible bag, capacity 500 ml. The bag is maintained open by a vacuum inside the shell. One end of the unit is connected to the joint drainage tubes, the device incorporating a 260 μ filter, and the other end, via a one-way valve and 0.2 μ antibacterial filter, to a suction pump. Aspiration pressure is maintained at ≤ 100 mm Hg. Prior to usage 40 ml of citrate anticoagulant is added to the inner bag. When the bag is filled the device is disconnected, inverted and the blood immediately reinfused via a 40 μ micropore filter. If necessary, subsequent Solcotrans® can be attached. Solcotrans® Orthopaedic is for post-operative usage only.

The study was an open, uncontrolled trial in 20 patients. The aim of the study was to evaluate safety, efficacy and practicability.

All patients studied underwent hip prosthetic surgery and there was no age limit for its use.

Patient exclusions were those suffering malignant or infective disease of the hip and those suffering a coagulation disorder or taking drugs that could affect coagulation.

Informed consent was obtained from all patients prior to entering the study.

Haematological baselines of haemoglobin, haematocrit, red cell count and platelet count were obtained pre-operatively and at the end of operation. These measurements were repeated immediately post-reinfusion of salvaged blood and 1, 4 and 8 days thereafter.

Record was made of all i.v. infusions given within 24 hours of operation and also any unexpected events.

Results

Twenty patients entered the study—14 female, 6 male.

Age: Female, mean 51 years, range 42–75 years

Male, mean 57 years, range 37–67 years

The mean volume of blood salvaged and reinfused per patient was 932 ml (range 400–1450 ml). Fourteen patients did not require homologous blood. Six patients were additionally given homologous blood either as whole blood, red cell concentrates or combinations of the two.

A total of 17 700 ml of autologous blood was salvaged and reinfused; Homologous blood requirements were 5650 ml.

The haematological parameter changes are as given in Table 1.

TABLE 1

Haematological parameter changes with Solcotrans® Orthopaedic usage n = 20

Parameters	Pre-operative (\pm SD)	Post-operative (\pm SD)	Post-Solcotrans® (\pm SD)	+ Day 1 (\pm SD)	+ Day 4 (\pm SD)	+ Day 8 (\pm SD)
Haemoglobin g/dl	13.5 (1.3)	11.8 (1.6)	9.1 (2.2)	9.5 (1.5)	9.9 (1.6)	10.7 (1.3)
Haematocrit %	43.3 (3.0)	37.5 (4.9)	29.2 (6.4)	31.2 (5.3)	32.7 (4.2)	35.2 (4.1)
Red cell count $\times 10^6/\text{mm}^3$	4.4 (0.3)	3.8 (0.5)	3.0 (0.6)	3.1 (0.4)	3.3 (0.4)	3.3 (0.7)
Platelet count $\times 10^3/\text{mm}^3$	211 (42)	196 (44)	170 (33)	171 (38)	195 (57)	232 (65)

Two patients were febrile post-infusion. In both instances the pyrexia promptly resolved following aspirin therapy.

An additional 2 patients developed pyrexia after the 3rd postoperative day. There was no suggestion nor probability that this was caused by the Solcotrans®.

The volume of colloid and crystalloid solutions given to the patients intra and post-operatively was a mean of 3.2 litres (range: 1–4.2 litres).

No patient post-operatively showed clinical evidence of adult respiratory distress syndrome, disseminated intravascular coagulation nor renal failure.

Discussion

With an increasing aging population the incidence of hip replacement is growing and a concomitant demand upon the Blood Transfusion Service will occur.

A zero risk with homologous blood transfusion is impossible to attain and demand for autologous blood usage is increasing among knowledgeable patients.

The efficacy of autologous blood transfusion has now been documented in a large number of studies and its application is rising in Europe and N. America. [4]

In this study the use of Solcotrans® Orthopaedic enabled us to effect a marked reduction—76%—in homologous blood usage, thus reducing the demand on increasingly limited homologous blood stocks and reducing the risk of disease transmission.

Three prime questions needed to be answered within this study:

1. Was Solcotrans® Orthopaedic safe to use?
2. Was it effective in salvaging and reinfusing whole blood?
3. Was it practicable?

To all these questions the answer was in the affirmative. No adverse effects of clinical significance occurred and use of the device enabled us to salvage and reinfuse a mean volume of 932 ml of blood that would otherwise have been discarded. Solcotrans® is simple to use and demanded no change in the operative procedure. The saving of 76% in homologous blood requirements was higher than we anticipated.

It has been our practice in patients undergoing hip prosthetic surgery to infuse an average of 3 units of blood per patient. By using Solcotrans® 14/20 (70%) of our patients did not require homologous blood.

Conclusions

Solcotrans® Orthopaedic is a safe and effective method of salvaging and reinfusing post-operatively shed whole blood from patients undergoing hip prosthetic surgery. No significant adverse effects were noted and its routine use would reduce the demands on the Blood Transfusion Service. The produce is simple to use and requires little training. Its use as a routine procedure in appropriate orthopaedic surgery is recommended.

References

1. Ritter M: Reinfusion of drained blood. State of the Art Ed R Coombes et al. Joint Replacement Chapter 68:401-405, 1990
2. Groh GI: Comparison of transfusion requirements after total knee replacement using the Solcotrans® autotransfusion system. Presented at AAOS meeting. New Orleans USA February 1990
3. Keim H, Behrman M: Perioperative blood salvage in spina surgery. Presented at AAOS meeting. New Orleans USA February 1990
4. Martindale J: Use of a disposable system to enable postoperative autotransfusion in total knee replacement. Presented at British Orthopaedic Association Meeting Glasgow April 1990. Submitted for publication
5. Howes K, Robbins G, Grech H: A study of autologous blood collected after Joint Replacement Surgery. AGM Br Haem Soc March 1990
6. Majkowski R, Currie I, Newman JH: Autologous blood transfusion and total knee arthroplasty. Presented BOA meeting. Glasgow April 1990
7. Silberstein LE: Strategies for the review of transfusion practices. JAMA 262:1993-1997, 1989

Successful Treatment of Erectile Dysfunction with Fortisex Coated Tablets

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After a brief survey of treatment, possibilities of erectile dysfunction, the Authors describe their results with FORTISEX coated tablets playing an important role in the conservative therapy even in our days. Their results suggest that the primary advantage of the product appears in increasing the libido in sexual problems of psychic origin, but its secondary field of application is the minor improvement of erectile parameters of dysfunctions of "mixed" history.

Male sexual activity is by no means a private affair, since erectile dysfunction may lead to daily discomfort, to reduced environmental tolerability and even to the disintegration of family life; so it may deteriorate not only the life of the individual, but also that of his environment. This recognition has, especially in the past two decades, remarkably activated the research in this field, a fact well proven by the appearance of many new stimulants and drugs on the market.

Gorm Wagner suggests [12] that the erectile cycle consists of four phases. The *first* is the *rest* phase, characterized by the constancy of the penis volume, the intracavernous pressure and the blood flow. In the *second* (tumescence) phase the volume increases and slow elevation in the intracavernous pressure is seen. In the *third* (erectile) phase, the penis volume is constant, and the intracavernous pressure increases to 80 mmHg. In the *fourth* (detumescence) phase, the volume and the erection are decreased, and the parameters return to the values of the rest phase [12].

The research and therapy of erectile dysfunction are an old endeavor in Hungarian andrology [3, 4].

In erectile dysfunction, erection is difficult or lasts only for a very short time, and differences may be seen in its degree, as well. These symptoms may also be associated with disorders of the libido, the orgasm or the ejaculation [5, 6].

This dysfunction may be treated either conservatively or by surgical intervention. Though *psychotherapy* is the most common method among the conservative treatments, the progress in medical science allows ever better knowledge of the physiology of the field, and so the "pure" psychotherapeutical

approach is losing its former monopoly. Also widely applied in Hungary, hormone therapies have not brought about the expected results in many cases (field of indication!), and the use of afrodysiacs offers good results in minor complaints only [1, 2, 8].

In present-day Europe the conservative treatments are focused partly on vacuum therapies and partly on injections of vasoactive substances into the cavernous body [11, 13, 14, 16].

While the publication of experience with the vacuum therapy is still in process, the intracavernous treatment can be regarded as a common method in Hungary [9]. Now, based on a large patient material, also the limits of application of the latter are well-known (complications, invasivity) [9, 10].

In our days the surgical approach is comprised of prosthesis implantation, of "empty vein" ligation (for open veins, i.e. that "steal" blood from the penis even in the erected position), and of vascular surgical solution of arterial inflow [6, 13, 15].

Besides the surgical and conservative "invasive" treatments, also the "non-invasive" conservative approaches are markedly and rightfully present in the current therapy of sexual dysfunctions.

Material and method

In the Andrology Center of the Urology Department of Semmelweis Medical School we treated a total of 50 patients with FORTISEX product of Pharma Bus GmbH in 1990 and 1991. The youngest patient was 21, the oldest 68 years old. The patients were ranged into two groups: the sexual dysfunction was of "pure" psychic origin in 18 cases, and of "mixed" origin (organic alterations with psychic superpositional in 32 cases.

Patients with "venous leak" and those with impotence requiring revascularization were excluded from the mixed group. However, half of the patients in this group were diabetics, though in different degrees and patterns.

The drug is a favorable mixture of animal pituitary gland and testis extracts, Muira-puma, vitamins and afrodysiacs, and is formulated as coated tablets. The daily oral dose is 3×1 coated tablets. Each patient received 100 tablets. The drug is recommended mainly for the treatment of potency problems of psychic and nervous origins. No adverse effects have been seen up to now, and the comprehensive use of the drug is promoted by its reasonable price of about DEM 40.

Trends in libido, in the erectile period and in the detectable differences in erection were monitored in both patient groups.

Results

Our results obtained in the "purely psychic" group are shown in *Table 1*.

TABLE 1

No. of patients	Increased libido	Erectile period	Erection
18	14	10	11

The table suggests that the libido has increased in the majority of the patients, they reported on prolonged erectile periods in 50% of the cases, and more marked erection was observed on the effect of the treatment in 11 patients.

TABLE 2

Illustrates the results in the "mixed history" group

No. of patients	Increased libido	Erectile period	Erection
32	12	5	6

Accordingly, in this group each parameter remained below that was seen in the former group: the libido had increased only in one third of the cases, and positive changes in the erectile period and in the degree of erection were observed only in a few patients.

Discussion

Conservative methods cannot be omitted in the treatment of mild erectile disfunctions [1, 7, 16]. Specially designed for the purpose, the Fortisex afro-dysiac product of Bus Pharma Company can be applied effectively only in impotence of "psychic" origin, and it promotes only the increase of libido even in this cases. If the psychic cause is associated with some organic components (urological alterations, liver disease, diabetes or hormona disbalance), then only modest results can be expected from the drug. Nevertheless the product should not be refused, since its libido increasing and mild erection improving effect entitles it to have a place in the so poor selection of potency improving products among conservative methods offering only partial results in themselves. The use of the drug is all the more reasonable in patients who refuse "invasive" help or in whom the "invasive" methods cannot be applied due to some organic or other problems.

References

1. Hagemann W, Steffens J: Interdisziplinäre Zusammenarbeit zwischen Urologie und Psychotherapie bei erectiler Disfunction. *Urologie* (8) 28:18–21, 1988
2. Junemann KP, Lue TF, Melchior H: Die Physiologie der Penilen Erection. *Urologie* (A) 26:283–288, 1987
3. Molnár J, Szarvas F: *Andrológia (Andrology)* Budapest, Medicina, 1973
4. Papp Gy, Molnár J: The andrological diseases of the penis and the urethra. Suppl V Symp Gynec, Lublin, 30–33, 1978
5. Papp Gy: Az impotencia coeundi organikus okairól (On organic causes of impotence coeundi) *Urol Nephrol Szle* 4:230, 1981
6. Papp Gy: Nemzőképességzavarok (Potency problems), Budapest, Medicina, 1985
7. Porst H: Stellenwert von Prostaglandin E₁ (PGE₁) in der diagnostik der erectilen disfunction (ED) im vergleich zu Papaverin und Papaverin/Phentolamin bei 61 patienten mit ED. *Urologie* (A) 27:22–26, 1988
8. Smith AD: Causes and classification of impotence. pp 79–89 In: *The Urol Clin of North America Vol 8. Male sexual dysfunction*. W B Saunders Comp Philad, London, Toronto, 1981
9. Török A, Székely J, Gotz F: Papaverine induced erection. *Int Urol Nephrol* 21:195, 1989
10. Török A, Jilling A, Götz F: Induced priapism and its management. *Int Urol Nephrol* 23:191–194, 1991
11. Virág R, Sussman H, Floresco J, Houkry K: Late results in the treatment of neurogenic impotence by self-intracavernous injection of vasoactive drugs. *World J Urol* 5:166–170, 1987
12. Wagner G: Erection physiology and endocrinology. p 25 In: *Wagner G, Green L: Impotence* Plenum Press, New York, 1981
13. Wespes E, Schulman CC: Vascular impotence. *W J Urol* 5:144–149, 1987
14. Wiles PG: Successful non-invasive management of erectile impotence in diabetic men. *Brit Med J* 296:161–162, 1988
15. Williams G, Mulchay MJ, Hartnell G, Kiely E: Diagnosis and treatment of venous leakage: a curable cause of impotence. *Brit J Urol* 61: 151–155, 1988
16. Witherington R: Vacuum constriction device for management of erectile impotence. *J of Urol* 141:320–322, 1989

Concomitant Incidence of Fertility Chance Reducing Varicocele and Chromosome Aberration

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Authors describe the case of a male patient with varicocele, oligozoospermism and subfertility, a 46 XY t (8; 10) (q22; p15) balanced chromosome carrier. Following varicectomy, successful pregnancy has developed even with balanced translocation meaning only 50% fertility chance. Prenatal diagnostics by chorion biopsy showed a fetus of normal chromosome constellation. Authors call attention to the fact that even minor, step-by-step improvements in fertility chance may lead to success in multiple aberrations.

The andrological role of various genetical differences has come to the foreground of scientific interest. The importance of disorders in number or in structure is more and more clarified, the fertility chances can ever better be estimated and assessed [2, 1, 12]. Besides clinical patterns associated with differences in the *number* of chromosomes, such as Klinefelter syndrome, “double Y” chromosomes of “XX male” chromosomes, ever more publications are devoted to the fertility aspects of intersexuality; while among *structural* disturbances the primary factors responsible for fertility problems are breaks of the long arm of the Y chromosome, reciprocal translocations and centric fusion [6, 7, 8, 10, 13, 15].

The concomitant incidence of fertility chance reducing varicocele and chromosome aberration being very rare, we think our case deserves attention.

Case report

Earlier, our patient was treated in other institutions for oligozoospermism; he received Andronal, Clostylbegyt and Vitamin E cures.

The patient reported in our Andrology Center for a general check-up in 1986. Grave oligozoospermism (sperm count: 5 millions/ml, 60% movement, intensivity: 1/3 are moderately vivid, the others showing minimal move-

ment) and medium degree left-sized varicocele were found with testicles of normal size and palpation. In the patient's history spontaneous abortions, 4 in his first, and 2 in his second marriage, all in the first trimester deserve special attention.

Considering the above facts, our plan included the surgical solution of the varicocele (with simultaneous testis biopsy), hormonal tests and genetical check-up. At the first andrological control examination after the varicocele we observed only minimal improvement in the spermal count (8 millions/ml, 70% moving, 2/3 moves intensively, 1/3 moderately), and the histological evaluation of the testicle biopsy sample showed inhibited maturation (spermatocyte level I) and interstitial fibrosis. Parallel hormonal tests (testosterone 30 nmol/l, FSH: 11 IU/l, LH: 14 IU/l, prolactone: 2.0 ug/ml) could not reveal the cause of infertility. We tried FSH stimulation of the maturity process with no significant results, and this was followed by the planned genetical check-up.

Chromosome analysis was made from lymphocyte culture by the G- and C-stripe techniques, by evaluating 100 metaphasic cells. The karyotype of our index patient was: 46, XY, t(8;10)(q22;p15). Figure 1 shows the karyotype of

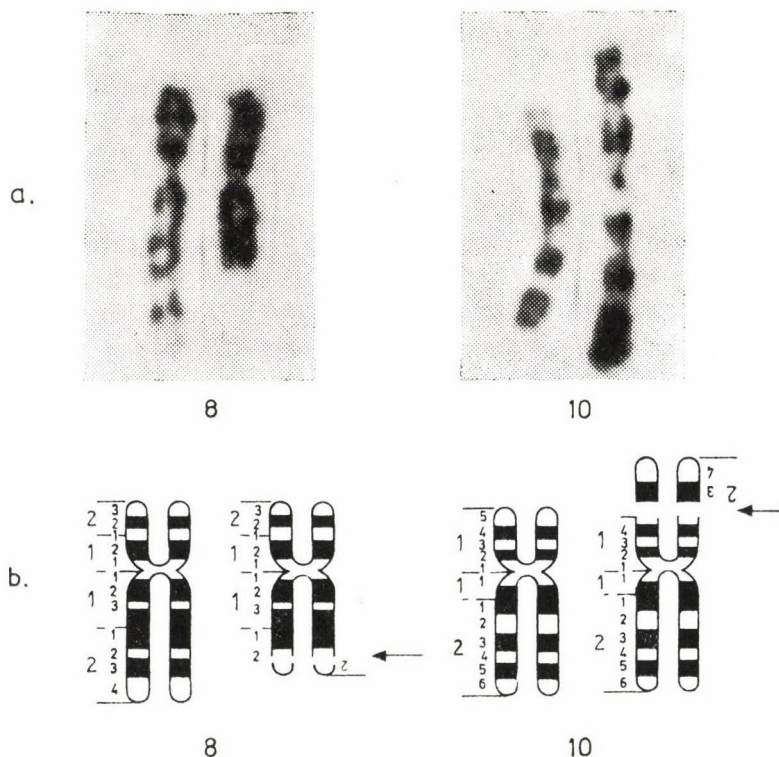


FIG. 1. a: Partial karyotype from the patient Sz. G. 28/M. 46, XY, t(8;10)(q22;p15)
Code: 120/87. ASG technique. b: Idiogram of the translocation

the index patient. His first and second wives were of normal karyotype. It was not possible to perform comprehensive family study to clarify whether the case was *de novo* or hereditary, translocation, because our index patient was a single child, and his parents had already died.

Discussion

Similar cases carrying t (8; 10) balanced translocation have been described several times, but with different chromosomal break sites. Because of the andrological status of our index patient, it is more important to consider the observations of Retief et al (9): [1] constitutional chromosomal abnormalities were found in 5.1% in 390 males with oligozoospermism; [2] in general, the rate sex chromosomal aberrations is 50%, and autosomal chromosome translocation is 50% in oligozoospermatic populations; [3] the average frequency in infertile males with chromosomal aberration, in whom the spermal count was below 10 millions/ml, is 7.1% [4] reciprocal translocations were found to be sporadic in azoospermic or subfertile males [3, 4, 14]. Our index patient is included as a balanced chromosomal aberration carrier in an article compiled in our institute which summarizes 418 couples with habitual spontaneous abortion [5].

The testicle size of our Hungarian index patient (volumes of the right and the left testicles are 18.1 cm³ and 17.0 cm³, resp.) corresponds to the Hungarian standard of testicle development [1]. The cause of childlessness is not only the fact that our patient is a balanced translocation carrier, but also his severe oligozoospermism associated with the tissular alteration of the testicles and his varicocele. Also his being a balanced translocation carrier can be responsible for the 4 spontaneous abortions in his first, and the 2 ones in his second marriage.

What is to be underlined is the fact that fertility chances can be improved even in balanced chromosomal aberrations associated with varicocele. The prolonged disappointment because of childlessness in our patient's private life was compensated by the hope of a baby. Indeed, his partner was found to be pregnant with a fetus as judged normal by prenatal diagnosis in this year (1991). And this means that step-by step, gradual improvement of the andrological status can be important for the patient as well.

References

1. Béres J, Papp Gy, Pazonyi I, Czeizel E: Testicular volume variations from 0 to 28 years of age. *Int Urol Nephrol* 21(2):159-167, 1989
2. Lantos I, Papp Gy, Wessely J: Una rara anomalia genetica causata da aspermia a due fratelli. *Urologia V Treviso* 20:1, 1980

3. Lyberatou-Moraitou E, Grigori-Kostaraki P, Retzpopolou Z, Kosmaidou-Aravidou Z: Cytogenetics of recurrent abortions. *Clin Genet* 23:294-297, 1983
4. Moreau N, Teyssier M: Ring chromosome 15: Report of a case in an infertile man. *Clin Genet* 21:272-279, 1989
5. Osztovics MK, Toth SP, Wesely JA: Cytogenetic investigations in 418 couples with recurrent fetal wastage. *Ann Genet* 25:232-236, 1982
6. Papp Gy: Nemzőképesség zavarok. *Andrológia és genetika (Fertility disturbances. Andrology and Genetics) Medicina, Budapest, 1985*
7. Papp Z: Testicular intersexuality. In: *Obstetric Genetics. Akademia Publishing House, Budapest, 1990*
8. Pusch H, Held KR, et al: Das XX-male Syndrom aus andrologischer Sicht. *Andrologia* 12:219, 1980
9. Retief AE, Van Zyl JA, Menkveld R, Fox MF, Kotze GM, Brusnick J: Chromosome studies in 496 infertile males with a sperm count below 10 million/ml. *Hum Genet* 66:162-164, 1984
10. Schirren C: Das Klinefelter Syndrom. In: *Praktische Andrologie 2. Auflage Schering A, Berlin 71, 1982*
11. Simpson JL: Genes, chromosomes and reproductive failure. *Fertil Steril* 33:107, 1980
12. Toth A, Gaál M, László J: Férfi meddőség citogenetikai háttere (Cytogenetic background of male infertility) *Orv Hetil* 28:1723, 1982
13. Tötörk L: Association of centric fusion of G-chromosome with impairment of spermatogenesis. *Andrologia* 13:556, 1981
14. Vigule F, Romani F, Dadoune JP: Male infertility in a case of (Y;6) balanced reciprocal translocation; mitotic and meiotic study. *Hum Genet* 62:225, 1982
15. Wegener RD, Nurnberg F: Clinical, cytological and biochemical investigations in case of an XX-male. *Andrologia* 15(3):253, 1983

Dopamine-induced Aggravation of Myocardial Ischaemia in the Paced Heart: Cardiosurgical Perspectives

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The action of dopamine on the blood supply to acutely ischemic cardiac areas was investigated at arbitrarily selected, fixed heart rates. The A–V node of open chest dogs was crushed and the ventricles were paced between 30 and 220 beats per minute (bpm). Ischemic blood supply was assessed by computer-aided infrared thermography. It was found that the ischemic (collateral-dependent) blood flow paralleled overall myocardial blood supply (coronary sinus outflow) and was directly related to heart rate between 30 and 100–140 bpm; above this frequency it decreased moderately. Dopamine (10 $\mu\text{g}/\text{kg}$ i.v.) elicited a marked increase of ischemic flow in the heart paced at 60 bpm, whereas the drug action was characterized by a long-lasting flow decrease (preceded by a slight dilation) at 200 bpm. It was concluded that the treatment of the tachycardic heart with dopamine, as it frequently occurs in postbypass cardiac and coronary surgery, may place the non-completely revascularized myocardium at risk.

During the past decade there has been a renewed interest in catecholamine-induced cardiac deterioration [12, 14], essentially ischemic in character. At the same time, treatment with cardiostimulatory agents often referred to as inotropic support is a well known therapeutic measure employed in cardiac surgery, especially at the late intraoperative and/or the early postoperative phases of interventions. In most instances catecholamines (usually dopamine or dobutamine) are utilized for this purpose. It is claimed that these agents are comparatively safe, because both of them exert an inotropic effect without increasing heart rate, a major hemodynamic determinant of adverse catecholaminergic effects. Experience has shown, however, that with dobutamine this is clearly not the case [5]; as to dopamine, although its action is seldom associated with tachycardia, coronary vasoconstrictor influences that markedly characterize the pharmacological spectrum of activation may arise as detrimental factors [8, 13]. Moreover, the high incidence of postoperative tachycardic episodes may in itself determine the hemodynamic background for dopamine actions in patients having widespread or extended cardiac ischemic foci. The aim of this study was, therefore, to examine in an experimental model how the dopamine action on the regionally ischemic heart is influenced by the changes of basic heart rates.

Methods

Eight mongrel dogs of either sex, weighing between 14 and 23 kg were anesthetized with pentobarbital sodium (30–35 mg/kg b.w., iv.). Using artificial ventilation (RO-5, volume-cycled respirator) the thorax was opened by making incisions in the 4th intercostal spaces on both sides and splitting the sternum transversely. The heart was firmly suspended in a pericardiac cradle and a short segment at the upper mid-portion of the left anterior descending (LAD) coronary artery was prepared free. The dogs were given heparin (500 I.U./kg) and the coronary sinus was cannulated through the azygos vein with a large-bore (≈ 5 mm i.d.) polyethylene tubing which was connected with an extracorporeal circuit delivering the outflow of the sinus to the cannulated central stump of a femoral vein. Coronary sinus flow representing blood supply to the left ventricle was measured with a Statham SP 2002 cannulating flow probe. Blood pressure was also monitored from a femoral artery with a Statham gauge. A monopolar pacing electrode was sutured to the lateral wall of the right ventricle. A large purse string suture was also placed on the right auricular appendage.

After completing the surgical preparations the A–V conduction of the heart was discontinued as follows: both venae cavae were temporarily occluded with snare occluders, the right auricular appendage was incised and, by using continuous blood suckling, the site of the A–V node was identified with the naked eye. The node was crushed by electrocauterization, the ventricular pacing was started by means of a programmable Medtronic stimulator, and the normal circulation restored. The circulatory arrest did not outlast more than 25–30 sec; after reinfusing the blood lost during this procedure, the normal circulatory equilibrium was reestablished in every case.

All tests were performed on the regionally ischemic heart in a stabilized state of the ischemic zone: Accordingly, after establishing the A–V block, the LAD artery was occluded at least 1 hour prior to testings. During this period the heart was paced at 140 beats per minute (bpm) which is close to the average heart rate of anesthetized dogs. The development of regional ischaemia was monitored by computer-aided thermography (AGA 750 camera) which senses local flow-dependent infrared irradiation from the cardiac surface. The sensitivity of the equipment was set to cover a range of 5 °C. The analysis of the thermographic images was performed according to the techniques described earlier in detail [11].

The experimental tests included: [1]. Ventricular pacing at fixed heart rates (30, 60, 100, 140, 200 and 220 bpm) in order to construct curves describing frequency-dependent thermographic changes in the ischemic zone. [2] Administration of dopamine (10 μ g/kg i.v.) at low (60 bpm) and high (200 bpm) heart rates, respectively; this was performed to determine whether or

not bradycardic and tachycardic basal rates influence *per se* the characteristic features of catecholamine-induced changes in ischemic blood supply.

The thermographic results were expressed as changes of computer-evaluated mean temperature ($\Delta^{\circ}\text{C}$), whereas coronary blood flow alterations as percent deviations from basic values measured at 140 bpm (100%). Comparison of these variables was made by graphic equalization of maximal extensions between 30 and 140 bpm, according to the routine developed in former studies [2, 3]. Statistical analyses were based on results obtained in five successful experiments. In two dogs out of eight, the idioventricular rhythm was too high to be suppressed reliably by pacing at low frequencies, while in another dog the pacing was poorly tolerated at frequencies higher than 140 bpm. All statistically compared values are mean \pm SEM. Calculations of significance were made by using Student's *t*-test for paired and unpaired data.

Results

Figure 1 depicts changes in mean temperature of the ischemic zone (representing collateral-dependent blood supply) and in coronary sinus outflow (representing overall myocardial blood supply). The astonishingly close parallelism between the *relative* alterations of these variables revealed a curvilinear relationship of both the ischemic and the overall flow to the heart rate: the blood supply increased from 30 bpm to 100–140 bpm with continuously regressive increments, whereas it remained fairly constant over 140 bpm. Ischemic mean temperature and coronary sinus flow were found to be usually higher at 200 bpm than at 60 bpm. However, the differences were not very pronounced and statistically not significant (not shown in Fig 1).

At the same time, the characteristic features of dopamine-induced changes at these arbitrarily selected heart rates were drastically different from

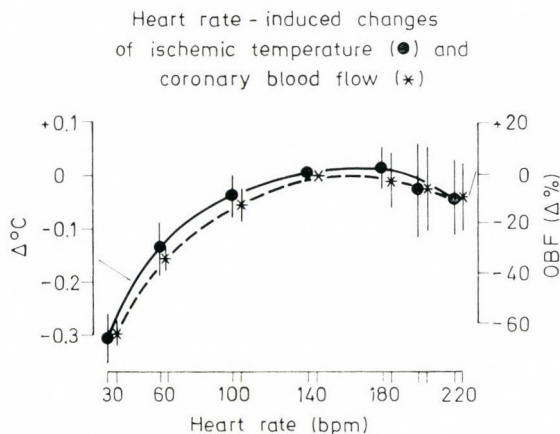


FIG. 1. Parallelism of thermographically recorded ischemic blood supply and coronary sinus flow in response to ventricular pacing

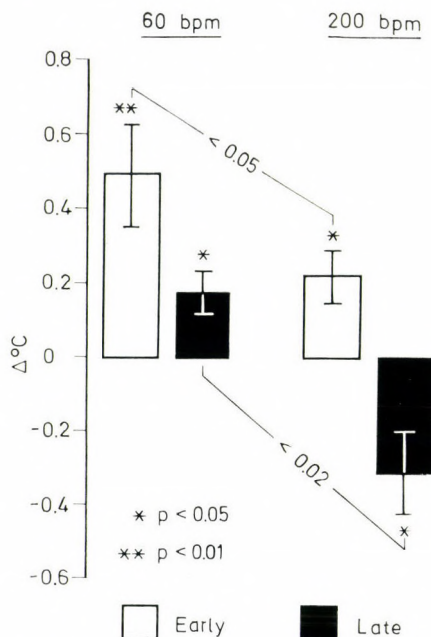


FIG. 2. Blood flow-dependent ischemic temperature changes induced by dopamine (10 $\mu\text{g/kg}$, i.v.). Note the decrease of the early (≤ 1 min) effect and the reversal of the late (4–5 min) effect in tachycardia (200 bpm)

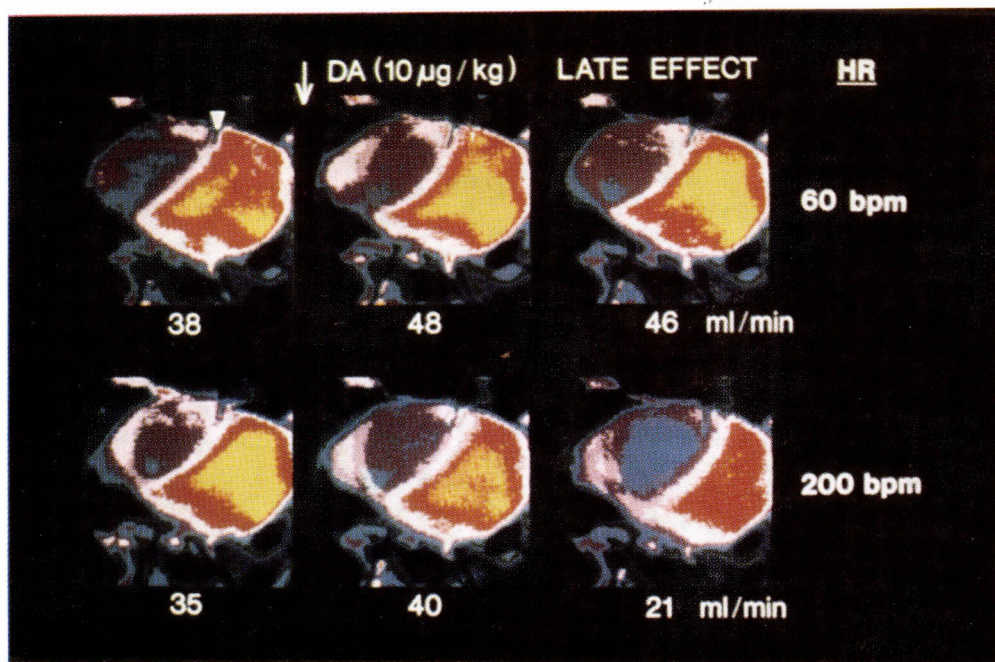


FIG. 3. Original thermographic cardiac images. White arrowhead denotes the site of LAD occlusion. (Note mirror image of the heart in the thermograms.) Each colour-band on the false-colouring represents a temperature range of 0.5 $^{\circ}\text{C}$. Direction of cooling: yellow (orange) – red – rose – lilac – mauve – green

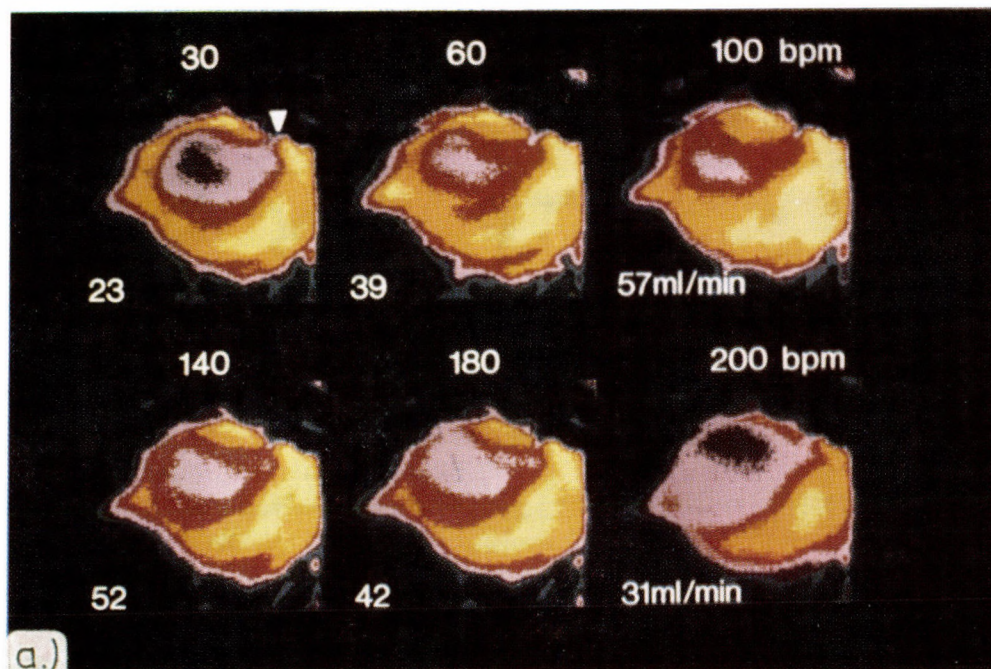


FIG. 4a. Example of the decrease of collateral-dependent ischemic flow and demarcation of ischemia upon heart rate increases. Arrangement as in Fig. 3

each other as shown in Fig 2. In the bradycardic state the immediate (≤ 1 min) warming action upon dopamine administration was followed by a prolonged (4–5 min) small temperature increase indicating a great flow overshoot followed by a slight vasodilation. In contrast, in the tachycardic state the early vasodilation was much smaller, while the late effect was diametrically opposite to this change indicating a marked flow decrease. A characteristic example is shown in Fig 3.

In one dog (not included in statistics) high-frequency pacing was in itself sufficient to elicit marked decreases in local flow. Heart rate-dependent relations of temperature and sinus outflow exhibited peculiar bell-shaped curves in this preparation (Fig 4a and 4b), the descending limb of which started over the frequency of 100 bpm.

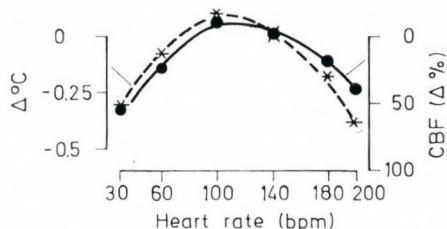


FIG. 4b. Graphic representation of experiment shown in Fig. 4a

Discussion

Reduction of perioperative cardiac morbidity and mortality is a major task of heart surgery. The recent studies of Papp and his co-workers [9, 12] have stressed the predictive role of perioperative dynamic circulatory changes in cardiosurgical patients who are diagnosed as having preoperative cardiac ischemic hazards and/or subjected to potential ischemic damages during operations. More specifically, treatment with catecholamines has particularly been implicated by Papp in the development and aggravation of postoperative ischemic cardiac deterioration. Consistent with this assumption by reducing intraoperative inotropic support to the necessary minimum, postoperative mortality also was found to be significantly reduced [12].

The results of the present investigations may provide a further indirect support to this thesis. A major finding of this study was that even dopamine, a comparatively safe inotropic drug might aggravate myocardial ischemia if administered to the (moderately) overdriven heart representing a high-risk state of cardiac activity. (It should be noted that in the dog the heart rate of 200 bpm at which these adverse actions developed cannot be considered as high as in humans, the "physiologic" cardiac frequency being about 140–150 bpm in the anesthetized animals.) Postoperative tachycardia often occurs after cardiac operations with or without rhythm disturbances. Theoretically, it can be detrimental because of its impact on ventricular filling and myocardial oxygen balance [6]. Recent clinical studies also suggest a close association between tachycardia and ventricular ischemia after cardiosurgical interventions [7, 10, 11]. It appears from the present study that the inotropic drug dopamine may place the tachycardic heart at an exaggerated risk: the results indicated that the actions of dopamine specifically targeted at improving cardiac functions can be transformed to an extent that they transcend physiologic limits and assume a pathologic significance, especially in the ischemic areas of the heart. Collateral vessels supplying these areas cannot be regarded passive conduit channels: In agreement with previous results [1, 4] the present studies suggest that hemodynamic factors that regulate collateral supply are closely related to and possibly identical with those regulating normal coronary blood flow (see Fig 1). However, an utilizable coronary reserve, if not totally exhausted, is apparently reduced by ischemia, and this renders collateral-dependent areas more vulnerable to adverse catecholaminergic influences. The substantial alpha-agonist properties of dopamine may play a decisive role in these effects [8, 13].

Another aspect of the present analysis related to operative risks is the question of incomplete revascularization of the heart muscle. Again, this problem should be addressed from the dynamic point of view, and, since at least partially, it is under the control of the coronary surgeon, from a practical standpoint.

Papp and one of us (A.K.) have recently established a principle which may be called the correlative law of ischemic hazards at incomplete revascularization [9]. This rule seems to be particularly important in cases of valvular surgery where the coronary circulation is also compromised. The law states that (other things being equal) the postoperative risk of incomplete revascularization is directly related to the *quotient* of postoperative and preoperative ventricular loads, while the *absolute extension* of areas omitted from revascularization is less important in this respect [9]. This explains the apparent paradox why incompleteness of revascularization is much better tolerated postoperatively by patients undergoing surgery for the correction of aortic stenosis, a disease notoriously associated with coronary insufficiency, than by patients undergoing surgical corrections for mitral stenosis usually not associated with coronary symptoms: in the former case the ventricular load (afterload) *decreases*, whereas in the latter the load (preload) *increases* following a successful operation. The physiologic value of blood supply to areas at or just below the ischemic threshold increases in the former, while it decreases in the latter case. In other words, the outcome depends on the myocardial demands for adequate blood supply rather than on the absolute level of flow.

An analogous situation may arise when dopamine (an agent possessing both coronary vasoconstrictor and cardiostimulator potencies) is administered to hearts having an already compromised coronary bed *and* an already increased metabolic demand (tachycardia). In these cases dopamine may multiply the patients' risks.

Acknowledgement

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References

1. Buffington CW, Feigl RO: Adrenergic coronary vasoconstriction in the presence of coronary stenosis in the dog. *Circ Res* 48: 416-423, 1981
2. Dóbi I: Alterations of vascular reactivity in the mesenteric circulation. Thesis Budapest 1990
3. Dóbi I, Juhász-Nagy A: Substitution by adenosine for glucagon as a surgical diagnostic tool to detect mesenteric vascular adaptation. *J Vasc Surg*, in press 1991
4. Heusch G: Koronare Vasomotion bei Myokardischämie. *Ztschr Kardiologie* 78: 485-499 1989
5. Hug CC Jr: Making a choice of inotropes and vasodilators in clinical situations. *J Cardiovasc Surg* 5: 272-281, 1990
6. Juhász-Nagy A: Risk factors of pharmacologic cardiostimulation at surgical myocardial ischemia: utilization of experimental model in the clinical practice. In: Szabó Z (ed): *Current Problems of Cardiovascular Surgery*, pp. 57-98, Akadémiai Kiadó Budapest 1986
7. Knight AA, Hollenberg M, London MJ, Tubau J, Verrier E, Bowner W, Magnano DT, SPI Research Group: Perioperative myocardial ischemia: Importance of perioperative ischemic pattern. *Anesthesiology* 68: 681-688, 1988

8. Kollár A, Kékesi V, Juhász-Nagy A: The dopamine-induced coronary vasoconstrictor response is potentiated by adenosine administration in the dog heart. *Jpn Heart J* 30: 709–721, 1989
9. Kollár A, Papp L: Surgery of cardiac valve diseases combined with coronary operations 1979–1990 *Orv Htlp*, in press, (in Hungarian)
10. Leung JM, O'Kelly B, Browner WS, Tubau J, Hollenberg M, Magnano DT, SPI Research Group: Prognostic importance of postbypass regional wall-motion abnormalities in patients undergoing coronary artery bypass graft surgery. *Anesthesiology* 71: 16–25, 1989
11. Magnano DT: Detection of perioperative myocardial ischemia. *Our Heart J* 10 (suppl H): 2–9, 1989
12. Papp L: Distribution of coronary flow of the normal and the diseased heart investigated with cardiotelethermography in experiments and in human cardiac surgery. Thesis, Budapest 1987
13. Rablóczky G, Kékesi V, Mader RM, Juhász-Nagy A: Dopamine-induced coronary effects in the dog heart attributed to β - and α -adrenergic mechanisms. *Arch Int Pharmacodyn* 293: 109–126, 1988
14. Rona G: Catecholamine cardiotoxicity. *J Mol Cell Cardiol* 17: 291–306, 1985

Comparison of Histological Effect of Electrocoagulation and Nd-YAG Laser Coagulation in Intact and Tumorous Rat Tissue

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In our animal experiments we used a chemical agent (dibutylNitrosamine) to induce urinary bladder tumor in rats, then this was implanted under the dorsal skin of rats of the same strain to gain a standard tumor preparation (10).

The histological effects of electrocoagulation and Nd-Yag laser coagulation were compared in rat striated muscle, liver, intact rat urinary bladder and in our standard tumor preparation.

The histological changes suggested that laser coagulation has advantages over electrocoagulation for inducing deep and homogenous necrosis in intact and tumorous tissues.

Dramatic progress of laser medicine has yielded a great number of publications also on the histological effects of laser radiation, and detailed studies have also been devoted to the transmission and morphological effects of laser rays in the living tissue [3, 5, 8].

However, sporadic data are available on the features of laser ray in the tumorous tissue, which can be explained by the small selection and poor availability of standard reproducible tumor preparations.

In our animal experiments we have developed a standard rat urinary bladder tumor line. If this is transplanted into an accessible site, the targeted tumor can be treated *in vivo* [10].

Material and method

Since 1968, urinary bladder tumors have been induced in F 344 female rats by administering N,N-dibutylNitrosamine in the drinking water. The so prepared transitional carcinoma was transplanted under the dorsal skin of rats of the same strain and was then passed continuously [10].

When reaching the 5 mm size, the skin was opened over the tumor growing under the dorsal area, and the visible tumor was coagulated by Nd-YAG

laser ray of 1064 nm wavelength, by 40 W performance and 3 second exposures using a KFKI MEDI-YAG 450 apparatus constructed for human use.

The laser light was transferred by means of a 600 μ lightguiding fibre, the end of which was placed at 1 mm from the tumor surface at the irradiation. Such interventions were performed in 10 animals.

In other experimental animals, artificial tumors in the same number and size were electrocoagulated by a filiformic electrode of ERBOTOM high frequency electric coagulation after placing the animals in water. The aim of this operation was to stimulate tissue alterations induced by the resection of transurethral vesical tumors. To compare the effect of these two types of interventions on various tissues, both treatments were repeated in *in vivo* preparations of rat striated muscle, liver and in intact rat urinary bladder mucosa.

Results

In accordance with literature data, Nd-YAG laser irradiation of 1064 nm wavelength induced homogenous, sharp-edged necroses in all tissue types which did not cause significant lesion to the tissue structures. No intact cell nuclei had remained in the laser induced necrotic areas (Figs 1, 3, 5, 7, 8).

The electrocoagulation induced tissue lesion was rougher, was not sharply demarkable from the environment, and the alteration was non-homogenous, involving "protrusions" toward sites of lower electric resistance, and caused

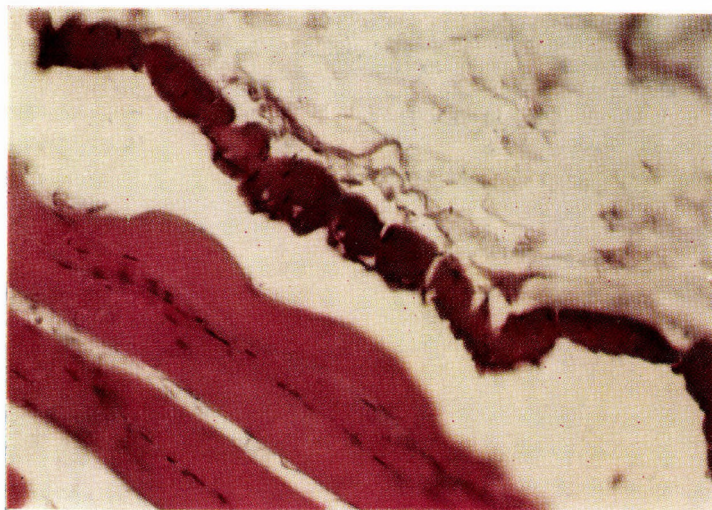


FIG. 1. Rat striated muscle after *in vivo* laser treatment. There are little morphological alterations in the tissue, but no intact cell nuclei have remained. Hematoxylin-eosin-alcyane blue (hereinafter: HEA) staining, 250 times magnification

remarkable damage to the tissue structures. Depending on the various tissue types, the electrocoagulation necrosis widespread towards the peripheral areas in uncontrollable depths.

In the areas of the electrocoagulation necrosis there remained intact cell nuclei and cells with presumable surviving capacity, which may form an eventual basis for recurrent tumors (Figs 2, 4, 6).

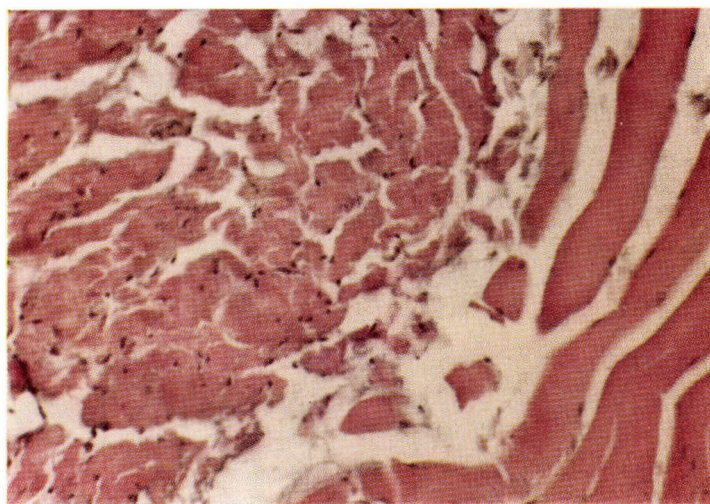


FIG. 2. Rat striated muscle after *in vivo* electrocoagulation. Rough necrosis with irregular outlines. Extended disintegration of tissular structures is seen. HEA, 250 times magnification

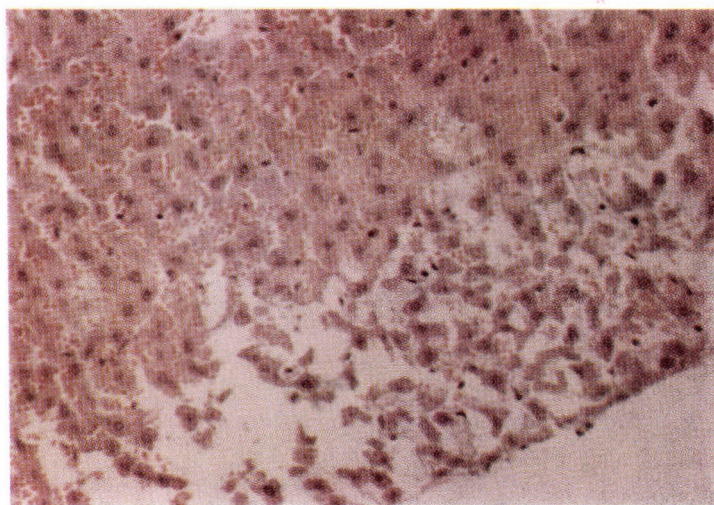


FIG. 3. Rat liver after *in vivo* laser coagulation. Bleeding and edematization; fine structural changes. HEA, 250 times magnification

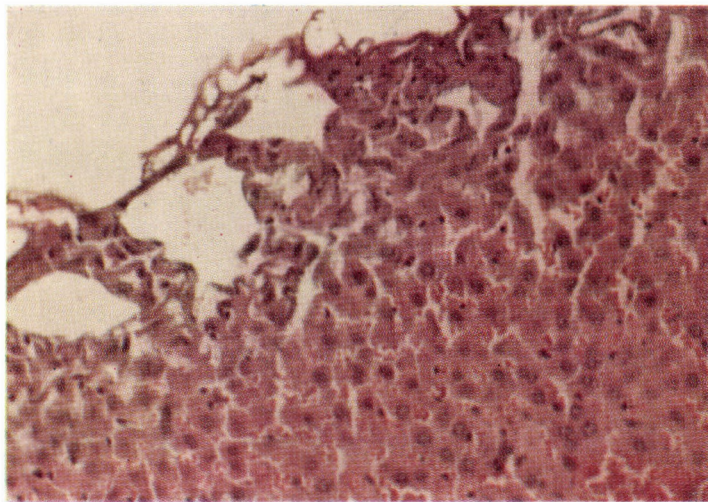


FIG. 4. Rat liver after *in vivo* electrocoagulation. Tissular deficiency, gaseous blister formation. HEA, 250 times magnification

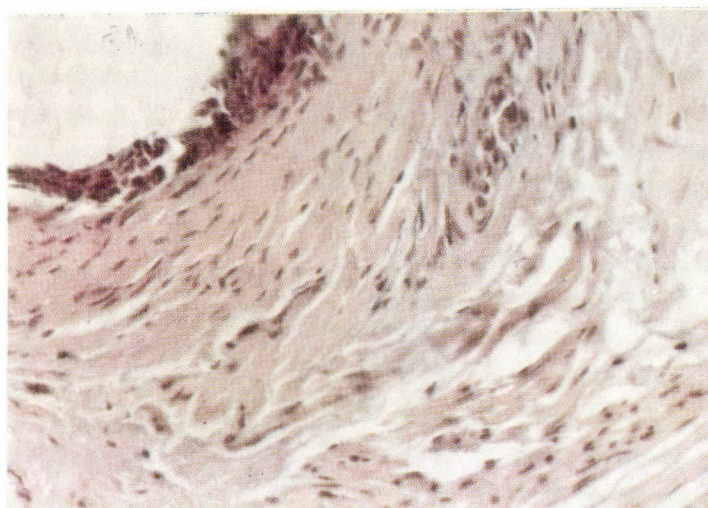


FIG. 5. Rat urinary bladder mucosa after laser coagulation. HEA, 400 times magnification

The above comparative statements were verified by our studies also for transitional cell urinary bladder carcinoma induced in rats.

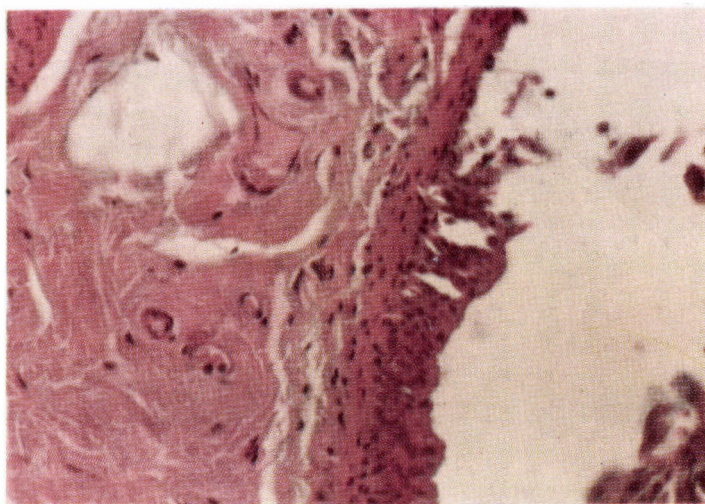


FIG. 6. Rat urinary bladder mucosa after electrocoagulation

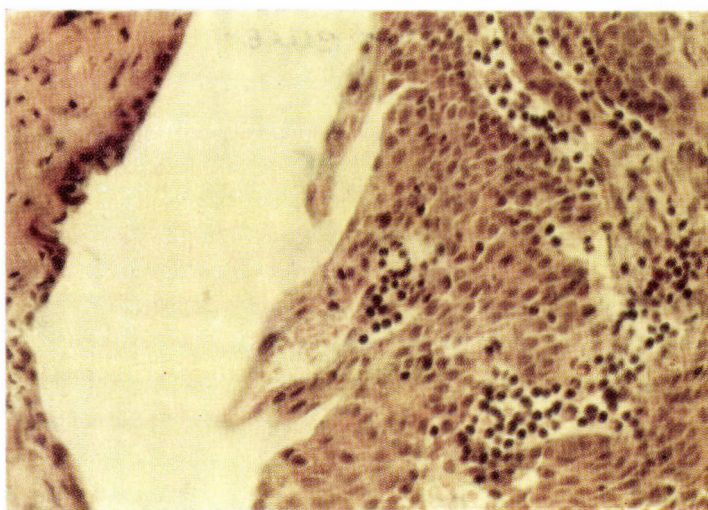


FIG. 7. Experimentally induced rat transitional cell carcinoma preparation after laser treatment. Cellular necrosis and hyperemia on the exposed areas. Sharply outlined, homogenous necrosis zone. The round cell infiltration is not a result of laser coagulation. HEA, 400 times magnification

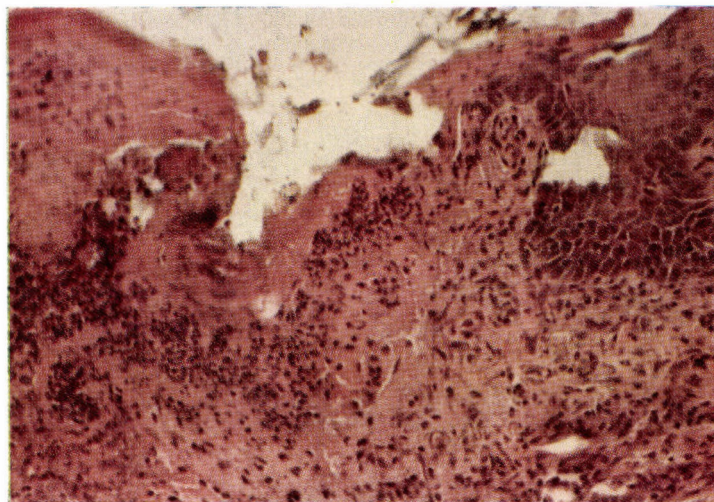


FIG. 8. Experimentally induced rat transitional cell urinary bladder carcinoma, peripheral part of an electrocoagulated area. Blisterous alterations, desquamated tumor cell groups. The cellular necrosis contains "protrusions" toward sites of lower resistance. HEA. 250 times magnification

Discussion

Our studies verified the observations described in other publications and suggested that these results apply to standard urological tumor preparations as well. Our observations verified that, due to its biophysical features, laser coagulation is more suitable for precise, well-designable treatments of organs of fine tissue structure, for that of the urinary bladder in our case, and the intervention causes only minimal damage to the tissues. For this reason, and for the homogenous, reliable, but still atraumatic necrosis caused by it, laser coagulation may favorably compare with the electroresection methods in tumor therapy.

References

1. Carter MB, Coffey DS: Cell surface charge in predicting metastatic potential of aspirated cells from the Dunning Rat Prostatic Adenocarcinoma Model. *The Journal of Urology* 140: 173-175, July 1988
2. Jeney A, Szende B, Lapis K, Institoris L: Citosztatikumok hatása az N-butyl-N-/4-hidroxi-butyl-Nitrosaminnal kiváltott preneoplasiás és neoplasiás elváltozásokra patkány vesica urinariában (Effect of cytostatics on N-butyl-N-/4-hydroxi-butyl-nitrosamine induced preneoplastic and neoplastic alterations in rat urinary bladder). 17th Congress of the Society of Hungarian Oncologists, 1987 Budapest. Proceedings, p 163
3. Keiditsch E: Histologische Grundlagen den endovesicalen Nd-YAG Laserbestrahlung. *Der Urologe* 20:300-304, 1981
4. Mardan AM, Williams RD, Lubaroff DM: Induction of urinary bladder papillary carcinoma in Fischer (F344) female rats with N-N-butyl-N-4-hydroxi-butyl-Nitrosamine (abstract). *The Journal of Urology*, 139:369A, April 1988

5. Rothenberger K, Pensel J, Hofstetter A, Keiditsch E, Stern J: Dosierung der Nd-YAG laserstrahlen zur endovesikelen Anwendung bei Blasentumoren. *Der Urologe* 20:310–314, 1981.
6. Schumann B, Szemes Z, Kovács R, Pulay I: Tumormarkerek alkalmazása hólyagrákos betegek vizsgálatában (Application of tumor markers in the examination of patients with urinary bladder cancer. 17th Congress of the Society of Hungarian Oncologists, 1987 Budapest. Abstract 30 #.
7. Schumann B, Szemes Z, Rimanoczy E, Kovács R: Komplex tumormarker vizsgálatok jelentősége az onkológiában (The importance of complex tumor marker studies in oncology). 4th Urologists Days in Kecskemét, 1989, Abstract # 40
8. See W, Chapman W: Tumor cell implantation following Nd-YAG injury – a comparison to electrocautery injury. *The Journal of Urology* 137:1266–1269, November, 1987
9. Szemes Z, Schumann B, Kovács R: Komplex tumormarker vizsgálatok a hólyagdaganatok diagnosztikájában (Complex tumor marker studies in the diagnostics of urinary bladder tumors). *Magyar Urologia*. In publication
10. Szemes Z, Számado I: Húgyhólyagtumor kísérletes előidézése patkányban (Experimental induction of urinary bladder tumors in rats) *Magyar Urologia*. In publication

Assessment of the Efficiency of Endovesical Laser Treatment of Urinary Bladder Tumors on the Basis of Polyamine Content Measured in the Eluent

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Authors describe a new analytical method for monitoring the treatment of vesicular tumors. Chromatographic analysis of the polyamine content of the eluent allows differential diagnostic judgement of the malignity of the laser treated tumorous tissue. The practical applicability of the method is demonstrated and evaluated on the basis of the analysis of 88 clinical cases.

In the recent years Nd-YAG laser irradiation has come into the foreground in the surgery of vesicular tumors in addition to TUR.

The method features the advantage to create deep, homogenous necrosis, to seal the neighboring lymph vessels, to prevent that living, adherable tumor cells can pass to the filling fluid of the bladder during the coagulation process. Furthermore, it has a low local recurrence rate, includes little or no complications, the bladder function is maintained, and a favorable basis is created for adjuvant chemo- or immunotherapies [4, 8, 9, 10].

Up to now, the single method for monitoring the depth extension of vesicular tumors has been TUR biopsy only, and no other diagnostic techniques supplementing endovesical laser treatment have been available.

To design such a technique, the most recent biochemical results of tumor research are employed.

Polyamines (PAs) are aliphatic amine compounds. The three major PAs, putrescine, spermidine and spermine, are present in almost all mammal cells. The intracellular role of PAs is connected to protein synthesis, and within this to cellular growth. They have a regulatory role in cell proliferation. They come into interaction with DNAs which are favorably competitive to histones, thereby decreasing non-specific repression of genetic activity, and this among others leads to the stimulation of RNA synthesis. Intracellular PA concentration will increase in all, either malignant or non-malignant proliferative tissues. PA concentration in malignant cells may 5 to 15 times exceed that in healthy cells, depending on the tissue type [2].

Through the process of cellular lesion or disintegration the intercellular PAs will pass into circulation, and this feature is used for the analysis of PA content of blood and urine as a tumor marker test [1, 3, 5, 6, 7].

Material and method

Endovesical urinary bladder tumor treatments have been performed by MEDI-YAG 450 (KFKI) type Neodym-YAG laser apparatus at the Urological Department of the Central Hospital and Related Institutions of The Ministry of Home Affairs since September 1, 1985. (Figs 1 and 2) Simultaneously we have analyzed the level and composition of PAs released from tumor destroyed cells to the vesicular eluent during laser treatment.

A total of 88 selected cases have been processed.

The age of our 64 male (73%) and 24 female (27%) patients ranged from 52 to 78 years, the mean age was 63.3 years.

The staging of the tumor was determined by cystoscopy, abdominal and endovesical ultrasound, computer tomography and magnetic resonance tests in all cases.

The tumor grading was evaluated by histological testing of tumorous tissue taken by cold biopsy, and this was transitiocellular carcinoma in each case.

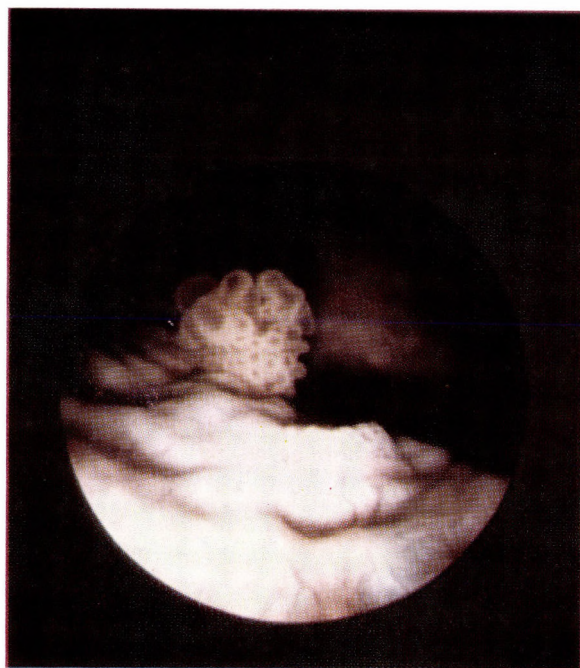


FIG. 1

Staging and grading data of the tumors are summarized in Table 1.

The distribution of tumor location in the bladder is shown in Table 2.

The distribution of tumor sizes is illustrated in Table 3. The smallest tumor was of 5 mm³ volume, the largest 35 mm³, and the mean size was 18 mm³.

The tumors were laser treated by means of a MEDI-YAG Neodym-YAG apparatus. The 40 W performance was administered in 3 sec impulses, with 120 J energy onto the vesicular bladder using the scanning ray beam technique.

TABLE I
Staging and grading data of vesical tumors

Stage Grade	T _a	T ₁	T ₂	T _{3a}	Total
G ₀	16(18%)	0	0	0	16 (18%)
G ₁	0	12 (13%)	12 (13%)	4 (4%)	28 (30%)
G ₂	0	20 (22%)	8 (9%)	4 (4%)	32 (36%)
G _{3a}	0	0	4 (4%)	8 (9%)	12 (13%)
Total	16 (18%)	32 (36%)	24 (27%)	16 (18%)	88 (100%)

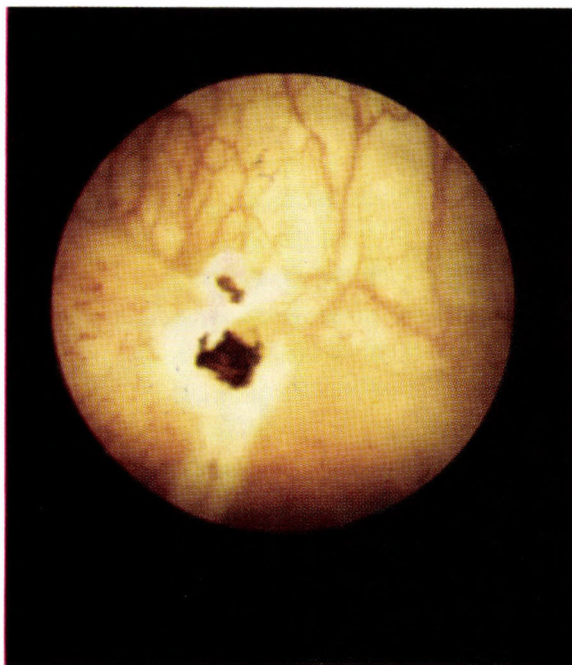


FIG. 2

TABLE 2
Distribution of the location of vesicular tumors

Location of tumors	Case No.	%
Bladder neck	0	0%
Anterior wall	8	9%
Posterior wall	20	22%
Cone	4	4%
Trigonum	24	27%
Lateral wall	28	32%
Diverticle	4	4%
Total	88	100%

TABLE 3
Distribution of tumor sizes

Tumor size	Case No.	%
0—5 mm ³	24	27%
6—10 mm ³	24	27%
11—15 mm ³	0	0%
16—20 mm ³	16	18%
21—25 mm ³	0	0%
26—30 mm ³	20	22%
31—35 mm ³	4	4%
Total	88	100%

We employed 2 mm fiber distance and 4 mm spot diameter, which corresponds to 1000 J/cm² energy density and 320 W/cm² surface performance density per impulse. The lowest irradiation energy was 480 J, the highest 36,360 J, and the mean was 14.420 J, depending on the size and location of bladder tumors.

The distribution of irradiation energies is shown in Table 4.

PAs releasing from laser destroyed vesicular tumor cells were determined as follows:

The whole volume, i.e. 150 ml of the bidistilled water vesical eluent was used for the analysis. The eluent pH was adjusted to 2 with concentrated hydrochloric acid, then it was evaporated to 10 cm³ volume. Then the pH of the mixture was adjusted to pH = 10–11 with solid Na₂CO₃, and 2 cm³ 10 mg

TABLE 4
Distribution of irradiation energy

Irradiation energy	Case No.	Relative Frequency	Cumulative Frequency
0 — 500 J	20	22%	22%
2 500 — 3 000 J	8	9%	31%
10 500 — 11 500 J	8	9%	40%
11 500 — 12 500 J	20	22%	63%
22 500 — 23 500 J	8	9%	72%
23 500 — 24 500 J	8	9%	81%
34 500 — 35 500 J	8	9%	90%
35 500 — 36 500 J	8	9%	100%
Total	88	100%	

dansyl chloride/1 ml acetone reagent was added. Then the mixture was kept at 55 °C for 1 hour, as protected from light. During this time the dansylation of PAs takes place quantitatively, i.e. a dansyl group is connected to the amino groups each, and the releasing HCl is continuously bound by the alkaline medium. Dansylated PAs (Dns PAs) obtained are highly fluorescent compounds. The Dns PAs are extracted from the reaction mixture with 2 × 5 ml ethyl acetate, the ethyl acetate phase is evaporated to dry, then it is resolved with 0.5 cm³ methanol, and this is analyzed by high pressure liquid chromatography [11].

Parameters of HPLC analysis

Apparatus: Varian 5020

Column: 250 × 4.6 mm RPB 5 μ

Column temperature: 50 °C

Injected sample: 50 μ l

Detector: fluorescent
Exc: 330 nm
Em: 450 nm

Separation: gradient

Eluents: A: Methanol/water = 60 : 40
B: Methanol

Gradient program: time (min.): % B:

0	0
16	100
21	100
22	0

Retention times: putrescine: 17.9 (min.)
 spermidine: 21.3 (min.)
 spermine: 23.3 (min.)

The separation of dansylated PAs is illustrated in Fig. 3.

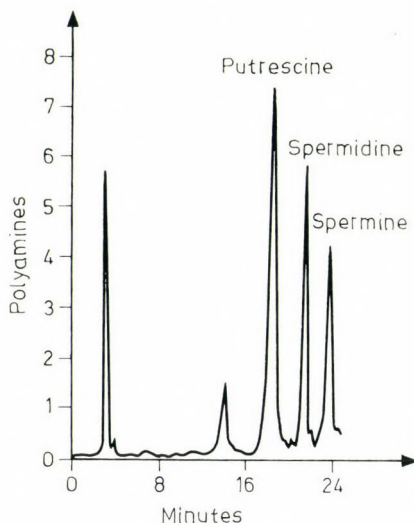


FIG. 3

Results

In our 88 test samples we were able to detect PAs in well measurable levels from the eluent. The PA quantity distributed in the 1.44–15.08 μg range, the mean PA release was 5.35 μg . Simultaneously we studied the PA level released after the irradiation of the intact, tumorous cell vesicular wall, and stated that this was near the limit of detection, i.e. less than 0.1 μg .

This had verified that our original hypothesis was correct, namely that the significantly higher PA content of the tumorous tissue can be used for the monitoring of the effects of laser intervention.

Mean values of the individual components:

Putrescine: 1.52 μg
 Spermidine: 3.10 μg
 Spermine: 0.70 μg

The distribution of the total PA content is shown in Table 5.

The table shows that the total PA content is in the 0.5 μg range in 72% of the cases.

We also studied the relationship between PA data and the tumor size and the applied radiation energies. Data of the correlation calculations are shown in Table 6.

TABLE 5
Distribution of total polyamine content

Total polyamine level	Case No.	Relative frequency	Cumulative frequency
0 — 1 μg	32	36%	36%
1 — 3 μg	24	27%	63%
3 — 5 μg	8	9%	72%
5 — 7 μg	8	9%	81%
7 — 9 μg	0	0%	86%
9 — 11 μg	8	9%	90%
11 — 13 μg	4	4%	95%
13 — 15 μg	4	4%	100%
Total	88	100%	

TABLE 6
Data of correlation calculations

Correlation data	Between tumor size (x) and total PA (y)	Between irradiation energy (x) and total PA (y)
Regression line	$y = 1.32x + 0.22$	$y = 3.20x + 1.47$
Correlation coefficient (v)	0.56	0.45
Covariance (S_{xy})	0.3	0.2

The table suggests that there is medium correlation between the total PA content and the tumor size. In evaluating this it is to be considered that the three-dimensional data of the tumor mass can be determined only with some inaccuracy as related to the error of the analytical test, so this data indicates hardly more than the obvious tendency itself.

The correlation coefficient between the total PA value and the irradiation energy indicates a weak relation. This explains why the applied irradiation energy is only one of the parameters characterizing the efficiency of laser removal of tumors. The spatial accuracy of irradiation is presumably a more important factor.

The regression lines are shown in Fig. 4.

The straight axial section of the tumor size is below the 1 μg PA level. From this it follows that the laser coagulation must concern some malignant tissue if the PA content of the eluent is over 1 μg .

If the PA content of the eluent is determined after the laser treatment of an individual tumor, conclusions can be drawn as to the size of the elimin-

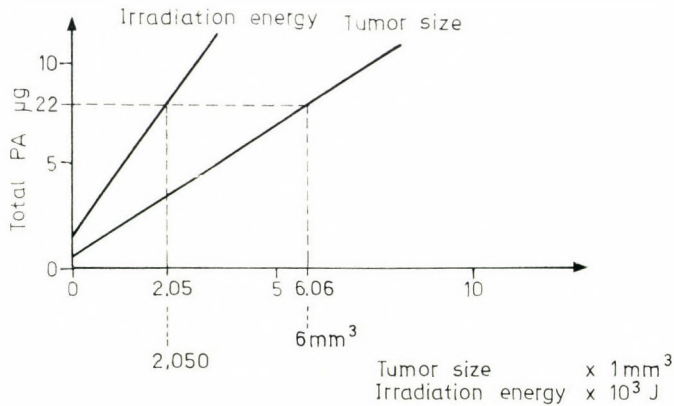


FIG. 4

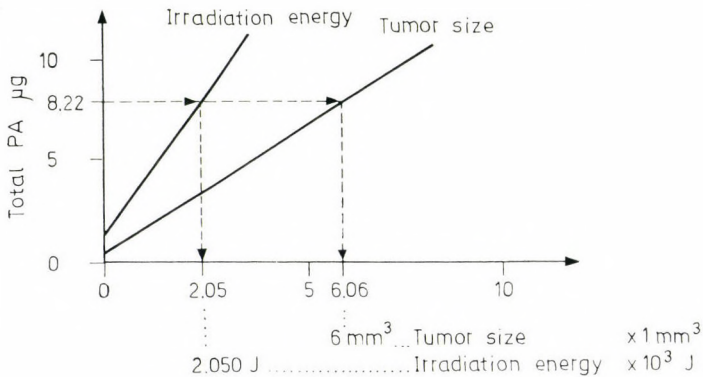


FIG. 5

ated tumor, which is shown in Fig. 5. This may be related to the visualized results obtained during the post-surgical examination, and can decide whether or not the tumor was completely destroyed.

Then perifocal laser irradiation is performed to seal the peritumoral lymph vessels. If in this case PA is released from vesicular areas thought to be macroscopically intact and tumor-free, this will mean that the lasered area contained tumor cells. On this basis conclusions can be drawn as to the tumorous involvement of the lasered area and the radicality of the intervention.

Earlier, such information was given by the histological processing of fractioned TUR performed according to the Bressel scheme.

Discussion

The determination of the polyamine content of the eluent after the endovesical Nd-YAG laser treatment of surfacial urinary bladder tumors allows the monitoring of the extension and efficiency of the intervention, without the risk of spreading or implanting tumor cells in the bladder.

Our method is especially suitable for the monitoring and checking of laser treatment of infiltrative urothelial tumors of low and medium grade.

Our future research will involve the study of relationship between the quantitative and qualitative composition of PAs releasing during laser treatment, and the histological and biological behavior of the tumor. The distribution of the individual polyamine components according to the type and stage of the tumor will also be investigated.

In addition, we will study the circulating tumor marker values of our bladder cancer patients (lipid bound sialic acid, neopterin, carcinoembryonal antigen, alpha fetoprotein, beta-human choriogonine, etc.) as compared to local PA values. When having a suitable number of cases, we will summarize these results in a publication.

References

1. Bachrach U: Function of naturally occurring polyamines. Academic Press, New York, 1973
2. Denton MD, Glazer HS, Walle T: Polyamines in normal and neoplastic growth. Raven Press, New York, 1973
3. Desser H, Luta D, Krieger O: *Onkology* 37:376, 1980
4. Hofstetter A: Neue Technologien in der Urologie. *Fortschr Med* 21:100(39), 1982 Oct, 1981-2
5. Russel DH: *Nature. New Biol* 223:144, 1971
6. Russel DH, Durie BGM: Polyamines as biochemical markers of normal and malignant growth. *Prog Cancer Res Ther. Vol 8*
7. Schumann B, Szemes Z, Rimanoczi E, Kovács R: Komplex tumor marker vizsgálatok jelentősége az onkológiában (The role of complex tumor marker studies in oncology) 4th Kecske-mét National Urological Days, Abstracts 41, 1989
8. Szemes Z: Neodym-YAG lézer intravezikális alkalmazásának elméleti és gyakorlati kérdései (Theoretical and practical aspects of intravesical application of Neodym-YAG laser). *BM Orvos*, 1-2:60, 1986
9. Szemes Z: MEDI-YAG 450 t'pusú lézerkészülék az urológiában (Application of MEDI-YAG 450 laser apparatus in urology) Symposium on Laser Therapy and Laser Diagnostics, Pécs, Abstracts 3, 1986
10. Szemes Z, Magasi P: Hólyagdaganatok kezelése Neodym-YAG lézerrel (Treatment of vesicular tumors by Neodym-YAG laser) *Urol Nephrol Szemle*, 15:2, 91-97, 1988
11. Vandemark FL, Schmidt GI: *J Chrom Sci* 16:465, 1978

Magnesium Transport in Human Pregnancy (Magnesium content of human gestation tissues and tissue fluids)

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Authors used atom absorption spectrophotometry to determine the magnesium content of gestation tissues (placenta, myometrium) and tissue fluids (maternal blood, cord blood, amniotic fluid) taken in different periods of gestation. Magnesium concentration was found higher in the cord blood than in the maternal serum. It was assumed that the concentration gradient between mother and fetus resulted from active transport. There was a significant difference between the magnesium content of the amniotic fluid and the cord blood sera ($P < 0.001$). The magnesium content of the mature chorion tissue was by nearly 40% lower than that of the immature one. The magnesium content of the myometrium decreased by 38% by Week 40 of gestation, as compared to the value in Week 37.

Fundamental research in the past decades has clarified many physiological and pathophysiological details of transplacental fetomaternal material exchange. Initially, the placental material transport was studied by the perfusion of the whole placenta. Recently, the preparation of human syncytiotrophoblast vesicles [9] made possible the study of transport mechanisms of many anions and cations [19], glucose [8] and several amino acids [24].

There are still no data available on human placental transport. Nevertheless, many details of the net magnesium transport of certain isolated mammal cells, such as erythrocytes, thymocytes, has been revealed in the recent years [5, 15].

It has been proven that the magnesium uptake of isolated mammalian cells takes place through a $Mg^{2+}/2HCO_3^-$ -symport, which can be modified by beta receptor activation. This effect, however, is cAMP mediated [5, 15]. On the other hand, the magnesium release takes place through an amiloride sensitive $2Na^+/mg^{2+}$ antiport. The process is ATP dependent, and does not depend on certain receptors [5, 6].

In the recent years it has also been clarified that the magnesium content of the maternal blood decreases by the end of gestation even in healthy pregnancy [18, 10]. One of the responsible factors is the increased magnesium demand with advancing gestation [11]. The elevated magnesium demand may be

in relation with the increased function of gestation tissues, the increased demand of the developing fetal organism, the altered nutritional habits [12], the increased maternal renal magnesium loss as compared to the non-pregnant condition [17, 23], and also with insufficient magnesium intake which cannot compensate the above demands.

Clinical observations suggest that the development and aggravation of certain clinical patterns, such as spontaneous abortion, preterm birth, intrauterine fetal retardation and preclampsy can be prevented by regular administration of magnesium [2, 11]. However, these are only empirical observations, and are not based on the knowledge of the mechanism of action and the biological role of magnesium.

It is therefore, important to gain a complete picture of the magnesium content of gestation tissues and fluids, of their changes with advancing pregnancy also in human gestation, to draw conclusions as to the mechanism of magnesium transport.

Material and method

The maternal and cord blood ($n = 38$) and the *amniotic fluid* ($n = 21$) samples were obtained during labor. The tissue fluid samples were spin dried, the supernatants were collected and stored at -18°C until the assay. The magnesium content of the blood sera and the amniotic fluid was determined after 25 times and 20 times dilutions, respectively.

The placental tissue was obtained at legal interruptions of 4–12 week pregnancies ($n = 14$) and at the end of 22–40 week pregnancies ($n = 29$).

The *myometrium* fragments were taken from the lower uterine segment (passive stage) in the course of caesarean sections performed due to maternal or fetal indications (maternal disease, problematic obstetrical or surgical history, spatial improporitions) on Week 37 ($n = 15$) and Week 40 ($n = 14$) of pregnancy.

The placental and myometrium tissue samples were carefully cleaned of blood and interstitial tissues, and homogenized with 10% TCA in Ultra-Turax apparatus (1 g tissue/2 ml TCA), washed with 5% TCA (1 g tissue/2 ml TCA), and the supernatants were diluted with bidistilled water to 10 ml. Magnesium contents were determined. The protein content of the placental homogenate was studied according to the method of Lowry et al [14].

The magnesium content of the test samples was determined by atom absorption spectrophotometry at 285.3 nm. The reference solution was made from 1000 ppm magnesium acetate solutin ($\text{Mg}/\text{C}_2\text{H}_3\text{O}_2/ \times 4\text{H}_2\text{O}/$ POB Sigma).

The mean values of the samples ($\times \pm \text{SD}$) were calculated from the results of 3 measurements. The Student t-test was used for mathematical analyses.

Results

Magnesium content of the maternal blood, the cord blood and the amniotic fluid

The magnesium content of blood samples taken during labor is shown in Table 1. The values are similar to those described by *Lechner, et al* [13], but are below those defined by *Nagel* [16] and *Anastasiadis* [1]. The differences can possibly be explained by the fact that the studies were performed by different methods, and by the different magnesium supply of the test groups involved.

TABLE 1

Magnesium content in maternal and cord blood and in the amniotic fluid

	n	mM ($\times \pm$ SD)
Maternal venous blood	38	0.77 \pm 0.065
Cord blood		
venous blood	38	0.848 \pm 0.050
arterial blood	38	0.81 \pm 0.030
Amniotic fluid	21	0.51 \pm 0.900

The magnesium concentration of the *amniotic fluid* was found to be 0.53 ± 0.9 mM on the average, and this value was similar to those published by *Baltzer et al* [3].

Magnesium content of the chorion tissue

Calculated per wet weight, the magnesium content of *placentas* born to term was 2.61 ± 0.85 mmol/l. This value is nearly the same as those published by *Widdowson and Spray* [25] (3.3 mmol mg^{2+}/kg) and by *Baltzer* [3] (2.73 mmol Mg^{2+}/kg , but is nearly twice as high as the value measured by *Lechner et al* [13] (1.375 mmol Mg^{2+}/kg).

The placental magnesium content calculated for protein can be seen in Table 2.

The magnesium content calculated for protein decreases by 40% by the end of pregnancy, as compared to the value measured in the immature placenta.

TABLE 2

Placental magnesium content calculated for protein content and wet myometrium weight

	n	Gestation weeks	$\bar{x} \pm \text{SD}$
Placenta	14	4–12	$53.34 \pm 2.9 \mu\text{mol/g protein}$
	29	22–40	$*31.07 \pm 0.6 \mu\text{mol/g protein}$
Myometrium	15	37	$3.8 \pm 0.15 \text{ mmol/kg}$ n. s.
	14	40	$**2.34 \pm 0.61 \text{ mmol/kg}$ n. s.

* $P < 0.005$ ** $P < 0.05$ *Magnesium content of the uterus*

The magnesium content values of *uterus* samples taken from colsarean sections on maternal or fetal indications are shown in Table 2. The magnesium value measured on Gestation Week 37 decreases significantly, by 38% by Week 40.

Discussion

The conclusions which can be drawn from the results of magnesium content determinations of maternal blood, cord blood and amniotic fluid samples, and which are in accordance with those described by *Spatling et al* [23], are as follows.

Magnesium concentration elevates from the maternal to the fetal direction: the *venous cord blood* contains by 10% more magnesium than the *venous maternal blood*. In the *arterial cord blood* the magnesium content is by about 5% lower than in the venous blood. Since on the fetal side the magnesium content is higher in the cord blood than in the maternal serum, it can be assumed that the concentration gradient results from an active transport mechanism. On the other hand, the fact that the magnesium concentration in the blood returning from the fetus to the placenta (umbilical artery) is lower than in the blood flowing from the placenta to the fetus (umbilical vein) suggests that the fetus takes up a substantial amount of magnesium, and this phenomenon cannot result from active transport.

The significant difference between the magnesium levels of the amniotic fluid and the cord blood sera ($P < 0.001$) may be in relation with the fact that

in late stages of pregnancy the fetus accumulates gradually more magnesium, and releases gradually less magnesium to the amniotic fluid [13].

In the *placental tissue*, a 40% Zn^{2+} decrease, similar to that of the magnesium content calculated for protein was seen in our earlier studies in mature placentas, as compared to immature ones [20]. This observation seems to be important, since an assumed role is attributed to zinc in signal transmission [4].

Our data on *myometrium* samples taken from healthy gestations born to term, agree with those described by *Lechner* [13] (0.38–3.15 mmol/kg) and *Spatling* [21] (2.69 ± 0.69 mmol/kg), but are nearly three times lower than those published by *Hawkins, et al* (6.75 mmol/kg) in 1958 [7].

Our results suggest that the magnesium content of the maternal venous blood decreases even in symptom-free gestations. There is a well measurable gradient between mother and fetus, which presumably results from active transport. In the late gestation period the magnesium content of both the placenta ($P < 0.005$) and the myometrium ($P < 0.05$) decreases significantly, as compared to the earlier values. It is not known, however, whether the decrease in magnesium content concerns the whole organism of the pregnant woman, or it develops only in the gestation tissues which are in organic biological connection with the fetus.

For the moment being we cannot answer the question whether the magnesium decrease in certain clinical patterns or forms as compared to normal gestations is to be evaluated as a primary or as a secondary factor. The fact, however, that remarkable improvement is seen on magnesium treatment in certain clinical patterns obviously supports the development and the necessity of treating conditions with relative magnesium deficiency.

However, until we do not understand the magnesium transport mechanisms of gestation tissues and the hormonal and other factors which regulate these processes, the underlying causes of conditions with magnesium deficiency in various gestation complications cannot be clarified.

The aim of our current studies on placental and myometric transport is to obtain a better knowledge of and to find answer to these questions.

References

1. Anastasiadis T, Kohler R, Rimpler M: Pathobiochemie von Mineral- und Spurelementen. III Magnesium Konzentration in Vollblut und Serum von Schwangeren und Neugeborenen. *Z. Geburtsh Perinat* 185:100–105, 1981
2. Balázs M, Morvay F, Székely A, Szücs M, Varenka Zs, Kuti V: A spontán vetélés és a magnéziumellátottság kapcsolata (The relation of spontaneous abortion and magnesium supply) *Medicus Universalis* XIV/1:15–19, 1981
3. Baltzer G, Pilz M, Schlag M, Knecht J, Deichert U, Schmidt-Rhode P: Untersuchungen zur Magnesiumkonzentration im Fruchtwasser und in der Plazenta bei normalem Schwangerschaftsverlauf. In: H. Weidinger (Hrsg.): *Magnesium in der Frauenheilkunde. Bayreuther Gespräch*, 44–49, 1985
4. Csermely P, Somogyi J: Zinc as a possible mediator of signal transduction in T lymphocytes. *Acta Physiologica Hungarica* 74:195–199, 1989

5. Gunther T: Biochemische Mechanismen des Mg^{2+} -Influx und $Mg + 2 \pm$ Efflux. In: H Weidinger (Hrsg.): Magnesium in Klinik und Fosschung. Bayreuther Gespräch, 3-8, 1987
6. Gunther T, Vormann J, Cragoe EJ, Holtriagl V: Characterization of Na^+ dependent and Na^+ independent Mg^{2+} efflux from erythrocytes by amiloride derivatives. *Magn Bull* 11:103-107, 1989
7. Hawkins DF, Nixon WCW: Electrolyte composition of human uterus in normal pregnancy and labour and in prolonged labour. *J Obstet Gynec Brit Cwlth* 65: 895-910, 1958
8. Johnson LW, Smit CH: Glucose transport across the basal plasma membrane of human placental syncytiotrophoblast. *BBA* 815:44-50, 1985
9. Kelley LK, Smith CH, King BF: Isolation and partial characterization of the basal cell membrane of human placental throphoblast. *BBA* 734:91-98, 1983
10. Kovács L, Rigó J: A few aspects of dietetic therapy in cases of pathological pregnancy. *Magy Nőorv L* 30: 485-489, 1967
11. Kovács L, Molnár GB, Huhn E, Bódis L: Magnézium pótlás a terhesség alatt (Magnesium supplementation during pregnancy) *Magy Nőorv L* 51:9-14, 1988
12. Kuti V, Balázs M, Morvay F, Varenka Zs, Székely A, Szűcs M, Hajdok K, Halmos K, Szabó I, Benkó L, Tas M, Pázsit L, Zmertlich A, Tüske Zs, Bálint I, Mélykúti M, Csuka J, Fodor M, Horváth I, Kobor T, Morva L: Az anya magnéziumellátottságának hatása a spontán vetélésre, koraszülésre, a magzat intrauterin fejlődésére és a csecsemőhalálózásra (The effect of maternal magnesium supply on spontaneous abortion, premature birth, fetal development and infant mortality) *Egészségtudomány* 26:62-73, 1982
13. Lechner W, Artner-Dworzak E, Jarosch E, Mayr P, Pastner E, Streit B, Marth CH: Untersuchungen zum Magnesiumgehalt von Myometrium, Plazenta, Nabelschnur, Blut, Fruchtwasser und Muttermilch. *Magn Bull* 10:69-71, 1988
14. Lowry OH, Rosenbrough NH, Farr AL, Randall RJ: Protein measurement with the Folin phenol reagent. *J Biol Chem* 193: 265-275, 1951
15. Maguire ME: Hormone sensitive magnesium transport and magnesium regulation of adenylate cyclase. *TIPS* 5:73-77, 1984
16. Nagel H, Düring R, Bendel L: Bestimmung von Zink, Kupfer und Magnesium im Nabelschnurblut hypotropher Neugeborener. *Zenbl Gynakol* 108:118-121, 1986
17. Quamme GA, Dirsk JA: Magnesium transport in the nephron. *Am J Physiol* 293: 393-401, 1980
18. de Ridder G, Gossen D: Magnesium in der Schwangerschaft unter besonderer Berücksichtigung von Prophylaxe und Therapie der Frühgeburtsneigung bei der drohenden Frühgeburt. In: H. Weidinger (Hrsg.): Magnesium in Klinik und Forschung. Bayreuther Gespräch, 161-175, 1987
19. Shennan DB, Boyd CAR: Ion transport by placenta: a review of membrane transport systems. *BBA* 906:437-457, 1987
20. Somogyi J, Ver A, Fodor P, Zsolnai B, Lintner F, Weidinger H: Konzentration im humanen Plazentagewebe. In: H Weidinger (Hrsg): Magnesium in Klinik und Forschung. Bayreuther Gespräch, 9-11, 1987
21. Spatling L, Kunz PA: Magnesium im während der Gravidität. In: H Weidinger (Hrsg): Magnesium und Schwangerschaft. Bayreuther Gespräch, 244-247, 1983
22. Spatling L, Kunz PA: Renaler Magnesium und Kalziumverlust in der Schwangerschaft. In: H Weidinger (Hrsg): Magnesium in der Frauenheilkunde. Bayreuther Gespräch, 130-136, 1985
23. Spatling L, Disch G, Classen HG: Magnesium in pregnant women and the newborn. *Magnesium Research*. 2,4:271-280, 1989
24. Yudilevich DL, Sweiry JH: Transport of amino acids in the placenta. *BBA* 822:169-201, 1985
25. Widdowson EM, Spray CM: Chemical development in utero. *Arch of diseases in childhood* 26:205-214, 1951

Biological valve Prosthesis Replacement — Experiences and Considerations

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Between 1976 and 1991. 1.017 tissue valve prostheses were implanted in 801 patients. During the same period 1876 mechanical valve prostheses were replaced. The hospital mortality was 8.1%. Till 1991 230 bioprostheses (22.6%) in the case of 166 patients (20.7%) had to be removed and replaced by other valve prostheses. There are no significant differences concerning the mortality between the first (8.1%) and the second operations (9.1%), and the durability of the various types of bioprostheses used, however, calcification, degeneration and other complications occurred more frequently and earlier in the case of mitral (24.5%) than in aortic (18.9%) bioprostheses, and in younger patients than in the older ones, as well. The mean age of patients was 46 years at the time of the first and 49 years at the time of the second operation. The incidence of reoperations was the highest in the seventh year after the first surgical intervention. In general, one size smaller prostheses were used in valve replacements after the removal of the first bioprostheses.

In our Department the first tissue valve prosthesis was replaced in mitral position in 1976 [9]. In the following years, like other cardiac surgeons, we also performed biological valve replacements in an increasing number, experiencing the several well-known advantages of the tissue valve prostheses. [1, 2, 4, 7]. The sudden boom was followed by a gradual decline. There can be read more and more about the calcification and degeneration of the biological valves, leaflet disruptions, structural failures, etc. [3, 5, 6, 8].

Although, in those days the bioprostheses implanted by us were still too young, and it would be premature to draw conclusions from our data, by now time has arrived to do so.

Materials and methods

Between 1976 and 1991 1.017 tissue valve prostheses were implanted in 801 patients in our Department.

During the same period 1857 mechanical valve prostheses were replaced. The mean age of the patients was 46 years. 472 (59.1%) of them were females and 329 (41.1%) were males. The hospital mortality was 8.1%.

TABLE 1

Number of single and multiple valve replacements, and per cents of hospital mortality

	Number of pts.:	Hospital mortality(%)
M V R	374	6.7
A V R	201	6.9
M V R + A V R	198	10.6
M V R + T V R	15	13.3
M V R + A V R + T V R	13	15.3
Sum total:	801	

Table 1 shows the number of the single and multiple valve replacements and the per cent ratio of hospital mortalities. Our operations were performed with hypothermic extracorporeal perfusion. Myocardial protection was obtained by infusion of cold (4 °C) cardioplegic ion solution in the aortic bulb or directly in the origins of the coronary arteries. Patients remained in the postoperative intensive care unit in average during 48 hours. Anticoagulant treatment started on the second postoperative day and was continued in general during three months. Patients who had atrial fibrillation and/or large left atrium were full anticoagulated indefinitely.

During the period past till 1991, 230 bioprostheses (22.6%) had to be removed and replaced in 166 patients (20.7%).

The mean age of this group was 49 years and their hospital mortality 9.1%.

The reasons for the removal of the bioprostheses were the following:
 calcification and/or leaflet disruption in 140 patients,
 paravalvular leak in 19 patients
 and prosthetic valve endocarditis in 7 patients
 altogether 166 patients

Figure 1 lists the size of the 390 bioprostheses implanted in aortic position. The number and the size of the 74 (18.9%) removed aortic bioprostheses are demonstrated in Figure 2 and the number and the size of valves replaced in aortic position are presented in Figure 3.

Comparing the data of the two figures (2-3), it can be seen that the replaced valves were slightly smaller than those implanted first.

Table 2 demonstrates the number of the various types of implanted and removed aortic bioprostheses.

As a matter of fact, the use rate of the various types of tissue valve prostheses which were implanted at various occasions, were depending rather on their acquisition possibilities than on their durability.

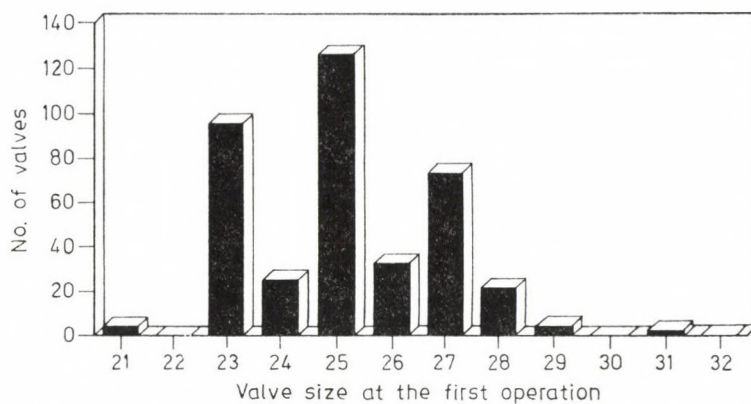


FIG. 1. Number and size of bioprostheses implanted in aortic position (N = 390)

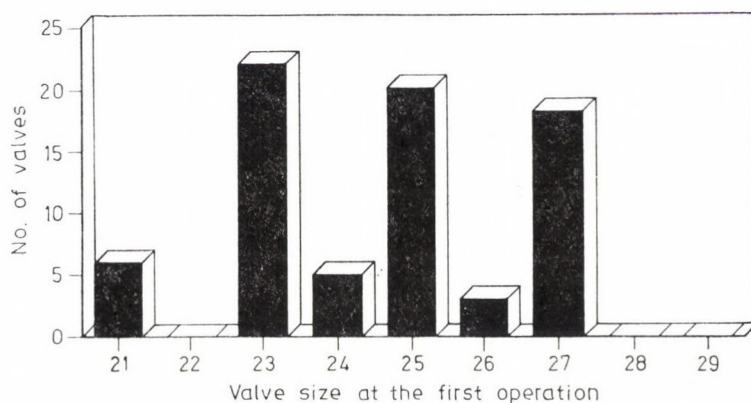


FIG. 2. Number and size of the removed aortic bioprostheses (N = 74)

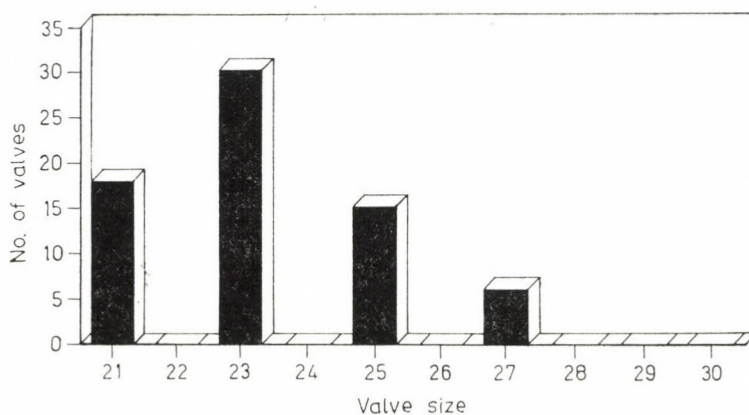


FIG. 3. Number and size of the replaced valve prostheses in aortic position (N = 74)

TABLE 2
Number of various types of implanted and removed aortic bioprostheses

	No. of implanted bioprostheses	No. of removed bioprostheses
Carpantier-Edwards	191	34
Xenomedica	91	17
Hancock	83	20
Mitroflow	18	1
Liotta	6	1
Ionescu-Shiley	1	1
	390	74

The size of the 599 prostheses in mitral position is listed in Figure 4. Of them 148 (24.7%) have been removed and similarly as in the case of aortic valve replacements, usually smaller valve prostheses were implanted. (Figure 5 and Figure 6)

The number of the various types of implanted and removed mitral bioprostheses are demonstrated in Table 3.

It can be seen in Table 4 that ten out of the 28 bioprostheses implanted in the tricuspid position, have been removed.

As it is shown by Figure 7, the frequency of reoperations was the highest in the seventh year after the first surgical procedure.

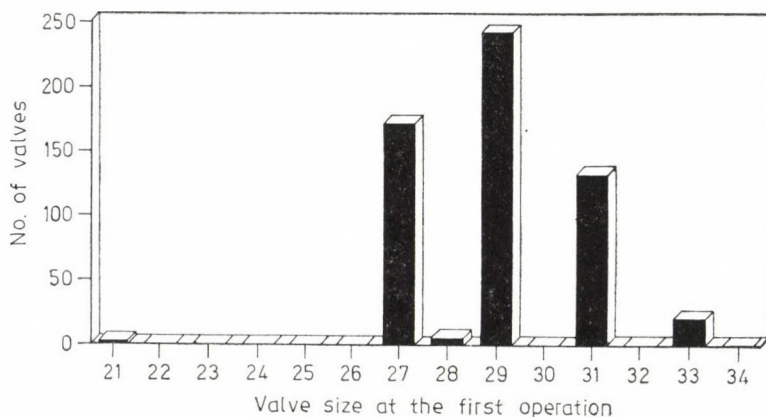


FIG. 4. Number and size of bioprostheses implanted in mitral position (N = 599)

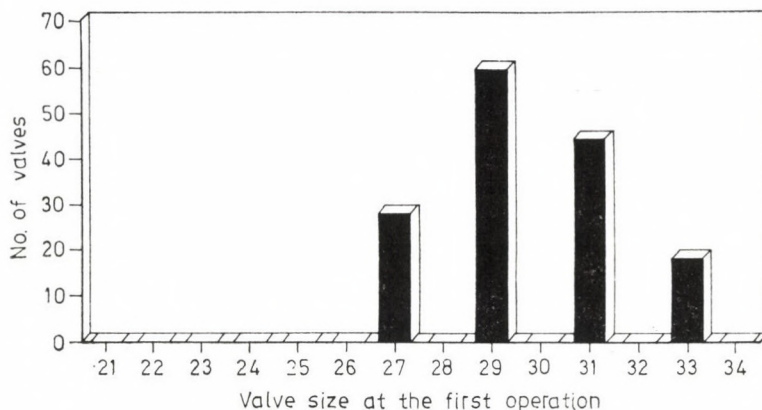


FIG. 5. Number and size of removed mitral bioprostheses (N = 148)

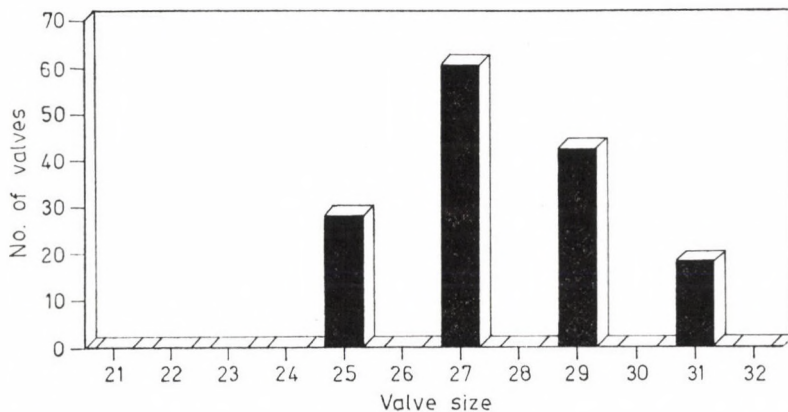


FIG. 6. Number and size of replaced valve prostheses in aortic position (N = 148)

TABLE 3

Number of various types of implanted and removed mitral bioprostheses

	No. of implanted bioprostheses	No. of removed bioprostheses
Carpantier-Edwards	197	52
Xenomedica	223	43
Hancock	148	49
Mitroflow	9	—
Liotta	22	4
	599	148

TABLE 4

Number of various types of implanted and removed bioprostheses in tricuspidal position

	No. of implanted bioprostheses	No. of removed bioprostheses
Carpantier-Edwards	13	5
Xenomedica	6	1
Hancock	9	4
	28	10

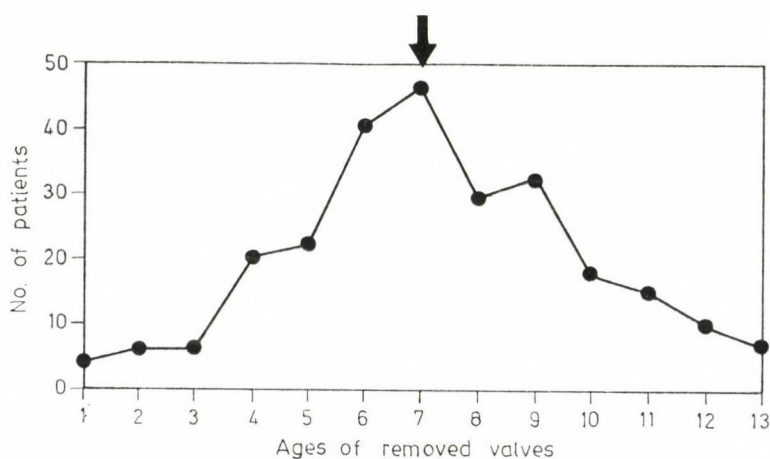


FIG. 7. Durability of bioprostheses. The arrow indicates that the removal rate of the 7 years old bioprostheses is the highest

Results

According to our experience there are no significant differences concerning the *mortality* of the first (8.1%) and the second operations (9.1%).

The *frequency* of reoperations was the *highest* during the seventh year after the first surgical intervention.

In general *one size* smaller prosthetic valves were used in course of valve replacements following the explantation of the bioprostheses.

There are no significant differences between the *durability* of the *various types* of bioprostheses.

Calcification, degeneration and other complications occurred earlier and more frequently *in the case of mitral* (24.5) then in aortic (18.9) bioprostheses, and in the younger than in the older patients.

The late results of biological valve replacements *do not* mean their explicit exclusion from our arsenal.

Bioprostheses, if necessary, can be used with good conscience, in *younger patients*, before delivery, or in the case of peptic ulcer, in older patients, because long-lasting peroral anticoagulant therapy can be avoided by this way.

References

1. Carpentier A, Dubost C: Biological Tissue in Heart Valve Replacement. London, Butterworth, 1971.
2. Cohn LH, Gallucci J: Cardiac Bioprostheses. York Medical Books, 1981, 79–90 p
3. Cohn LH, Mudge GH, Pratter F, Collins JJ: Five to eight year follow-up of patient undergoing heart valve replacement. *N Engl J Med* 304: 258–262, 1981
4. Craver JM, King SB, Doughlas JS: Late hemodynamic evaluation of Hancock modified orifice aortic bioprostheses. *Circulation* 60 (Suppl. I.): 93–102, 1979
5. Gonzales-Lavin L, Chi S, Blair TC, Jung JJ, Fabaz AG: Five year experiments with the Jonescu-Shiley bovine pericardial valve in the aortic position. *Ann Thorac Surg* 36:270–280, 1983
6. Janusz MT, Jamieson WRE, Allen P, Munro AI, Miyagishima RT: Experience with the Carpentier-Edwards porcine valve prosthesis in 700 patients. *Ann Thorac Surg* 34:626–633, 1982
7. Kirklin JW: The replacement of cardiac valves. *N Eng J Med*, 304: 291–292, 1981
8. Oyer PE, Stinston EB, Reitz BA, Miller DC, Rossiter SJ, Shumway NE: Long-term evaluation of the porcine xenograft bioprosthesis. *J Thorac Cardiovasc Surg* 78: 343–350, 1979
9. Szabó Z: Szívbillentyűpótlás bioprotézisekkel: 5 éves tapasztalataink. *Orv Hetil* 833–837, 1982

Book review

A. TANKO: *Functional Diagnostics of the Lower Urinary Tract* (in English). pp. 201, 146 figs. Academia Publishing House, Budapest, 1990. Price: USD 38. HUF 440.-

Methods for the functional diagnostics of the lower urinary tract that were regarded earlier solely as experimental techniques have by now become integral in clinical practice all over the world. Data collected by these methods allow the examiner to set more accurate and objective diagnoses in patients with micturition or urinary incontinence problems. The selection of recent techniques for revealing the background of symptoms appearing in comprehensive and frequently in mixed forms is now referred to as urodynamical methods.

The Author summarizes our current knowledge of these techniques in six chapters, sequentially focused on uroflowmetry, cystometry, pressure/flow measurements, urethral pressure profile determination, urethral sphincter EMG and radiological methods related to the topic.

The next chapter provides a complete current terminology issued by the International Continence Society (ICS) for the international standardization of definitions related to the function of the lower urinary tract and for the technical characteristics of urodynamical examinations. The last chapter describes the technical modifications and developments designed by the Author and his coworkers, which have contributed to the easier availability and simplification of some diagnostic methods. The contextual figures, photos, original recordings and X-ray pictures are of good quality and are easy to survey. The legends and the figures are in good concordance, and as a whole, they well illustrate the written text. This monograph provides the reader with the physiological principles of particular examinations, the conditions of technical performance, the sources of error and with the evaluation of the results. Thus, it offers a useful help to specialists having the task of diagnosing and treating patients with micturition and urinary incontinence problems in their everyday practice. The book can be recommended to urologists, gynecologists, neurologists, radiologists and also to internists and general practitioners.

S. Csata, M. D.

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CONTENTS

Complications following major abdominal surgery in cirrhotic patients. <u>F. Jakab, Z. Ráth, I. Sugár and J. Faller</u>	279
Parenteral and enteral nutrition and the enterocutaneous fistula treatment I. Investigations on fistula output, nutritional status and complications. <u>E. Dárdai, Sz. Pírityi and L. Nagy</u>	287
Parenteral and enteral nutrition and the enterocutaneous fistula treatment II. Factors influencing the outcome of treatment <u>E. Dárdai, Sz. Pírityi and L. Nagy</u>	305
Experience with a new combined method in the differential diagnostics of early endometrial changes. <u>K. Patai, Zs. Jakab, P. Siklós, Z. Vigváry and J. Balogh</u>	319
Operative treatment of malformations of the middle ear. <u>Gy. Szabó and O. Ribári</u>	323
Vacuum therapy in the treatment of erectal impotence. <u>Gy. Papp, A. Hoznek, E. Juhász and Zs. Kopa</u>	331
Acute acalculous cholecystitis. <u>L. Kiss, L. Nagy, F. Juhász, Z. Nagy and Á. Soós</u>	337
Study on dysphagia after proximal selective vagotomy. <u>A. Bálint, P. Balázs, J. Bátorfi, T. Fazekas, M. Réfi and M. Ihász</u>	341
Endoscopic diagnosis and therapy of urothelial tumours of the upper urinary tract. <u>P. Magasi, A. Karsza and M. A. Heggagi</u>	347
Evaluation of 1000 percutaneous nephrostomies with a special view to efficiency and complications. <u>A. Karsza, M. A. Heggagi and P. Magasi</u>	355
Use of different types of dilator systems in the prevention of complications of percutaneous (PC) renal surgery. <u>M. A. Heggagi, A. Karsza and E. Szüle Jr.</u>	365
Preservation of ejaculation in stage I. Non-seminomatous testicular tumours. <u>M. Fehér, L. Korányi, V. Szokoly and S. Kéry</u>	371
BOOK REVIEW	377

COMPLICATIONS FOLLOWING MAJOR ABDOMINAL SURGERY IN CIRRHOTIC PATIENTS

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(Received: June 11, 1991)

The morbidity and mortality of major abdominal surgical interventions in 34 histologically proven cirrhotic patients are analysed by the authors.

The surgical interventions were carried out based on vital absolute and elective indications. 37 general and surgical complications were observed following the major abdominal surgery of 34 cirrhotics. 7 out of 34 patients died, the mortality was 21%. Suture insufficiency, peritonitis, sepsis and other inflammatory processes occurred most frequently among the complications. The Child criteria, the prothrombin level and white blood cell count proved to be useful prognostic factors.

3400 deaths occurred due to liver cirrhosis in 1981, while 5480 deaths in 1985 /15, 16/. The number of cirrhotic cases has increased for the past decade all over the world /1, 5/. The main etiologic factors of the disease seem to be alcohol abuse and hepatitis B virus /8, 14/. By contrary to other surgical activities, the high death rate due to major abdominal interventions performed on cirrhotic patients has not decreased /1, 2, 4, 9/. On the other hand, more and more data show a favourable mortality and morbidity rate in portosystemic shunt, expanded devascularisation of bleeding esophageal varices or even in liver transplantation performed because of cirrhosis /7, 10, 11, 13/.

The cause of this significant difference is not yet clear, but an abdominal surgeon often faces the need to assess the risk of an elective or urgent operation of a cirrhotic patient. The aim of our present study is to draw conclusions from the analysis of the complications and deaths of abdominal surgery performed on cirrhotic patients and — identifying risk factors — make our statement on abdominal interventions in cirrhotic patients.

Patients and Methods

Abdominal surgery has been applied in 34 histologically proved cirrhotic patients at the Department of Surgery of the Semmelweis University Medical School between 1st January 1987 - 31st December 1989. Patients were enrolled in the study in whom cirrhosis was verified by preoperative liver biopsy, operational findings and biopsy of pathological and histological results.

The patients were classified on the basis of Child-Turcotte /14/ criteria (Table 1). Preoperative data contained age, sex, associated disease, disease requiring operation, encephalopathy, nutrition, ascites and inflammatory processes. Major laboratory findings referred to albumine, bilirubin, WBC and prothrombine.

Table 1
Classification of cirrhotic patients on the basis of
Child-Turcotte criteria

Child	A	B	C
Se bilirubin mmol/l	36	35 - 54	54
Se albumine g/l	35	30 - 35	30
Ascites	no	reacts well on treatment	does not react on treatment
Encephalopathy	no	minimal	expressed (coma)
Nutrition	excellent	medium	poor

Surgical interventions were performed on the basis of vital, absolute or elective indications. As vital indication, perforation of the intestinal tract into the abdominal cavity, massive bleeding from a gastroduodenal ulcer, hernia, ileus and acute appendicitis were regarded. Malignant tumours were taken as an absolute indication. Elective indication involved cholelithiasis, choledocholithiasis or mechanical icterus due to ventricular or duodenal ulceration.

General and surgical complications were classified on the basis of the Child criteria, the origin of cirrhosis and the groups of indication. Death were analysed on the same basis; etiology necessitating operation was also investigated.

For statistical analysis the χ^2 formula was used. In another classification patients were grouped as survivors and lost, deaths were evaluated on the basis of the mentioned preoperative variables (ascites, albumin, WBC, etc.) with variance analysis (Mattheas programme). Statistical significance was accepted in case $p \leq 0.05$.

Results

The most frequent causes of the 34 histologically verified cirrhotic cases were alcohol abuse and hepatitis. Distribution by the Child criteria seems to be relatively homogeneous (Table 2).

Table 2

The origin of cirrhosis and stage - classification of patients

Origin	No. of patients	Child stage	No. of patients
- alcoholic	15	Child A	12
- posthepatic	10	Child B	12
- primary biliary	2	Child C	10
- unknown	7		

Table 3

Postoperational complications of cirrhotic patients

	No.		No.
Surgical:	13	General:	24
- suture-line insufficiency	5	- sepsis	7
- peritonitis		- cardiopulmonary	3
- biliary flow	1	- urogenital	4
- haemorrhage	3	- liver failure	2
- pyosis - disruption	4	- neurological	3
		- "multiorgan failure"	5

Surgical indication was vital in 20 cases, absolute in 9 and elective in 5 cases. There were 37 postoperative complications (Table 3). Suture insufficiency and peritonitis were the most frequent among surgical complications, while sepsis and failure of other organs (known as "multi-organ failure" in the literature) among general complications.

Table 4
Analysis of postoperative complications of cirrhotic patients

	General		Surgical	
	No. of patients	Significance	No. of patients	Significance
<u>Child grading</u>				
Child A	4/12	$p \leq 0.05$	1/12	insignificant
Child B	10/12		4/12	
Child C	10/10	insignificant	8/10	$p \leq 0.01$
<u>Origin of cirrhosis</u>				
Alcoholic	11/15	insignificant	6/15	insignificant
Posthepatic	6/10		1/10	
Primary biliary	1/2	insignificant	1/2	insignificant
Unknown	6/7	insignificant	3/7	insignificant
<u>Indication</u>				
Urgent	14/20	insignificant	7/20	insignificant
Absolute	7/9		6/9	
Elective	3/5		0/5	

Table 4 contains the analysis of complications by the Child criteria, origin of cirrhosis and indication. It is striking that B and C stages by the Child criteria are accompanied with a statistically significant number of complications.

The results of the analyses of deaths from identical aspects are similar (Table 5).

The prognostic values of survivors and those who died in Table 6 differed significantly by multifactorial variance analysis. The examined factors or survivors and lost were evaluated by multifactorial discriminative analysis (Table 7). Factors are listed in order of importance. The data show the primary importance of the Child stages.

Table 5
Postoperative deaths in cirrhotic patients

	Total No.			
<u>Child grading:</u>	Died	/	of patients	Significance
Child A	1	/	12	insignificant $p \leq 0.05$
Child B	1	/	12	
Child C	5	/	10	
<u>Child of cirrhosis:</u>				
Alcoholic	5	/	15	insignificant insignificant insignificant insignificant
Posthepatic	1	/	10	
Primary biliary	0	/	2	
Unknown	1	/	1	
<u>Indication:</u>				
Urgent	5	/	20	insignificant insignificant insignificant
Absolute	1	/	9	
Elective				

Table 6
Preoperative variables of survivors and the dead

Preoperative variable	Survivor (n=27)	Died (n=7)
Bilirubin mmol/l p^+	27 \pm 4.5	72.2 \pm 7.1
Albumine g/l p^+	36.5 \pm 4.5	26.5 \pm 3.9
WBC 10^3 adv. p^+	8.9 \pm 1.1	16.5 \pm 2.1
Prothrombine % p^+	80.5 \pm 7.2	20.8 \pm 2.1
$p^+ \leq 0.01$ variance analysis		

Table 7
Preoperative prognostic factors. Variance analysis

Prognostic factor	Probability of death in the presence / lack of the factor	
Inflammation, peritonitis	70%	21%
Ascites	58%	11%
Acute intervention	25%	10%
Undernutrition	62%	22%
Bilirubin ≥ 54 mmol/l	62%	17%
Albumine < 30 g/l	58%	12%
Prothrombine $< 20\%$	63%	18%
WBC $> 10\ 000$	54%	19%
$p \leq 0.01$ in all values		

Discussion

Abdominal interventions on cirrhotic patients are of high risk and of high mortality /1, 4, 9/. On abdominal surgery due to cirrhosis in 34 histologically verified cases we found a death rate of 21% and a high number of complications. The most frequent cause of death was sepsis and "multiorgan failure".

From the prognostic point of view it was stated that neither the type of operation nor its organic localization have an impact on complications or deaths. However, the cause of death was peritonitis in 71% of cirrhotic patients. Vital surgical intervention may lead to poor results in cirrhotic patients either. Garrison /5/ found a 57% mortality rate with vital, and 10% mortality rate with elective operations. Doberneck /4/ found a 42% mortality rate with vital and 11% with elective interventions. We found 25% and 14% rate, respectively; no statistical difference was observed. On variance analyses vital intervention seemed to be a significant prognostic factor even in the small number of our cirrhotic patients.

There is a close relation between the Child criteria and death or complications, which we can also support. Originally the Child criteria were used in the prognosis of portocaval shunt operations of cirrhotic patients; however, it seems to be applicable in prognosing the results of large abdominal and even of esophageal operations in cirrhotic patients /2, 5, 12/.

Doberneck /4/ claims that elevated serum bilirubin level, hypoalbuminaemia and ascites have a significant impact on survival. Aranha and Schwartz /1, 9/ attached prognostic importance to prothrombin level. It is worth investigating the mentioned prognostic values separately, as they support the prognostic value of the Child criteria in abdominal surgery on cirrhosis.

Statistical analysis showed that WBC is of importance among preoperative data, as an elevated WBC shows significant relation to higher mortality rate which supports the fact that intraabdominal bacterial contamination or peritonitis are among the leading causes of death of cirrhotic patients /5/.

During our study we found a high number of complications, generally the patient / complication ratio was 1:2. Most of the complications were of bacterial origin. Although the cause and importance of the cumulative occurrence of septic complications in cirrhosis are well known, we would like to call attention to it.

We can conclude that the high mortality - and complication rates of abdominal surgery performed on cirrhotic patients call attention to the importance of careful indication in choosing the type of operation. Before operation nutrition should be improved, prothrombin-level normalized and ascites ceased.

Taking into account the Child criteria in the case of indication for elective operation is absolutely justified. Elective operation — in our opinion — can be performed at Child stage A in the case of tumours, risk of malignancy or unbearable pains. In Child stage B management of the mentioned abnormalities and getting back to stage A are desirable. Elective operation is not recommended in Child stage C.

The necessity of intervention in case of vital indication is unquestionable; attention is called to increased risk.

References

1. Aranha VG, Sontag JS, Greenle HB: Cholecystectomy in cirrhotic patients: A formidable operation. *Am.J.Surg.* 143:55-59, 1982
2. Belghiti J, Chargui D, Langonnet F, Fékété F: Esophagogastrectomy for carcinoma in cirrhotic patients. *Hepato-Gastroenterol* 37:388-391, 1990
3. Child CG, Turcotte JG: 1964. Surgery and portal hypertension. In Child CG (ed) *The liver and Portal Hypertension*. WB Saunders Co. Philadelphia P.: 50
4. Doberneck CR, Sterling WA, Allison DC: Morbidity and mortality after operation in non-bleeding cirrhotic patients. *Am.J.Surg.* 146:306-309, 1983
5. Garrison NR, Cryer HM, Howard AD, Polk HC: Classification of risk factors for abdominal operations in patients with risk factors. *Am.Surg.* 199:648-655, 1984
6. Garagliano CF, Lilienfeld AM, Mondelhoff AI: Incidence rates of liver cirrhosis and related disease in Baltimore and selected areas of the United States. *J.Chronic Dis.* 32:543-544, 1979
7. Iwatsuki S, Starzl TE, Todo S: Liver transplantation in the treatment of bleeding esophageal varices. *Surgery* 104:697-705, 1988
8. Saunders JB, Walters JRF, Davies P et al.: A 20 years postoperative study of cirrhosis. *Brit.Med.J.* 282:263-266, 1981
9. Schwartz SI: Biliary tract surgery and cirrhosis: A critical combination. *Surgery* 90: 577-583, 1981
10. Smith RB, Warren WD, Salam AA: Dacron interposition shunts for portal hypertension. *Am. Surg.* 192:9-17, 1980
11. Starzl TE, Demetris AJ, Van Thiel D: Liver transplantation I.-II. *New Engl. J. Med.* 321:1092-1099, 1983
12. Stone HH: Preoperative and postoperative care. *Surg.Clin. North Am.* 57:409-419, 1977
13. Sugiurawa M, Futagawa: Results of six hundred thirty-six oesophageal transections with paraesophagogastric devascularisation of oesophageal varice. *J.Vasc.Surg.* 1:254-557, 1984
14. Tanaka R, Itosima T, Nagashima H: Follow-up study of 582 liver cirrhosis patients for 26 years in Japan. *Liver* 7:316-324, 1987
15. World Health Statistics Annual WHO 1983. Genève pp.: 168
16. World Health Statistics Annual WHO 1986. Genève p. 392

PARENTERAL AND ENTERAL NUTRITION AND THE ENTEROCUTANEOUS
FISTULA TREATMENT I
INVESTIGATIONS ON FISTULA OUTPUT, NUTRITIONAL STATUS COMPLICATIONS*

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(Received: June 6, 1991)

Prospective evaluation were made of 45 patients with postoperative small bowel fistulas treated with total parenteral nutrition (TPN) and enteral nutrition (EN) between 1971-1988. The administration of TPN in the early treatment of enteric fistulas decreased the mean fistula output significantly ($p < 0.05-0.001$) and provided an effective tool in the control of high-output fistulas.

The electrolyte contents of different fistula secretions were unchanged and the losses through the fistulas depended on the daily output. In patients with high-output fistulas acid-base balance disturbances had to be corrected.

When comparing two parenteral nutrition regimens (carbohydrate+amino acids /CH+AA/ versus carbohydrate+amino acids+fat /CH+AA+F/) both facilitated the reduction of fistula secretion (in high-output fistulas. CH+AA = -50.2%; CH+AA+F = -49%).

Positive nitrogen balance was achieved in non-septic patients after 13 days of treatment. Improvement of serum protein and albumin occurred by the time of fistula healing. In non surviving patients significant decrease in protein synthesis was observed. Out of 7 of 75 central venous catheters yielded positive bacterial cultures (9.3%). In 5 patients autopsy proved generalized sepsis.

The use of parenteral and enteral nutrition proved to be a powerful method for controlling the enterocutaneous fistulas and maintaining the nutritional integrity of patients.

Introduction

The development of postoperative enterocutaneous small bowel fistulas has frequently been reported to be accompanied by high morbidity and mortality. Malnutrition and sepsis are the major determinants of the adverse clinical outcome /1, 21, 24, 34, 36, 45/.

The provision of optimal nutrition via parenteral or enteral routes is now a mandatory component of postoperative care of these patients. How-

*Presented at the 5th World Congress on Intensive and Critical Care Medicine. Kyoto, Japan, 1989

ever the general advances in fluid and electrolyte therapy, intensive care patient monitoring have contributed to the overall salvage of the fistula patients as much as the nutritional management /40, 44, 45/. The outcome of therapy does not depend on the nutritional therapy alone but is influenced by other factors, such as the localization of the fistula and the concomitant septic complications. In the last decade the use of parenteral and/or enteral nutrition together with highly developed diagnostic and therapeutic methods have resulted in increased rates of spontaneous closure and in decrease of the mortality of those individuals. The operative therapy of fistulas has also been expanded due to the increased use of nutritional programs /19, 20, 21/.

Unfortunately there are no prospective, randomized, controlled trials to confirm the efficacy of parenteral and enteral nutrition in the treatment of patients with enteric fistulas. Because of the ethical concerns in obtaining an adequate control population and the lack of homogeneity among the fistula patients, there will probably never be a totally objective study of this type /40/.

Despite of the absence of controlled trials, many reports have examined the impact of parenteral and enteral nutrition on the clinical results of postoperative enterocutaneous fistula treatment /1, 10, 14, 15, 34, 35, 43, 45/. The aim of this study is to investigate the different effects of nutritional care on postoperative enterocutaneous fistula management of the upper gastrointestinal tract.

Patients and Methods

At the 2nd Department of Surgery, Semmelweis University Medical School 64 patients were treated because of 71 gastroenterocutaneous fistulas from 1971 to 1988.

The localization of fistulas, the distribution of sex and age of the patients are shown in Table 1. Twenty-two patients had daily fistula drainage of more than 500 ml, we classified those as high-output fistulas /1, 19, 24/.

The schedule of treatment of enteric fistula patients was divided into three phases: fluid and electrolyte resuscitation, the evaluation and treatment of sepsis and the institution of proper nutritional regimen (Fig. 1) /1, 19, 40/.

Table 1
Distribution of 64 patients with 71 postoperative gastrointestinal
fistulas treated between 1971-1988

Localization	No.	Sex		Age (years)			
		Female	Male	25	26-45	46-65	> 65
Gastric	4	2	2	-	1	2	1
Duodenal	21	4	17	1	5	8	7
Jejunal	9	2	7	-	1	5	3
Ileal	37	16	14	8	6	8	8
Total	71	24	40 (64)	9	13	23	19

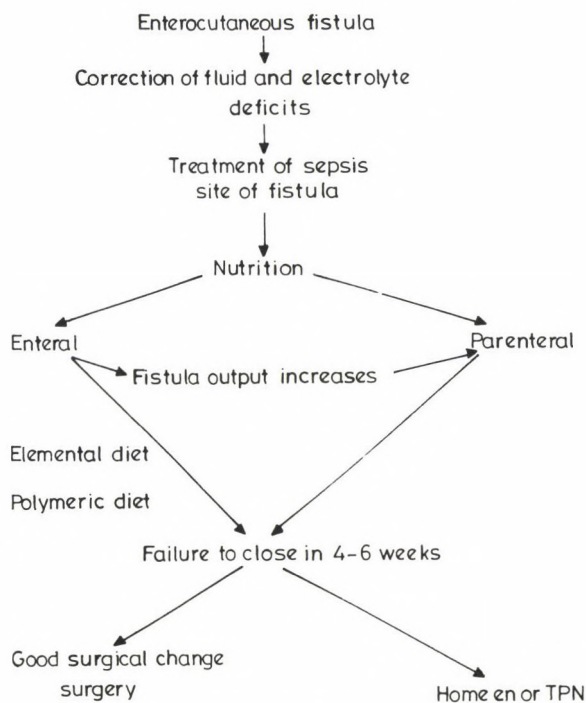


Fig. 1. Schematic illustration of scheduled fistula treatment

In the case of an established enterocutaneous fistula appropriate drainage was applied at the suture line of the abdominal wall or at the cutaneous orifice of the fistula. The skin around the orifice of the fistula was protected by Stomahesive® (Squibb Surgicare Ltd.) so that a collection bag (Coloplast Ltd.) could be attached /22, 25, 28, 30/. Large number of drainage modalities was developed using suction, gravity drainage or collection bags in order to collect the fistula secretion as completely as possible. The gastrointestinal tract was kept in rest, the patients received nothing per os and nasogastric suction was instituted during the early state of treatment. In the unstable initial phase blood, plasma, albumin and electrolytes were given to restore the circulating blood volume and to replace the fluid loss. An accurate intensive care was required to correct the metabolic and cardiorespiratory disturbances.

Twenty-eight acute abdominal operations were performed in order to control the intraperitoneal abscesses, peritonitis or bowel obstruction. In 2 patients a bleeding gastric ulcer was sutured.

In 45 patients with 48 fistulas TPN and/or tube feeding were performed as an adjuvant therapy. The rest of the patients received only fluid and electrolyte supplementation. In the initial period of the treatment we administered TPN via a central venous catheter. The nutritive solution consisted of 40% glucose, 10% fructose, 5-6% synthetic amino acids (Aminoplasma LX-5, B. Braun; Infusamin S5 or X5, Human; Aminomel LX-6, Salvia) and 10-20% fat emulsions (Intralipid, KabiVitrum; Lipofundin S, B. Braun), electrolyte supplementation, vitamins and trace elements in multi-bottle system /2/. The daily energy intake reached $1.56 \pm 0.21 \times \text{BEE}$ calculated by the modified Harris-Benedict equation /12, 33/.

In 15 of the patients we have continued the TPN with EN. In 8 cases of duodenal stump fistula we inserted nasojejunal feeding tubes under radiological control. In 7 cases thin catheter jejunostomy was performed either during the elective operation or during the emergency surgery performed for septic complications /42/. A formula diet was mostly employed for feeding (Salvimulsin, Salvia; Nutrocomp F, B. Braun; Cosilat, Egis) in gastric, duodenal and jejunal fistula cases. Our experience with elemental diet in ileal fistula cases were less favorable. We often had to discontinue it due to increased fistula output and return to TPN.

In 32 patients with well-controlled fistula drainage the fistula mean output was calculated from the sum of the daily secretion in a week by dividing it by 7 in order to get the mean daily secretion. By this cal-

culatation the weekly changes in fistula output were statistically comparable. The effects of different parental nutritional regimens (CH+AA versus CH+AA+F) on fistula output were evaluated by similar method. In the collected fistula secretions the electrolyte and protein content were determined. The daily electrolyte loss and the serum electrolytes were analysed and corrected. In 13 patients an appropriate fistula output collection was impossible due to extended disruption of the abdominal wound. In these cases we estimated the daily fluid, electrolyte and protein loss. The direct determination of base loss proved to be very uncertain due to technical reasons, therefore we measured the blood acid-base data with the micro-Astrup method three times a day and the means of the measurements were evaluated. The nitrogen loss was determined by micro-Kjeldahl method from the collected urine, fistula and nasogastric suction fluid. Nitrogen balance was calculated.

The serum protein and albumin level of patients were examined on every 5th day of the nutritional therapy. Statistical analysis of data was made by Student's t-test.

Results

The daily mean fistula output decreased significantly after two weeks of TPN. The data of 3 patients with high-output gastroduodenal fistula showed a decreasing tendency (Fig. 2).

In evaluation of different nutritiv regimens (CH+AA versus CH+AA+F) on fistula secretion showed similar effects. Marked decrease in fistula mean output was observed both with low- and high-output fistulas in comparison to the first week fistula secretion. In patients with high-output fistulas with CH+AA: -50.2% and CH+AA+F: -49% changes occurred on the second week of treatment (Fig. 3).

In all types of fistulas the examined ion composition of secretion seemed to be unchanged. The daily electrolyte loss was influenced by the amount of fistula secretion (Fig. 4). With proper replacement of electrolyte loss we were able to maintain the plasma electrolyte level in normal limits in patients with properly collected fistula output (Fig. 5).

In high-output fistula patients at the beginning of the nutritional support metabolic acidosis was observed (Fig. 6). The base-losses were continuously corrected by the i.v. infusion of 4.2% bicarbonate solution.

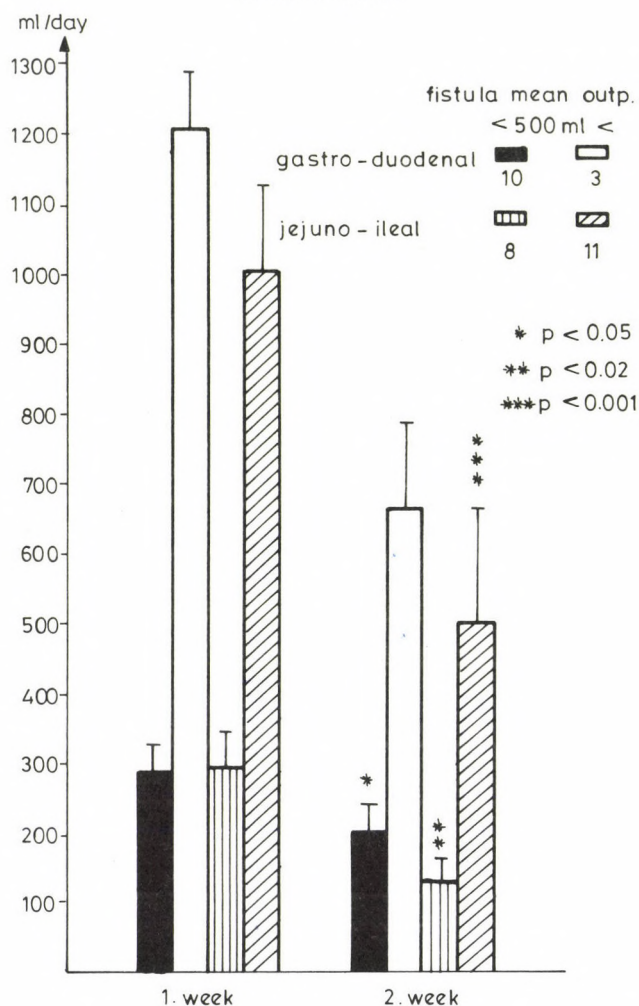


Fig. 2. Changes in fistula mean output during two weeks of TPN and nothing per os treatment. (I = SEM)

In 20 patients meticulous nitrogen balance study was carried out. Positive nitrogen balance could be achieved on the 2nd week of TPN (Fig. 7). Septic episodes, surgical interventions had negative effects on nitrogen balance that improved when the hypermetabolic condition abolished.

The plasma protein and albumin level declined significantly between the 2nd and 5th days of treatment. In surviving patients ($n = 30$) it reached the preoperative level after the fistula closure (Fig. 8). In 15 patients no improvement of plasma proteins was observed despite of human

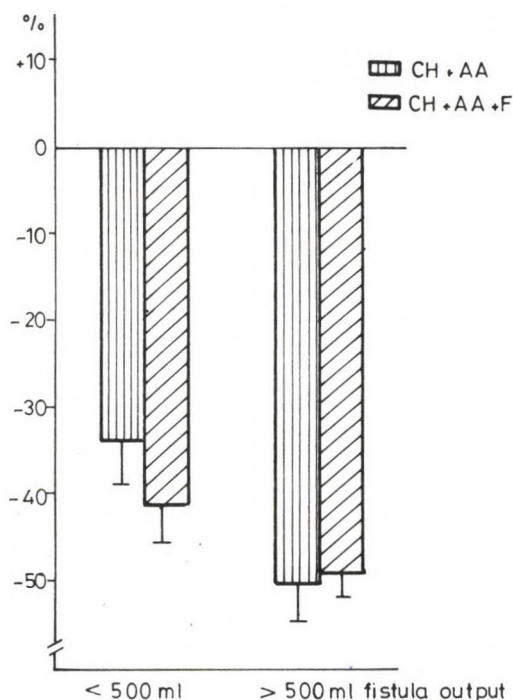


Fig. 3. Percentage changes in low- and high-output fistulas mean secretions on CH+AA versus CH+AA+F parenteral nutrition. (The fistula mean output of first week served as control)

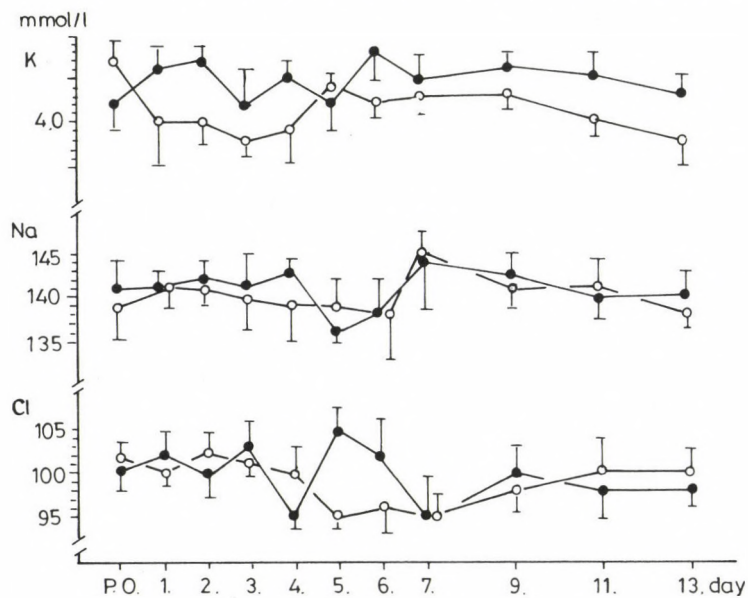
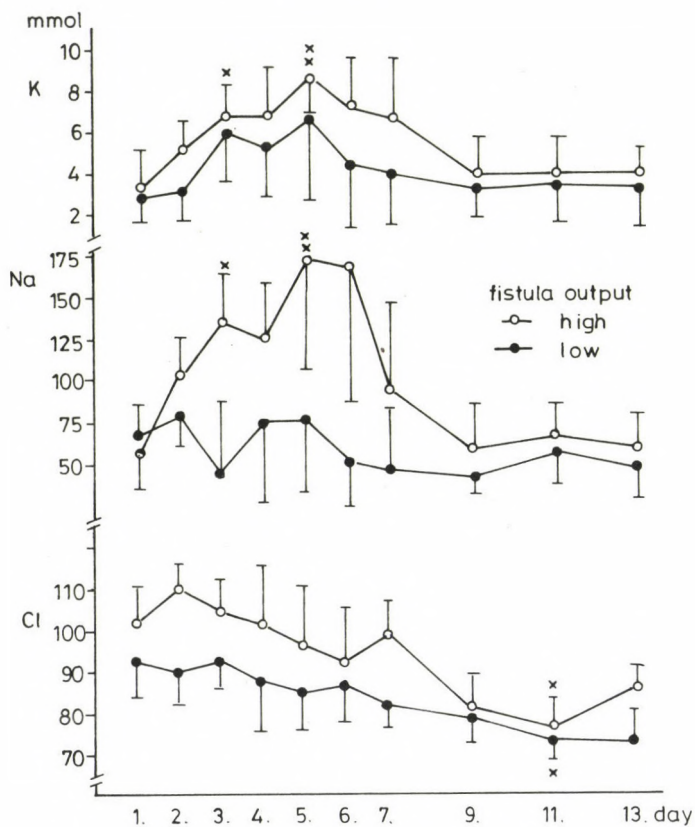
albumin or plasma supplementation even after the 20th day of the treatment (Fig. 9).

All patients lost body weight during the surgical complications and the fistula treatment. The mean rate of weight loss was: $19.5 \pm 8.5\%$.

Complications with parenteral and enteral nutrition

Percutaneous or surgical introduction of catheters into the superior vena cava can be considered a routine procedure during TPN. The need of central catheters is necessary because of the high concentration of nutritive solutions, the administration of other supplementary drugs and the better monitoring of circulatory functions in critically ill patients /38, 41/.

The technical complication rate is related to the experience of the physician inserting the catheter and increases when performed under



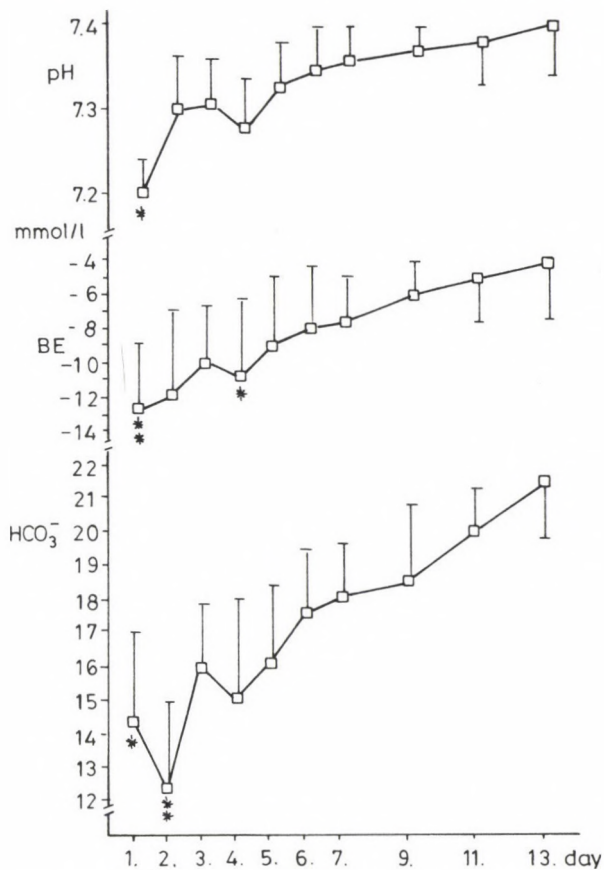
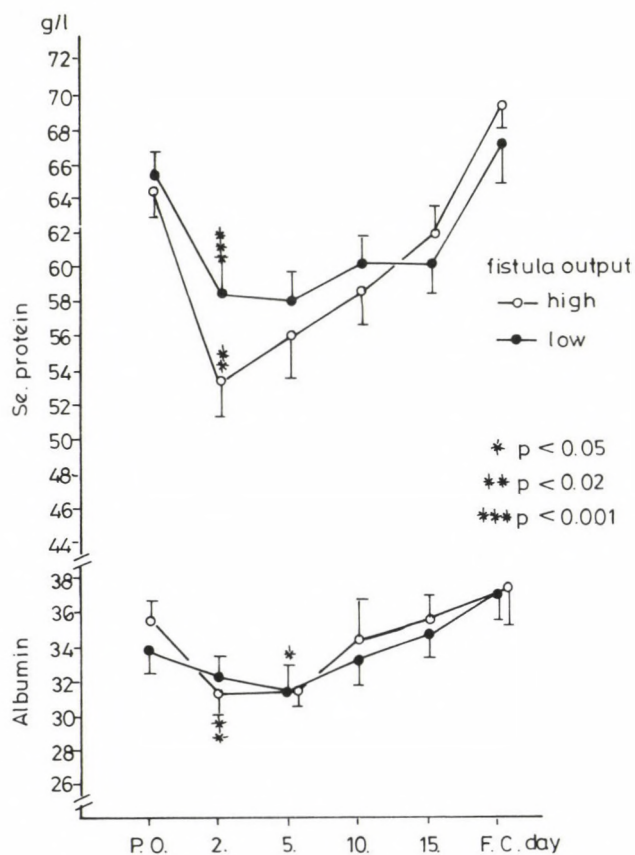
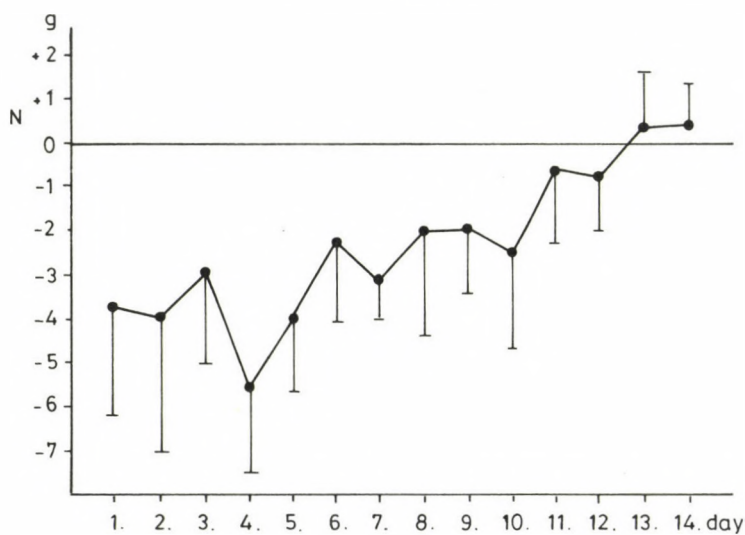


Fig. 6. The blood gas data of 14 patients with high output fistulas and the result of therapy with base (4.2% bicarbonate) replacement



Fig. 4. The daily electrolyte losses through the fistulas in 32 patients

Fig. 5. The changes in plasma electrolyte data during two weeks of TPN



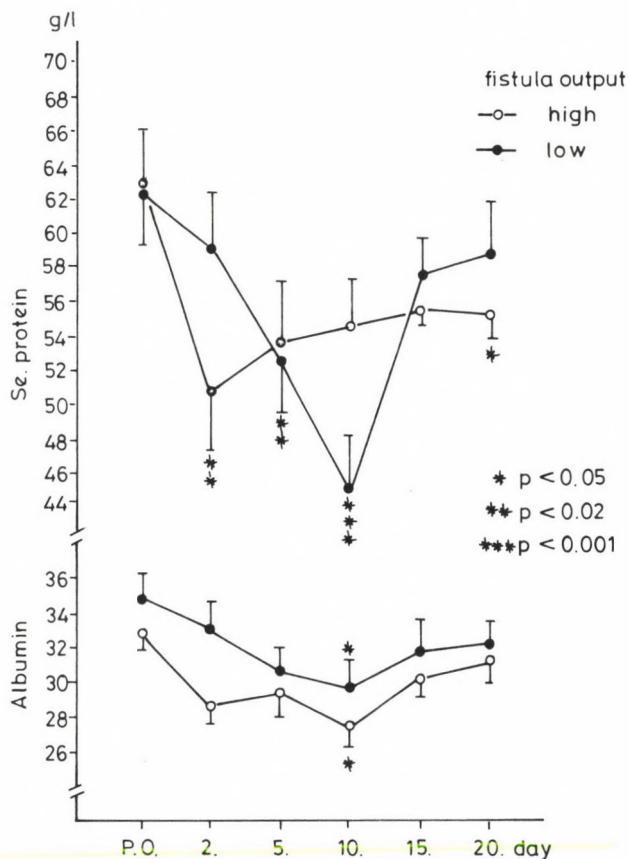


Fig. 9. Changes in plasma protein and albumin of non surviving patients up to 20th day of nutritional treatment

Fig. 7. Data of nitrogen-balance study in 20 surviving fistula patients

Fig. 8. Changes in plasma protein and albumin in early phase of treatment of surviving patients. (P.O. = preoperative; F.C. = fistula closure)

Table 2
Localization and methods of central vena catheterization

Localization of insertion	n	Method
Subclavian vein	20	percutaneous puncture
Right or left juglar vein	37	surgical preparation
Right or left vena basilica	18	surgical preparation
Total	75	

emergency conditions. Chest X-ray is essential after central vein catheterization to control the proper location of the catheter and to detect unsuspected complications such as: bleeding, pneumothorax, infusothorax, etc. /21/.

In the 45 TPN patients 75 central catheters were inserted and total or supplementary parenteral nutrition was administered lasting 1511 days altogether. The mean infusion duration reached 33.5 days per patients. The localization and method of central catheterization are presented in Table 2. X-ray control detected catheter tip location abnormality in 5 cases (axillary vewin: 1, external or internal jugular veins on the opposite sides: 3, kinkig catheter: 1). In 20 patients with percutaneous subclavian vein catheters a single case of pneumothorax and 2 cases of infusothorax were found. An appropriate treatment of the technical complications was initiated after detection.

Catheter contamination was related to the poor technique during insertion or removal or to the immigration of microorganisms along the catheter from the skin puncture site and the wound. Further contamination may have resulted from the presence of microorganisms in the nutritive solutions or administration sets, manipulations with the central catheters: monitoring of circulatory parameters, drug administration. Beside the antimicrobial therapy when unexplained fever and other septic symptoms occurred the central venous catheter was withdrawn and culture was taken from it. The positive culture result does not prove that the catheter is the source of infection because microorganisms may lodge on the catheter during a transient episode of bacteremia. Only when no other source of infection can be identified will the central line be designated as the origin of sepsis /6, 7, 41/.

Table 3
Distribution of contaminated central venous catheter tips

Pathogens	No. of positive cultures
Gram negative	
<i>Pseudomonas aeruginosa</i>	1
Gram positive	
<i>Staphylococcus aureus</i>	2
Mixed bacteria and fungi	
<i>Staph. aur.</i> + <i>Candida alb.</i>	1
<i>Enterococcus</i> + <i>E coli</i>	3
Total	7

Seven of 75 inserted central catheters were positive for pathogenic bacteria or fungi (Table 3). In 5 patients with operative wound and urine infection the same bacteria were identified in the haemoculture. In 2 cases the positive catheter tip culture was not accompanied by clinical signs of sepsis.

The frequency of minor catheter related thrombosis occurred in 10 cases in this study. In one patient superior caval vein thrombosis was diagnosed. After removal of the central catheter and anticoagulant therapy the patient recovered.

The metabolic complications of TPN are common during enteric fistula treatment. Elevated blood glucose levels, glucosuria are the symptoms of hypercatabolic metabolism and limited tolerance of glucose /3, 39/. In 36 patients Insulin supplementation was needed during TPN. One diabetic patient died in consequence of septic complications and metabolic disorders. At autopsy fatty liver degeneration was found in 10 cases, the liver damage was detected clinically by jaundice and elevated enzyme data only in 4 cases. No adverse effects of fat administration was detected.

Tube feeding had well-defined indications when bowel motility could be proved /16, 42/. The EN started with incremental doses of enteral nutrients and reached the daily intake of 2000 ml. In 5 of 15 patients diarrhoea was observed. With proportional feeding and administration of Lactobact^R (Human) and Reasec^R (G. Richter) solutions the diarrhoea could be controlled when the fistula secretion increased readministration of TPN was necessary.

Discussion

In the 1960s the conservative and surgical treatment of enterocutaneous small bowel fistulas was associated with a mortality rate of 50% /17, 45/. Deaths were attributed to fluid and electrolyte imbalance, infections and malnutrition. The development of improved broad-spectrum antibiotics resulted in decreased mortality and morbidity, but postoperative enterocutaneous small bowel fistulas still represented a significant risk for the patients /34, 35/. However, the recent addition of TPN and/or EN to the management of enteric fistulas has substantially decreased the mortality rate /10, 11, 40/. Several factors are responsible for this improvement. After the development of a postoperative fistula fluid is replaced intravenously and oral intake is eliminated, thus decreasing intestinal secretion and reducing fluid and electrolyte loss through the fistula /46/.

The results of our clinical study demonstrate that TPN, elimination of oral intake decreased the enterocutaneous fistula secretion significantly. The high-output fistulas changed their characters and they could be controlled by the end of two weeks of treatment.

Human and animal studies indicate the intravenous nutrients have direct effects on gastro-entero-pancreatic enzyme secretion /8, 9, 13, 23, 47, 48/. The data of Isenberg and Maxwell demonstrated stimulation of gastric acid secretion in man during amino acid infusion with or without glucose that could be inhibited by infusion of fat emulsion /26, 47/.

The effect of different intravenous nutrients on pancreatic exocrine secretion are contradictory /23, 29, 31/. The recent data of animal experiments and clinical observations have proved that neither amino acids nor fat emulsion had secretagogue effect on the exocrine pancreas /13, 29, 46/.

In comparison of two parenteral regimens (CH+AA versus CH+AA+F) on fistula output we could not find any significant difference. The secretory data emphasize the important role of TPN in reduction of fluid and electrolyte loss that makes the proper fluid and electrolyte replacement and correction of acid-base disturbances possible.

The efficacy of nutritional therapy on malnutrition seemed to be very difficult to assess in the early phase of fistula treatment /4, 37/. TPN and EN are very effective in the treatment of malnutrition when no uncontrolled sepsis coexists /45/. Sepsis cannot be treated by nutritional

therapy alone without effective surgical drainage. As long as uncontrolled sepsis persists, the patient's condition deteriorates.

The nitrogen balance study proved to be relatively sensitive estimating the metabolic changes /5, 32/. Positive nitrogen balance could be only achieved when the septic foci were eliminated.

The changes in serum protein and albumin level and the response of these parameters to nutritional support have both been proposed to be used as prognostic indicators of the morbidity and mortality. Hypoproteinemia and hypalbuminemia are often associated with impaired wound healing, decreased resistance to infections and total body water imbalance /36/. Because endogenous protein and albumin synthesis require the provision of adequate substrates over an extended period of time and intact liver function, the repair of the deficit by the administration of exogenous protein and albumin in selected cases has been recommended /25/. Then the serum level can be maintained with adequate nutritional support /4, 18/.

In 30 surviving patients the serum protein and albumin level reached the preoperative level by the fistula closure. In non surviving patients with different septic complications the improvement in serum proteins was not observed despite of exogenous protein and albumin supplementation.

The use of TPN and EN as supportive treatment of enterocutaneous fistulas has certain advantages in increasing the survival rate of septic hypercatabolic patients. However, central venous catheters and continuous infusion of hyperosmolar nutritive solutions involve the possibility of superinfection and metabolic disorders /10, 43/. The enteral feeding has advantages in comparison to TPN with respect to infectious and metabolic complications, but in fistula treatment the administration of EN is limited by the localization of the fistula, the prevailing surgical abdominal complications and the intolerance to the diets /11/. These patients require TPN. In the early period of fistula treatment the TPN proved to be the only suitable method for controlling the fistula output and to replace the fluid and electrolyte loss.

The management of enterocutaneous fistulas is still a challenging task in postoperative intensive therapy. There is no doubt that parenteral and enteral nutrition represent a powerful tool for maintaining nutritional integrity of the patients. When no sepsis is present, the parenteral and enteral nutrition combined with proper diagnosis and intensive care offers promising chances for spontaneous healing of enteric fistulas or may improve the operative results after a course of nutritive support.

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References

1. Aguirre A, Fischer JE: Intestinal fistulas. In: Total Parenteral Nutrition. Ed. Fischer JE, Little, Brown, Boston 1976, p 203
2. Alánt OI, Weltner J: Amino acids in continuous mixing system for total parenteral nutrition. Clin.Nutr. 1: Suppl. p 16, 1982
3. Allison SP: Insulin and carbohydrates in parenteral feeding. In Wilkinson J.: Parenteral nutrition. Churchill-Livinstone, London 1972, p 275
4. Apelgren KN, Wilmore DW: Nutritional care of the critically ill patients. Surg. Clin. North Am. 63:497, 1983
5. Bagényi J, Horváth M, Imre J, Petri G, Gaál T: A N-mérleg vizsgálatának jelentősége a műtét utáni szövődményekben. (The importance of nitrogenbalance studies in evaluation of postoperative complications.) Magy. Sebészet 24:391, 1971
6. Bismar B, Hardstedt C, Malmberg A: Bacteriology and phlebography in catheterization for parentral nutrition. Acta Chir Scand 146:115, 1980
7. Bozzetti F, Regalia E, Pinardi L, Terno G: Central venous catheter sepsis: Prognosis and treatment. Clin Nutr 5:113, 1986
8. Dárdai E, Heavner JE: Effect of TPN on gastrointestinal secretion in rats. Clin Nutr 5: Suppl. 111, 1986
9. Dárdai E, Heavner JE: Effect of parenteral nutrients on enterocutaneous fistula output in rats. Clin Nutr 6: Suppl. 72, 1987
10. Dárdai E, Erdős, L, Stefanics J: Vollständige parenterale Ernährung bei Patienten mit enterokutaner Darmfistel. Zbl Chir 108:77, 1983
11. Dárdai E, Szabó J: Parenterale oder enterale Ernährung in der Behandlung der postoperativen enterokutanen Dünn darmfisteln? Infusionstherapie 17: Suppl. 9, 1990
12. Dárdai E: Indirect calorimetry methods for determination of energy expenditure. Acta Chir Hung 31:47 1990
13. Dárdai E, Heavner JE: Effect of intravenous nutrients on upper gastrointestinal secretion in rats. Acta Chir Hung (in press)
14. Deitel M: Nutritional management of external gastrointestinal fistulas. Acta Chir Scand Suppl 494:154, 1979
15. Deitel M: Management of gastrointestinal fistulas. In Deitel M: Nutrition in clinical Surgery. Williams-Wikins, Baltimore 1980, p 173
16. Dietze G: Fehler und Gefahren der enteralen und parenteralen Ernährung. Chirurg 54:18, 1983
17. Edmunds HL, Williams GM, Welch CE: External fistulas arising from the gastro-intestinal tract. Ann Surg 152:445, 1960
18. Elwyn DH: Nutritional requirement of adult surgical patients. Crit Care Med 8:9, 1980
19. Fischer JE: The pathology of enterocutaneous fistulas. World J Surg 7:446, 1983
20. Goodgame JT: A critical assessment of the indications for total parenteral nutrition. Surg Gyn Obst 151:433, 1980
21. Grant JP: Handbook of total parenteral nutrition. Sanders, Philadelphia 1980
22. Gross E, Irving M: Protection of the skin around intestinal fistulas. Brit J Surg 64:258, 1977
23. Hamilton RF, Davis WC, Stephenson DV, Magee DF: Effects of parenteral hyperalimentation on upper gastrointestinal tract secretions. Arch Surg 102:348, 1971
24. Hardy JD: High-output gastrointestinal fistula. In Hardy JD: Critical Surgical Illness. Sanders, Philadelphia 1971

25. Irving M: Local and surgical management of enterocutaneous fistulas. *Brit J Surg* 64:690, 1977
26. Isenberg JI, Maxwell V. Intravenous infusion of amino acids stimulates gastric acid secretion in man. *New Engl J Med* 298:27, 1978
27. Kelemen E: A fehérje szerepe a parenterális táplálásban. (The role of proteins in parenteral nutrition.) *Mesterséges Táplálás Symposium 1964. Országos Traumatológiai Intézet Kiadványa, Budapest 1965*
28. Kiss L, Stefanics J: Stomahesive anus praternaturalis záróval szerzett tapasztalatok. (Clinical experiences with Stomahesive.) *Magy. Sebészet* 34:46, 1981
29. Klein E, Shneebaum S, Ben-Ari G, Dreiling DA: Effect of total parenteral nutrition on exocrine pancreatic secretion. *Am J Gastroenterol* 78:31, 1983
30. Knighton DR, Burns K, Nyhus LM: The use of Stomahesive in the care of the skin of enterocutaneous fistulas. *Surg Gyn Obstet* 143:449, 1976
31. Konturek SJ, Tasler J, Cieszkowski M, Javorek J: Intravenous amino acids and fat stimulate pancreatic secretion. *Am J Physiol* 236:E678, 1979
32. Loirat P, Roham JE, Chapman A, Peaufils F, David R, Nedey YR: Positive nitrogen balance in hypermetabolic states: Results obtained with parenteral feeding after major surgical procedures. *Europ J Intensive Care Med* 1:11, 1975
33. Lon CL, Schaffel N, Geiger JW, Schiller WR, Blakemore WS: Metabolic response to injury and illness: estimation of energy and protein needs from indirect calorimetry and nitrogen balance. *JPEN* 3:452, 1979
34. MacFadyen BW, Dudrich SJ, Ruberg LR: Management of gastrointestinal fistulas with parenteral hyperalimentation. *Surgery* 74:100, 1973
35. Monod-Broca P: Treatment of intestinal fistulas. *Brit J Surg* 64:685, 1977
36. Mullen JL: Consequence of malnutrition in the surgical patient. *Surg Clin North Am* 61:465, 1981
37. Mullen JL, Buzby GP, Wladman MT, Gertner MH, Hobbs CL, Rosato EF: Prediction of operative morbidity and mortality by preoperative nutritional assessment. *Surg Forum* 30:80, 1979
38. Padberg FT, Ruggiero J, Blackburn GL, Bistrian BR: Central venous catheterization for parenteral nutrition. *Ann Surg* 193:264, 1981
39. Robin AP, Carpentier, YA, Askanazi J, Nordenström J, Kinney JM: Metabolic consequences of hypercaloric glucose infusions. A review. *Acta Chir Belg* 80:133, 1981
40. Rombeau JL, Rolandelli RH: Enteral and parenteral nutrition in patients with enteric fistulas and short bowel syndrome. *Surg Clin North Am* 67:551, 1987
41. Ryan JA, Abel RM, Abbott WM, Hopkins CC, Chesney TM, Colley R, Phillips K, Fischer JE: Catheter complications in total parenteral nutrition. A prospective study of 200 consecutive patients. *New Engl J Med* 290:757, 1974
42. Schmoz G, Wilde J, Hartig W, Weiner R, Reimann S: Die Katheterjejunostomie - ein Beitrag zur künstlichen enteralen Ernährung in der Chirurgie. *Zbl Chir* 109:192, 1984
43. Sitges-Serra A, Jaurrieta E, Sitges-Creus A: Management of postoperative enterocutaneous fistulas: the role of parenteral nutrition and surgery. *Brit J Surg* 69:147, 1982
44. Soeters PB: Parenteral nutrition and gastro-intestinal fistulas. In Greep JM, Soeters PB, Westdorp RIC, Phaf CWR, Fischer JE: *Current Concept in Parenteral Nutrition*. Nijhoff, The Hague 1977, p 99
45. Soeters PB, Ebeid AM, Fischer JE: Review of 404 patients with gastrointestinal fistulas. Impact of parenteral nutrition. *Ann Surg* 190: 189, 1979
46. Towne JB, Hamilton RF, Stephenson DV: Mechanism of hyperalimentation in the suppression of upper gastrointestinal secretion. *Am J Surg* 126:714, 1973
47. Varner HA, Stenberg, JI, Elashoff JD, Lamers CBH, Maxwell V, Shulkes AS: Effect of intravenous lipid on gastric acid secretion stimulated by intravenous amino acids. *Gastroenterol* 79:873, 1980
48. Wolfe BM, Keltner RM, Willman VL: Intestinal fistula output in regular, elemental and intravenous alimentation. *Am J Surg* 124: 803, 1972

PARENTERAL AND ENTERAL NUTRITION AND THE ENTEROCUTANEOUS
FISTULA TREATMENT II
FACTORS INFLUENCING THE OUTCOME OF TREATMENT*

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An 18-year review of 64 patients treated with 71 postoperative enterocutaneous fistulas of the stomach /4/, duodenum /21/, jejunum /9/ and ileum /37/ was carried out to identify the factors affecting morbidity and mortality. Age, localization, output, inflammatory or malignant bowel disease, nutritional status and associated sepsis were analysed.

The administration of total parenteral nutrition (TPN) or/and enteral nutrition (EN) as adjuvant therapy in the management of gastrointestinal fistulas increased the fistula closure rate (64%) and decreased mortality (33%). In patients over 65 years a rise in mortality rate (69%) was found. TPN and EN support yielded the best results in duodenal and jejunal fistula patients (closure rate 83% and 71%, respectively). In patients with high-output fistulas, inflammatory bowel disease and malignancy good results could be achieved with nutritional treatment. The presence of malnutrition had an adverse effect on the outcome in the non-TPN group with a mortality rate of 49%. In 43 patients severe septic complications occurred and 21 died due to septic multiple organ failure proved by autopsy. The overall mortality rate was 39%.

Timing of fistula surgery had little impact on the fistula closure rate, but better results were obtained when reconstructive surgery was deferred beyond 6 weeks from fistula onset. Mortality has decreased since 1980.

While many factors influence the outcome of fistula disease, adequate antiseptic treatment is assumed of primary importance.

The nutritional therapy facilitated the spontaneous fistula healing and allowed the elective intestinal reconstruction to be scheduled at an optimal time.

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Introduction

Most enterocutaneous fistulas arise postoperatively as complications of a surgical procedure in which the surgeon has encountered extensive adhesions, inflammatory bowel disease, malignant tumour or radiation injury to the intestine. Fluid therapy, antibiotics, surgical drainage and skin protection have become an essential part of the fistulous patient's treatment. Several authors have recognized that undernutrition is a bad prognostic factor /12, 15, 19, 23, 29, 37, 39/.

Before the widespread availability of safe parenteral and enteral nutrition, attempts of early surgical fistula closure were usual, but the results were dismal. Fistula recurrence with fluid, electrolyte and acid-base imbalance often occurred; sepsis and marked wasting resulted in a high mortality rate /2, 5, 8, 14, 24/.

The value of parenteral and enteral nutrition in the treatment of enterocutaneous fistulas has been emphasized. A marked decrease in mortality and an improvement in spontaneous fistula closure rate were demonstrated /3, 13, 16, 20, 23, 29, 33, 40, 43, 44/.

Our experience with 45 patients with postoperative gastrointestinal fistulas who received total parenteral or enteral nutrition (TPN and EN group) as a part of their therapy is reviewed. These results have been compared with those obtained from 19 patients treated without nutritional support (non-TPN group) at the same institution either at the same time or prior to the introduction of parenteral nutrition.

Patients and Methods

Sixty-four patients (40 men and 24 women, between 15 and 82 years) with 4 gastric, 21 duodenal, 9 jejunal and 37 ileal fistulas were treated in our department from 1971 to 1988. Aetiological factors of postoperative fistulas are summarized in Table 1. In 45 cases (63.3%) enterotomy or anastomotic suture line failure occurred. Twelve fistulas were caused by direct surgical injury or drain decubitus. The majority of fistulas developed between the 6th and the 15th postoperative days (Table 2). All enterocutaneous fistulas were documented by phystulography, intraluminal dye or contrast studies and/or chemical analysis of the fistula secretion (electrolyte, pH, bilirubin and amylase level). Certain principles of

Table 1
Aetiology of postoperative enterocutaneous fistulas

	No. of fistulas	%
Suture line leakage	45	63.3
Surgical injury	7	9.9
Disruption of abdominal wall	8	11.3
Drain decubitus	5	7.0
Recurrent fistula	6	8.5
Total	71	100.0

Table 2
Development of enteric fistulas in the postoperative period

Postoperative days	No. of fistulas	%
0 - 5	15	21.1
6 -15	34	47.9
16 -30	12	16.9
-30	10	14.1
Total	71	100.0

Table 3
Results of operative treatment of postoperative fistulas

Operations	No.	Closure	Fistula recurrency	Mortality
Primary suture	3	2	1	0/3
Resection and anastomosis	9	5	2	2/9
Exteriorisation of fistula	2	0	1	1/2
Total	14	7	4	3/14

early fistula management were common in both groups of patients. The patients received nothing orally, appropriate nasogastric suction was instituted and fluid and electrolyte imbalances were corrected. The daily energy intake of 19 patients (non-TPN group) was less than 4000 kJ. In this group the surgical fistula closure was attempted rather early. Since the institution of parenteral and enteral nutrition early surgical inter-

vention for closing the fistulas has been rare and was delayed until the fistula had been persisting for four to six weeks.

During the fistula management the patients required surgical interventions for control of sepsis as well which allowed the spontaneous or definitive surgical closure of fistula. The different surgical methods for closing the enterocutaneous fistula, the results of the operations and the mortality due to surgery are shown in Table 3. Seven fistulas were closed by surgery, the remaining unsuccessful surgical attempts were due to untreated sepsis and malnutrition.

Results

Table 4 shows the final outcome of fistula treatment in the 64 patients. In the TPN and EN group 24 fistulas closed spontaneously, 29 patients left the hospital with cured fistula (64%). In the non-TPN group only 3 spontaneous fistula closures were achieved, 2 fistulas were closed by surgery, in 4 patients the low-output fistula persisted. Marked difference was observed between the mortality rate (33% versus 53%) of the two groups.

A higher mortality rate and decreasing healing tendency were associated with age over 65 years (Table 5).

Table 4
Results of treatment in 64 patients with 71 postoperative
enterocutaneous fistulas (1971-1988)

	F/Pts	Fistula spontaneous closure	Permanent fistulas	Healed Pts	Mortality
TPN and EN	48/45	24 (50%)	1	29 (64%)	15 (33%)
non-TPN	23/19	3 (13%)	4	5 (26%)	10 (53%)
Total	71/64	27 (38%)	5	34 (53%)	25 (39%)

(F = fistula; Pts = patients)

Table 5
Influence of age on results of fistula treatment

Age (yr)	No.	TPN and EN		Non-TPN	
		Survived + cured pts	Deaths	Survived + cured pts	Deaths
65	45	25	8	8	4
65	19	5	7	1	6

(yr = year)

Table 6
Localization of fistulas and effect of nutritional therapy
on outcome of fistula treatment

Loca- lization	F/Pts	TPN and EN		F/Pts	Non-TPN	
		Closed fistula	Deaths		Closed fistula	Deaths
Stomach	2/2	1	1	2/2	0	2
Duodenum	18/18	15	3	3/3	1	2
Jejunum	7/7	5	2	2/2	1	1
Ileum	21/18	8	9	16/12	3	5
Total	48/45	29	15	23/19	5	10

Table 7
Effects of diseased alimentary tract on outcome of fistula treatment

	No. of pts	Closed fistulas	TPN and EN Permanent fistulas	Mortality
Crohn's disease	5	4	-	1/5
Carcinoma	14	9	-	5/14
non-TPN				
Crohn's disease	3	-	3	-
Carcinoma	9	-	1	8/9

Table 8
Closure rate and mortality rate related to fistula output

TPN and EN			
Output	Fistula	Closure rate	Mortality
500 ml		18/27	6/24
500 ml		11/21	9/21
Total		29/48	15/45
non-TPN			
500 ml		5/22	9/18
500 ml		0/1	1/1
Total		5/23	10/19

Table 9
Malnutrition and the results of fistula treatment

non-TPN group (n = 19 pts)			
Nutritional status	No. of pts	Survival + fistula closure	Mortality
Normal	6	5/6	1/6
Malnutrition	13	4/13	9/13
TPN and EN group (n = 45 pts)			
Normal	21	15/21	6/21
Malnutrition	24	15/24	9/24

The ileum and the duodenum were the most common sites of origin for the postoperative fistula development. With nutritional support and surgical treatment the best results could be obtained in the duodenal (15 of 18 fistulas closed) and jejunal fistula management (5 of 7 fistulas closed) (Table 6). Healing tendency was lower and mortality was higher of ileal fistulas in both groups. These unfavorable results were attributed to Crohn's disease (8 patients) and cancer (21 patients).

The beneficial effect of nutritional therapy on Crohn's fistula is

evident as seen in Table 7. Patients operated because of malignant tumours with preexisting nutritional disturbances are known to have poor prognosis in outcome if a major surgical complication occurs. These patients with enteric fistulas had no chance for survival without intensive nutritional support.

Fistula output had a strong impact on mortality rate (Table 8). According to our experience mortality rate was higher when comparing high-output to low-output fistulas. The increased fistula closure rate in the TPN and EN group may be explained by the decreasing secretory activity of the gut due to parenteral nutrition.

In of malnutrition (loss of body weight > 15%), anaemia (haemoglobin < 10 g/100 ml), hypoproteinaemia (Se. protein < 60 g/l) or hypalbuminaemia (Se. albumin < 35 g/l) the mortality rate was greatly increased in the non-TPN group (Table 9). Nearly equal survival and decreased mortality rates were achieved by nutritional therapy in previously malnourished patients in comparison to patients without nutritional disorders.

The existence of intraperitoneal infection was the factor that had the worst effect on the prognosis. Several forms of intraperitoneal infection were observed. Sometimes peritonitis developed together with early postoperative fistulas or at a later stage, perifistulous aggregates may have suppurated. In certain cases the septic focus was difficult to detect despite of modern diagnostic methods (such as ultrasound, computerized tomography, isotopic scans, etc.). Multiple organ failure developed due to bacteremia and endotoxemia. In non-TPN group 2 patients had severe atelectasia and bronchopneumonia. Ten patients died because of autopsy proved septic multiple organ failure (Table 10). In the TPN and EN group septic organ failure occurred in 31 patients. Four of 20 patients died due to pulmonary, cardiac and gastrointestinal septic complications. In 11 cases death could be related to uncontrolled sepsis and multiple organ failure (Table 11).

Table 12 presents the results and the way they changed the fistula treatment, observed during the 18-year period covered by this study. From 1971 to 1979 patients were cared for mainly by their own surgeon and treated at the surgical ward. These included the non-TPN group as well. Since 1980 the responsibility of fistula management has been in the hands of Intensive Care Unit staff as well as in the surgeon's. In the last years more experience has accumulated in the recognition and management of enterocutaneous fistulas that resulted in increased survival rate (76%) and decreased mortality rate (24%).

Table 10

Sepsis related complications and mortality in the non-TPN group of patients

In 2 patients non lethal pulmonary complications occurred						
Septic multiple organ failures						
No. of deaths	Pulmonary	Manifestation of damage				
		Cardiac	Renal	Hepatic	Gastrointestinal	Blood coagul.
1	+			+		
3	+*	+				
2	+		+			
2	+					+
1		+				
1		+	+			
10	(* = acute pancreatitis; * = septic endocarditis)					

Table 11

Sepsis related complications and mortality in the TPN and EN group of patients

Diagnosis	No. of pts					Deaths
Atelectasia						
Pneumonia		11				1
ARDS		2				1
Myocardial infarction		1				1
Gastric bleeding		5				1
Pulmonary embolism		1				-
Total		20				4
Septic multiple organ failures						
No. of deaths	Pulmonary	Manifestation of damage				
		Cardiac	Renal	Hepatic	Gastrointestinal	Blood coagul.
1	+		+		+	
3	+*	+	+			+
1	+*			+		
1	+*				+	
1	+					+
2	+	+			+	
2	+		+	+		
11	(* = Adult respiratory distress syndrom (ARDS))					

Table 12
Change in results of postoperative enterocutaneous fistula treatment
(2 time periods)

Years	Healing rate	Permanent fistulas	Mortality
1971-1979	15/39	5	19/39
1980-1988	19/25	0	6/25

Discussion

Surveying the literature of the last 15 years shows that the frequency rate of postoperative enterocutaneous fistulas following laparotomy has been changing between 0.5% and 5.6% (Table 13) /5, 8, 25/. The Hungarian reports focused on the surgical attempts to close the enteric fistula, only a few papers were published on the benefit of early fistula secretion control and nutritional support /7, 11, 18, 26, 32, 41/. Parenteral nutrition was proved to reduce the volume of gastro-entero-pancreatic secretion in animal experiments and in clinical studies. Parenteral nutrition made the patients' nutrition easier and more effective and it became routinely used in all cases of enteric fistula.

Table 13
Frequency rate of gastroenterocutaneous fistula development
related to laparatomies

Chevrier et al. (1968)	1.5%
Bouré et al. (1971)	3.0%
Hollender et al. (1974)	0.5%
Dárdai et al. (1988)	5.6%

However, it also became evident that some fistulas closed spontaneously after bowel rest and intravenous feeding, while others were associated with severe intraabdominal infections. This dilemma was also reflected in early papers dealing with the parenteral nutrition treatment of fistulas /2, 3, 6, 12, 23, 38/. Some surgeons pinned their faith on nutritional management /14, 16, 23, 34, 36, 39, 40/, while others still preferred early surgery for most upper gastrointestinal high-output fistulas /24, 31, 35/.

The work by Kaminsky and Deitel underlined the relevance of proper nutritional therapy which in their hands lowered the mortality of enteric fistulas from 40% to 12.5% and increased the spontaneous closure rate from 34.4% to 80% /29, 38/. This paper failed to compare similar series, but stressed the point that homogeneity between series would be desirable if true benefit from nutrition regimens was to be assessed objectively. In our study the comparison of a prospective assessment with a retrospective one may involve similar difficulties. In our case there was a similarity between the groups with respect to the type of fistula, disease process, surgical therapy and intensive care. The patients and the method of selection was similar to those reported elsewhere /24, 30, 43/.

The important findings in the present study was that the results of treatment with nutritional regimen showed a higher rate of spontaneous fistula closure (50%) when comparing with the non-TPN group (13%). Marked improvement has been observed in the mortality rate (33% versus 53%). If we compare our data with the chronologically parallel series the results are found to coincide very closely /2, 3, 6, 13, 14, 15, 23, 33, 34, 42/. We have also noted a significant improvement in fistula healing (76%) and a decline in mortality rate (24%) in the last 9 years.

A postoperative enteric fistula involves grave consequences and these consequences are to be reduced still further. A better definition of factors affecting prognosis seems to be necessary in order to evaluate the therapeutic measures.

Among factors that are believed to have a determining effect on prognosis seems to be necessary in order to evaluate the therapeutic measures.

Among factors that are believed to have a determining effect on prognosis the following are to mention: age, localization and output of fistula, disease of the fistulized alimentary tract, malnutrition and existence of different septic complications.

Age appears to make the prognosis less favorable. Lévy et al. observed significant increase in mortality over the age of 50 ($p < 0.01$) /30/. Hollender et al. reported a 76% mortality rate for patients over 70 years as compared with an overall mortality rate of 48% /24/. In our series the overall mortality rate over the age of 65 reached 69% as compared with the younger age of fistula patients (27%).

There is some evidence that proximal localization of the fistula means an aggravating factor. Gastro-oesophageal anastomosis fistulas are characterized by high mortality. The conservative treatment: parenteral

and/or enteral nutrition, suture line drainage and control of infection offer good clinical results /28, 36, 44/. We had only a single surviving patient treated with the regimen mentioned. The gastro-oesophago-pleural fistula closed spontaneously after 114 days of treatment /10/.

In duodenal and jejunal fistula treatment the mortality rate of our non-TPN group was as high as reported in the literature before the nutrition era /6, 12, 26, 40, 41/. The increased number of spontaneous fistula closure appeared only in patients with nutritional support /14, 16, 20, 31, 33, 35, 38, 42/. Recently, the thin catheter jejunostomy feeding has proved to be advantageous in the fistula management of the upper alimentary tract /4, 9, 19, 29, 44/.

Inflammatory and malignant diseases of the gastrointestinal tract involve a higher coincidence of postoperative fistula development and lead an unfavorable prognosis for fistula treatment /1, 3, 21, 27, 37/. The use of nutritional therapy as a supportive agent in patients with Crohn's disease improved healing tendency. It was obviously important to support malnourished patients who were undergoing resection for carcinoma and also in fistula management if developed postoperatively. If a neoplasm involved the fistula tract particularly after incomplete resection of stomach or colon cancer, closure was not obtained in patients on nutrition therapy /40, 43/. Our high mortality rate in ileal fistulas could be related to the great number of ileocolic anastomosis insufficiencies after colon cancer resection.

The voluminous fistula secretion was regarded as a determining factor in the early treatment of enterocutaneous fistulas. Electrolyte disturbances, nutritional insufficiency and sepsis stimulated the surgeons to close the fistula as early as possible /12, 17, 22, 23/. On the basis of the rather poor results the advantages of better patient monitoring including correction of electrolyte disturbances and volume replacement were realized. The elimination of oral intake and total parenteral nutrition reduced the fistula output. This made the timing of operation for fistula cure possible.

Undrained abscesses, peritonitis, haemorrhage or bowel obstruction required urgent surgery independent of what period of time has elapsed since the fistula developed. For less urgent situations in which sepsis was controlled we preferred deferring the fistula operation 6 weeks, then intra-abdominal conditions were likely to allow safe definitive surgery. During this time the nutritional therapy could be particularly efficacious in maintaining the patient's nutritional state.

Malnutrition leads to high incidence of suture line insufficiency. The development of postoperative fistula makes the patient's condition worse. There are identifiable sources of malnutrition in enteric fistulas such as the lack of proper food intake, the hypercatabolism because of the associated sepsis and loss of protein-rich energy requiring secretion from the fistula. Bowel rest and parenteral nutrition decrease the fistula output. However, the energy expenditure of fistula patients are highly dependent on the elimination of septic foci. This fact underlines the need of adequate surgical drainage during the course of conservative management. After obtaining appropriate cultures, antibiotics with a spectrum also covering aerobic and anaerobic gram-negative bacilli are used in persisting sepsis. The nutritive solutions and sets used for parenteral nutrition can be regarded as additional sources of infection. When detecting clinical symptoms of sepsis without any other evidence, these sources should be taken into consideration. There is no doubt that enteral nutrition may be equally effective in specific situations with a lower complication rate.

However, malnutrition in the presence of uncontrolled sepsis cannot be treated by nutritional regimen without effective surgical drainage otherwise multiple organ failure develops and death ensue.

When compared with the data referred in the literature, our experience confirms that the application of a comprehensive treatment program which includes early introduction of nutritional support results in an improvement in morbidity and mortality as well as the spontaneous closure rate of enterocutaneous fistulas of the gastrointestinal tract. Uncontrolled sepsis proved to be the one major determinant of unfavorable outcome of fistula treatment.

References

1. Alexander Williams J: Surgical management of fistulae in Crohn's disease. Symposium on Present Management of Ulcerative and Crohn's Colitis. Rotterdam, 1982
2. Ali SD, Lefall LD: Management of external fistulas of the gastrointestinal tract. *Am J Surg* 123:535, 1972
3. Allan R: Treatment of fistula by parenteral nutrition. *Gastroenterology* 80:215, 1981
4. Bodoky Gy, Harsányi L: Korai posztoperatív tű-katéterjejunosztómia táplálással szerzett tapasztalatok. (Experiences with needle-katheter jejunostomy feeding in the early post-operative period.) *Orv. Hetil.* 127:2251, 1986
5. Boure J, Asshdouria R, Randrianonimandimby J, Lamy J: Les fistules digestives externes post-operatoires. Consideration étiopathogénique et clinique (a propos de 40 observations). *Ann Chir* 25:25, 1971
6. Brown RR, Speir RC, Trenton JW: Duodenal fistula. *Ann Surg* 132:913, 1950

7. Bucšina O, Kolb J: Többszörös gyomor-bélsipoly sikeres zárása a negyvenkilencedik hasi műtét után. (Successful closure of multiple gastrointestinal fistula after 49th abdominal surgery.) *Magyar Sebészet* 24:302, 1971
8. Chevrier JL, Despretz R, Bonzet P, Mailleux M: Les fistules postopératoire de l'intestine grêle. *Mém Acad Chir* 94:160, 1968
9. Dárdai E, Bite Á: Behandlung der enterokutanen Dünndarmfisteln mit Hilfe der parenteralen Ernährungstherapie. *Deutsche Zeitschr. Verdauungs- Stoffwechselkrankh.* 44:149, 1984
10. Dárdai E, Szabó K: A mesterséges táplálás jelentősége a nyelőcsőperforatio postoperatív kezelésében. (Importance of artificial nutrition in postoperative treatment of perforated oesophagus.) *Anaesth Intensiv Ther* 7:49, 1977
11. Dubecz S, Bárdosi Z: Gyomor resectiot követő idült külső duodenális sipoly kezelése. (Treatment of chronic external duodenal fistula following gastric resection.) *Magyar Sebészet* 28:372, 1975
12. Edmunds HL, Williams GM, Welch CE: External fistulas arising from the gastro-intestinal tract. *Ann Surg* 152:445, 1960
13. Fazio VW, Coutsoftides T, Steiger E: Factors influencing the outcome of treatment of small bowel cutaneous fistula. *World J Surg* 7:481, 1983
14. Freund H, Anner C, Salz NJ: Management of gastrointestinal fistulas with total parenteral nutrition. *Surgery* 61:273, 1976
15. Fujita H, Shoji M, Noto H, Ueda H, Kusajima Y, Sabe Y, Miyazaki I: Management of post-operative gastrointestinal fistula. *World J Surg* 5:743, 1981
16. Garden OJ: Surgical and nutritional management of postoperative duodenal fistulas. *Dig Dis Sci* 33:30, 1988
17. Gülzow M, Koelsch KA, Kuntzen H: *Gastroenterologie*. Fischer, Jena 1969
18. Haas P, Rónai J: A gyomor-bélszatorna külső sipolyai. (External fistulas of gastrointestinal tract.) *Orv Hetil* 107:390, 1966
19. Hartig W, Schmoz G, Weiner R, Matkowitz R: *Künstliche Ernährung*. Barth, Leipzig 1988
20. Hartig W: *Moderne Infusionstherapie, Parenterale Ernährung*. Barth, Leipzig 1979
21. Hawker PC, Givel JC, Keighley MRB, Alexander Williams J: Management of enterocutaneous fistulae in Crohn's disease. *Gut* 24:284, 1983
22. Hill GL: Operative strategy in the treatment of enterocutaneous fistulas. *World J Surg* 7:495, 1983
23. HIMAL HS, Allard, JR, Nadeau JE, Freeman JE, MacLean LD: The importance of adequate nutrition in closure of small intestinal fistulas. *Br J Surg* 61:724, 1974
24. Hollender LF, Meyer C, Avet D, Zeyer B: Postoperative fistulas of the small intestine: Therapeutic principles. *World J Surg* 7:474, 1983
25. Hollender LF, Otten F, Meyer C, Marrie A: Notre expérience du traitement chirurgical des fistules externes post-opératoires de l'intestin grêle. *J Med Strasbourg* 5:415, 1974
26. Ihász M, Réfi M, Bátorfi J, Jakab F, Regös J: Duodenumcsomok insufficiencia gyakorisága a klinika 12 éves anyagában. (Frequency of duodenal-stump insufficiency in 12 years clinical material.) *Magyar Sebészet* 26:9, 1973
27. Ihász M, Réfi M, Szabó K, Bátorfi J, Vályi S, Kiss S: A Morbus Crohn szövődményei és a recidiva gyakorisága. (Frequency of complications and recurrency of Crohn's disease.) *Magyar Sebészet* 32:369, 1979
28. Jørgensen ST, Pedersen H, Larsen V: Conservative treatment with total parenteral nutrition in patients with gastro oesophageal anastomosis leaks (anastomotic leaks conservatively treated). *Acta Chir Scand* 145:173, 1979
29. Kaminsky VM, Deitel M: Nutritional support in the management of external fistulas of the alimentary tract. *Br J Surg* 62:100, 1975
30. Lévy E, Cugnenc P, Parc R, Bloch P, Hugué J, Frileux P, Loygue J: Fistules jejuno-iléales s'ouvrant dans une éviscération. Expérience de 120 cas. *Gastroenterol Clin Biol* 5:497, 1981
31. McIntyre PB, Ritchie JK, Hawley PR, Barthram CI, Lenhard-Jones JE: Management of enterocutaneous fistulas a review of 132 cases. *Br J Surg* 71:293, 1984

32. Molnár J, Kudász F: Hasüregi fistulák. (Abdominal fistulas.) Orv Hetil 103:2085, 1962
33. Nassos TP, Braasch JW: External small bowel fistulas. Current treatment and results. Surg Clin North Am 51:687, 1971
34. Pearlstein L, Jones CE, Polk HC: Gastrocutaneous fistula. Etiology and treatment. Ann Surg 187:223, 1978
35. Reber HA, Roberts C, Way LW, Dunphy EJ: Management of external gastrointestinal fistulas. Ann Surg 188:460, 1978
36. Riboli EB, Bertoglio S, Arnulfo G, Terrizzi A: Treatment of esophageal anastomotic leakage after cancer resection. The role of total parenteral nutrition. J P E N 10:82, 1986
37. Rombeau JL, Rolandelli RH: Enteral and parenteral nutrition in patients with enteric fistulas and short bowel syndrome. Surg Clin North Am 67:551, 1987
38. Sandler JT, Deitel M: Management of duodenal fistulas. Can J Surg 24:124, 1981
39. Sheldon GF, Gardiner BN, Way LW, Dunphy EJ: Management of gastrointestinal fistulas. Surg Gynec Obstet 133:385, 1971
40. Soeters PB, Ebeid AM, Fischer JE: Review of 404 patients with gastrointestinal fistulas: impact of parenteral nutrition. Ann Surg 190:189, 1979
41. Stefanics J, Bánki F, Farkas I, Juhász M: Duodenum sipoly. (Duodenal fistula.) Sebész Nagygyűlés. Budapest, 1964 p 224
42. Tarazi R, Coutsoftides T, Steiger E: Gastric and duodenal cutaneous fistulas. World J Surg 7:463, 1983
43. Thomas RJS: The response of patients with fistulas of the gastrointestinal tract to parenteral nutrition. Surg Gynec Obstet 153:77, 1981
44. Wolf G von, Steindorfer P, Piber G: Parenterale oder enterale Hyperalimentation in der Behandlung enterokutaner Fisteln, Zentbl Chir 113:973, 1988

EXPERIENCE WITH A NEW COMBINED METHOD IN THE DIFFERENTIAL DIAGNOSTICS OF EARLY ENDOMETRIAL CHANGES

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The authors have performed in 30 cases ultrasonic examination of the endometrium followed by vacuum aspiration with TIS-U-TRAP device (Milex Prod. Inc., Chicago) with equipped a transvaginal head, to obtain samples for histological examination. In 8 of the 30 cases endometrial hyperplasia, while in 2 cases endometrial adenocarcinoma was verified. The authors suggest that transvaginal ultrasonic examination together with vacuum aspiration is suitable for oncological screening of the endometrium.

Combined colposcopic and cytological examination is applied in gynecological oncological screening which reveals most of the pathological changes in the portio. However, the pathological, oncological changes in the endometrium are not revealed by this technique /7/. The endometrium is usually examined by curettage.

This examinational method is suitable for testing the temporary state of the uterine mucous membrane after cervical dilatation. This intervention - which seems to be one of the most frequent gynecological interventions - can only be performed in a hospital, with general or local anaesthesia. It can be followed by complications due to the both operation and anaesthesia. Expenses of hospital treatment should also be reckoned with. This is the reason which curettage cannot be used for screening. The so-called suction curettage which does not require cervical dilatation - seems to be appropriate for sampling of uterine mucous membrane. A periodical routine use of a reliable screening method seems to be necessary in women with increased risk of malignant disorders of the uterine corpus (hypertension, diabetes, not delivered, late menopause, excess weight, infertility, oestrogen treatment) /15/. Sampling with aspiration technique seems to meet the above requirements /3, 6/. The application of transvaginal ultrasonic technique /9/ would be a useful addition to aspi-

rationsampling in the morphological examination of the abnormalities of the uterine mucous membrane calling attention to cases when the thickening of the mucous membrane calling attention to cases when the thickening of the mucous membrane is expected. In our study we report on the results of microscopic examinations of samples obtained from women with risk by vacuum aspiration technique following ultrasonic examination with the use of a transvaginal head.

Patients and Methods

Screening examination was performed in 30 women without symptoms. Pregnancy test was negative in all cases. All women examined belonged to a high risk group of malignant disorders of the uterine corpus. The examined women were informed about the nature of the examination, it was performed with their consent. In case of appropriate vaginal cleanness the first step of examination was sonography (Fig. 1).

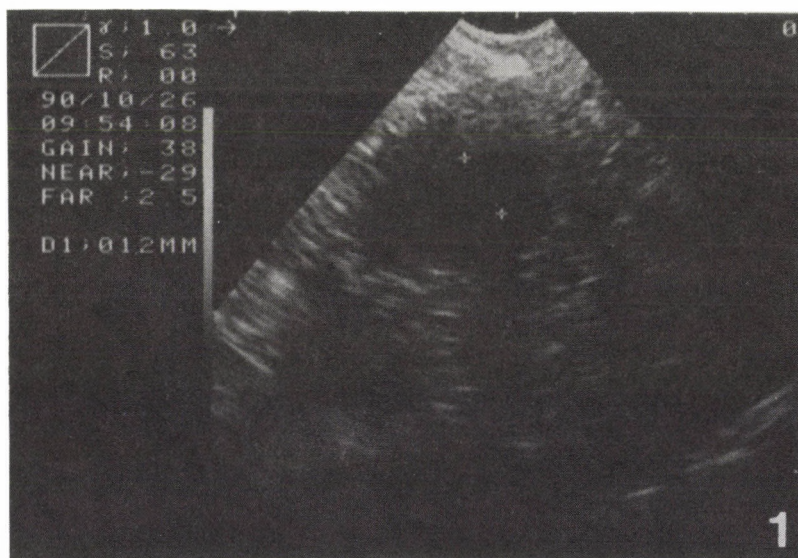


Fig. 1. Transvaginal ultrasonic picture of uterine cancer in a 56-year-old woman

Ultrasound examination was performed with the use of Toshiba Sono-layer, SAL 388 device supplied with a 5 mHz intravaginal head. The transducer had a fluid gel gum and a gel layer. The test head was introduced into the vagina. Then samples were taken with vacuum aspiration from the thickened mucous membrane defined by ultrasonic technique.

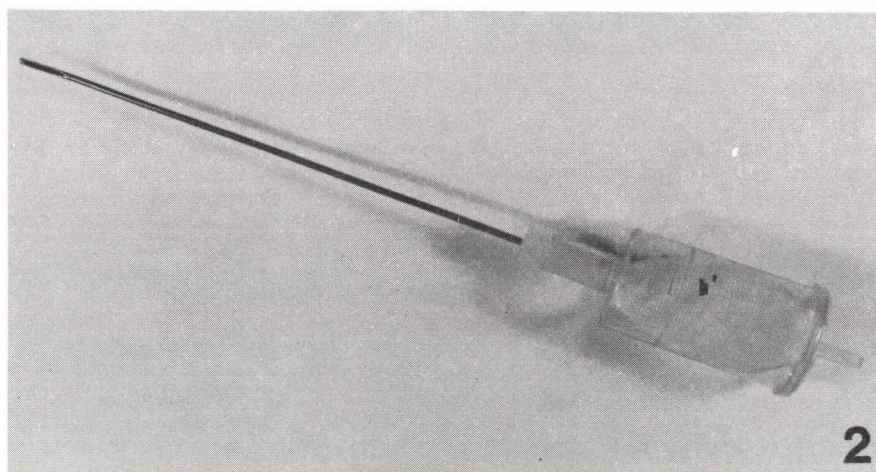


Fig. 2. Vacuum aspirator - can be used outpatiently

Vacuum aspiration was performed with the use of TIS-U-TRAP (Milex Product. Inc., Chicago) device (Fig. 2). The examinations were performed outpatiently. Before introducing the 3 mm diameter steel suckle curette the portio was fixed with a ball-fixer and curettage performed with 500-600 mm Hg suckle after disinfecting the vagina. On ultrastructural examination samples were fixed in 2.5% glutaraldehyde, 1% osmium-tetroxide or 4% formaldehyde solutions.

Results

Changes in the structure or size can be defined even during the menstrual cycle with ultrasonic examination. If the thickness of the endometrium seems to be abnormal on ultrasonic examinations, a pathological change - most frequently hyperplasia, adenomyosis, chronic endometritis or pyometra - is suspected. Ultrasonic examination alone can reveal endometrial carcinoma, however - according to some publications - it shows an echo-full or echo-poor structure in adenocarcinoma [1, 2, 4, 9, 10].

Fifteen negative results were obtained out of 30 sonographic examinations when the endometrium did not seem to be thickened. Morphological examination performed with suction also showed normal mucous membrane in these cases.

Ultrasonic examination revealed the thickening of the mucous membrane

in 15 cases. On histological examination of the suction material 5 normal and 10 pathological mucous membrane results were obtained. In 8 of the 10 abnormal cases glandular cystic endometrial hyperplasia and adenocarcinoma was found in two cases.

Discussion

The number of endometrial carcinoma cases is increasing all over the world as well as in Hungary. Because of this a screening method would be necessary to recognize the disease before as early. Ultrasonic examination if supported by a simple light, or electron microscopic or - when needed - electrocytochemical method. On using these methods no other complications than slight discomfort and lower abdominal spasms have been observed. In our cases sufficient test material was available for histological examination and no contraction in the portio hindered intervention.

On the basis of our preliminary examinations the combined screening method - described above - is a useful tool in women with increased risk because of the cancer of the uterine corpus. However, we would like to emphasize, that this is a screening, not a diagnostic method, whose use would not eliminate the use for curettage in positive cases.

References

1. Fleischer A, Dudley BS, Entman SS, Baxter JW, Kalmeris GC, James AE: Myometrial invasion by endometrial carcinoma: sonographic assessment. *Radiology* 162:307-310, 1987
2. Forrest TS, Elyaderani MK, Muilenburg MI, Bewtra C, Kable WT, Sullivan P: Cyclic endometrial changes: US assessment with histologic correlation. *Radiology* 167:233-237, 1988
3. Goldrath MH, Sherman AJ: Office hysteroscopy and suction curettage: Can we eliminate the hospital diagnostic dilatation and curettage. *Am J Obstet Gynecol* 152:220-229, 1985
4. Johnson M, Graham M, Cooperberg P: Abnormal endometrial echoes, sonographic spectrum of endometrial pathology. *J Ultrasound Med* 1:161-166, 1982
5. Lacey CG: Premalignant and malignant disorders of the Uterine Corpus In: Pernoll ML and Benson RC: *Current Obstetrics and Gynaecologic Diagnosis and Treatment*. p 847, 1987
6. McKenzie IZ: Routine outpatient diagnostic uterine curettage using a flexible plastic aspiration curette. *Br J Obstet Gynecol* 92:1291-1293, 1985
7. Nagy P, Keller G, Csaba I: Cytohormonal and cancer screening procedure for endometrial carcinoma. *Zbl. Gynäkol.* 107:169-174, 1985
8. Nagy P, Keller G, Csaba I, Garadhy B, Török A: Recognition of endometrial carcinoma with the help of Milan-Markley endometrial helix. (Az endometriumcarcinoma felismerése Milan-Markley-féle endometrialis helixszel.) *Magyar Onkológia* 30:65-72, 1986
9. Patai K, Jakab Zs, Harkányi Z, Balogh I: New possibilities of recognizing early endometrial changes. *Acta Chirurg Hung* 30:333-339, 1989
10. Van Roessel J, Wamsteker K, Exalto N: Sonographic investigation of the uterus during artificial uterine cavity distention. *J Clin Ultrasound* 15:439-450, 1987

OPERATIVE TREATMENT OF MALFORMATIONS OF THE MIDDLE EAR

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The authors give a review of their experience with the surgical treatment of developmental disorders of the middle ear. They introduce to the findings and surgical solutions in the tympanum of their cases. In shaping the acoustic meatus they recommend the closed approach developed by Marguet.

One out of 3500 live-born children has a congenital auricular malformation. This relatively high frequency can be explained with the sensitivity of the developing foetus to teratogenous effects on days 30-50 of intrauterine life. This is the period when the organs of hearing and balance develop /3, 5/.

The basic condition of the formation of this organ seems to be the development of the labyrinth, which induces the development of the malleus, the incus and the mandibula as well as the first third of the outer ear from the first branchial arch. The stapes, processus styloideus and the back 2/3 of the auricle develop from the second branchial arch. The tympanic cavity originate from the tubotympanal gap of the front of the throat, while the external acoustic meatus from the first branchial sulcus. Auricular malformations mainly occur in the external - less frequently in the middle - and least frequently in the internal ear /2, 3/.

Malformations of the external and middle ear often occur together, also in association with the anomalies of other organs (kidney, heart, eyes, etc.) developing simultaneously with the ear in the 2nd-3rd month of gestation, so in the case of congenital disorders of the mentioned organs the presence of auricular malformation should be searched with a view to early diagnosis.

Patients and Methods

Twenty-six ear operations have been performed due to the developmental disorder of the middle ear at our clinic for the past 5 years. The malformation was bilateral in 10 and unilateral in 16 cases; 15 of the patients were women and 11 men. The mean age was 15.2 years. Intervention was performed most frequently at the age of 5-7 years. Other developmental disorders (vitium, Treacher-Collins syndrome) were found in 4 cases.

Preoperative diagnosis is based on Schüller-Stenvers X-ray, CT and audiometry. Hypoplasia of the internal ear due to full atresy of the osseous acoustic meatus is, of course, contraindication. As it was mentioned, the labyrinth has an inductive role in the formation of the tympanum and the cells of the mastoid. The well-pneumatized mastoid process on the Schüller picture is the origin of the internal ear. Indication is supported by 40-60 dB air-bone gap and by symmetrical arcuate eminences on the Stenvers picture.

Operations were performed in intratracheal narcosis. A segment-shape piece from the skin above the planum mastoideum is dissected during retroauricular dissection. An approx. 2 mm^2 oval piece is taken and pressed from the temporal fascia. After removing the soft tissue, right mastoidectomy is performed with a drill. We get into the antrum through the cell-system of the operative cavity limited by the three main directions (apex-zygomatic root-Citelli corner).

The tympanum is exposed through posterior atticotomy from the antrum. In most /14/ of our cases malleus-incus body conglomerate, intact and mobile stapes and good contact between the conglomerate and the stapes were found in the area of the atticus. The malleus evolving from the ectoderm - which develops together with the tympanic membrane - was, of course, missing in all cases. The operative technique to be applied is to cover the conglomerate or the tympanum with temporal fascia.

There was no contact between the conglomerate and the stapes in 4 cases. In such cases the conglomerate is removed, the mobile stapes is covered with a short cortical columella and the tympanum with temporal fascia.

Middle ear homograft preserved in Thiomersal was applied in 4 cases /7/. The tympanum + hammer partial homograft functioned well for a long time in all cases, while the full homograft in 50% of the cases. The homografts were fixed with a two-component fibrin adhesive (Immuno Co.,

Austria). The homografts are safely stabilized and adhered with this method /4, 6/. Stapes developed in itself proved to be fix in one case. The solution is to form a short cortical columella after mobilizing the stapes. In one case the tympanum was filled with undifferentiated mesenchyma where tympanoplastics was not possible because of the risk of the opening of the labyrinth.

The operation was considered successful if at least 30 dB improve in hearing was recorded on day 14 after operation (Table 1). The whole section of the facial nerve in the tympanum was free in two cases in the first group. Lumen-preserving acoustic meatus was shaped in two ways. The bone, which would be the bridge evolving on posterior atticotomy, was removed. The acoustic meatus-forming operations were small radical operations. Epithalization went out from the retroauricular petiolated gill turned into the cavity, the gill was cut through on second operation.

Table 1
Intratympanic findings and solutions

Situation	Solution	Cases	Result (30 dB)
Malleus-incus body conglomeratum with intact and mobile stapes	Covering by fascia	14	10
No connection between the conglomeratum and stapes	short cortical columella + fascia	4	2
Mobile stapes only	2 partial homograft 2 total homograft 2 short cortical columella	2	2
Fixed stapes only	short cortical columella + mobilization	1	1
Undifferentiated mesenchymal tissue	-	1	-

These small radical cavities were later often superinfected resulting in real chronic otitis with "running ear", abundant granulation or metaplastic cholesteatoma. This is why we recommend the approach developed by prof. Marquet.

When evolved, the bridge is never removed. In the knowledge of the position of the tympanum exposed from the back, and incision is made before the intact or aborted auricle where the normal access to the tympanum can be found. The tympanum is formed from the transplant from the reticulo-auricular skin in its whole thickness, which is stitched elliptically to the edges of the wound. The tympanum is covered by temporal fascia from the back, then bended on the neomembrane. Lumen is preserved by a plastic tube which is removed in three month. All of our 10 operations performed with this technique were successful (independently from the findings of the tympanum).

Our experiences with the correction of aborted auricle often associated with auricular malformations or shaping it were unfavourable. Although we have applied several methods (own rib-cartilage, cadaver-cartilage), they did not give the expected results.

SUMMARY

In the case of bilateral developmental disorder of the middle and external ear - if the mastoid is well developed and mental development is normal - forming the auditory meatus with operation is justified at any case, if possible, at the age of about 5. Until that time ability of speech is developed by using a hearing aid. Operation is justified even in unilateral cases because of small operational stress and with a view to establish the hearing of space and direction or a reserve ear. From the operational technique point of view we would like to stress the advantages of the closed technique. In the case of series of difficult plastic operations appropriate hair-styling is recommended.

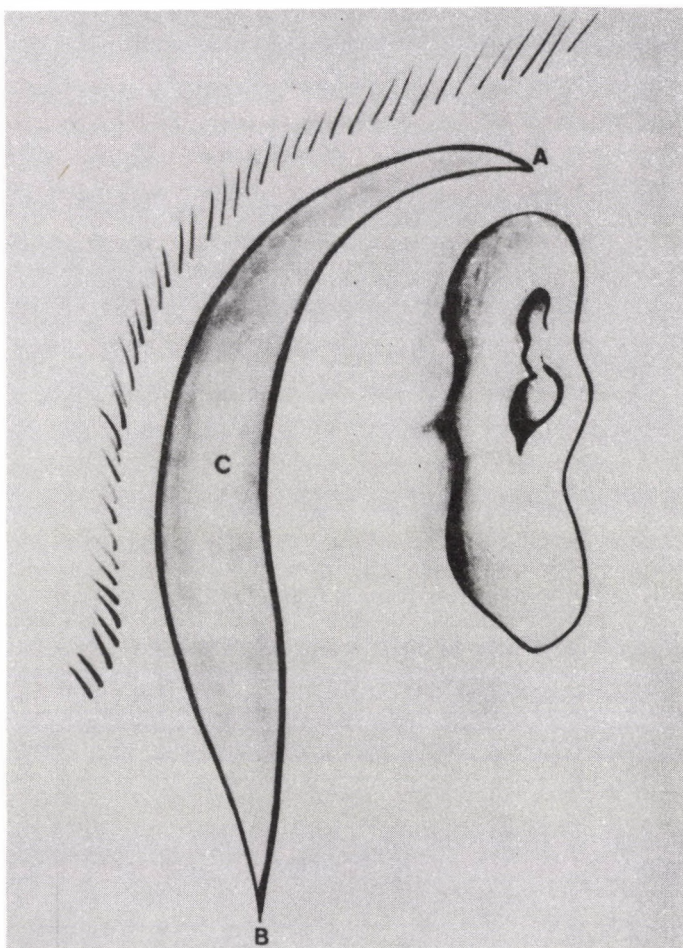


Fig. 1. Retroauricular incisions of the skin (A-B), area for prelevation of a free skin graft (C)

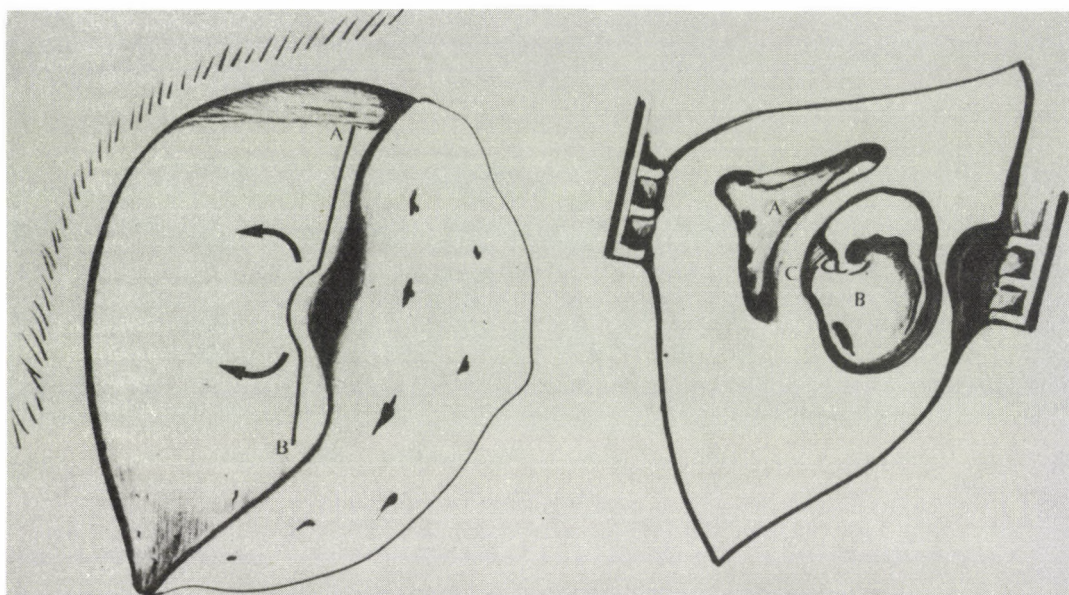


Fig. 2. Incision of the periosteum and posterior-superior exploration opening of the mastoid and the tympanic cavity

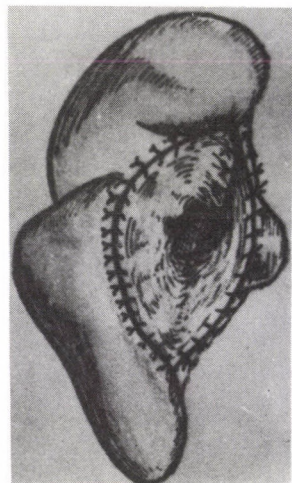
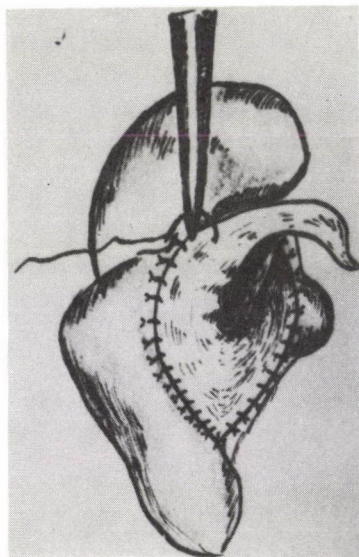
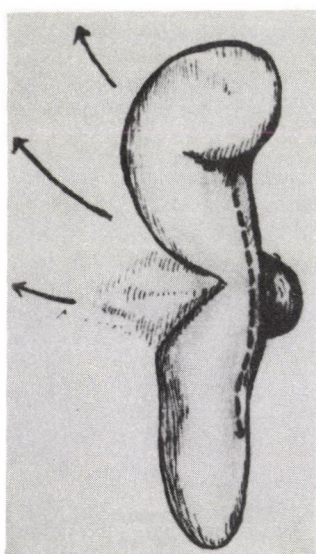


Fig. 3. Drawing showing the restoration, by means of full free skin autograft, of the function between the external skin and the implanted meatal autograft skin

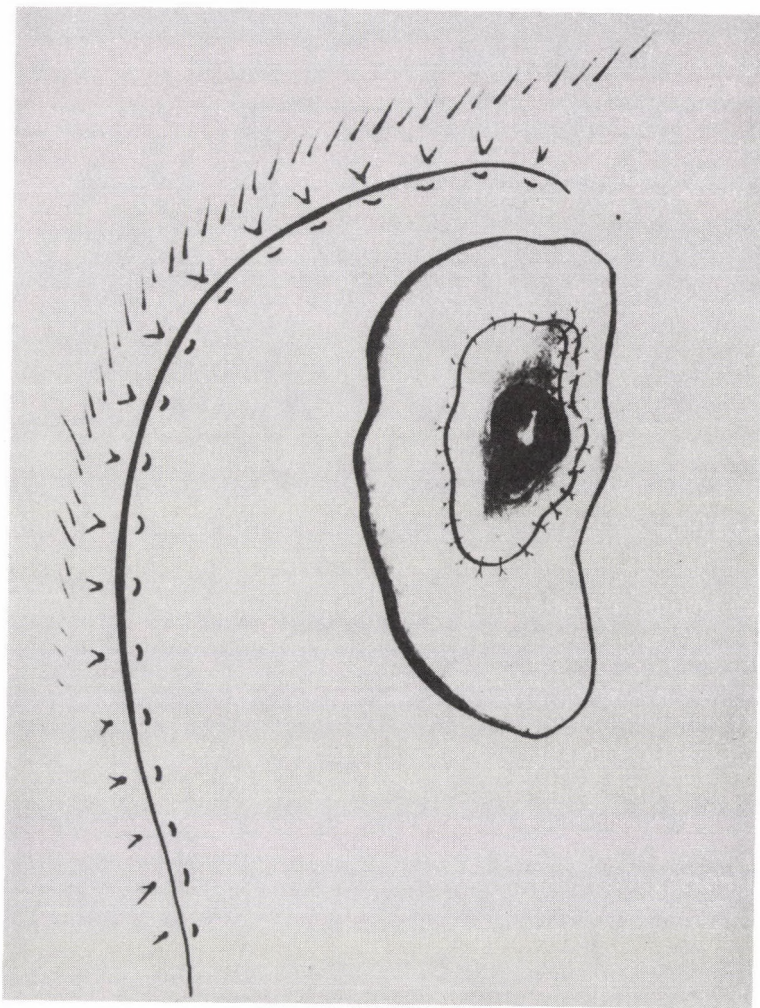


Fig. 4. Final stage showing the meatal and retroauricular sutures

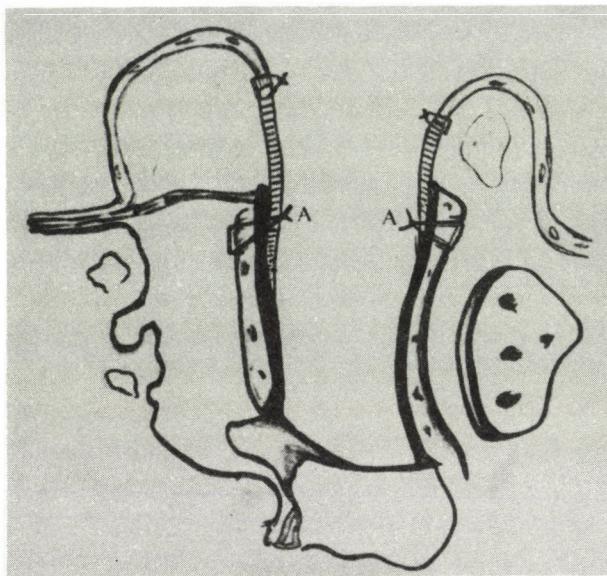


Fig. 5. Section showing the restored continuity between the external skin and the homografted meatal skin

References

1. Belluci, RJ: Congenital auricular malformations. *Annals of Oto-rhino-laryngology* 81:659, 1972
2. Gill NW: Surgery of meatal atresia. *Operative Surgery*, Vol. Ear 6-14. London: Butterworth. 1976
3. Marquet JF: Congenital Conductive Deafness. *Clinical Otolaryngology*, Blackwell Scientific Publications, 501-513. 1979
4. Marquet JF: The fibrin seal in otorhinolaryngology, *J Head Neck Pathology* 3:71-72, 1982
5. Manson I: Diseases of the Ear. Edward Arnold Ltd. London, 4-9, 1967
6. Ribári O: Fibrin Sealant in *Operative Medicine Otorhinolaryngology*, Vol. 1:75-81, Springer-Verlag Berlin-Heidelberg.
7. Takáts J, Ribári O: Preparation and application of middle ear homograft. (Hun.) *Fül-orr-gégegyógyászat* 29:205-211, 1983

VACUUM THERAPY IN THE TREATMENT OF ERECTAL IMPOTENCE

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The authors were the first in Hungary to use vacuum-induced erection in the treatment of erectile dysfunction. Negative pressure was induced by OSBON ERECAID SYSTEM. Erectile impotence was successfully treated with this non-invasive and complications-free method in patients with diabetes and psychic problems. The method was applied first for ameliorating sexual complaints due to virile climacteric and - based on the results - its application is recommended.

The view that 80% of erectile impotence is of psychic origin has completely changed for the past decade. Pharmacological, physiological and haemodynamic research revealed underlying organic and functional causes as a result of which currently not more than 20% of impotence is related to psychic origin alone /7, 8, 10/.

The change in views has led to significant development of therapy as well. There are two trends: a conservative (drugs, psychotherapy) and a surgical approach (prosthesis implantation, arterialization, "venous leak"). Diagnostic possibilities have improved (cavernosometry, cavernosography, Doppler) and indications of different therapeutic methods have been defined /7, 10, 11, 12/.

One group of conservative therapeutic methods comprises artificial erection induced by the intracavernous application of vasoactives (papa-verine, phentolamine, VIP, prostaglandine). This method which is widely applied also in Hungary is an invasive way of conservative therapy with all its early and late complications known from both literature and practice /1, 9/. In view of the complications of different surgical interventions the interest taken in "less harmful" (non-invasive) ways of conservative treatment must be understood /3, 4, 15/.

Herewith we are not going to deal with either psychotherapy or drug-treatment with hormones or aphrosidiacums rather we give an evaluation of our own experience - the first in Hungary - with the method of vacuum-

induced erection based on the erection-inducing impact of "negative pressure" which belongs to the "non-invasive" approach in which interest has increased lately /3, 4, 15/.

Patients and Methods

Forty-eight patients have been examined (treated with the OSBON ERECAID SYSTEM device inducing erection by vacuum-technique) at the Centre of Andrology of the Department of Urology of the Semmelweis University Medical School since April 1990. The first treatment chosen on the basis of appropriate indication is an examination as well as this is the time to decide whether erection can be induced in the patient with the help of the device. In Hungary it is also of importance because of the approx 300 USD price of the device, so it seems reasonable to decide before investment if the problem really can be solved by the purchase of the ERECAID SYSTEM. (Fig. 1)



Fig. 1. The OSBON ERECAID SYSTEM device

The youngest patient was 21, the oldest 68 years old. Patients were divided into 3 groups as it is shown in Table 1.

Table 1

No. of patients	Diabetes	Psychic origin	Virile climacteric
48	20	10	18

The application of vacuum therapy in patients with diabetes is well known from literature; it was tried in the group of psychic origin on the basis of the "theory of the least invasion"; while in virile climacteric we tried this method - the first to the best of our knowledge - considering the risk of the known complications (cancer of the prostate gland) due to different virile hormone compounds beside that of other invasive therapies.

The ERECAID SYSTEM contains a plastic cylinder (to be placed on the penis) in which vacuum can be proceeded pumping it manually. The corpora cavernosa are filled with blood on the sucking effect of the negative pressure in the pump which results in erection. Reflux of blood is prevented with the use of an elastic ring-clamp which can be placed from the cylinder to the root of the penis ensuring continued erection. Maintaining the erection induced and fixed this way is recommended for max 30 minutes; removing the ring-clamp detumescency takes place. Attention must be called to that vacuum can be produced only with the use of a contact material applied on the root of the penis and the bottom of the cylinder. Learning this method is simple, it does not need any special skills. (In contrary to the use of "own cavernous injections".)

The cylinder can be cleaned easily with soap and water.

Results

We examined four factors in connection with the use of the device:

1. Can erection be induced with its help? (Table 2)
2. Is the induced erection appropriate? (Table 3)
3. Are there any complications or adverse effects during treatment (bleeding, painful erection, etc.)?
4. Does the coitus with artificial erection lead to orgasm? (Table 4)

Table 2
Erection with the help of ERECAID SYSTEM

<u>No. of patients</u>	<u>Diabetes</u>	<u>Psychic origin</u>	<u>Virile climacteric</u>
48/40	20/16	10/8	18/16

As it can be seen from the Table the answer to the first question is that vacuum-induced erection was successfully applied in all the three groups.

Table 3
Vacuum-induced erection and rigidity

<u>No. of patients</u>	<u>Diabetes</u>	<u>Psychic origin</u>	<u>Virile climacteric</u>
	20/14	10/7	18/13

Thirty-four of 48 patients reported appropriate erection. Fourteen of the 20 in the diabetic group were satisfied with the degree of erection, while only one of the group with psychic problems but producing erection was unsatisfied with the degree of rigidity, 7 were fully satisfied with it. Almost 1/3 of the climacteric group was unsatisfied with the degree of erection. No complications occurred in the 48 treated patients, no adverse effect in the 40 produced erections were found.

Table 4

<u>No. of patients</u>	<u>Diabetes</u>	<u>Psychic origin</u>	<u>Virile climacteric</u>
48/39	20/15	10/8	18/16

Vacuum-induced artificial erection resulted in perfect orgasm. Once erection was produced (even in patients whose rigidity was imperfect), the orgasm was as usual.

Discussion

Vacuum-induced erection - known as non-invasive method - has received an important role in the treatment of erectile dysfunction having occurred

more frequently in recent years; more and more information on the experience gained with this method are published in literature /2, 4, 5, 6, 11, 13, 14, 15/.

Both literary and our own data prove the successful applicability of this method in coital disturbances due to diabetes /11/. Its effectiveness in impotence of "psychic" origin - besides the sucking effect of negative pressure - can be explained with the trust in its use. While its use in virile climacteric problems seemed to be merely an attractive hypothesis for us when we started this trial, by now it has become a very useful element of our everyday work. Although we have not got an own experience with its use as a supporting aid to earlier implanted penis prosthesis, literature proved its usefulness in this field as well /4/. Together with other authors we also find the ERECAID SYSTEM device produced by OSBON Co. appropriate and amenable in producing vacuum-induced erection /13/.

Erectile dysfunction can be treated in several ways. As the problem has not been solved even with the great advance in this field, we recommend the application of vacuum therapy in the mentioned groups of patients because of its successful use and lack of complications.

References

1. Desai KM, Gingel JC, Feneley RC: Penile corporal fibrosis following papaverine self-injection therapy for impotence. *Eur Urol* 15:132-133, 1988
2. Marmar JL, DeBenedictis TJ, Praiss DE: Penile plethysmography on impotent men using vacuum constrictor devices. *Urology* 32/2:198-203, 1988
3. Montague DK: Periprosthetic infections. *J Urol* 138:68, 1987
4. Moul JW, McLeod DG: Negative pressure devices in the explanted penile prosthesis population. *J Urol* 142:729, 1988
5. Nadig PW: Utility of the vacuum constriction device for men WHO have failed penile prosthesis. *J Urol* 135:232 A, Abstr. 512, 1986
6. Nadig PW, Ware JC, Blumoff R: Noninvasive device to produce and maintain an erection-like state. *Urology* 27:126, 1986
7. Papp Gy: Potency problems. (Nemzőképességzavarok.) Budapest, Medicina, 1985
8. Papp Gy: The organic causes of erectile impotence. (Az impotencia coeundi organikus okairól.) *Urol Nephrol Szle* 4:230, 1981
9. Török A, Jilling Á, Götz F: Induced priapism and its management. *Int Urol Nephrol* 23: 191-194, 1991
10. Wespes E, Schulman CCF: Vascular impotence. *W J Urol* 5:144-149, 1987
11. Wiles PG: Successful non-invasive management of erectile impotence in diabetic men. *Brit Med J* 196:161-162, 1988
12. Williams G, Mulchay MJ, Hartnell G, Kiely E: Diagnosis and treatment of venous leakage: a curable cause of impotence. *Brit J Urol* 61:151-155, 1988
13. Witherington R: The OSBON erect: Aid system in the management of erectile impotence. *J Urol* 133:190 A, Abstr. 306, 1985
14. Witherington R: Vacuum constriction device for management of erectile impotence. *J Urol* 141:320-322, 1989
15. Zasler ND: Managing erectile dysfunction with external devices. *Pract Diabetol* 8/3:1-9, 1989

ACUTE ACALCULOUS CHOLECYSTITIS

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In 1884 Duncan was the first to report on acute postoperative acalculous cholecystitis (ref.: 14). Initial publications reported a small number of cases. Literary data have shown a change of the situation for the past few decades /16/. It was most frequently observed following surgical intervention, trauma, delivery or parenteral nutrition /1, 13, 16/. The number of new acalculous cholecystitis cases often requiring surgical intervention and causing death in elderly male patients has increased /5, 16/. Therefore we decided to undertake a clinical study. In Hungary the authors who deal with this theme are: Csengődy /2/, Sándor /17/, Lukács /12/ and Ezer et al. /3/.

Case History

1992 cholecystectomies were performed at the 2nd Department of Surgery of the Semmelweis University Medical School between 1st March 1979 - 1st April 1991. Fourteen patients died after operation (0.71%). Twenty-four patients were operated because of acalculous cholecystitis (1.25%). Six patients died in this group (25%). Patients were enrolled in the study who did not have calculi in their anamnesis, in whose inflamed gall bladder calculi were not found on operation and if histological examination of the removed gall bladder verified acute inflammation. Patients' age ranged between 20-92 years (mean:64 years). Male to female ratio was 9:15; which was different from literary data. In 3 of 24 operated patients the disease appeared as postoperative complication following coronary bypass, embolectomy or peritoneal dialysis. 19 patients were admitted because of acute abdominal symptoms, suspect of cholecystitis. The most characteristic symptom was an increasing pain in the right upper abdomen and febrile condition with nausea, vomiting and jaundice.

Diagnosis and indication for operation were established on the basis of the anamnesis, physical and ultrasound examination as well as progredient abdominal symptoms. 19 of the operated patients had other underlying disease. Artherosclerosis was found in 8 patients, coronary sclerosis in 6

- with myocardial infarction in their anamnesis - alcoholic liver cirrhosis, obstructive pulmonary disease, peptic ulceration or serous renal failure in one patient each. Eleven patients had more than two underlying diseases. Cholecystectomy was performed in all operated patients. Upon exposure perforation of the gall bladder or gangraenous cholecystitis was found in 4 cases, two patients with the latter died. Postoperative complications were: cardiopulmonary in 5 cases, septic peritonitis or disturbance in wound healing in 4. Altogether 6 patients were lost. The causes of death were: cardiac failure in 3 cases and peritonitis in another 3 cases.

Discussion

Acute acalculous cholecystitis is a disease requiring usually conservative therapy. It generally heals on staying in bed, applying compress, cooling, diet, spasmolytics, infusion or antibiotics. Prostaglandine inhibitor and opiate antagonist have been included recently in therapeutics /10/. With the administration of cyclooxygenase - inhibitors the prostaglandine - level can be decreased and pain due to cholecystitis ameliorated, so they can be applied in the treatment of acute calculous or acalculous cholecystitis /18/.

Acalculous cholecystitis has a multifactorial background, e.g. relative visceral hypoperfusion frequent in hypovolaemic, septic shock, decreased portal circulation, hyperbilirubinaemia, biliary stasis, accumulation of prostaglandine or distension of the wall of the gall bladder /3, 7, 9/. An important factor in etiology is the stenosis of the cystic duct due to different causes accompanied by biliary atony /4, 6/. Infection has a secondary role /11, 19/. Acute inflammation progresses - mainly in the elderly - in some cases in spite of conservative treatment with the threat of complications (necrosis, perforation), which necessitates surgical intervention.

Continuous observation of the patient is important in preoperative diagnosis. No other diagnostic means existed prior to the development of current. Nowadays cholescintigraphy (HIDA), ultrasonic examination and computer tomography are of help in establishing the diagnosis /13/. Ultrasonic examination is available in almost all of our hospitals. It is a cheap, reproducible way of examination which can be performed also at the patient's bed and facilitates the observation of the inflammatory process. The signs

appearing on the ultrasound device are the following: the wall of the gall bladder is 4 mm thick, accumulation of fluid in the pericholecyst, the presence of subserosal oedema or intramural gases and irregular picture of the mucousmembrane. In our cases clinical observation and ultrasound examination were of greatest help. We do not have the possibility to perform HIDA examination at our Department, CT was not necessitated in setting up the indication for operation.

Careful observation, early diagnosis, ultrasonic examination and timely operation are of great importance as acalculous cholecystitis is frequent in patients with other underlying diseases. Death rate is higher (6-67%) as compared to the 3% death rate of calculous cholecystitis /15/, which can be explained that the symptoms - primarily in postoperative cholecystitis cases - are less expressed, can be masked by the symptoms of the underlying disease which may result in a late diagnosis.

Early surgical intervention is justified in the case of progressing clinical and radiological symptoms before complications occur, similarly to the treatment of acute calculous cholecystitis /8/. With some exceptions cholecystectomy is usually easy to perform, so earlier generally applied cholecystostomy is not recommended.

Attention should be paid to acute cholecystitis following operation, delivery or trauma. Acute postoperative cholecystitis can be prevented with adequate fluid- and electrolyte therapy, the prevention and treatment of paralytic atony in the stomach and the bowels, avoiding the application of spasmolytics to Oddi-sphincter spasms or drugs decreasing motility. The only way of decreasing the number of complications and postoperative death is careful observation and - if necessary - immediate operation.

References

1. Cornwell EE: Acute acalculous cholecystitis in critically injured patients. *Ann Surg* 210: 52, 1989
2. Csengődy J, Mészöly I, Juhász M: Postoperative necrosis and casting of the gall bladder. (Postoperatív epehólyag-elhalás és kilökődés.) *Orv Hetil* 108:466, 1967
3. Ezer P, Takátsy Z, Tihanyi M: The surgical aspects of acalculous cholecystitis. (A kő nélküli epehólyaggyulladás sebészeti vonatkozásai.) *Magy Seb* 43:9, 1990
4. Glenn F: Acute acalculous cholecystitis. *Ann Surg* 189:458, 1979
5. Glenn F, Becker CG: Acute acalculous cholecystitis. An increasing entity. *Ann Surg* 195: 131, 1982
6. Howard RJ: Acute acalculous cholecystitis. *Amer J Surg* 141:194, 1981
7. Jizegard L, Thornell E, Svanvik J: Pathophysiology of acute obstructive cholecystitis implications for non-operative management. *Brit J Surg* 74:1084, 1987

8. Johnson LB: The importance of early diagnosis of acute acalculous cholecystitis. *Surg Gynec Obstet* 164:197, 1987
9. Kaminski DL et al.: The role of prostanooids in the production of acute acalculous cholecystitis by platelet-activating factor. *Ann Surg* 212:455, 1990
10. Kaminski DL, Deshpanden YG, Thomas LA: The role of prostaglandins E and F in acalculous gallbladder disease. *Hepatogastroenterology*, 34:70, 1987
11. Lee AW: Acalculous cholecystitis. *Surg Gynec Obstet* 159:33, 1984
12. Lukács G, Nagy T, Kozlowszky B: Acalculous gall-bladder in surgery. (Kőnénkűli epehó-lyag a sebészgi gyakorlatban.) Magyar Sebész Társaság Kongresszusa, Szeged, 1980
13. Mirris SE et al.: The diagnosis of acute acalculous cholecystitis: a comparison of sonographia, scintigraphy and CT. *Amer J Roentgenol* 147:1171, 1986
14. Orbán L et al.: Acute-, reactive- or stress-cholecystitis. (Heveny, reaktív vagy stressz cholecystitis.) *Magy Seb* 35:69, 1982
15. Orlando R, Glenson E, Drezner B: Acute acalculous cholecystitis in the critically ill patient. *Amer J Surg* 145:472, 1983
16. Savoca PE et al.: The increasing prevalence of acalculous cholecystitis in outpatients. *Ann Surg* 211:433, 1990
17. Sándor J: Postoperative gangraenous cholecystitis. (Postoperatív gangraénás cholecysti-tis.) Magyar Sebész Társaság Kongresszusa, Szeged, 1980
18. Thornell E, Jansson R, Svanvik J: Indomethacin intravenously - a new way for effective relief of biliary pain: a double blind study in man. *Surgery*, 90:468, 1981
19. Truedson H: The incidence of bacteria in gallbladder bile et acute and elective chole-cystectomy. *Acta Chir Scand* 149:307, 1983

STUDY ON DYSPHAGIA AFTER PROXIMAL SELECTIVE VAGOTOMY

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The authors examined one of the characteristic complications - dysphagia - of proximal selective vagotomy widely applied in the surgical treatment of duodenal ulcerations. To gain a better knowledge of the causes of this type of complications measuring the pH value for 24 hours and manometric examinations of the lower esophageal sphincter were performed in 12 patients without complaints following operation and in 22 with the complaint of dysphagia. No significant changes were observed between the two groups either in basal sphincter pressure or in the two parameters characteristic for reflux activity, e.g. the number of reflux episodes and reflux index. Operation resulted in a slight increase of the basal pressure and the decrease of reflux activity in both groups. It is likely that postvagotomical dysphagia has a multifactorial background: denervation or mechanical trauma of the lower oesophagus and the uncoordinated and insufficient relaxation of the lower oesophageal sphincter following swallowing.

The development of the physiological basis and technique of proximal selective vagotomy seems to be one of the significant results achieved in functional surgery. The operative technique was developed by Griffith and Harkins in dogs /7/ and by Holle and Hart in humans /8/ completed with the plastics of the pylorus. It is remarkable that 7 years later a Hungarian author, Berger reported on his early experience in this field /4/. This type of operation is widely applied all over the world; several publications have appeared. However, in Hungary it has become more frequent recently /1, 3, 10, 11, 12/.

Experience gained for years have shown not only its advantages - low mortality- and morbidity rate, good functional results - but also its characteristic complications. Some of them are: the ischaemic necrosis in the mesenteric artery, early repletion after meals, diarrhoea or dumping syndrome /1, 2, 10, 11/. Slight postoperative dysphagia occurs in approx 30% of the cases, while it is serious in 1% /6, 9, 13/.

Dysphagia was observed in 112 (14.4%) of 778 patients having proximal selective vagotomy performed of 11 years. The complaints ceased in all cases spontaneously or on conservative therapy (diet, sedatives, prokinetic drugs) within 1-6 months. No reoperation or dilation was needed because of these complaints.

We undertook our study to have a better understanding of the nature and background of this phenomenon. We have examined 12 patients without postoperative complaints and 22 with dysphagia.

Material and Methods

Patients were selected for study who had in their history proximal selective vagotomy because of chronic duodenal ulceration without dysphagia and abnormal swallowing on preoperative radiological examination. The measurement of pH values for 24 hours and manometric examination of the lower oesophageal sphincter were performed in 12 patients free of complaints and in 22 with dysphagia 6-8 weeks after operation. The values were compared to those obtained before operation. Male to female ratio in the group without complaints was 10:2; mean age 37.9 years. Male to female ratio in the group with dysphagia was 19:3; mean age 39.1 years. Dysphagia was slight in 20 cases, moderate in 2 patients. Dysphagia was taken slight if it occurred rarely, after having solid food, moderate if it occurred frequently, after having pulpy food.

Measuring of pH-value: Measurements were performed with the use of portable digital data-collection system (GASTROpH, ASK-OMIKRON Ltd.). Combined glass-electrode (Radiometer GK 2802 C) was introduced and fixed at 5 cm above the lower oesophageal sphincter in the oesophagus. Appropriate location of the probe was determined by using an X-ray intensifier. The device was calibrated in buffer solutions with 3 known pH values before and after measuring. Data of measurements were evaluated on IBM compatible PC/XT according to the criteria defined by Johnson - De Meester.

Manometry: Single channel fluid-perfusional measurement of pressure was performed with the so-called "quick-pull" method. Low compliance flow of fluid (3.0 ml/min) was provided by an infusion pump altered for this purpose with 4 90° lateral gaps at the olive-shape end of the polyethylene probe with an interior diameter of 1.5 mm. The probe is attached to an exterior pressure-transforming head which is placed at the axillary-height

of the patient. Data were recorded with PRESSTOMACH device (Omikron Ltd). The location of the probe in the stomach was checked by increased intra-abdominal pressure and respiration. Then the probe was pulled out of the lying, relaxed patient at a 3 cm/s speed after breathing out and pressure curve in the lower oesophageal sphincter was recorded. Ten measurements were taken and mean value calculated in each of the cases. Pressure in the sphincter was obtained from the difference between maximum pressure and that in the fundus, taking the latter as a reference.

On evaluation of the results one- and two-sampled t -probes were applied.

Results

No significant changes were observed in the two parameters characteristic for reflux activity, the number of reflux episodes and reflux index, between the two groups. It is worth mentioning that proximal selective vagotomy resulted in a significant decrease of reflux index in the group of patients free of complaints, while both in reflux index and the number of reflux episodes in the group with dysphagia ($p \leq 0.05$).

No significant difference was found between the two groups in relative sphincter pressure either. Although there was a slight increase of pressure in both groups due to operation, this increase was not significant either. Preoperative low sphincter pressure (3.3 mm Hg) increased to above the average (26.1 mm Hg) after operation in one of the two patients with slight dysphagia.

Table 1

Groups	Free of complaints SD	Dysphagias SD
Pressure in the sphincter before operation (mm Hg)	14.4 + 4.4	15.1 + 5.0
Pressure in the sphincter after operation (mm Hg)	16.3 + 3.1	17.2 + 3.3
No. of reflux episodes before operation	58.7 + 71.8	46.1 + 14.6
No. of reflux episodes after operation	30.5 + 25.6	28.1 + 15.7
		p 0.05
Reflux index before operation (%)	4.6 + 3.4	5.5 + 3.0
Reflux index after operation (%)	3.2 + 2.5	3.8 + 2.0
	p 0.05	p 0.05

Discussion

Dysphagia is resulted from the failure of urthering of the swallowed bolus. Theoretically this may happen in two ways: the oro-aboral pressure gradient is insufficient to prevent the resistance of organic stenosis or the advance of the bolus is prevented by positive aboro-oral pressure gradient opposite to the physiological /14/. In this case - excluding organic obstruction - positive aboro-oral pressure gradient is may be due to several causes with uncoordinated and incomplete relaxation in the lower oesophageal sphincter following swallowing and the decrease of the amplitude of peristaltic pressure due to denervation or mechanical trauma in the lower third of the oesophagus among them. In summary: There are several factors in the occurrence of dysphagia following proximal selective vagotomy. They include the denervation of the sphincter of the lower oesophagus, traumatization of the lower 4-6 cm tract of the oesophagus due to its bareness and the resulting perioesophageal inflammation and oedema /9/. Literary data on the changes of the pressure of the lower oesophageal sphincter are contradictory. Both the decrease, constancy and increase of pressure in relaxation were observed /5, 6, 13/. In our study we experienced a slight increase of pressure in relax. In postvagotomial dysphagia rather the degree and disconcordance of the relax of the sphincter than repose pressure was of importance. Further examinations are needed to support this and to clarify the role of other - e.g. endocrine - factors (hypergastrinaemia).

References

1. Baltás B, Nagy A, Garas F et al.: Early experiences with superselective vagotomy in the treatment of duodenal ulceration. (Superselectiv vagotomiával szerzett korai tapasztalataink a duodenalis ulcus kezelésében.) Orvosi Hetilap, 125:2231, 1984
2. Bátorfi J, Ihász M, Balogh I et al.: A special complication of proximal selective vagotomy: Ischaemic necrosis of the mesenteric artery. (A proximális selectiv vagotomia speciális szövődménye: a kisgörbületi ischemias necrosis.) Magyar Sebészet, 35:251, 1982
3. Bátorfi I, Ihász M, Bálint A et al.: The technique of expanded proximal selective vagotomy. (A kiterjesztett proximális selectiv vagotomia technikája.) Magyar Sebészet, 44:3, 1991
4. Berger R: Selective proximal vagotomy without drainage. (Selectiv proximális vagotomia drainage-műtét nélkül.) Magyar Sebészet, 28:285, 1974
5. Emde C, Konradt J, Vosberg W: Manometrische Untersuchung zur Wirkung der selektiv proximalen Vagotomie nach Hedenstedt auf den unteren Osophagussphincter. Zbl. Chirurgie, 109:797, 1984
6. Guelrud M, Zambrano-Ricones V, Simon C et al.: Dysphagia and lower esophageal sphincter Abnormalities after proximal gastric vagotomy. Am J Surg 149:232, 1985
7. Griffith CA, Harkins HN: Partial Gastric Vagotomy: Experimental Study. Gastroenterology, 32: 96, 1957

8. Holle F, Hart W: Wege der Chirurgie des Gastroduodenalulkus. Med Klin 62:441, 1967
9. Ihász M: Postvagotomische Dysphagie. Zbl. Chirurgie, 100:603, 1975
10. Ihász M: Vagotomia. Akadémiai Kiadó, Budapest, 1980
11. Ihász M, Bálint A: Modern surgical treatment of peptic ulcerations. (A pepticus fekélyek korszerű sebészi kezelése.) Orvostképzés, 62:285, 1987
12. Jordan PH: Indications for parietal cell vagotomy without drainage in gastrointestinal Surgery. Ann Surg 210:29, 1989
13. Martinoli S, Müller C, Allgöwer M: Prä- und postoperative endomanometrische Befunde im Ösophagus bei proximalselectiver Vagotomie. Helv Chir Acta, 45:75, 1978
14. Vantrappen G, Janssens J: Recent studies of the Pathophysiology and Diagnosis of Esophageal Symptoms. Scand J Gastroenterol 25(Suppl 175):34, 1990

ENDOSCOPIC DIAGNOSIS AND THERAPY OF UROTHELIAL TUMOURS
OF THE UPPER URINARY TRACT
(AN ANALYSES OF OUR OWN CASES WITH LITERARY REVIEW)

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The authors review the importance of ureteropyeloscopy and nephroscopy in the diagnostics and endoscopic treatment of urothelial tumours of the upper urinary tract, in view of their two-year experience and discuss indications and technical difficulties compared to those described in the literature. Practice is demonstrated with the description of two cases. Follow-up and care-tactics are detailedly described.

Radical nephro-ureterectomy with the collar-like resection of the meatus urethrae has been applied for decades in the surgical therapy of urothelial tumours of the upper urinary tract /11/. However, alternative approaches have for years been available and applied for saving the organ in the therapy of identical or similar urothelial tumours. The choice primarily depends on the histological malignancy, location, multicentre or solitary occurrence and extension of the urothelial tumour. In spite of that the diagnostic criteria of urothelial tumours listed above could not be reliably tested in the tumours of the pyelum and the ureter until recently, there were operative technics for organ preservation. Some of them were applied in necessity, i.e. in the case of anatomically or functionally solitary kidney, others because of the situation found on operation and intraoperative biopsy. Organ preservation was also dependent on the patient's age and condition /1, 4, 12, 15, 17/. Drawing conclusion from a few cases is certainly not possible. However, the retrospective study of Murphy et al. on operative techniques of the different stage and differentiated tumours of the upper cavity system may be of use in this context /13/.

The routine application of uretero-pyeloscopy and nephroscopy facilitated the visualization of the tumours of the ureter, pyelum and bladder. With their use the size, surface and surroundings of the tumours can be well detined, and as multilocality can be excluded or confirmed. The clinical stage can be identified in some instances on the basis of the

above, with complementary examinations. Histological processing of biopsy material also provides information about grading /6/. The results of retrospective analyses of conservational operations and the development of endoscopic technique facilitated the performance of conservational operations not only in necessity or in open surgery but with a planned endoscopic approach. In the present study we try to answer the currently emerging questions in this field on the basis of our experience gained with the endoscopic diagnosis and treatment of urothelial tumours of the upper urinary tract, and on the survey publications available.

Patients and Methods

Uretero-pyeloscopy has been performed at our clinic in 48 cases over a more than two-year study period (1 January 1987 - 30 April 1989); in 27 cases as a therapeutical solution of stone, and because of differential diagnostic problems - primarily in ureter- and pyelotumours - in 23 cases. In 4 of 23 cases percutaneous (PC) antegrade intervention was also applied, primarily in the case of suspect of a tumour in the meatus or close to it or in the pyelum. Table 1 contains the clinical, X-ray and cystoscopic signs. Percutaneous uretero-pyeloscopy of the tumours close to the meatus are justified by prevention of implantation of the tumour in the upper urinary tract. We did not find any data referring of the spread of the tumour during transurethral intervention. In accordance with other authors, we find the antegrade examination of the renal cavity system and the ureter more reliable /8/. Diagnostic examinations have been performed with the use of a flexible ureteroscope (with Storz 9 Ch, 3,5 Ch drains) for the past year. With the use of flexible forces samples can be obtained. However, in some tumour cases we used the rigid ureteroscope instead of the flexible device in order to assess the surroundings better and to obtain a larger field of vision and multifocal biopsy. The intervention begins with ureter-catheter examination introduced through the urethro-cystoscope. Retrograde ureteropyelography is performed. X-ray examination may field important additional data on the extent and location of the changes in i.v. urography (lack of contour, block of flow). Also more precise information can be obtained about the course and ruptures in the ureter which is of practical importance in the introduction of the ureteroscope. The meatus urethrae is usually dilated up to 13 Ch. In the case of tumours biopsy is

Table 1
Symptoms of upper tract urothelial tumours

Indication for ureteropyeloscopy	No. of patients
<u>Upper tract haematuria</u>	14
Normal X-ray	6 (1)
Lack of contour	5 (2)
X-ray showing obstruction	3 (2)
<u>Without haematuria</u>	9
Tumour in the meatus or close to it	3 (1)
X-ray showing obstruction	2 (0)
Lack of contour	4 (2)

The numbers in the brackets show tumorous cases

made with a flexible device which is useful for histological sampling if the rigid device cannot be introduced (it occurred in one case).

With the use of a flexible device most of the cavity system and the whole ureter can be traversed. A rigid device is required only for the careful investigation and biopsy of the suspicious area. Through the device smaller, unambiguously superficial, well-differentiated papillomas can be resected with an appropriate electric snare or coagulation performed with a coagulation probe. Prior to operational intervention in the ureter percutaneous nephrostomy (PCN) is performed with two aims: examination of the cavity system above the tumour in the case of tumours of the lower and middle ureter following the dilation of the nephrostoma. The other cause is of practical consideration: when using an ureteroscope, overpressure can be avoided with all its consequences. During diagnostic interventions max. 30-50 cm H₂O pressure is applied, as a result of which the cavity system is often emptied by sucking in cases without PCN. Following ureteroscopic interventions ureterocatheter is kept in for 48-72 hours depending on the severity of intervention. Table 2 contains the results. In Table 3 the location, histological features and clinical stage of the tumours of the cavity system as well as the chosen operative techniques are summarized.

For the identification of clinical stages of tumours in the pyelum ultrasound and CT examinations, careful intraluminal examination of the tumours of the ureter, assessment of the environment and targeted CT examinations are used. Remote metastases were not seen in any of the cases. In patients 3, 4 and 5 tumour of the bladder also occurred. In patients 3

Table 2
Classification on the basis of diagnosis

Diagnosis	No. of cases
Tumour in the ureter or the pyelum	8
X-ray negative stone	6
Exterior compression	3
Ureteritis cystica	1
Negative result	5
	23

Location, histological characteristics and clinical stage of upper tract
tumours and chosen operative technique

No.	Location	Clinical stage	Grading	Operation
1	Middle ureter	T ₂	G ₂	Nephro-ureterectomy
2	Middle ureter	T ₂	G ₁	Electrical resection through an uretero- scope
3	Pyelum calyx of solitary kidney, upper ureter	T ₃	G ₂	PC palliative resection, coagu- lation through ureteroscope
4	Pyelum	T ₁	G ₁	PC electrical resection
5	Pyelum/ureter	T ₂	G ₃	Nephro-ureterectomy
6	Middle ureter	T ₂	G ₂	Nephro-ureterectomy
7	Pyelum, calyx	T ₃	G ₂₋₃	Nephrectomy
8	Upper ureter, multiple	T ₂	G ₁₋₂	Nephro-ureterectomy

tumour of the bladder was detected in 1983; 4 years later nephro-ureterectomy was performed because of tumours in the right kidney and ureter. In patients 4 the tumours both of the pyelum and the bladder were discovered simultaneously. The tumour of the bladder in patient 5 was discovered on examination because of haematuria 5 months after a left nephro-ureterectomy. We give a short history of patients 3 and 4.

Mrs I. M. (born 27.05.1919) The G₁ type tumour of the bladder was detected in 1982. TUR was performed 20 times between 1982-1986. The last histological result was G₂. Nephro-ureterectomy was performed in 1986 because of tumour in the right cavity system. Repeated TUR was performed in 1988 because of a tumour in the bladder followed by a PCN because of oligoanuria

due to a tumour in the upper urinary tract, which was removed 2 weeks later. She was admitted to our clinic in April 1989. Main laboratory results: ESR: 35 mm/h, CN: 10 mmol/l, Se-creatinine: 198 mol/l, Se-electrolytes: normal. Blood-count: HB: 118 g/l, HTC: 0.36, WBC: 4.4 g/l, Se-bi: 5.9 mol/l, glucose: 5.6 mmol/l. Urine: pH 6, Protein: opale, other: neg. Sediment: full of WBC and RBC. Culture: *Proteus mirabilis* - significant bacteriuria. Sensitive to: Ceftriaxon, Gramurine, Ofloxacin. Blood-group: "AB" Rh neg., the serum contains anti-D antibody. On urography the upper calyces of the left solitary kidney cannot be seen, lack of contour at the initial ureteral tract. On the ultrasound picture an area of poor reflexion can be seen in the central echotexture. Angiography was normal.

In view of the limited function of the solitary kidney cytostatic treatment was out of question. Because of stagnant haematuria and obstructed flow we had to apply palliative endoscopy. Percutaneous nephrotomy was performed. Nephroscopy revealed solid and rough villous tumours in the upper calyx and the pyelum. Papillomatosis in the upper tract of the ureter could also be seen. Accessible structures (histology: $G_{2p}Tx$) were resected by pyeloresectoscopy. The tumour in the upper ureter was coagulated with ureteroscopy. (Laser coagulation was tried to be performed through the ureteroscope - Nd: YAG - without success.) Urine cleared and renal functions returned to normal after operation. The mentioned operations were performed in May 1989. The patient was discharged home with a transrenal drain, whose removal depended on the results of control examination. Mrs J. W. (born 31.05.1922) had haematuria since 1988. She was admitted to our clinic on 15.02.1989. Cystoscopy showed an approx cherry-size, fine villous papilloma slightly laterally from the left meatus. Biopsy gave G_1 result. A pulp-size lack of contour could be seen in the right pyelum on i.v. urography.

CT and ultrasound examinations gave negative results. PC nephroscopy was performed because of the location of the tumour. After taking biopsy the formula was resected. Histological results was: $G_{1p}T_a$. No pathological changes were observed in the ureter with flexible ureteroscopy. 2x10 mg of Adriamycin was given through the PC drain. PC nephrostomy ceased in 10 days. After resecting the tumour in the bladder local Adriamycin treatment was started. Neither the i.v. urography nor tomography performed two months after operation showed any abnormalities. Cytoscopy and cytology gave negative results.

Follow-up periods were short: from two months to 1.5 year. In view of this and the small number of cases they are not appropriate for drawing conclusions. One complication was found in 23 diagnostic - inclusive 3 therapeutical - interventions with ureteropyeloscope. In case 3 the wall of the pyelum perforated during the resection of the multiple tumour. Resection was accomplished at low pressure beside the small perforation gap and UK removed on day three. No other complication was found on PCN and targeted combined antibiotic therapy. The rigid ureteropyeloscope could not be introduced in one case.

Patients with nephro-ureterectomy were examined in every six months following control examination performed three months after operation. If the result of urethrocystoscopy is negative after six months, further only sedimentary, cytological and ultrasound examinations are performed. Regression occurred only in patient five, which was a tumour in the bladder. We find flexible ureteroscopy necessary as control examination, 3.5 years after endoscopic operation. Control ureteroscopy performed on patient two did not show any regression half-a-year later. On nine months follow-up the patient is free of complaints, sedimentary and cytological examinations gave negative results.

Discussion

Beside widely applied percutaneous nephroscopy ureteroscopy is getting an increasing role in endourological interventions. It is particularly important in the differential diagnosis of the ureter and in diagnosing its tumours. Performing uretero-pyeloscopy is justified in cases of symptom-free, unilateral haematuria or that with clinical complaints referring to obstructed flow shown either micro- or macroscopically, when the cause could not be defined on i.v. urography /9/. In setting up a diagnosis a flexible ureteroscope can be used alone. However, in intraureteral interventions it is more appropriate to use a rigid ureteroscope /14/. With it not only the abnormality can be seen, but the stage of the tumour can be identified on the basis of the change, size, location and assessment of the environment. Biopsy can be obtained from different parts; the tumour can be removed or coagulated with laser technique through the ureteroscope in some instances.

The greatest problem which excludes the possibility of choice in the therapy of the tumours of the upper cavity system was for a long time the difficulty in defining the tumour stage (ultrasound and CT examinations proved to be ineffective in the tumours of the ureter and some small tumours in the pyelum of low grading). Cytological examinations, the so-called brush biopsy has fallen short of expectations /3, 5/. With the histological examination of biopsy material obtained by ureteroscopy not only the degree of differentiation of the tumour, but - beside the pathological state - the clinical stage can also be identified. Several studies attest on the basis of retrospective studies that stage can be identified from the degree of differentiation of the tumour, especially in the case of low grading /2, 7/. Resection of the tumour, coagulation and laser-aspiration through a ureteroscope or a nephroscope have been applied first of all in palliative cases (anatomically or functionally solitary kidney or poor general condition). A further problem in conservative surgery of upper tract urothelial tumours was the appearance of recidivation, e.g. a tumour on the same or the other side. Statistical analyses have shown that the appearance of a tumour in the bladder is independent either of the type of operation or the degree of differentiation of the tumour. The simultaneous or later appearance of a tumour in the bladder is likely to occur in 25-30% of the cases /7/. Recidivation in the ureteral stub is expected in 35-40% the cases after nephrectomy /16, 17/. When choosing the type of operation, it may be of importance to consider that nearly all of the tumours regressed if the removed ureteral stub was of type G_2 . It was commonly stated in literature that regressions in the renal cavity system on the other side are extremely rare. Recidivations on the same side of conservational surgery on tumours type G_1 of the peripheral cavity system are also uncommon /6/. On the basis of the above, the conservational surgery of small, peripheral tumours type G_1 in the cavity system can be recommended. Resection and laser coagulation through a rigid ureteroscope seem to be a reasonable alternative to segmental resection.

References

1. Carroll G: Bilateral transitional cell carcinoma of the renal pelvis. J Urol 93:130, 1965
2. Chesko SB, Gray GF et al.: Urothelial neoplasia of the upper urinary tract. Sommers SC, Rosen PP eds, New York, p 127, 1981
3. Gibod LB, Chiche R et al.: Upper tract urothelial tumours - Diagnostic efficiency of radiology and urinary cytology. Eur Urol 8:145, 1982

4. Gibson TE: Local excision in transitional cell tumours of the upper urinary tract. *J Urol* 97:619, 1967
5. Gill WB, Lu C: Retrograde brush biopsy of the ureter and renal pelvis. *Urol Clin North Am* 6:573, 1979
6. Grossmann HB: The late recurrence of grade 1 transitional cell carcinoma of the ureter after conservative therapy. *J Urol* 120:251, 1978
7. Heney NM, Nocks BN et al.: Prognostic factors in carcinoma of the ureter. *J Urol* 125:632, 1981
8. Huffman JL, Morse MJ et al.: Ureteropyeloscopy: the diagnostic and therapeutic approach to upper tract urothelial tumours. *World J Urol* 3:58, 1985
9. Huffman JL, Bagley DH et al.: Extending cystoscopic techniques into the ureter and pyeloscopy. *JAMA* 250:2002, 1983
10. Huffman JL, Bagley DM et al.: Endoscopic diagnosis and treatment of upper-tract urothelial tumours. *Cancer* 55:1422, 1985
11. Kimball FN, Ferris HW: Papillomatous tumour of the renal pelvis associated with similar tumours of the ureter and bladder. *J Urol* 31:257, 1934
12. Murphy DM, Zinke H et al.: Primary grade 1 transitional cell carcinoma of the renal pelvis and ureter. *J Urol* 123:629, 1980
13. Murphy DM, Zinke H: Management of high grade transitional cell cancer of the upper urinary tract. *J Urol* 125:25, 1981
14. Perez-Castro E, Pineiro JA: Transurethral ureteroscopy: A current urological procedure. *Arch Esp Urol* 33:445, 1980
15. Petkovic S, Mutardzic M: The late results of conservative surgery for ureteral tumours. *Brit J Urol* 40:412, 1968
16. Schneller NT, Nofstetter AG: LASER treatment of ureteral tumours. *J Urol* 141:840, 1989
17. Strong DW, Pearse HD: Recurrent urothelial tumours following surgery for transitional cell carcinoma of the upper urinary tract. *Cancer* 38:2178, 1976

EVALUATION OF 1000 PERCUTANEOUS NEPHROSTOMIES WITH A SPECIAL VIEW TO EFFICIENCY AND COMPLICATIONS

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The authors summarize the experience gained with 100 percutaneous nephrostomies including the evaluation of the efficiency of the applied technique, complications and the possibilities to decrease the number of complications in 900 nephrolithotomies. Discussing efficiency, they stress the importance of appropriate indication, to which low failure rate (3%) is attributed. In the prevention of complications accessories are of importance. Experience has shown that the number of perforations in the cavity system can significantly be decreased in multi-operated, cicatrized kidney - where perforations occur most frequently - with the use of the Amplatz dilator system. This type of dilator system is also recommended to unexperienced endoscopic specialists for use in primary cases. Favourable experience was gained with the use of the so-called swab balloon catheter in haemorrhages from nephrostomy. In the end they give a summary of the present fields of application of this technique and its role in the treatment of nephrolithiasis.

The aim of the first percutaneous nephrostomy performed in the case of obstruction was to provide urinary outlet. This technique was introduced by Goodwin et al. /6/. Thousands of PCN have been performed since then. Indication field has significantly expanded for the past decade. Besides drainage aiming at providing simple urinary outlet, this technique facilitated the removal of certain renal and ureteral calculi without a necessity to open surgery /5/, endoscopic approach in some pyeloureteral- and ureteral coarctations /2/, percutaneous histological examination of inflammation or tumours in the renal cavity system and the removal of tumours in selected cases /7/. The method is also applied in setting up operational indication of dilation of the renal cavity system and measuring the pressure in it /17/. The first in Hungary to apply this type of intervention in therapy were Tóth and Rosdy, while in diagnostics Karsza /8, 11, 15/. The number of complications has naturally increased in consequence of the widened and more frequent application of this new technique. Several devices promoting precise puncture and ensured performance have been developed lately.

In our study we primarily deal with the efficiency of PC technique in nephrolithotomy, complications due to this intervention and the ways of prevention.

Patients and Methods

Percutaneous nephrostomy was performed in 1000 cases at the Department of Urology of the Postgraduate Medical University between 1st January 1986 30. April 1989. Indications are grouped in Table 1.

Table 1
Distribution of 1000 PC punctures on the basis of indication

Indication	No. of patients
Stone in the renal cavity system and the upper tract of the ureter	935
Tumour in the pyelum or the ureter	5
Endoplastics of the pyelo-ureteral barrier	8
Functional examination (2-3 weeks drainage)	28
Palliative therapy	24
Totally	1000

Complications in the first 35 nephrolithiac cases were not included either in the retrospective study or the assessment of the results (so-called trial period). Efficiency of accessories used in PCN was evaluated. We have had ultrasound equipment and TV intensifier since the first interventions. Three different devices were used in dilating puncture channel for the past two years. They are shown in Figs 1, 2 and 3. The Alken telescope - Amplatz polyethylene - and balloon dilator systems were used to study which of them can be applied in different anatomical situations with the least complications. The main aspects were haemorrhage, perforation of the renal cavity system and unsuccessful dilation. Postoperative febrile state and sepsis were also taken as complications. In the case of residual stones and early regression we tried to find the causes. One of the main advantages of using PC technique is its efficiency as suggested by the duration of operation and period of hospitalization.

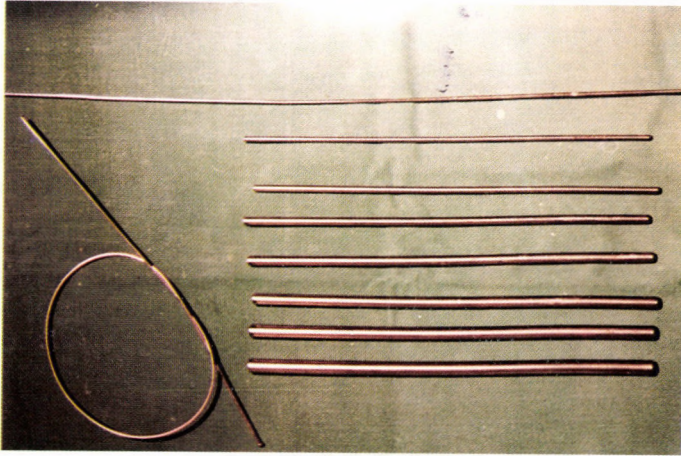


Fig. 1.

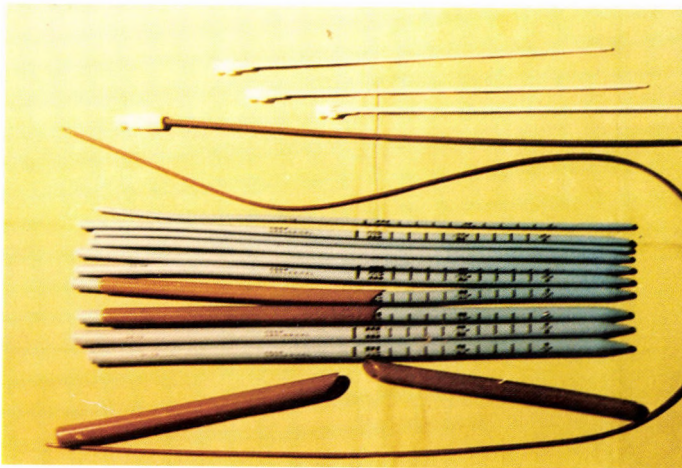


Fig. 2.

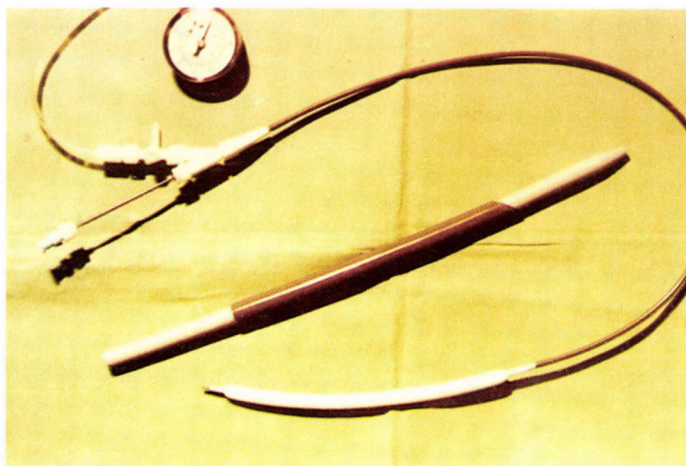


Fig. 3.

Results and Complications

In 115 of the 900 patients of the study, calculi could be found in the upper and middle tract of the ureter. 560 of the 785 calculi in the renal cavity system seemed to be solitary pyelolithotomes. Coral stones were removed in 8 cases with 2 or 3 treatment sessions. Joint occurrence of calculi in the pyelum and the calyx was recorded in 182 cases. Partial coral stones were found in 35 patients. Repeated PC intervention or open surgery was necessary because of technical difficulties in 21 cases. Initial failure was due to two causes: the inappropriate access to the stone and difficulties emerging during manipulation. Detailed causes and outcome are shown in Table 2. The 8 cases where anterograde removal was planned as first approach following unsuccessful trial to obtruse the calculi in the upper and middle ureterial tract, are not included in the table. In four out of these cases PC approach proved to be unsuccessful; ultrasonic lithotripsy was performed in two cases with stones in the middle tract and open surgery in other two cases. Failure ratio is 2.77%, if the latter four patients are involved in failure due to initial technical difficulties (21+4 patients). Literary data contain a 2-4% failure rate in similar cases.

Table 2
Causes of initially unsuccessful PC interventions

Cause	Outcome		
	No. of cases	Repeated successfully	Open surgery
Inappropriate puncture perforation, extravasion	5	4	1
Repeated puncture-trial perforation during dilation	2	2	1
Unsuccessful introduction of device	5	5	-
Haemorrhage	5	5	-
Unsuccessful dilation	3	2 (ESWL)	1
Totally	21	15	6

Stone fragments recognized by native kidney X-ray, tomography or antero-grade urography performed before removal of the transrenal drain (TRD) in the postoperative period were taken as residual stones. Little fragments whose size did not exceed that appropriate for spontaneous leave after ESWL treatment, were not considered as residual stones. In view of the above criteria residual stones were recorded in 24 patients on discharge; which is 2.7% of our cases treated successfully. Recidivations were observed of our cases treated successfully. Recidivations were observed in 10 cases after PCN. In all of the cases ultrasonic lithotripsy was performed during operation.

Treatment days

Treatment days we count from the day of operation. Figure 4 shows the number of treatment days. Most patients were discharged on days 4-6 after operation. Mean treatment period was 5, 6 days (shortest: 3 days, longest: 29 days). Several weeks hospitalization is reasonable in the case of patients with coral or multiple stones where stone removal was performed on two or three occasions. Days 5-9 were characterized by pain, discomfort and macroscopic haematuria in some instances because of the closed TRD. Complaints sometimes were due to stone fragments, more often to the location of TRD or obstructed urinary flow because of coagulation.

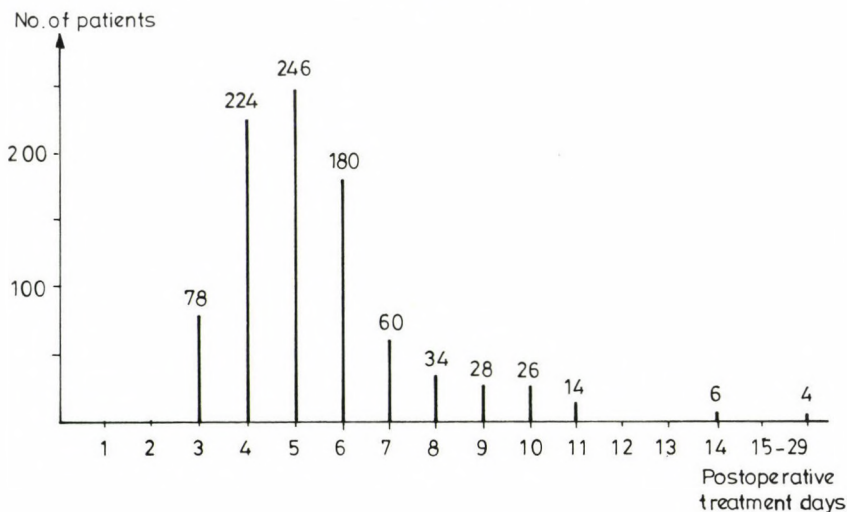


Fig. 4. Postoperative treatment days of 900 percutaneous nephrolithotomies

Duration of operation

Starting time of operation we considered the time of puncture on a narcotized patient with continuous epidural anaesthesia or paravertebrally narcotized with puncture anaesthesia lying on his front. Narcosis through intubation was applied in the first 150 patients. The operation was finished with sticking the TRD. The mean duration of operation was 52 minutes. In the evaluation of the time of operation we also have to take in consideration that 2-3-hour interventions were common in the first 100-150 cases. Operational time has shortened to 25-40 minutes for the past two years which resulted in the decrease of mean duration, which does not mean, however, that there are not some operations which last for 1.5-2 hours.

Complications

Literary data give a wide range of ratio of complications due to PC interventions: between 4-30% [3, 14]. The explanation for this may be that some authors include into complications also small perforations of the renal cavity not requiring treatment and punctural haemorrhage requiring transfusion in small quantity.

We took for complication only cases requiring further operation or more than 48 hours observation. Table 3 shows typical complications. The analysis of different types of complications shows that haemorrhage more frequently occurs with the use of Amplatz dilator system, while perforation occurred only when using the Alken telescope dilator system. No complications occurred with the balloon dilator system which was used in 40 cases.

In nearly 90% of febrile complications preoperative examination of the urine showed pyuria or significant bacteriuria. 80% of the pathogens belonged to the E. coli group and reacted well to combined targeted treatment. In our septic patients with a shock preoperative culture showed *Proteus* in two cases and bacteria belonging to the *Pseudomonas* line in one case.

Table 3

Intra and direct postoperative complications of 900 PC nephrolithotomies

Complication	No. of cases	Treatment	
		Surgical	Conversation
Haemorrhage	7	sutura 2 nephrectomy 1	swab catheter 4
Rupture in the renal material (inappropriate dilation)	2	suture 2	-
Bowel fistula	1	-	1
Perforation of the renal cavity system	10	sutura 1	TRD, UK 9 for 3-4 days
Postoperative febrile state	54	-	targeted antibiotic
Septic shock	3	nephrectomy 1	appropriate

Discussion

PC removal of stones from the renal cavity system or the upper tract of the ureter seemed to be nearly the only way of intervention in the early 80s /1, 12/.

With the increase of the number of cases complications decreasing the circle of indications appeared /4, 9, 10, 16/. PC lithotomy has received its real place in available, optional possibilities in the removal of renal and ureter calculi on the joint impact of complications and the

spread of ESWL treatment. Appropriate indication, available tools and - last but not least - individual skills have a decisive role in the efficiency of PC interventions and the wide range of the occurrence of complications. Our low failure rate can be explained with the fact that the scale of indication was not broadened more than necessary when introducing PC technique at our clinic. PC interventions were indicated in exceptional cases with anatomical and local disturbances of development or flow disturbances due to ptotic kidneys. The low number of our patients with coral stones shows that PC monotherapy is rarely considered in these cases. Recent literary data support our practice /13/.

What is less frequently mentioned in literature and we would like to stress is PC lithotripsy, supportive therapy following ESWL treatment and the importance of a careful follow-up. Ruptured parts in the mucous membrane remaining after lithotripsy, concretions in the injured mucous membrane or small sand-grains in the coagulum serve as a basis for recidives. If the renal cavity system cannot be fully cleared with the available tools and careful intervention, continuous irrigation through TRD in the defence of UK is reasonable. The content of the irrigation fluid can be changed depending on the material of the stone; local and parenteral administration of targeted antibiotics can be added. Indication has an important role in the ratio and types of complications during and after PC interventions. Serious complications (haemorrhage, injury to adjacent organs are more frequent in the cases of authors who extend the indication of PC interventions on the operation of horseshoe - or dystopic kidneys, when intruding between ribs X-XI, pneumo-haemothorax can be expected. Serious complications occur in 4-5% of the cases on PC interventions performed on the basis of justified indication /10/. The other important factor - beside indication - is the availability or lack of accessories. To make an appropriate and quick puncture an ultrasound and X-ray intensifier are needed, which is of particular importance in case of infected urine. Difficult puncture, multiple trial occurred in the surgical report of the majority of our steadily febrile patients and in 2 of 3 septic patients in the post-operative period. (Most of them had infected urine before operation.)

Urine must be cleared before operation in all patients whose urine is infected, and if possible, operation must be performed applying targeted broad-spectrum antibiotics. If puncture cannot be appropriately performed after 2 or 3 trials, operation should be postponed in case of infected urine.

Our experience shows that haemorrhagic and perforational complications can be prevented to a great extent with the use of a dilator system suited to the case and the experience of the operating surgeon. In the case of multioperated kidneys in cicatrized environment and parenchyma the Amplatz polyethylene dilator system can reliably be applied. The 8 Ch teflon catheter on the leading wire prevents not only from the perforation of the renal cavity system but from the break or sliding out of the wire which is quite common with the unexperienced endoscopist. However, greater damage can be done in the parenchyma especially when introducing a teflon suspension sheath compared to telescopic dilation which results in haemorrhagic complication. The Alken dilator system can be used successfully in the above average mobile ptotic kidneys, where dilation can be performed more safely fixing the kidney with the leading wire. We consider balloon dilation favourable first of all because it is quick and causes minimal mechanical damage to the parenchyma, but only in primary cases. Its use is recommended in the case of inflamed kidneys and after acute pyelonephritis.

The so-called swab balloon catheter seems to be useful in the treatment of haemorrhagic complications. Bleedings from nephrostomy rapidly cease after introducing the catheter. If haemorrhage cannot be stopped, a swab catheter can be placed instead of the nephrostomy catheter, with the help of a leading wire, which - after pumping the balloon blocking the puncture - not only stops haemorrhage, but provides urinary drainage.

On the basis of our experience and available publications, PC nephrolithotomy has an important role beside ESWL in the treatment of urolithiasis. Its role has significantly decreased in monotherapy but it has several advantages in removing small stones from the renal cavity system without lithotripsy. Anyhow, ESWL treatment seems to be also inconceivable without the knowledge of PC technique. This concerns both combined therapy and the frequent necessity of PC interventions before or after ESWL treatment.

Besides lithotherapy PC technique is expected to have a growing role in the treatment of patients with upper tract tumours, constriction of the pyelo-ureter barrier and primary and secondary constrictions of the ureter.

Concerning complications, the risk of PC intervention - with well grounded indication and with accessories providing greater reliability - is no greater than that of open surgery; on the other hand, it is quicker and much more efficient.

References

1. Alken P, Hutschenreiter G et al.: Percutaneous stone manipulation. J Urol 125:463, 1981
2. Badlani G, Smith AD: Percutaneous surgery for ureteropelvic junction obstruction (endopyelotomy): techniques and early results. J Urol 133:215, 1985
3. Clayman RV, Surya V et al.: Percutaneous nephrolithotomy: extraction of renal and ureteral calculi from 100 patients. J Urol 131:868, 1984
4. Clayman RV, Surya V et al.: Renal vascular complications associated with the percutaneous removal of renal calculi. J Urol 133:228, 1984
5. Fernström J, Johansson, B: Percutaneous pyelolithotomy. Scan J Urol Nephrol 10:257, 1976
6. Goodwin WE, Casey WC, Wolf W: Percutaneous trocar (needle) nephrostomy in hydronephrosis. JAMA 157:891, 1955
7. Huffman JL, Morse MJ et al.: Endoscopic diagnosis and treatment of upper tract urothelial tumours. A preliminary report. Cancer. 55:1422, 1985
8. Karsza A, Banyó T, Engert Z: Surgical indication of dilatation in the renal cavity system. Acta Chirurgica Hungarica 26(6), 201, 1985
9. Lee WJ, Smith AD et al.: Complications of percutaneous nephrolithotomy. AJR 148:177, 1987
10. Marberger M, Stackl W et al.: Late sequelae of ultrasonic lithotripsy of renal calculi. J Urol 133:170, 1985
11. Rosdy E: Approaches increasing the efficiency of percutaneous nephrolithotomy. (Perkután veseköeltávolítás eredményességét fokozó eljárásokról.) Urol Nephrol Szemle 14 (2), 107, 1987
12. Segura JW, Patterson DE et al.: Percutaneous removal of kidney stones: review of 1000 cases. J Urol 134:1077, 1985
13. Schulze H, Hertle L et al.: Critical evaluation of treatment of staghorn calculi by percutaneous nephrolithotomy and extracorporeal shock wave lithotripsy. J Urol 141:822, 1989
14. Stables DP, Ginsberg NJ, Johnson NL: Percutaneous nephrostomy: a series in review of the literature. AJR 130:75, 1978
15. Tóth Cs: Endoscopic nephrolithotomy. (Endoszkópos vesekösebészet.) Medicina, Budapest, 1987
16. Vallancien G, Capdeville R et al.: Colonic perforation following percutaneous nephrostomy and renal calculus removal. Radiology. 155:83, 1985
17. Whitaker RH: The Whitaker test. Urol Clin North Am 6:529, 1979

USE OF DIFFERENT TYPES OF DILATOR SYSTEMS IN THE PREVENTION OF COMPLICATIONS OF PERCUTANEOUS (PC) RENAL SURGERY

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The authors deal with the causes of frequent complications observed in 1300 PCN performed. The retrospective study focuses on haemorrhagic and perforative complications. Relation between the type of the applied dilator system and the frequency of complications was observed. Emphasis should be put on the preliminary mapping of anatomical conditions and the use of appropriate dilator system. In the case of cicatrized, multioperated kidneys the application of Amplatz polyethylen dilator system is recommended, especially if the operating surgeon is unexperienced. In primary cases and developmental disorders the use of Alken telescopic dilator is recommended. They have favourable early experiences with balloon dilatation of the parenchyma.

The number of publications dealing with the assessment of the forms and causes of complications has increased for the past decade as PC renal operations became a routine. The publications most often stress the experience of surgeons performing the operations and the role of existing tools. The most important of the latter are targeting and forming the puncture channel in the right direction /8, 13/. Less emphasis is put on the complications and the possibilities of prevention during dilating the puncture channel.

At our clinic we have used three different types of dilator systems since PC interventions were introduced. In the course of our retrospective study on complications and their causes we found a context whose analysis seems to be justified.

Patients and Methods

1300 PC interventions have been performed because of urinary calculus at the Department of Urology of the Postgraduate Medical University between 1 January 1986 - 31 December 1990. Puncture of the renal cavity

system was initially performed mainly by ultrasound targeting. Later - on the basis of experience - the direction of puncture was corrected with the help of a TV intensifier.

On retrospective analyses the following points related to the most frequent complications (perforation requiring treatment, haemorrhage) were attended:

- preliminary open operation,
- the anatomical and morphological abnormalities of the kidneys,
- presence of inflammation in the parenchyma,
- type of the dilator system,
- experience of the surgeon performing the operation.

The three types of dilator systems we use, are the following: Alken telescopic dilator, Amplatz polyethylene - and balloon dilator /2, 3, 12/. Dilation of the puncture channel is most frequently up to 28 CH thickness.

Results

Table 1
Complications during dilating the puncture channel and their management

Type of complication		Therapy			
		Conservative		Open surgery	
Bleeding	40	Swab catheter	18	Sutura	2
		Coagulation	4	Nephrectomy	3
		Transfusion	13		
Perforation	28	PCN or DJ for more than 72 hours	26	Sutura	2

Prevalence of the two significant groups of complications can be seen in Table 1. The most frequent problem is haemorrhage. Most bleedings on the drain put in at the end of operation or along it, could be controlled by placing a thicker, 18-20 CH drain in or a so-called swab catheter. Bleeding in the lumen causing visual disturbance during operation was stopped by coagulation through a nephroscope in 4 cases. In 30 out of the 1300 performed interventions we had to apply transfusion in addition to the treatment methods given in the table, while in 13 cases transfusion was applied

as single therapy. Perforation in the renal cavity system requiring treatment was recorded in 28 cases.

Perforations caused by UC or leading wire were not included in the above-mentioned cases as they had no impact either on the process of the operation or follow-up. We decided on exposure in two cases because of perforation due to the use of the dilator system. Exposure had to be performed because of the inappropriately deep introduction of the last element of the Amplatz dilator system, i.e. the suspension sheath which led to a rupture of the lower calyx and the pyelum. In the remaining 26 cases keeping in the transrenal drain (TRD) and/or double J (DJ) catheter for 72-88 hours proved to be sufficient for recovery.

On the retrospective analysis of complications it was striking that haemorrhage occurred in a significantly higher number with the use of the Amplatz dilator system, while perforations were mainly association with the use of the Alken dilator system (Table 2). In the anamnesis of haemorrhagic

Table 2

Context between the use of different dilator systems and the occurrence of complications

Complication		Type of dilator system		
		Amplatz polyethylene 482 cases	Alken telescopic 767 cases	Balloon 51 cases
Bleeding	40	28 previous inflammation developmental disorder	12 previous inflammation	4 -
Perforation	8	6 preliminary operation	22 preliminary operation	- 15

complications inflammation or developmental disorders (ptotic kidney, horseshoe kidney) are common, while in the case of perforations a striking number of previous operations. Table 2 also contains the number of these operations.

Discussion

Literary publications on the effectivity of PC interventions and complications focus on accurate targeting and the right direction of the puncture channel. Haemorrhage in the renal cavity system and the parenchyma due to multiple unsuccessful trials to puncture, release of the contrast material and broken puncture channel seem to be the frequent cause of failure /4, 6, 8, 9, 11, 13, 14/.

The leading wire led into a broken puncture channel often slides out or breaks during dilation which may cause complications. Our analyses showed the determining role of the type of the applied dilator system in perforating or haemorrhagic complications.

The choice of the way of operation depends on the previous operations performed, anatomical abnormalities or past inflammation. We found perforating complications in an extremely large number in patients having had renal surgery especially if Alken dilator system was used. The reason for this may be a puncture channel passing a cicatrized area must be dilated with greater strength and if the leading wire of the dilator system is not appropriately fixed in the surgeon's hand, it can break easily and perforates the wall of the cavity system. The 8 CH teflon catheter applied on the leading wire of the Amplatz polyethylene dilator system does not allow its break even in the case of a sudden display of greater strength and leads the elements in the right direction. Anyhow, perforation may occur with the use of Amplatz dilator system as well /2/. Our experience shows that the position and introductory technique of the suspension sheath plays an important part in this. If the sheath is led in without rotating and too deep, it may lead to the rupture of the calyx and the wall of the pyelum. This mainly occurs in the case of penetrating the lower calyces with narrow calyx.

The greater number of haemorrhagic complications with the use of Amplatz dilator systems can also be explained with the inappropriate, careless introductory technique of the suspension sheath. If the teflon sheath is introduced not in a standard way, its shovel-shaped end may tear off parts of the parenchyma and the fascia which prevent the free introduction of the last element of the dilator system and holding the right direction resulting in an injury and rupture of the parenchyma /6/.

The cause of more frequent occurrence of haemorrhagic complications with the use of this type of dilator system could also be that the puncture

channel was dilated up to 30 CH in case of large calculi requiring lithotripsy, so the bleeding was more expressed and difficult to swab by catheter. This method is of great use primarily in subacute or preoperational acute inflammations. This was supported by our own experience. Its disadvantage lies in its high costs.

In summary we can conclude that the occurrence of complications due to PC interventions depends on the experience of the surgeon on the one hand, and the type of the dilator system chosen according to anatomical conditions on the other /10/.

Amplatz dilator system seems to be advantageous in multioperated, cicatrized kidneys, while the Alksen system in the case of anatomical disorders. Telescopic dilators are significantly faster in primary cases. Amplatz polyethylene dilator system is recommended for surgeons without or with little experience.

References

1. Alken P, Günther R, Thuroff J: Percutaneous nephrolithotomy - a routine procedure. *Brit. J Urology Suppl.*, 1-5, 1983
2. Alken P: The telescopic dilators. *World J Urology*. 3:7-10, 1985
3. Clayman RV, Castaneda-Zuniga WR, Hunter DH, Miller RP, Lange PH, Amplatz K: Rapid balloon dilatation of the nephrostomy tract for nephrostolithotomy. *Radiology*, 147:884-885, 1983
4. Clayman RV, Castaneda-Zuniga WR: Nephrolithotomy, percutaneous removal of renal calculi. *Urologic Radiology*, 6:95-112, 1984
5. Elyoderani MK, Kandzali S: Percutaneous antegrade pyelography and nephrostomy guided by ultra sound. *West Virginia Med J* 76:5, 1980
6. Karsza A, Magasi P: Evaluation of thousand percutaneous interventions with particular respect of the efficiency and the complications. *Magyar Urológia* 1:71-79, 1989
7. Kovács A, Szolnoki Gy: Percutaneous nephrostomy under ultrasonographic control. *Int Urol Nephrol* 21:131, 1989
8. Lee WJ, Smith AD, Cubelli V et al.: Complications of percutaneous nephrolithotomy. *A.J.R.* 148:177, 1987
9. Miller RA, Wickham JEA: Percutaneous nephrolithotomy: advances in equipment and endoscopic technique. *Urology* 23:2-6, 1984
10. Miller RA, Payne SR, Wickham JEA: Review of accessories for percutaneous renal surgery. *Brit J Urology* 56:577-581, 1984
11. Rosdy E, Török P: Experiences with 150 percutaneous nephrolithotomies. (Perkután vesekő-eltávolítással szerzett tapasztalataink 150 eset kapcsán.) *Orvosi Hetilap* 128:1875, 1987
12. Rusnack B, Castaneda-Zuniga WR, Kotusa F, Herrera M, Amplatz K: An improved dilator system for percutaneous nephrostomies. *Radiology* 144:174, 1982
13. Sequerra SW, Patterson DE, le Roy J et al.: Percutaneous removal of kidney stones: review of 1000 cases. *J Urol* 134:1077, 1985
14. Tóth Cs: Endoscopic nephrolithotomy. (Endoszkópos vesekősebészet.) *Medicina Könyvkiadó*, Budapest 1987
15. Wickham JEA, Miller RA, Kellett MJ, Payne SR: Percutaneous nephrolithotomy, results and cost effectiveness. *Brit J Urology Suppl.* 103-106, 1983

PRESERVATION OF EJACULATION IN STAGE I. NON-SEMINOMATOUS TESTICULAR TUMOURS

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(Received: January 24, 1992)

The loss of ejaculation is the most serious postoperative complication of patients having stage I non-seminomatous testicular tumours. In order to preserve the capability for ejaculation even after retroperitoneal lymphadenectomy (RPA) the preservation of paravertebral sympathetic ganglia but that of the sympathetic nerves in the territory of aortic bifurcation and common iliac arteries to be unnecessary.

The first publications on the problems of ejaculation and fertility of patients with testicular tumours after retroperitoneal lymphadenectomy appeared in the 60s /1, 3, 11, 12, 13/. In this period nearly 90% of patients lost their capability of ejaculation which was considered an evidence of successful bilateral retroperitoneal lymphadenectomy (RLA;4). As a result of operation and the application of new cytostatic drugs more and more patients recover; most of them of course belong to pathological or clinical stage I. These young men with lasting remission have a just claim for the same quality of life that their healthy fellows have.

Patients and Methods

167 different types of RLA have been performed on patients with testicular tumours in different stages and of various pathology for the past 13 years. The routinely applied way of operation was bilateral RLA at our clinic (Fig. 1) later the knowledge of the lymphatic system of the retroperitoneal area facilitated the introduction of altered RLA in clinically stage I patients (Fig. 2). This means that the paravertebral sympathetic ganglia area spared on at least one side. Applying this method ejaculation is preserved in appr. 70% of the patients /7/.

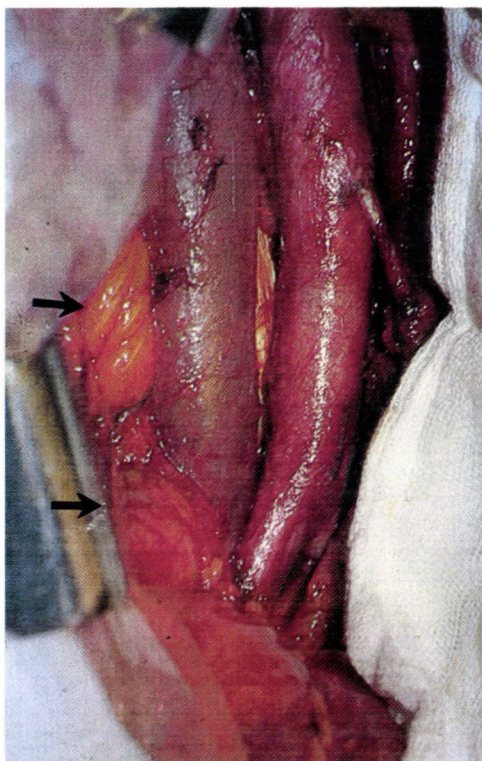


Fig. 1.

A year ago, the nerve-preserving operative technic recommended by Javadpour and later of Donohue was introduced with the aim of further improving the results, which is based on the preservation of the paravertebral sympathetic ganglia and concentrates on the sympathetic nerves in the territory of aortic bifurcation and common iliac arteries [2, 9, 10]. This type of operation can be performed on patients in whom metastases were not found either by CT or ultrasound examination or their markers are normal.

In the case of a tumour on the right side the right paravertebral ganglia and the sympathetic nerves in the aortocaval territory must be preserved. In order to preserve the sympathetic nerves in this territory, we must leave the interaortacaval region intact in the area of the inferior mesenteric artery. The operation on the left side is technically more com-



Fig. 2.

plicated as the sympathetic nerves emerging from both the left and the right side ganglia can be found on the front side of the aorta, so departing the nerve fibres and lymphatic system is a time-consuming process requiring patience.

Ejaculation seems to be safely preserved if the front side of the aorta is left intact distally from the inferior mesenteric artery and the nerves above the common iliac arteries are preserved /2, 10/ (Fig. 3).

We must stress that block dissection is applied in this case as in bilateral or altered RLA; the difference is that block dissection is preceded by the partition of the sympathetic nerves.

Donohue and colleagues performed this nerve preserving retriperitoneal RLA in 75 stage I patients; their data show that the capability of ejacu-



Fig. 4.

lation is preserved in all of their patients /2/.

This method has been applied for one year in our clinic. This type of operation was performed on 10 patients; andrological examination could be performed in 9 of them. Eight of them have normal ejaculation, it ceased in one case.

Table 1

Type of RLA	No. of patients	Ejaculatory disorders (%)
Bilateral	13	85
Altered	21	33
Nerve-preserving	10	12

Types of RLA performed on patients with clinical stage I non-seminomatous testicular tumours and the % rate of ejaculatory disorders (N=44)

Discussion

Ejaculation is a two-phased process: the sperm first gets into the prostatic section of the urethra then it gets out with the contraction of the muscles of the pelvic floor. If the sympathetic ganglia between the lumbar disks 2-4 or the hypogastric plexus are hurt during RLA, the first stage of the above process is missing, that is the sperm does not enter the rear urethra.

The paravertebral sympathetic ganglia and the nerves of the hypogastric plexus are near the abdominal aorta and the common iliac arteries, their network is blended with lymphatic systems. Even if the paravertebral ganglia can be preserved on RLA, the nerves on the front side of the aorta and the common iliac arteries can be hurt easily when removing the lymphatic systems and lymph nodes in this region.

In the knowledge of the path of the retroperitoneal lymphatic system and the most frequent localization of metastases the area of dissection can be reduced and the aortic bifurcation and the nerves above the common iliac arteries can be preserved - if no malignant cells from the specific area could be seen either in the intraoperative cooled sections and the pre-operative tumour markers were negative /8/.

Supposed the sympathetic ganglia were preserved on RLA, the reduction of the dissected area alone is not enough to preserve ejaculation, but the accurate and patient partition of the nerves and lymphatic system is required in the area of the removal of the lymphatic tissue so that we can preserve the nerves.

Our experience shows that nerve-preserving retroperitoneal lymphadenectomy can well be applied in the clinical treatment of patients with stage I. Non-seminomatous testicular tumours, who belong to a group of patients where recovery is approx 95%; anyhow, they are expected to survive longer

and - preserving ejaculation - normal sexual and harmonic family life is provided to them.

References

1. Albrecht D, Nagel R: Verlust der potentia generandi nach retroperitonealer Lymphadenectomie bei malignen Hodentumoren. Act Urol 4:91, 1972
2. Donohue JP, Foster RS, Geier G et al.: Preservation of ejaculation following nerve-sparing retroperitoneal lymphadenectomy. J Urol 139:
3. Donohue JP, Rowland RG: Complications of retroperitoneal lymphadenectomy. J Urol 125:338, 1981
4. Fehér M: The surgical treatment of testicular tumours at our clinic. (A heredaganatok sebészki kezelése klinikánkon.) Urol Nephrol Szle Suppl. 73, 1985
5. Fehér M, Bányai B: Ejaculatory impotence of patients with testicular tumours following the dissection of retroperitoneal lymph node. (Heretumoros betegek impotentia ejaculandi-ja retroperitoneális nyirokcsomó dissectio után.) Orv Hetilap 122:2659, 1981
6. Fehér M, Kéry S: Preservation of capability of ejaculation on retroperitoneal lymphadenectomy. (Az ejaculatio képesség megőrzésének lehetősége a retroperitoneális lymphadenectomia során.) Urol Nephrol Szle 12:38, 1985
7. Fossa SD, Klepp O et al.: Unilateral retroperitoneal lymph node dissection in patients with non-seminomatous testicular tumour in clinical stage 1. Eur Urol 10:17, 1984
8. Fossa SD et al.: Distribution of retroperitoneal lymph node metastases in patients with non-seminomatous testicular cancer in clinical stage 1. Eur Urol 17:107, 1990
9. Foster RS, Donohue JP, Bihrlé R: Stage A non-seminomatous testis carcinoma. rationale and results of nerve-sparing retroperitoneal lymphadenectomy. Urol Int 46:294, 1991
10. Javadpour N: Nerve-sparing retroperitoneal lymphadenectomy for non-seminomatous testicular cancer. J Urol 139:435, 1988
11. Kom C, Mulholland SG, Edson M: Etiology of infertility after retroperitoneal lymphadenectomy. J Urol 105:528, 1971
12. Leiter E, Brendler H: Loss of ejaculation following bilateral retroperitoneal lymphadenectomy. J Urol 98:375, 1967
13. Lenz P, Meredies R: Fertilitätsstörungen nach retroperitonealer Lymphknotenausraumung wegen teratoider Hodentumoren. Act Urol 4:87, 1972

BOOK REVIEW

Reconstruction of the mamma (Rekonstrukcija zenskoj molocnoj zelezey)

János Zoltán

Akadémiai Kiadó, Budapest 1989, pp. 237; price: 6 Roubles 80 kopek

Mamillary cancer seems to be one of the most frequent malignant tumours in women. Its likely occurrence is 6-7%. In Europe the mortality rate is the highest in the Benelux countries and in Great Britain. Modern treatment may improve the potential survival of thousands of individuals every year. In addition to complex treatment methods applied with the aim of decreasing the mortality rate, the search for an operative technique ensuring the patients' physical and mental rehabilitation has come into prominence. The book of János Zoltán "Reconstruction of the mamma" was written in this spirit which focuses on these actual and important problems and their potential solutions in mamillary surgery.

The book consists of 11 well-constructed chapters, a comprehensive review of the literature on the subject, 133 illustrations and 30 pages of black and white photos based on the author's many decades experience.

Chapters 1 and 2 written by two co-authors, deal with the psychic impacts of mamillary operations and the classic, radical as well as the new altered ways of operation applied in the treatment of mamillary cancer.

Chapter 3 describes the indications, contraindications for mamillary surgery and reconstructional problems.

Chapter 4 contains the anatomy of the mamma. The author discusses the anatomical conditions in which reconstructional operation can be performed with respect to oncological aspects.

Chapter 5 contains the description of modern ways of replacing skin deficiencies due to amputation. It also deals with the treatment of cutaneous injuries and strictures due to postoperative irradiation.

Chapter 6 deals with the reconstructional possibilities after the radical removal of the mamma. It describes the different ways of alloplastic reconstruction, the applicability of silicon- and gel prostheses, operative technique and postoperative complications.

Chapter 7 is an introduction to immediate or early alloplastic or prosthetic transplant possibilities following the extirpation of mamillary cancer recognized at an early stage.

Chapter 8 gives a detailed description of combined procedures leading to the best results in the reconstruction of the mamma. It also deals with the possibility of free cutis-fat lobe transplantation performed with a microsurgical technique.

Chapter 9 is about the possibilities and results of reconstruction of the nipple and the areola.

Chapter 10 focuses on the indication and technique of subcutaneous mastectomy and the possibilities of reconstruction.

Chapter 11 discusses the replacement of mammary defects of non-tumour origin.

The reader - who is interested in the subject - is holding in his hands a book of superior quality with excellent illustrations whose 1517 references give a good volution in the field. The book is supplemented with a series of photos of excellent quality on the last 30 pages which show the results of the author gained from this own experience. The author - using his own experience and giving a comprehensive review of the literature on the subject - published a modern textbook obridging a gap existing in Hungary in every-day surgical practice: it can be recommended not only for specialists of plastic surgery but for all practicing surgeons.

Mihály IHÁSZ

Akadémiai Kiadó, Budapest.

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VOLUME 32

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INDEX

Advantage of transvaginal over transabdominal sonography. <u>K. Pataki, Zs. Jakab, Z. Harkányi and Z. Vigváry</u>	3
A case of Fournier's gangrene. <u>H. Czalbert, L. Hornok and L. Ritter</u>	13
Intraoperative injuries during transperitoneal urological operation. <u>L. Pajor, J. Lip-ták and M. Szűcs</u>	17
Ultrastructural changes in the nerve elements in Chron's disease. <u>V. Szabó and Erzsébet Fehér</u>	25
Motor response to electric spatial stimulation of isolated intact and inflamed human ap-pendix. <u>A. Antal, J. Szolcsányi and L. Bartho</u>	33
The potentials of CO ₂ laser in the surgery of the liver, biliary tract and pancreas. <u>I. Tóth and J. Bátorfi</u>	39
A case of multiple cholangiogenic liver abscess due to residual biliary stone cured by percutaneous drainage controlled by CT and endoscopic papillotomy. <u>I. Fazekas, F.I. Todua, M.Y. Vilyavin and A. Bálint</u>	45
Gastrointestinal angiodysplasia. <u>F. Jakab, Márta Balázs, J. Fallér and S. Kiss</u>	57
Percutaneous cholecysto-lithotripsy. <u>Cs. Tóth</u>	69
Rupture of the splenic artery aneurysm during pregnancy. <u>D. Hunka, Teréz Csordás and Z. Domány</u>	77
Virus-host studies in human seminal and mouse testicular cells. <u>S. Csata and Gizella Kulcsár</u>	83
Sonographic scan of the normal and pathological endometrium. <u>K. Patai, Z. Harkányi, Zsuzsa Jakab and Z. Vigvári</u>	91
Effect of different intravenous nutrients on upper gastrointestinal secretion in rats. <u>E. Dárdai and J.E. Heavner</u>	101
Coronary artery revascularization after myocardial infarction. <u>F. Tarr, Gy. Lakos, I. Tomcsányi, T. Sugár, L. Hajdu and T. Lónyay</u>	109
Treatment experiences with intracavitary ¹³⁷ Cs after-loading in a five-year patient material with uterine-cervical carcinoma. <u>S. Csömör, Z. Vigváry and L. Szanyi</u> ..	119
Intra-abdominal desmoids observed after total proctocolectomies. <u>K. Szilágyi, K. Kett and G. Hegedűs</u>	127
Follow-up of the effect of BCG in bladder tumour patients. <u>P. Tenke, S. Csata and Gizel-la Kulcsár</u>	131

Technique of extensive proximal selective vagotomy. <u>J. Bátorfi, M. Ihász, A. Bálint, K. Szabó, T. Fazekas and I. Koiss</u>	141
Effect of orchiopexy on human testicular ultrastructure. <u>Y. Martinova, D. Tzvetkov and M. Nikolovsky</u>	153
Our experiences with the management of pyogenic liver abscesses by percutaneous trans-hepatic puncture and permanent drainage guided by computed tomography. <u>M. Ihász, T. Fazekas, F.I. Todua, J. Bátorfi and M. Máté</u>	159
Pregnancy in women with chronic renal disease: A 14-year study. <u>A. Pajor, L. Lukácsi, L. Bakos, F. Lintner and B. Zsolnai</u>	175
Early complications of gastric resection. <u>M. Ihász, Z. Radnai, A. Bálint, F. Szalay, M. Máté, M. Bereczky and G. Pósfai</u>	183
Endothelin-induced long-lasting mesenteric vasoconstriction: a hypothetical mechanism of non-occlusive intestinal infarction. <u>I. Dóbi, Violetta Kékesi, M. Tóth and S. Juhász-Nagy</u>	199
CO ₂ laser in septic surgery. <u>I. Tóth and Gy. Benedek</u>	209
Surgical treatment of the hip in cerebral palsy. <u>I. Vizkelety, A. Rényi-Vámos and Gy. Szőke</u>	215
Experience with Solcotrans ^R orthopaedic in hip arthroplasty. <u>Anikó Faluhelyi and J. Koczor</u>	225
Successful treatment of erectile dysfunction with Fortisex coated tablets. <u>Gy. Papp and Zs. Kopa</u>	229
Concomitant incidence of fertility chance reducing varicocele and chromosome aberration. <u>J. Béres and Gy. Papp</u>	233
Dopamine-induces aggravation of myocardial ischaemia in the paced heart: cardiosurgical perspectives. <u>A. Kollár, Violetta Kékesi and A. Juhász-Nagy</u>	237
Comparison of histological effect of electrocoagulation and Nd-YAG laser coagulation in intact and tumorous rat tissue. <u>Z. Szemes and I. Számadó</u>	245
Assessment of the efficiency of endovesical laser treatment of urinary bladder tumours on the basis of polyamine content measured in the eluent. <u>Z. Szemes, B. Schumann, R. Kovács and E. Rimanóczy</u>	253
Magnesium transport in human pregnancy (Magnesium content of human gestation tissues and tissue fluids). <u>L. Lukácsi, F. Lintner, B. Zsolnai and J. Somogyi</u>	263
Biological valve prosthesis replacement — experiences and considerations. <u>Z. Szabó, E. Bodor, T. György, E. Moravcsik, L. Papp, Z. Szabolcs and E. Bartha</u>	277
Complications following major abdominal surgery in cirrhotic patients. <u>F. Jakab, Z. Ráth, I. Sugár and J. Faller</u>	279
Parenteral and enteral nutrition and the enterocutaneous fistula treatment I. Investigations on fistula output, nutritional status and complications. <u>E. Dárdai, Sz. Piritiyi and L. Nagy</u>	287
Parenteral and enteral nutrition and the enterocutaneous fistula treatment II. Factors influencing the outcome of treatment. <u>E. Dárdai, Sz. Piritiyi and L. Nagy</u>	305
Experience with a new combined method in the differential diagnostics of early endometrial changes. <u>K. Patai, Zs. Jakab, P. Siklós, Z. Vigváry and J. Balogh</u>	319
Operative treatment of malformations of the middle ear. <u>Gy. Szabó and O. Ribári</u>	323
Vacuum therapy in the treatment of erectal impotence. <u>Gy. Papp, A. Hoznek, E. Juhász and Zs. Kopa</u>	331

Acute acalculous cholecystitis. <u>L. Kiss, L. Nagy, F. Juhász, Z. Nagy and Á. Soós</u>	337
Study on dysphagia after proximal selective vagotomy. <u>A. Bálint, P. Balázs, J. Bátorfi, T. Fazekas, M. Réfi and M. Ihász</u>	341
Endoscopic diagnosis and therapy of urothelial tumours of the upper urinary tract. <u>P. Magasi, A. Karsza and M.A. Heggagi</u>	347
Evaluation of 1000 percutaneous nephrostomies with a special view to efficiency and complications. <u>A. Karsza, M.A. Heggagi and P. Magasi</u>	355
Use of different types of dilator systems in the prevention of complications of percutaneous (PC) renal surgery. <u>M.A. Heggagi, A. Karsza and E. Szüle Jr.</u>	365
Preservation of ejaculation in stage I. Non-seminomatous testicular tumours. <u>M. Fehér, L. Korányi, V. Szokoly and S. Kéry</u>	371

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