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The Modern Approach of Hangman's Fracture

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Upper cervical spine injuries associated with the characteristic alterations of the axis are termed by the international literature as hangman's fracture (HF). The specific changes of the clinical picture include fracture of the bilateral pedicles of the axis, dislocation of the arch, luxation and discopathy between the second and third (C2–C3) vertebrae, eventually other accessory fractures of vertebrae C2–C3 (Fig. 1). There are two kinds of it, i.e. (i) one of a hyperextensive-distractive mechanism with the very severe neurological lesion leading to the classical injury due to hanging and (ii) one of a hyperextensive-compressive mechanism without neurological lesion of current traffic injuries or with slight neurological symptoms. The latter more often occurring type of injury encompasses a relatively wide range, which can be classified into three types: The stable injuries can be managed by conservative treatment, the unstable ones by Halo treatment or ventral surgical therapy meeting the up-to-date requirements. Prognosis is good. The authors have been the first in Hungary to present a critical and detailed survey of the world literature and their 11-year experience, in the form of a clinical study.

Introduction and Historical Review

Hangman's fracture was originally observed in execution victims. The first reports, that this kind of injury had been more widespread than formerly assumed, were published by Haughton in 1866 [34], then by Wood-Jones in 1913 [74]. An increasing number of authors were dealing with this kind of injury also due to traffic accidents. Grogono [32] noticed the similarity between the 'ideal fracture' due to hanging and the cervical injury of one of his patients suffered in a car accident. The subsequent reports were highly controversial. In 1964 Garber [30] reported eight cases of spondylolisthesis of the axis due to trauma associated only with minimal neurological symptoms. All these occurred in traffic accidents, in cars, or as a result of frontal collision. Schneider et al. [65] treated this type of injury as a well-differentiable clinical entity and termed it hangman's fracture. In 1967, 40 cases of the fracture of the isthmus of the axis pedicle were analysed by DeLorme [22]. In 1968 Cornish [19] dealt with 14 cases, which he assumed to have occurred as a result of the extension and compression of the upper cervical spine. Surveying a large material of spinal injuries in 1970, Norrell and Wilson [45] published 5 operated cases of the analysis of unstable HF, while he considered conser-

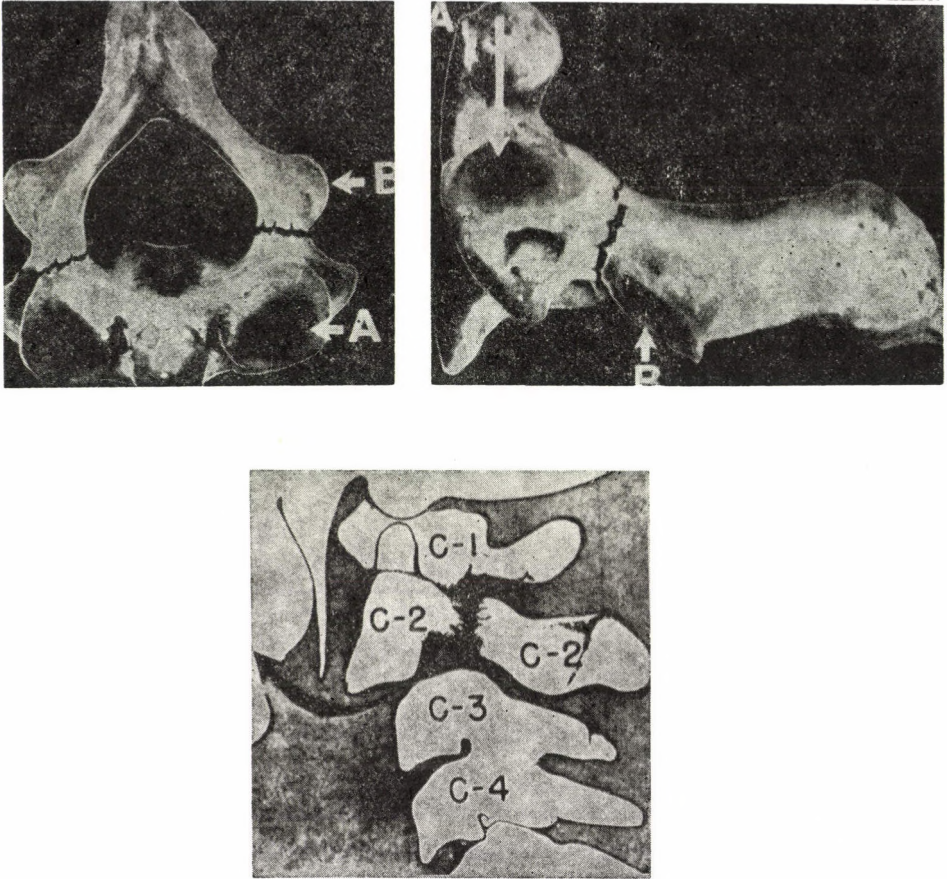


FIG. 1. Typical picture of HF

vative treatment to be justified in 7 cases which proved to be stable. In 1967 Saldeen [60] also reported on a case which resembled the mechanism occurring due to hanging but it still occurred in a traffic accident. The loose safety belt had practically beheaded the injured. A similar injury was reported by Edgar et al. [24] in 1972 when a motorcyclist was caught on a stretched rope which injured his cervical spine in the height of the submental region. Reference on HF can be found, beside the above-mentioned reports concerned exclusively with this issue, also in several summarizing studies [46, 55].

Pathomechanism

From a biomechanical point of view, the special role of the axis within the spine lies in the fact that the forces acting downwards (in the line of the atlanto-occipital and atlanto-axial joints) and divided in two parts in the frontal plane of segments I-II of the occipital bone unite in the body of axis and turning immediately by 90 degrees in the sagittal plane, they continue downwards in the line of the bodies and the articular processes (Fig. 2).

The basic difference in the pathomechanism of the two forms of injury summarized as HF is determined by the opposing forces acting in the moment of injury. During the classical judicial hanging, the injury is caused by hyperextension and distraction, while in car accidents by hyperextension and compression.

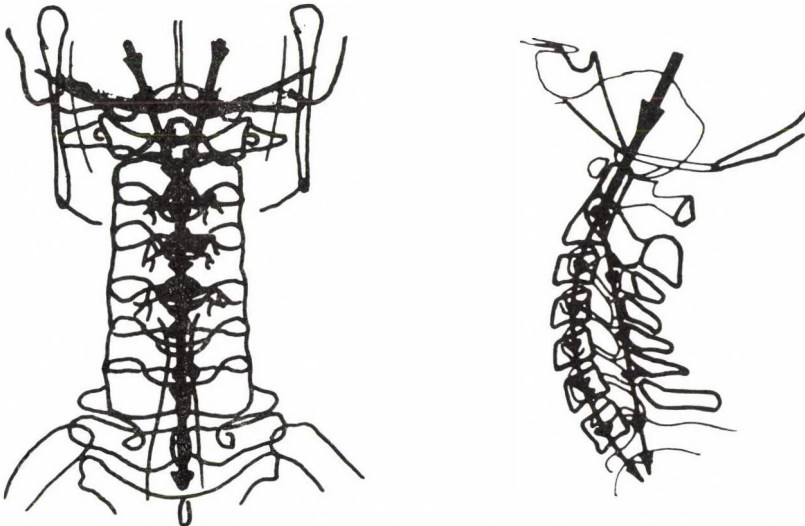


FIG. 2. Biomechanical role of the axis. Forces acting downwards through the atlanto-occipital and atlanto-axial joints, distributed in the frontal plane are united in the axis body and are divided again in the sagittal plane, acting downwards to the lower cervical spine via the bodies and the articular processes. The turning by 90 degrees of the distribution planes is located at the axis body

During execution, the knot on the hanging rope is placed under the victim's chin, then by eliminating the support under his feet, the convict falls down and so partly a longitudinal traction and partly a shock-like hyperextensive effect of the knot on the chin are there and head is exerted on the cervical spine. As a result, rupture of the ligament system fixing the cervical spine ventrally, the leaning of arch C2 on C3 and its consequential fracture then, due to the continuously effected longitudinal traction, complete detachment

from the lower cervical segment of the cervicocranium occurs (Fig. 3). This results in extremely serious neurological consequences, it is usually fatal. A similar injury can, however, be produced also in traffic accidents, when the transverse part of the loose safety belt enables that, during frontal collision, the driver be caught on the safety belt while slipping under it, simulating the classical mechanism of hanging. In this case, the axis can be torn, moreover, even the head can become detached [24, 60].

Concerning the pathomechanism of the other type of injuries occurring in car accidents, it is a hyperextensive and compressive injury. The moving human body in the car, falling forwards, brings the head, corresponding to its propping position, in the moment of shock, into a hyperextensive position,

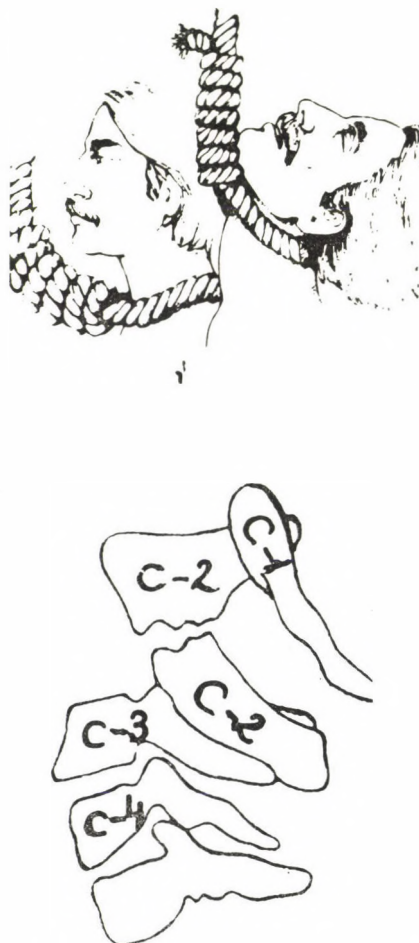


FIG. 3. Judicial hanging. The mechanism of injury is hyperextensive and distractive

meanwhile a longitudinal compressive force is acting. Depending on the magnitude of forces, the propping of the arch C2 against C3 can occur with its consequential rupture, partial or complete injury of the ventral longitudinal ligament system and fracture of the bodies of C2-C3 (Fig. 4). Depending on the extent of the above changes, the injury can occur without dislocation of the vertebral body. In this case only the pedicle is broken or torn. Injuries associated with dislocation of the vertebral body show various degrees of dislocation. It is usually characteristic of the type of injury that impairment of the neural elements is fairly rare or slight, because the neural canal is dilated at this segment (cisterns) and fracture of the arch provides further space for the spinal cord (Fig. 5). Here, direct spinal cord injury occurs very rarely regarding that no distractive mechanism is involved. Another characteristic of this form of injury is that, beside the specific HF injury, compressive ver-

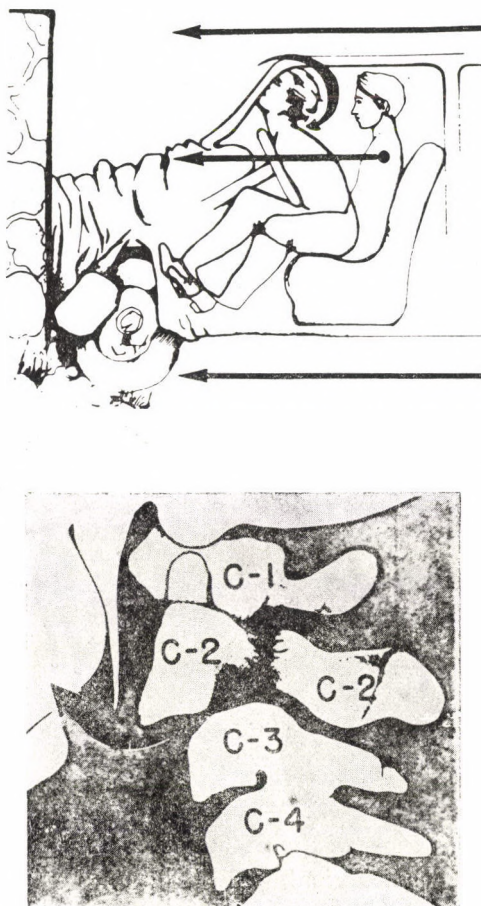


FIG. 4. Car accident. The mechanism of injury is hyperextensive and compressive

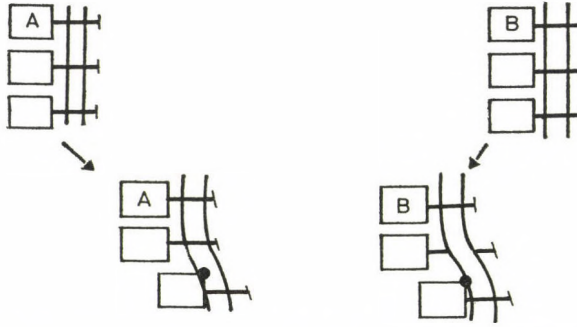


FIG. 5. Biomechanical explanation of cervical spinal cord lesion. In vertebral dislocation the interspinous space for the spinal cord depends on the fracture of the arch. *A.* No fracture of the arch, narrow space, spinal cord lesion. *B.* Fracture of the arch with large dislocation, wide space, no lesion of the spinal cord

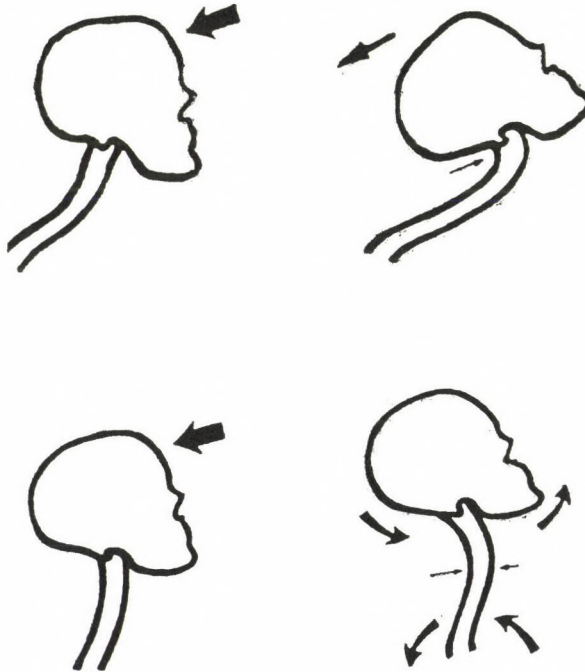


FIG. 6. In the current form of HF additional injuries of the lower cervical spine, the forehead and the face may also occur

tebral body fractures or those of the processus spinosus also occur at the middle and lower segment of the cervical spine (Fig. 6).

In the following, only the type of injury produced in traffic accidents is discussed because this is only of diagnostic and therapeutic importance.

The pathomechanism of the injury is closely linked with the problem of stability and instability. In 1981 Effendi et al. [25] studied and followed up in their summarizing work 142 cases from 4 months up to 4 years. They aimed at formulating a classification defining stability. In their opinion, the roentgenologically detectable changes depend on three fundamental factors:

1. The site of the fractured ring.
2. The dislocation of the anterior fragment (axis body) as compared to the line of fracture.
3. The position of the posterior fragment (arch and lower articular process). (The larger dislocation of the posterior fragment is usually associated with the slipping forwards and flexion of the anterior fragment, and the widening of the vertebral canal.)

Based on the degree and type of dislocation of the anterior and posterior fragments, the changes of the intervertebral disc between C2 and C3, the injuries of the ventral and dorsal longitudinal ligament system and on the change in the position of the articular surface, concerning stability, fractures are divided into three types (Fig. 7):

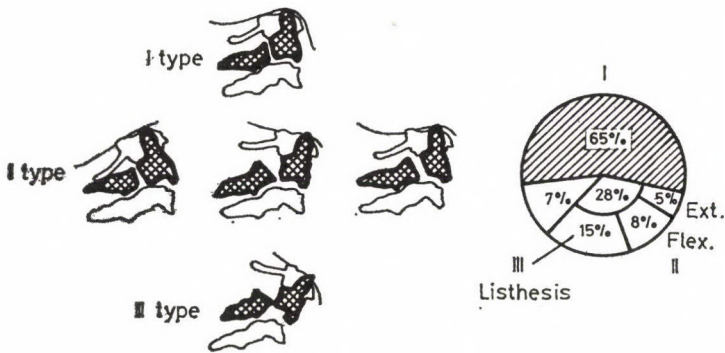


FIG. 7. Classification of HF cases according to stability. Stable type I, unstable type II, unstable type III with large dislocation (for frequency of the different types see references)

I. Stable type: Isolated fracture of the axis ring without an essential dislocation of the body of C2. The fracture can involve any part of the axial ring so it can also affect the body of C2, but it most often runs through the pedicle. The line of fracture is transversal involving in general one or both posterior angles of the C2 body. The subaxial disc-space is of normal width and does not change (Fig. 8).

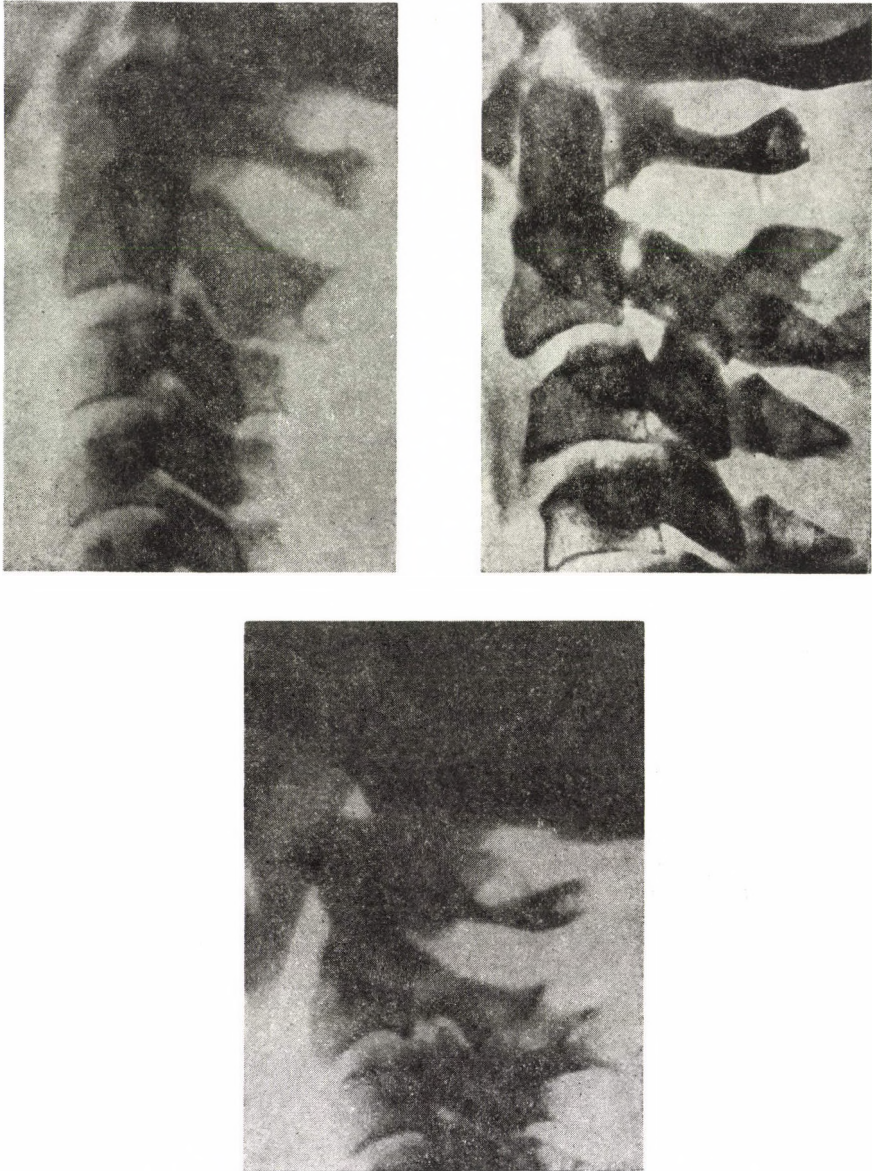


FIG. 8. Three different cases of type I (stable) HF

II. Unstable type: Dislocation of the anterior segment with injury of the disc and a widened intervertebral space between C2 and C3. The dislocation of the axis body can be a tilting of the extension-type (Fig. 9a), of the flexion type (Fig. 9b), or a slipping forwards of the listhetic type (Fig. 9c).



FIG. 9. Three different cases of type II (unstable) HF with dislocation of the axis body.
a. extensive type. b. flexion type. c. listhetic type

III. Unstable type with large dislocation: This type is characterized by considerable dislocation of the anterior fragment by flexion and the rough dislocation of the articular processes C2-C3. It is unambiguously the most severe form of instability and can even result in the desorganization of the cervicocranium (Fig. 10).



FIG. 10. Type III. HF case with large dislocation

Clinical Symptoms. Diagnostics

The clinical symptoms of HF can be classified into three main groups:

1. Local symptoms in the cervical spine.
2. Neurological symptoms.
3. Symptoms of associated injuries.

1. Symptoms localized to the cervical spine are mostly characterized by the pain of the upper cervical spine and occipital region, the limited movement of the cervical spine and the painful rigidity and forced position of the upper cervical spinal segment and muscles.

2. The neurological changes are specified by their rare occurrence. Of them various manifestations of organic neurological changes can be found ranging from the mildest change to each degree of severe tetraparesis. Numerous authors [4, 6, 7, 10, 19, 22, 24, 25, 27, 32, 40, 49, 56, 69, 67] consider distinctively characteristic the lack of neural lesion as opposed to the relatively severe osseous spinal change. There are others who regarded the presence of a neurological change as a feature of neurological injury occurring along other spinal segments and so they make the detailed examination of the other spinal segments obligatory [25, 65].

The classical HF is naturally associated with neurological lesions and death, but in this case another force and a mechanism of other direction are involved, which aim at blotting out life.

3. Symptoms of the accessory changes are primarily caused by alterations localized to other segments of the cervical spine. In addition, symptoms of the frontal, splanchnocranial and occipital regions as well as of those of chest injuries are encountered.

Diagnosis is based on a thoroughgoing clinical examination and the X-ray. Of the latter the lateral view of C2 of a good quality is decisive but complementary tomograms may also be necessary. In differentiating the individual types, functional pictures are of great importance. As reported by Brashear et al. [10], static roentgenograms in HF are similarly misleading or provide inadequate information as injuries of the ankle or knee ligaments. Therefore in every case suspicious for instability lateral view pictures of flexion and extension should be taken with slight traction of the head. If no change is observed, the position is stable. If there is change in flexion-extension or listhesis, it is an unstable case. If, however, the intervertebral space between C2 and C3 is largely widened, ventral dislocation of C2 and dislocation of the ruptured portions of the arch and of the articular processes increases, an unstable type of fracture of large dislocation is established. Naturally, in dislocations exceeding a certain degree, instability is evident also without functional symptoms.

In some cases, details of the ring fracture or of bone fragments having drifted into the vertebral canal can only be classified by CT.

Diagnostic difficulties are posed by the frequent neurologically symptom-free state and the relatively mild local symptoms. Based on them, in associated injuries causing more serious complaints, HF often escapes detection and is diagnosed only later or by chance.

Therapy

Views concerning the management of HF differ greatly the world over. This is partly caused by the fact that there is a broad spectrum of injuries even within the well-demarcable clinical picture of HF. On the other hand, different approaches and different technical conditions and treatments have developed within the various schools.

On the basis of the various approaches of the international literature and on that of the specificities of various types of injuries, the principles of up-to-date management can be summarized as follows:

Type I stable HF cases can readily be managed by conservative treatment. In these instances, there is no vertebral body dislocation posing a static

problem, only the fixation of the injured cervical spinal segment should be taken care of. This is possible by the use of cervical plaster collar, a head-trunk (Minerva plaster) plaster, soft collars and rigid supporting collars made of synthetic material, Halo fixation. Fixation time ranges from 3–4 to 12–16 weeks.

In type II unstable and type III unstable cases with large dislocation, management is divided into two phases, i.e. reduction and stabilization.

Up-to-date reduction is made by Crutchfield's or Halo extension. Both provide reduction by skeletal traction acting through the cranial bone as the most considerate and most effective procedures. In contrast to the traction at two points of the Crutchfield brace, the Halo method fixes the skull at 4 points and so the latter can provide traction of determined direction and head position. Complete reposition can be achieved in 80–90% of the cases by traction increasing from a few up to 15 kg.

Stabilization (preservation of the reduced position) can be performed by conservative methods or by operation.

The conservative fixing procedures are the same as enumerated under the stable type. The best results of them are ensured by the Halo-fixateur. The ring used for traction in the stage of reposition is propped against the shoulders through a system of bars by applying a specially designed vest made of synthetic material (Fig. 11). So a favourable external fixation ensuring reduction can be used in which mobilization of the patient can be started early and which is usually well tolerated by the patients. Fixation time is 12–16 weeks. The procedure is new in Hungary, but it has been applied in the United States and several European countries for 15–20 years [18, 26, 37, 44, 51, 66]. It is accepted all over the world as one of the best ways of treating HF, because reduction and stabilization can be secured by the same procedure, the degree of fixation being very high.

The results of the above-mentioned conservative fixations greatly lag behind those of the Halo treatment. Earlier it has been applied more often, but currently—for want of an even better method—is less often used.

Of the operative stabilizing procedures, ventral spondylodesis can be looked upon as an up-to-date fixation method in the management of HF [5, 8, 17, 39, 47, 50, 52, 53, 54, 68, 70]. It essentially involves the removal of the intervertebral disc C2–C3 from a ventral incision, if necessary spinal decompression, implantation of autologous corticocancellous bone block and fixation by plate and screw (Fig. 12). No external fixation is needed postoperatively. Bony union occurs within some months. During this time mobilization or the eventually necessary rehabilitation can be made unheeded. It should, however, not be ignored that a high cervical ventral exposure is much more difficult and it involves the risk of more complications than in the lower cervical spine.

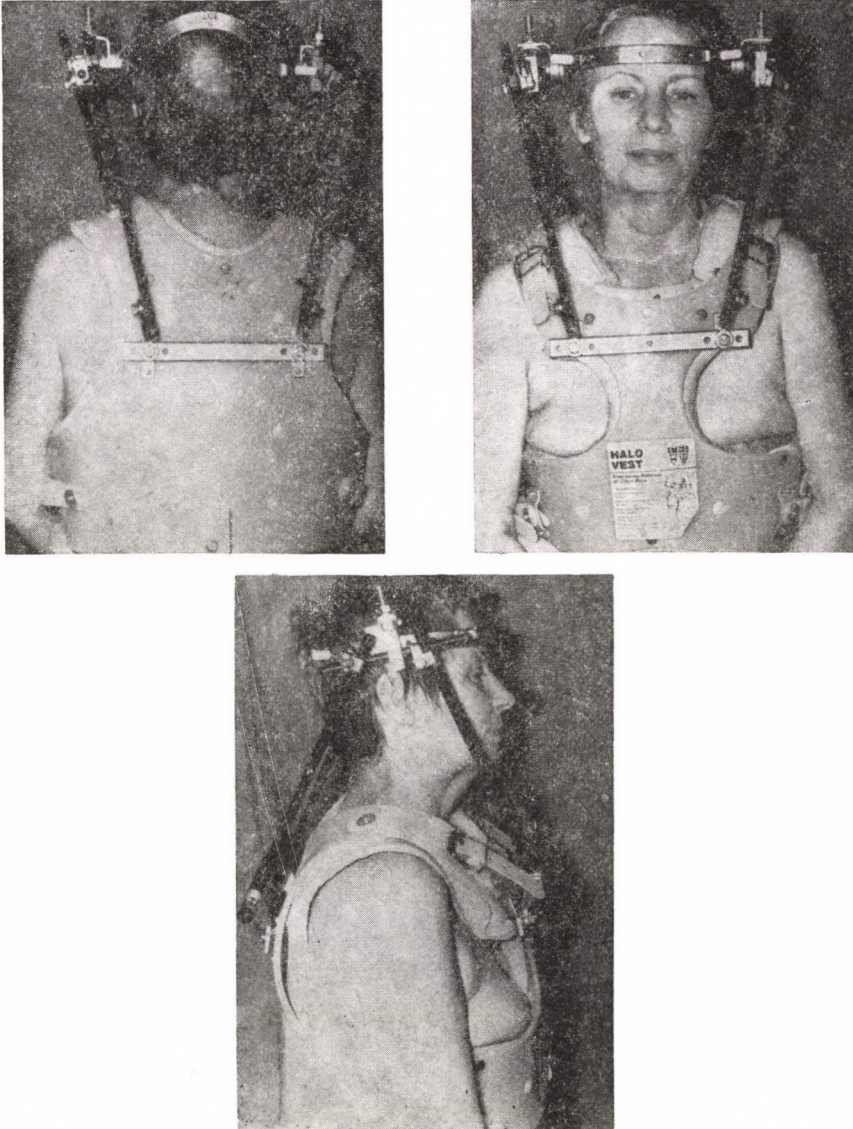


FIG. 11. Application of Halo fixateur for the treatment of a HF case

The posterior operative exposures are less suitable for stabilization of HF (fixations by wire loop, plate, screw along segments C O—I–II–III) [43, 52, 57, 58, 64, 70].

The prognosis of HF is good. After a good reduction bony consolidation occurs within 2–3 months even in injuries with a frighteningly large dislocation. In cases with rare neurological lesions (these are partial ones), rapid neurological improvement can be observed during the rehabilitation treatment.

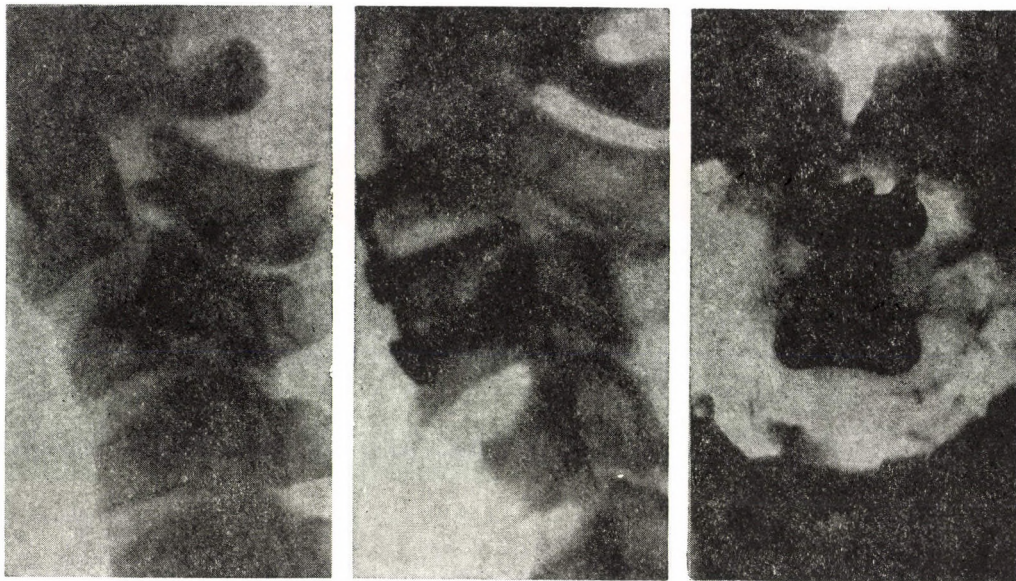


FIG. 12. Operative treatment of unstable HF case by high cervical ventral spondylodesis

Own Material and Results

During the 11 years from 1976 to 1986 a total of 608 patients with cervical spine injuries have been treated at the Department of Neurosurgery of our Institute. Thirty-four of them were HF cases. This means 5.6% of the overall cervical spine injuries. In 11 cases operation was performed. Twenty-three patients were managed by conservative treatment:

	Operation	Conservative	Total
Other cervical spine injuries	205	369	574
HF	11	23	34
Total	216	392	608

The annual distribution of the injured patients is shown in Fig. 13. Their age ranged from 12 to 78 years, the majority being in their third or fourth decade, with a mean age of 42.

The male-female ratio was 21 to 13.

Processing our material, essential differences were noted in comparison to the literature. For example, in the summarizing basic paper of Effendi et al. [25], the classification according to the stability of the various types

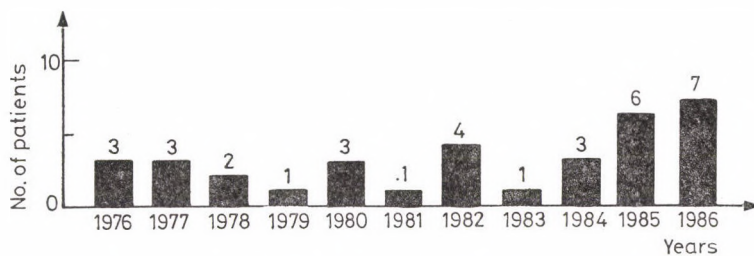


FIG. 13. Annual distribution of HF cases in the authors' own material (1976–1986)

showed a distribution totally different from our material. In their material stable injuries occurred in 65%, unstable in 28% and unstable ones with large dislocation in 7% of the cases, while our ratios were 37, 41 and 22%.

The different incidence ratios can be ascribed to the greater number of traffic and agricultural accidents in Hungary, the alcoholic state in 57% of the cases, the lacking safety belt in 30% of traffic accidents, the loose safety belt in other cases, and the lacking head rest in 95% of the cases. However, it should not be overlooked that in the first years of the study-period in Hungary, HF diagnostics did not achieve the present up-to-date level, and it is also obvious that there is a concentration of the injured in a national traumatological centre.

In 11 of the 34 cases studied, neurological changes of various degrees were found. This represents a higher ratio of neurological change in comparison to the international literature on HF due to traffic accidents. We have observed the most diverse manifestations of organic neurological changes to vary by the type of injuries. In injuries without dislocation, no organic neurological change was observed. In the group of unstable injuries where dislocation was only minimal, i.e. of slightly radicular nature, hyperaesthesia involving the dermatome C3–C5 or hypaesthesia was noted in 7 cases. In other cases hemiparesis of one or the other upper extremity, stopping after a time from a few days up to 3 months (3 patients). Among our unstable cases with large dislocation, severe tetraparesis was encountered. In one patient, tetraparesis partly decreased during rehabilitation after half a year: his lower extremital movement totally normalized, while the upper one improved only partially. The relatively high ratio of neurological lesion in our material seems to be related to the pooling of the material of neurological changes in special centres.

Management in the earlier years consisted, beside the Halo treatment, mainly in applying conservative methods, i.e. Crutchfield reduction and fixation by plaster or cervical support. Bony consolidation occurred in all of the 23 patients treated conservatively, in a favourable position in 10 and

in a less redislocated position causing no essential complaints in 13 cases. For illustration one case each of good position and of dislocated position is shown in Fig. 14.

Ventral spondylodesis has been performed for managing patients since 1980. Ventrofixation was made from a high cervical exposure mainly after reduction by Crutchfield, in a smaller number by Halo extension in 11 patients. According to Smith-Robinson or Caspar, similar to the technique used in the

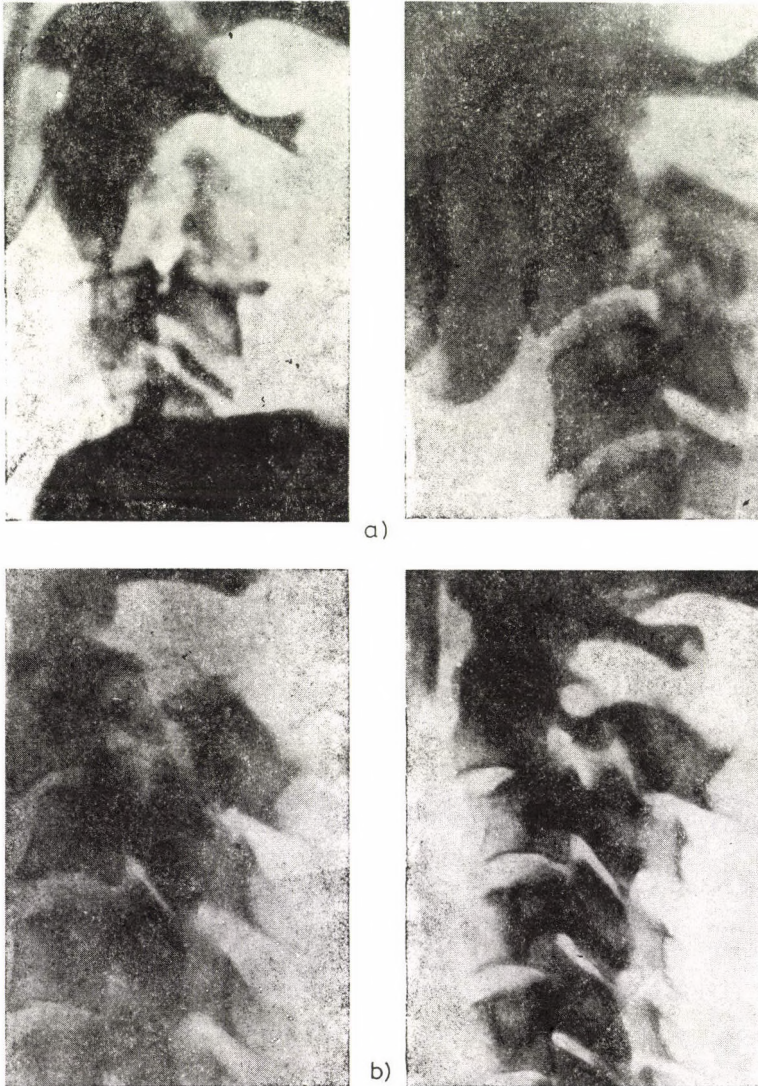


FIG. 14. Two cases of HF treated conservatively. *a.* Consolidation in a good position. *b.* Consolidation in a dislocated position. Clinically, both patients have become symptom- and complaint-free since their recovery

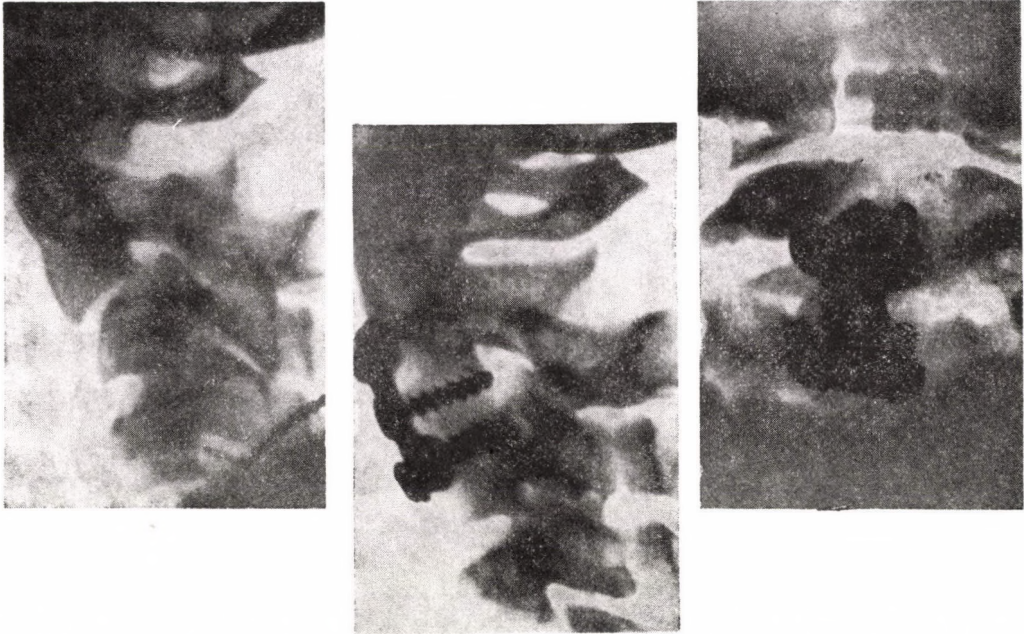


FIG. 15. A case of type II HF from the authors' own material treated by ventral spondylo-
desis. Conservative reduction by skeletal traction was followed by high cervical ventral
approach, removal of the injured disc from spaces C2-C3, spondylo-
desis between C2 and C3 by autologous corticocancellous bone grafting and H-plate fixed with cortical screws.
Solid union in a good position after three months

lower cervical spine segments [3, 5, 8, 39, 45, 52, 68]. Except for one case, bony consolidation occurred in each patient in a stabilized good position which is illustrated in the case shown in Fig. 15. The only exception was the HF case associated with comminuted fracture of the body of axis, where the screws were not right enough and redislocation followed. In this case Halo treatment helped us to achieve consolidation of a good position (Fig. 16).

It is more difficult to perform high cervical ventral exposure and it also incurs the risk of several complications. Opening of the pharynx occurred twice. These cases could be managed by direct sutures with no fistula formation. Other major complications were not encountered, but it is to be stressed that these operations have to be made by experts with great experience working in a centre of spinal surgery.

Following ventral spondylo-
desis, no external fixation was applied, only a soft foam-rubber collar was used postoperatively to reduce pain and muscular spasm.

During the monthly checkups bony reconstruction occurred usually during 3-4 months. Metal implants were not removed because it is unneces-

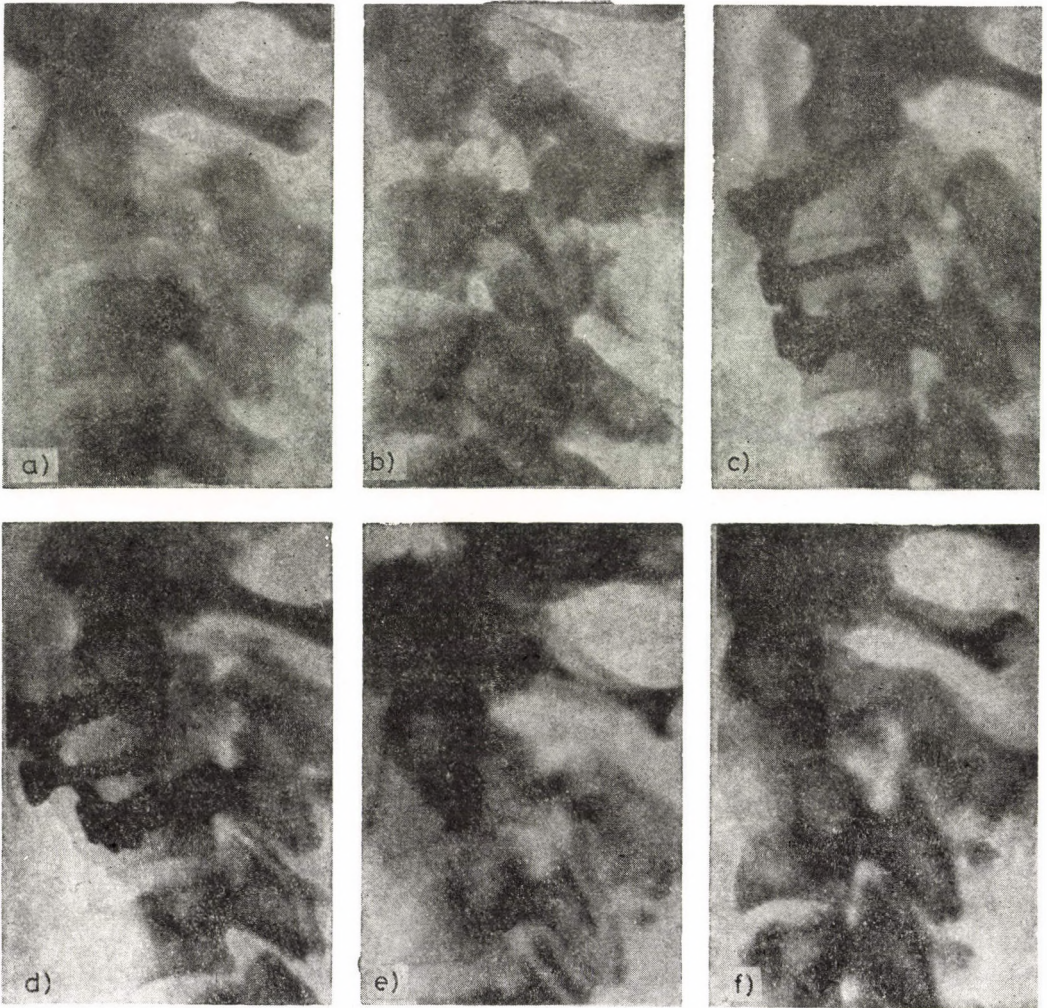


FIG. 16. Severe and complicated HF case from the authors' material treated by combined surgical and conservative methods. *a.* Initial picture of the injury. *b.* Position of reduction reached by skeletal traction. *c.* Ventral spondylodesis with plate fixation in a reduced position. *d.* Redislocation two weeks postoperatively. The screws could not fix the reduced position in the multiply fractured axis body. *e.* Halo fixation and removal of metal implants. *f.* Solid union in a good position after three months. Complete clinical healing without any symptoms and complaints

sary or involves an increased risk of complications in the formerly operated scarry site of operation.

Halo treatment has been applied since the end of 1985. It was made for HF in 3 patients. In all of them consolidation of a good position occurred. During 12 weeks there were no complications whatsoever [69]. Our initial

experience has been very promising, just in the management of the most severe cases of HF or in those associated with a systemic disease (as e.g. Bechterew's diseases, PCP) but currently our indications are very much limited by the small number of Halo fixateurs available to us.

Conclusions

HF, as a well-circumscribed type of injury ranges widely in addition to the two basic forms and the three types of stability. Currently, the classical form of execution after which the term has been coined, is the least frequent, and also the justification of this term having been widely accepted is disputable because of its illogic form.

It is rare and unusual that two types of injury of so different pathomechanism and course, like the hyperextensive-distractive injury due to hanging and the hyperextensive-compressive ones due to car accidents, should manifest in so similar changes and they should even be recorded under a common name in the literature.

Diagnostically, beside a relatively poor symptomatology, the importance of functional X-ray, even deciding therapy, can be stressed.

In the therapy of unstable injuries two up-to-date methods compete with each other, i.e. the Halo treatment and ventral spondylodesis. Naturally, both have their advantages and limitations. The view emerging from the predominantly English-language literature have gained more advocates to the use of Halo treatment. We, however, are in favour of the surgical management. We admit and stress that Halo treatment is the best in many cases but when contraindicated [18, 26, 44, 51, 66, 69] as well as under limited financial condition we have to resort to surgery yielding also good results and meeting up-to-date requirements, all the more because this has several advantages over Halo treatment.

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Zeitgemäße Anschauung der Hangman's Fracture

S. ZSOLCZAI und T. PENTELENYI

Die »Hangman's Fracture« — auf deutsch »Frakture des gehängten Menschen«, des weiteren HF — bedeutet in der internationalen Literatur die mit charakteristischen Epistropheusabweichungen einhergehende Verletzung der oberen Halswirbelsäule. Die charakteristischen knöchernen Veränderungen des Krankheitsbildes sind zweiseitige Pedunkulusfraktur des Epistropheus, Dislokation des Bogens, Luxation und Knorpelscheibenverletzung zwischen den Wirbeln C II und III sowie eventuell sonstige akzessorische Frakturen der Wirbeln C II und III. Zweierlei Formen sind bekannt: HF, mit einem Hyperextensions-Distraktions-mechanismus, klassische Erhängungsverletzung, mit tödlichen, äußerst schweren neurologischen Schädigungen und die HF mit einem Hyperextensions-Kompressionsmechanismus, eine moderne Verkehrsverletzung ohne neurologische Schädigungen oder mit relativ milden Nervensystemsychtomen. Die heutzutage immer häufiger vorkommende, letzterwähnte Verletzungsform meldet sich mit einem ziemlich breiten, in 3 Type einreihbaren Spektrum. Die stabil Verletzungen können mit konservativer Behandlung, die instabilen mit Halo-Behandlung oder mit ventraler chirurgischer Behandlung den zeitgemäßen Ansprüchen entsprechend versorgt werden. Die Prognose ist gut. In der Arbeit werden aufgrund des gründlichen kritischen Überblicks der Weltliteratur und der Verarbeitung des eigenen 11jährigen Materials stammenden Erfahrungen, das erstmal in der ungarischen Literatur in Form einer klinischen Studie erläutert.

Современный взгляд на «фрактуру хангмана»

Ш. ЖОЛЦАИ, Т. ПЕНТЕЛЕНИ

«Фрактура Хангмана» — по-венгерски «травма повешенного человека» — в международной литературе обозначается HF и представляет собой травму верхнего шейного отдела позвоночника, сопровождающуюся характерными изменениями эпистофея. Типичные костные изменения при этой патологии — двусторонний перелом ножки эпистофея, дислокация дужки, люксация и травма хрящевого диска между позвонками C_{II-III}, иногда другие дополнительные переломы C_{II-III} (рис. 1). Известны две формы: классическая травма повешенного с гипертензионно-дистракционным механизмом, с ведущими к смерти тяжелыми неврологическими поражениями, и разновидность современной транспортной травмы гипертензионно-компрессионного механизма без неврологических симптомов, или с относительно легкими симптомами. Все чаще встречающаяся в наши дни, эта последняя форма имеет весьма широкий спектр, в котором можно выделить три типа. Стабильные травмы обеспечиваются консервативным лечением, нестабильные повреждения лечением Halo или вентральным хирургическим вмешательством, в соответствии с современными требованиями. Прогноз хороший. Авторы знакомят с критически рассмотренными литературными данными и с результатами обработки собственного 11-летнего материала, в форме клинического очерка — первого в венгерской литературе.

Effect of Small Bowel Resection on Fecal Bile Acid Excretion and on Experimental Colon Tumour in Rats.

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Ileal and jejunal resections were carried out to investigate their effect on the faecal bile acid excretion and on the development of 1,2-dimethylhydrazine (DMH)-induced colonic cancer in rats. Both resection types raise the total daily faecal bile acid level compared to the control sham-operated group, whereas ileal resection has a more pronounced effect. The incidence of tumours was found higher in groups with enhanced faecal bile acid level. Our findings show a connection between the daily faecal bile acid excretion and the incidence of DMH-induced colonic cancer.

Introduction

Various endogenous and exogenous factors are considered to be involved in the appearance of tumour of the lower intestinal tract. Previous epidemiological, clinical and experimental studies have shown that the bile acids and their metabolism may be important factors in the development of colonic cancer.

After cholecystectomy the bile acid metabolism is altered and the composition of bile acids changes which might predispose the colon to tumour development. Several case-control and experimental studies have supported [6, 9, 16, 17, 18, 21, 30, 33, 36] or refuted [5, 34] this hypothesis. Aries et al. [1] postulated that high dietary fat increases the concentration of bile acids in the large bowel with subsequent metabolism by bacterial flora to co-carcinogens. Supportive evidence has been found in international comparative studies [11, 25, 31] that the stool from risk population for colon cancer has a higher concentration of faecal bile acids compared to those from low risk populations. On the other hand, increased fibre intake which decreases the concentration of faecal bile acids, reduces also the risk of colonic cancer development [2, 26]. However, studies on large bowel carcinoma patients have yielded

conflicting results regarding the question of whether they excrete a greater amount of bile acids than healthy persons [3, 10, 12, 14, 29, 35]. Experimentally increasing the faecal bile acid level in different ways, (e.g. by feeding of fat rich diet [7, 13, 28] or cholic acid [4], direct intrarectal instillation of various bile salts [27], by diversion of the bile into the mid small bowel [20, 38], or by small bowel resection [15, 24]) also raises the incidence of cancerous lesions in animal models.

In the following study we investigated the effect of the ileal and jejunal resection on the quantitative changes of total faecal bile acid excretion and on the DMH-induced tumour development in rats.

Materials and Methods

Eight-week-old rats (Wistar: Han: Lati, Gödöllő, Hungary) of 200–250 g in weight were used. The animals were housed 5 per cage, fed with standard rat diet and provided with tap water ad libitum. The 65 rats were randomly arranged in the following groups (Fig. 1):

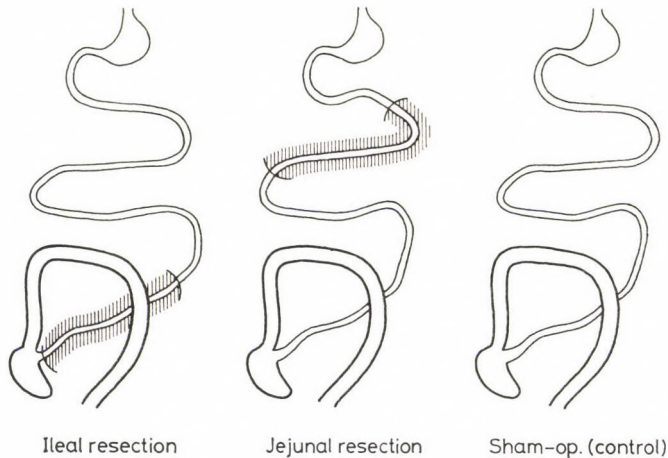


FIG. 1. Schemes of the applied surgical models

- Group 1. a, Ileal resection + DMH (20 rats)
- b, Ileal resection without carcinogen (5 rats)
- Group 2. a, Jejunal resection + DMH (20 rats)
- b, Jejunal resection without carcinogen (5 rats)
- Group 3. a, Sham-operation + DMH (10 rats)
- b, Sham-operation without carcinogen (5 rats)

Surgical technique: After 24 hours of starvation the rats were anaesthetized with intraperitoneal Nembutal in a dose of 40 mg/kg and operated on. A midline laparotomy was done on each of them. In Group 1 the distal 20 cm segment of the ileum was removed with preservation of the ileocaecal valve, and end-to-end anastomosis was performed using a single-layer of continuous 6/0 silk (Ethibond). In Group 2 we resected a 20-cm-long jejunum segment starting 5 cm distal from the ligament Treitz. We sutured the end-to-end anastomosis in the above-mentioned way, with 6/0 silk. Group 3 was formed by the sham-operated animals. Ten minutes after laparotomy we closed the abdomen with a double-layer of continuous 3/0 Mersilen, similar to the other groups. The animals were permitted to drink, but not to eat for 24 hours after the operation, then feeding was restored. In the fourth postoperative week the daily amount of faeces and the daily total faecal bile acid level were determined for 5 animals randomly chosen from each group. The quantitative analysis of bile acids was carried out by thin-layer chromatography.

Starting with the fourth postoperative week 50 rats were subcutaneously injected once weekly for 15 weeks with 20 mg/kg of 1,2-dimethylhydrazine (SIGMA 105F-3690). Five operated rats from each group did not receive carcinogen and served as controls.

The planned sacrifice of rats was done thirty-two weeks after the operation by an overdose of Nembutal. A complete autopsy was performed on each animal with particular attention to the large bowel. The large bowel mucosa was opened lengthwise, cleaned and photographed then checked for tumour using stereomicroscope with a four-fold magnification. The whole large bowel was stretched out and fixed in 4% formaldehyde-solution and processed for histological examination. Student's *t*-test was employed for statistical analysis.

Results

Fifty-eight from the 65 animals survived the eight-month experimental period. The mortality rate was 10.8%. None of the 13 surviving rats in groups without carcinogen treatment developed tumours.

Table I shows the mean faecal bile acid level and standard deviation as well as the incidence of tumours for rats treated with 1,2-dimethylhydrazine.

In both groups with small bowel resection we found higher daily bile acid level than in the sham-operated group. The highest bile acid excretion was found in the group with ileal resection, in accordance with the known facts that the ileum plays an important role in bile acid reabsorption.

In both resected groups the incidence of DMH-induced colonic cancer was higher than in the control group. Examination of the relationship between total faecal bile acid levels and the average number of tumours showed that

TABLE I

Colonic tumour incidence and faecal total bile acid level after small bowel resection in rats treated s.c. with DMH

Groups	No. of rats	Faecal bile* acid level ($\mu\text{mol/day/rat}$)	No. of + tumours per rat
Ileal res.	17	29.7 \pm 8.0	1.94 \pm 1.92
Jejunal res.	20	20.8 \pm 11.8	1.25 \pm 1.24
Sham-op.	8	5.1 \pm 0.7	0.75 \pm 0.65

The values *, + shown: mean \pm SD

the group with ileal resection, which manifested the highest total bile acid levels, showed also the highest number of tumorous lesions.

In all groups, the incidence of DMH-induced cancerous lesions was higher on the left side of the colon.

Discussion

In our study we changed the daily faecal bile acid excretion by resecting different parts of the small bowel and investigated the relationship between these changes and the DMH-induced colonic cancer.

The ileum plays an important role in the reabsorption of bile salts. The deficiency of this function caused by ileal disorders or ileal resection increases the bile acid excretion in the stools [8, 19, 32]. Besides partly intercepting the enterohepatic circulation of bile acids the ileal resection changes the transit-time of stools [32] and produces colonic cell proliferation as well [22, 24]. These are the most frequently studied factors which might influence the tumour development under experimental circumstances. Previous studies showed that colonic hyperplasia can be recognized not only after ileal [22, 24] but also after jejunal resection [23, 37]. Koga et al. [15] found that the increase of faecal total bile acid level was proportional to the length of ileal resection, and higher cancer incidence was observed in groups with higher total bile acid levels. The different length of resection varies the transit-time to different degrees. To eliminate this factor we resected the same length of both parts of the small bowel, 20 cm out of the terminal ileum and 20 cm out of the upper jejunum. The highest daily total bile acid excretion was found in the group with ileal resection, and also the highest incidence of tumours was observed in this group.

Figure 2 shows the connection between bile acid excretion and tumour development. Although the differences observed are not significant, probably

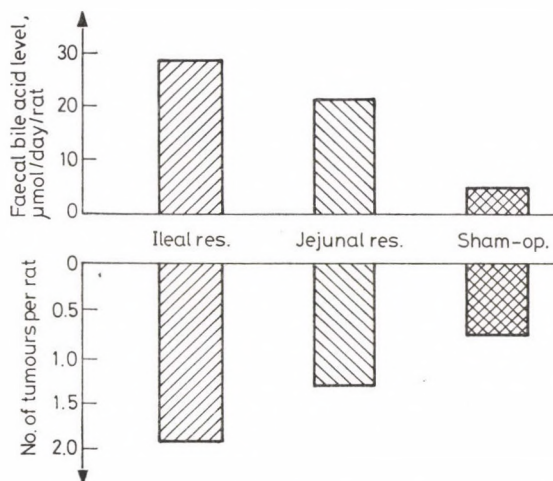


Fig. 2. Relationship between the daily total faecal bile acid excretion and the incidence of 1,2-dimethylhydrazine induced colonic cancer according to the surgical procedures used

due to the insufficient length of resection, we think that with a longer resection we might achieve significant differences.

Our findings lend support to the hypothesis that faecal bile acids are involved as promoters in colonic carcinogenesis by rats.

*

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Über die Wirkung der Dünndarmresektion auf die Menge der mit dem Stuhl entleerten Gallensäure und auf die Entwicklung des experimentellen Dickdarmtumors bei der Ratte

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Bei Ratten wurde die Wirkung der vorangehend durchgeführten Ileum- und Jejunumresektion auf die Menge der täglich mit dem Stuhl entleerten Gallensäure und auf die durch 1,2-Dimethylhydrazine (DMH) induzierten Dickdarmtumoren untersucht. Im Vergleich zu den scheinoperierten Kontrolltieren hat sich auf Wirkung beider Verfahren, insbesondere jedoch auf Wirkung der Ileumresektion die Tagesmenge der mit dem Stuhl entleerten Gallensäure erhöht. In den Gruppen, in denen sich die entleerte Gallensäuremenge erhöhte, war eine größere Häufigkeit des Tumorvorkommens zu verzeichnen. Die Ergebnisse wiesen auf eine Korrelation zwischen der Gallensäureentleerung mit dem Stuhl und der Häufigkeit der durch DMH induzierten Dickdarmtumoren hin.

Влияние резекции тонкой кишки на количество выделяемой с калом желчной кислоты и возникновение экспериментальной опухоли толстого кишечника у крыс

K. MORVAI, K. SENTLÉLEKI, G. TÖRÖK и A. ПИНТЕР

Авторы производили резекцию подвздошной и тощей кишок у крыс и исследовали влияние, оказываемое резекцией, на суточное количество выделяемой с калом желчной кислоты и на возникновение опухолей толстой кишки, индуцированное посредством 1, 2-диметилгидразина (DMH). Оба способа, но резекция подвздошной кишки более выражено, способствовали увеличению суточного количества желчной кислоты, выделяемой с калом, по сравнению с контрольными, ложно-оперированными животными. Установили, что опухоли чаще встречаются в тех группах, где количество выделяемой желчной кислоты увеличилось. Полученные результаты указывают на связь между выделением с калом кислоты и частотой индуцированных DMH опухолей толстой кишки.

Factors Affecting the Cold Transfer during Cryotherapy

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Cryotherapy of the cervix was made in 40 patients for chronic cervicitis, and the thickness of the ice zone around the probe was measured in function of treatment time, under standard cooling conditions. The pace of growth of the ice zone allowed the author to draw conclusions as to the conductivity of the studied tissue. It was established that in the study-group, the patient's age and their histories of abortions did not influence the cold transfer significantly. The difference between the average values of ice zone thickness measured in the groups of nulliparae and multiparae was, however, significant. Findings have shown that the spread of cold in the cervical tissue in nulliparous women is better than in multiparae and so a greater efficacy of cryotherapy can be expected in nulliparae.

The basic problems of cervical cryotherapy are the deep transfer of cold, the assessment of the spread of its necrotizing effect and the insufficient knowledge of all factors which may influence, with a given cooling energy, the spread of cold effect and the desired therapeutic effect.

In our study an answer was sought to the question to what extent cold transfer in the cervical tissue is affected by previous obstetric events and by the patient's age.

Materials and Methods

Cryotherapy by a cryoprobe was applied in 20 nulliparae and 20 multiparae after termination of their periods because of chronic cervicitis. The cooling energy was provided by an Erbokryo-Amoils 40/a equipment, the working pressure of the N₂O gas ranging, in all cases, between 4.0 and 4.2 MPa. Prior to treatment, the cervical mucus was removed and the surface of the cryoprobe was coated with gel improving heat contact. Freezing was begun after insertion of the probe and the width of the ice zone around the probe was measured in function of freezing time.

The patients' mean age was 31.9 years, the youngest being 19, the oldest 40 years of age.

Maximal treatment time was 8 minutes. In a part of the cases freezing lasted for 5 minutes if the thickness of the ice zone did reach, during this time, the 8 mm width around the probe.

The probe fitted well the surface of the portio in all cases, and the changes in the shape of the cervix did not influence the heat contact of the probe. For statistical analysis, Student's one-sample *t*-test was used.

Results and Discussion

It is known that with the increase of freezing time, the size of the ice zone around the probe increases at a diminishing pace with the progress of time until a heat balance is reached between the heat loss ensured by the equipment and the heat release ensured by the circulation of blood in the tissues. Beside the above two factors, several others play a role in reaching heat balance, such as heat contact, the heat conductivity of tissues, etc. Heat contact is improved by removal of the cervical mucus, use of gel on the surface of the probe, careful insertion of the probe and by the starting of freezing after application. Differences in heat contact could be neglected in our cases. Cooling energy and cooling surface were constant by using the same cooling equipment and probe.

The velocity of cold transfer was examined in the cervical tissue in relation to the patients' age and the number of abortions and deliveries in their histories. The patients were divided into groups of under and over 35 years of age. In the two groups the average ice zone thicknesses during freezing in the function of time are shown in Table I. In the group under 35, the average thickness of the ice zone was larger in each of the measured freezing times of 1, 3, 5, and 8 minutes than in the group over 35. Differences were not significant in either of the cases.

Assessing the larger average ice zone thickness values in the group under 35, it should be taken into account that there were more nulligravidae and nulliparae in this group.

TABLE I
Cold transfer in the cervical tissue according to age

Age	n	Freezing time (min)			
		1	3	5	8
Average < 35 thickness of ice zone (mm)	17	1.66±0.49*	4.33±0.8	5.6±0.67	7.0±0.70
> 35	23	0.57±0.40	2.57±0.44	4.42±0.34	6.57±1.17
p value		0.1 > p > 0.05	0.1 > p > 0.05	0.7 > p > 0.6	0.4 > p > 0.3

*SEM

If the velocity of cold transfer in the cervical tissue was examined in relation to previous deliveries, it was found that the average ice zone thickness was larger each time measured than the values in the multiparae, and the difference between the 1, 3 and 5-min data was significant, while being non-significant between the 8-min values (Table II). An additional finding was that the difference between the average values of ice zone thickness in the two groups decreased with time. The p value for the one-minute values was strongly significant ($p < 0,001$) and in case of the 3 and 5-min data, significant ($0.01 > p > 0.01$ and $0.02 > p > 0.01$), while in case of the 8-min values non-significant ($0.2 > p > 0.01$).

TABLE II

Cold transfer in the cervical tissue according to deliveries

	Deliveries	n	Freezing time (min)			
			1	3	5	8
Average thickness of ice zone (mm)	Nulliparae	20	2.50±0.28*	5.00±1.08	6.3±0.88	8.00±0.48
	Multiparae	20	0.44±0.50	2.66±0.16	4.66±0.23	6.77±0.40
	p value		$p < 0.001$	$0.01 > p > 0.001$	$0.02 > p > 0.01$	$0.2 > p > 0.1$

* SEM

Studying the cold transfer among nulligravidae and among those having had abortions but still being nulliparae, the average ice zone thickness values differed only to a small extent, the difference being non-significant and non-characteristic. The one-minute average value was higher in the group of nulligravidae, while the 3, 5 and 8-min average values were higher in the groups having had abortions but still being nulliparae.

On heat conduction, heat is transferred in some substance from the warmer towards the colder places without any microscopic flow of material. In the substance the molecules and atoms are in chaotic motion, they pass on a part of the energy of their heat movement through collision. In the case of heat conduction, the amount of heat (thermal electric density) transmitted per unit cross-section per unit time is according to Fourier's law proportional to the negative temperature gradient in the direction of flow and to the heat conduction factor, depending on the quality of the substance

$$q = -\lambda \frac{\delta t}{\delta t} \text{ w/m}^2$$

where φ = the passing amount of heat (thermal electric density), λ = heat conduction factor, $\delta t/\delta t \cdot \% / m$ = heat gradient (the differential coefficient of the heat gradient in the normal direction of the isothermic surface).

The heat conduction factor is defined as the amount of heat transmitted per unit time, per unit cross-section (m^2) per unit temperature gradient.

Exact measurement results for the heat conductivity of living tissues are hardly available. The cervix is composed of several rather heterogeneous tissues of a varying water content. Heat conductivity increases in the function of the water content, the relationship can be expressed by an exponential curve. Naturally, the heat conductivity of the portio is largely influenced by its blood supply as well but also by other factors. It is known that, e.g. the heat conductivity is about 1.1–1.2 times that of the values measured perpendicularly [1].

Studying the transmission of the ice zone around the probe under standard cooling conditions in the function of the age of patients and the number of their deliveries and abortions, it was found that during the same time, in multiparae an ice zone of a smaller diameter is formed than in nulliparae and the difference is significant. In this respect, the comparison according to the patients' age and their histories of abortions did not show any significant differences.

During delivery, the tissue of the portio undergoes a considerable change. Following delivery there is always an accumulation of connective tissue substance and, as a result, the water content of the tissue of the portio is reduced which may account for the changes in heat conduction. The cooling conditions standardized for the heat conductivity of the cervix can be deduced from the pace of growth of the ice zone around the probe. According to our results, cold transfer is more favourable in the cervical tissue of nulliparae as compared to that of multiparae, so better results of cryotherapy can be expected in nulliparae, particularly with treatments of a shorter time, i.e. 3–5 minutes.

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Die, die Fortpflanzung der Kälte beeinflussenden Faktoren anlässlich der Kryobehandlung der Zervix

S. MATÁNYI

Bei 40 Patientinnen wurde wegen chronischer Zervizitis die Kryobehandlung der Zervix durchgeführt und in der Funktion der Behandlungszeit die Dicke der sich in der Umgebung der Sonde entwickelten Eiszone unter standardisierten Abkühlungsverhältnissen gemessen. Aus dem Wachstumtempo der Eiszone konnten betreffs der Wärmeleitfähigkeit des untersuchten Gewebes Folgerungen gezogen werden. Im untersuchten Krankengut übten das Lebensalter der Patientinnen bzw. die vorangegangenen Aborte auf die Fortpflanzung der Kälte keinen signifikanten Einfluß aus, demgegenüber war in der Gruppe der Nulliparen und der Frauen, die bereits Kinder gebären, die Abweichung zwischen den Durchschnittswerten der gemessenen Dicke der Eiszone, signifikant. Aus den Ergebnissen folgt, die Fortpflanzung der Kälte im Zervixgewebe bei den Nulliparen besser als bei den schon Kinder auf die Welt gebrachten Frauen ist, d.h. daß sich die Kryobehandlung bei den Nulliparen voraussichtlich als erfolgreicher erweist.

Факторы, влияющие на распространение холода при криотерапии шейки матки

Ш. МАТАНИ

Автор провел криотерапию шейки матки у 40 женщин с хроническим цервицитом, и, в связи с продолжительностью времени лечения, определял толщину зоны льда, возникающую вокруг зонда, в условиях стандартизированного охлаждения. На основании темпов роста ледяной зоны, автор судил о теплопроводной способности исследуемой ткани. Показал, что в исследованной группе больных ни возраст пациента, ни аборт в анамнезе не оказывали достоверного влияния на распространение холода. В противоположность этому, различие между средними значениями толщины ледяной зоны, определенными в группах нерожавших и рожавших женщин, было статистически значимо. Как показывают результаты, распространение холода в случае нерожавших женщин в ткани шейки матки лучше, чем у рожавших, поэтому лучший результат от криотерапии ожидается у нерожавших женщин.

Invasive Intrauterine Procedures in Twin Pregnancies Discordant for Fetal Malformation*

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Invasive intrauterine procedures in two twin pregnancies for exencephaly and multiple malformations are reported. In the first case, to ensure the development of the normal fetus, selective feticide of the affected fetus was undertaken by transabdominal intracardial injection of 20% NaCl solution. A healthy newborn infant with normal weight and a fetus papyraceus were delivered at term. In the second case, because of monoamniotic placentation, the procedure was regarded too dangerous, therefore, only therapeutic amniocentesis was carried out to decrease the volume of amniotic fluid. The fetuses were delivered in the preterm period. The advantages of the procedure of selective feticide developed by the authors are also discussed.

The spread of ultrasound diagnosis has made it possible to recognize multiple pregnancy and fetal abnormalities at an early stage. If the fetus proves to be abnormal the couple may choose either termination or continuation of the pregnancy. In a twin pregnancy, if only one fetus is affected (discordant twin-pregnancy) there are three possible courses of action: (i) continuation of pregnancy; (ii) termination of pregnancy and (iii) selective feticide of the affected co-twin.

In the case of continuation of discordant twin-pregnancy, it usually ends up with spontaneous abortion or premature birth [2]. Under these circumstances, it may often be necessary on maternal indication to perform therapeutic amniocentesis on account of polyhydramnios. While if on termination the healthy fetus is lost, it can, on the other hand, be saved by selective feticide.

The aim of the present paper is to describe our experience in invasive intrauterine procedures performed in two discordant pregnancies.

Case Report

1. T. H., age 22. At the 24th week of her pregnancy, ultrasound examination (Picker LS 2000) revealed discordant twin pregnancy for exencephaly. No severe malformation was found in fetus A, but in fetus B severe neural

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tube defect (exencephaly) was diagnosed. Since the presence of septum between the sacs confirmed diamnial placentation, 10 ml of amniotic fluid were aspirated from each sac. In the amniotic fluid of fetus *B*, AFP concentration was high (95,256 ng/ml) and in the cytological smear a high number of phagocytic macrophage cells was found. The biochemical and cytological structures of the amniotic fluid of fetus *A* excluded the possibility of neural tube defect. In order to increase the viability of fetus *A*, selective feticide of fetus *B* was performed.

Ultrasound-monitored drainage of 8 ml blood from the fetal heart (fetus *B*) was followed by the injection of 10 ml of 20% sterile NaCl solution. Soon after the injection bradycardia developed and within a few hours pulsation of the heart stopped. The further course of the pregnancy was uneventful. Examination of the possibility of DIC carried out in the Central Laboratory of Clinical Chemistry showed no difference. The development of both fetuses was followed by ultrasound till the end of pregnancy; the healthy fetus developed in the normal way, whereas the other fetus (*B*) gradually degenerated. In the 40th week a 2550 g living mature female infant was born via spontaneous vaginal delivery, and preceding placental separation, the other fetus was born as fetus papyraceus.

2. Á. H. aged 24, primigravida. Ultrasound examination performed at 16 weeks due to high serum AFP level (140 ng/ml) revealed twin-pregnancy discordant for exomphalos. The absence of septum between the sacs confirmed monoamnial placentation, thus only one amniocentesis was done. The amniotic fluid AFP concentration was high (83.248 ng/ml) and in the cytological smear there were no phagocytic macrophage cells. Ultrasound examination repeated in the 20th week also showed hydrocephaly and lumbosacral neural tube defect. On account of monoamnial placentation selective feticide could have been dangerous, thus only bed rest was advised. At 27 weeks 100 ml, at 31 weeks 150 ml, at 35 weeks 250 ml amniotic fluid was drained. In the 36th week of pregnancy two infants were delivered: (*A*) a 1750 g healthy female, (*B*) a 1800 g female with severe malformations.

Discussion

It is well known that in twin-pregnancy discordant for fetal malformation the viability *in utero* of the healthy co-twin is worse than in singular pregnancy [4]. Therefore it is desirable from an obstetrical point of view that the affected fetus should not develop. It was first Aberg and his co-workers [1] and Kerényi and Chitkara [3] who reported selective invasive procedure in order to stop the growth of the affected fetus. Cardiac arrest was performed through intracardiac air embolization (on account of discordant Tay-Sachs

disease in the affected fetus), by Petres and Redwine [5] and through intracardiac injection of formaldehyde in the affected fetus for trisomy 21 by Palle and co-workers [4].

According to the degree of malformation, fetal diseases indicating selective feticide can be divided into two groups. The first group contains those genetic diseases which are compatible with life (e.g., chromosome aberrations, enzymopathies), thus without the procedure, the affected fetus is likely to be delivered and to live for a while. The presence of the affected fetus usually does not disturb the growth of the healthy co-twin. In these cases, similar to the practice followed in singular pregnancy, diseases resulting in severe mental retardation indicate selective feticide.

The second group contains malformations which are incompatible post-natal life. On account of ever-growing polyhydramnios a.o. the presence of these malformations gives the healthy co-twin a smaller chance of viability *in utero*, therefore, in these cases, selective feticide is indicated, mostly for helping the normal growth of the healthy co-twin. Such affected fetuses would not live long after delivery.

The first condition for performing the procedure is, of course, correct prenatal diagnosis. After progress, counselling the couple may decide to go ahead with the procedure.

The next step is to decide how the procedure should be performed technically. Contrary to cases described in the literature, we did not choose exsanguination [1, 3] or air embolization [5] or the formaldehyde method [4], but intracardiac injection of hypertonic NaCl solution. We did not draw more than a few ml of blood in order to avoid loss of blood in the healthy fetus through a potential shunt.

Before the procedure, it is important to identify the septum between the sacs by ultrasound. In our second case, placentation was found mono-amnial, therefore the procedure would have been dangerous. The affected fetus hindered the growth of the healthy fetus, which was born with a weight of only 1750 g in spite of therapeutic amniocentesis performed on account of polyhydramnios. Contrary to the second case, pregnancy in our first case continued in a normal way until the 40th week, and a healthy infant of 2550 g was born. In this case, the fact that polyhydramnios usual in malformations could not develop must also have played an important role. It is essential to observe the rules of asepsis during the performance of selective invasive procedure.

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Intrauterine Intensiv Eingriffe im Falle fötaler Malformation bei diskordanter Zwillingschwangerschaft

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In der Arbeit wird über bei zwei Mehrlingsschwangerschaften wegen Exenzephalie bzw. einer multiplen Entwicklungsanomalie durchgeführte invasive, intrauterine Eingriffe berichtet. Im ersten Fall wurde zwecks Gewährleistung der ungestörten Entwicklung des gesunden Fötus bei der in Hinblick auf die Exenzephalie diskordanten Zwillingschwangerschaft in das Herz des kranken Fötus transabdominal 20%ige NaCl-Lösung injiziert. Die gesunde Frucht kam termingerech, mit reifem Gewicht auf die Welt. Im anderen, mit multipler Entwicklungsanomalie verbundenen diskordanten Fall ein solcher Eingriff wegen der monoamnialen Plazentation zu riskant schien, wurden im Interesse dessen, daß das Gewicht des gesunden Fötus das reife Gewichtsbereich erreiche, serienweise entlastende Amniozentesen vorgenommen. Anschließend werden die vor der Durchführung der selektiven Eingriffe zu berücksichtigenden Gesichtspunkte sowie die Vorteile der im ersten Fall angewandten intrakardialen Technik beschrieben.

Инвазивные внутриматочные вмешательства из-за мальформации плодов при дискордантной беременности близнецами

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Авторы сообщают о инвазивных внутриматочных вмешательствах, произведенных из-за эксэнцефального и мультиплексного нарушений развития при двух многоплодных беременностях. В интересах обеспечения нормального развития здорового плода относительно эксэнцефалии при дискордантной многоплодной беременности, авторы ввели в сердце больного плода трансабдоминально 20%-й раствор хлористого натрия. Здоровый плод родился в срок с зрелой массой тела. В другом случае с дискордантностью, сопровождавшимся мультиплексным нарушением развития, вследствие моноамниальной плацентации такого характера, вмешательство считали сопряженным с риском, поэтому с помощью серийного разгрузочного амниоцентеза авторы попытались добиться того, чтобы масса тела здорового плода достигла бы зрелую весовую область. Они перечисляют точки зрения, которые следует принимать во внимание перед выполнением селективных вмешательств, упоминают о преимуществах интракардиальной техники, примененной в первом случае, по сравнению с другими методами.

Bilateral Spontaneous Pneumothorax Associated with Metastasis of a Malignant Fibrohistiocytoma

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The case of a 34-year-old female patient is presented. The patient was admitted because of bilateral pneumothorax caused by the metastasis of a malignant histiocytoma originating in the left gluteus.

Bilateral chest-suction was made and the patient received complex chemotherapy.

The chest X-ray taken 4 months later showed considerable regression of the lymph node metastases.

Neither the time of development of pneumothorax nor its mechanism is known. There are only assumptions about it. Authors have considered their case worthy of publication because the lymph node metastasis of bilateral simultaneous pneumothorax due to histiocytoma has not so far been known in the literature.

A 30-year-old woman, who had undergone surgery for a malignant fibrohistiocytoma in her left gluteus 4 months earlier, was admitted with a one-week history of severe dyspnoea and pain in both hemithorax that increased with breathing.

Physical examination showed a healthy-looking woman with decreased breath sounds on both sides and a surgical scar on her left gluteus with no pathological evidence. The only remarkable laboratory finding was an elevated alkaline phosphatase. The electrocardiogram was normal. Spirometric and gasometric values all fell within normal ranges.

A chest roentgenogram (Fig. 1) showed bilateral pneumothorax that increased during expiration, and multiple nodules in both lung fields. Bilateral pleural drainage was instituted until full lung expansion was achieved and the persistent air leak stopped. Resolution was first achieved in the right hemithorax.

The patient was started on 3 courses of combined chemotherapy (adriamycin 60 mg/m² on day 1; vincristine 2 mg on days 1, 7 and 14; cyclophosphamide 600 mg/m² on day 1; actinomycin D 0.50 mg/m² on days 1, 7, 14 and 21). She was kept on this chemotherapeutic regimen on an outpatient basis. A second roentgenogram (Fig. 2) four months later revealed a marked remis-



FIG. 1. Bilateral pneumothorax due to metastasis of a malignant fibrohistiocytoma

sion of the metastasis. The diagnosis of bilateral pneumothorax due to metastasis of a malignant fibrohistiocytoma was made.

Simultaneous bilateral pneumothorax associated with metastatic pulmonary disease is very rare. To our knowledge, no case of bilateral pneumothorax from a malignant fibrohistiocytoma has been reported in the literature, whereas a unilateral association has been described mainly in children with osseous sarcoma [1].

The first case was reported in 1937 by DeBarrin [2] who observed a hemipneumothorax as a complication of metastatic pulmonary osteogenic sarcoma. To date, the underlying mechanism of pneumothorax remains unclear. Thornton and Bigelow [3] suggested that rapid tumour growth might outstrip its blood supply with subsequent formation of a bronchopleural fistula due to the subpleural localization of the tumour. Lodmell and Capps [4] and Macklin [5] suggested that the tumour itself obstructs a bronchus or bronchiole resulting in a ball-valve system which overinflates the alveolus resulting in air rupturing into the pleural cavity.

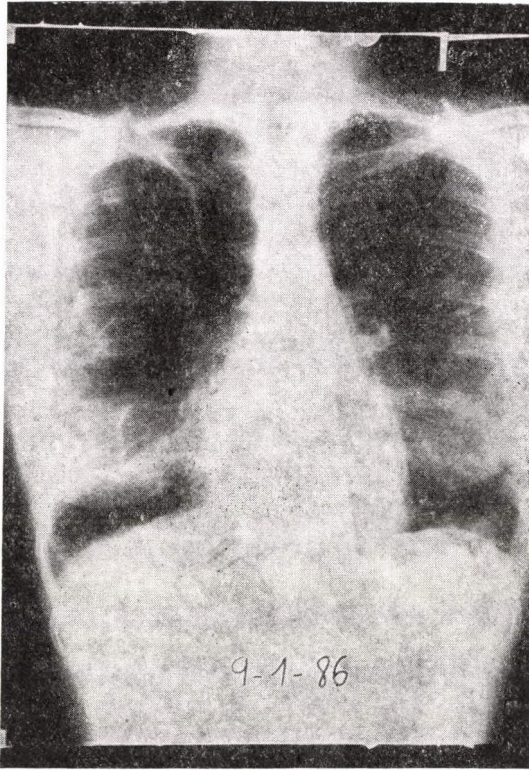


FIG. 2. Marked remission of the lesions (4 months later)

Recently, the incidence of pneumothorax observed in these patients has increased due to the use of chemotherapy [6] which induces tumour necrosis and interferes with tissue repair systems. In some cases, pneumothorax might present before the metastasis is observed radiologically [7]; thus, conventional and computerized tomography are important tools in the early diagnosis of these patients.

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Im Falle von zweiseitigem spontanem Pneumothorax diagnostiziertes, mit Metastasen kompliziertes malignes Fibrohistiozytom

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Die 34jährige Patientin wurde wegen zweiseitigem Pneumothorax aufgenommen, für den die Metastase des aus dem linken M. gluteus ausgegangenen malignen Histiozytoms war.

Bei der Patientin wurde bilaterale Thoraxabsaugung durchgeführt und komplexe Chemotherapie angewandt.

Auf der nach 4 Monaten gefertigten Thoraxaufnahme zeigten die Lymphknotenmetastasen eine wesentliche Regression.

Weder der Zeitpunkt, noch der Mechanismus der Entwicklung des Pneumothorax sind bekannt, damit im Zusammenhang gibt es nur Vermutungen. Die Darstellung des Falles schien deshalb als lohnhaft, weil durch Histiozytom herbeigeführter, zweiseitiger Pneumothorax mit pulmonaler Lymphknotenmetastase in der Literatur noch nicht beschrieben wurde.

Случай сочетания двустороннего спонтанного пневмоторакса с метастазами злокачественной фиброгистиоцитомы

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Авторы описывают случай 32-летней больной, которую приняли в отделение с двусторонним пневмотораксом, который был вызван метастазом злокачественной гистиоцитомы, находившейся в левой ягодичной мышце.

Больной произвели двустороннее отсасывание из грудной клетки и провели комплексную химиотерапию.

На рентгеновских снимках грудной клетки, сделанных спустя 4 месяца, была отмечена значительная регрессия метастазов в лимфатические узлы.

Ни время возникновения пневмоторакса, ни его механизм не известны, имеются только предположения. Авторы считают, что с описываемым случаем стоит ознакомиться, поскольку до сих пор в литературе не был описан двусторонний, одновременный пневмоторакс как следствие метастазов в легочные лимфатические узлы злокачественной гистиоцитомы.

Indirect Calorimetry Methods for Determination of Energy Expenditure*

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Brief history and development of calorimetric methods for the determination of energy expenditure are discussed. The author demonstrates the measuring principles of direct and indirect calorimetry. In two clinical studies the practical use of closed and open technique of indirect calorimetric measurements are presented.

In 10 operated patients under isoflurane-nitrous oxide anaesthesia in closed breathing circuit dose related decrease of oxygen consumption and carbon dioxide production was found. The indirect calorimetry showed higher mean energy expenditure (+14%) than was calculated by the Brody-Kleiber formula. These values indicate that the metabolic response due to surgical stress exceeds the metabolism decreasing effect of anaesthesia.

The modalities of exact determination of energy expenditure of septic patients under respiratory treatment are discussed. Data of modified Harris-Benedict equation adapted to clinical conditions and of continuous indirect calorimetric measurement of energy expenditure were compared in 25 septic patients. The measured and the calculated mean values showed good correlation ($r = 0.82$). The modified Harris-Benedict equation may be properly used in clinical practice, when indirect calorimetric measuring instrument is unavailable.

Introduction

Metabolism or cellular respiration are the means by which cells maintain their integrity. The energy requirement for synthesis or cellular function as muscle contraction, nerve conduction or glandular secretion is derived from the potential energy of organic foods. Organic foods either of vegetable or animal origin are absorbed, stored or oxidized in a series of graded enzymatic reactions designed to maximize the biological use of energy in a controlled fashion [3]. The released energy is utilized for cellular function, enzymatically stored in the form of high energy phosphates (ATP) or dissipated in the form of body heat. The efficacy of energy conversion to work can be calculated from the ratio of external work to internal conversion rate. At maximum efficiency, about 25% of chemical energy is converted to mechanical work,

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the remainder to heat. At rest almost all oxidized energy may be accounted for, by heat loss from the body [6, 13].

Energy can be neither created nor destroyed, hence the energy or heat produced by the body can be accounted for as heat loss, because man is homoiotherm and maintains stable body temperature within narrow limits [8].

Direct Calorimetry

Calorimetry is the measurement of energy expenditure. Heat lost from the body may be measured directly by whole-body or direct calorimetry (Fig. 1).

The subject is placed into a small insulated chamber in which all the heat evolved can be measured by water circulating through the coils which are inside the chamber. The rate of heat transfer from the individual to the coils is computed from the increase in water temperature and the rate of water flowing through the coils. Air is circulated through the chamber and its water vapour analysed to determine wet heat loss. The use of such a chamber for direct calorimetry is an arduous and slow process. These problems have been resolved in part by the development of gradient layer calorimeters for direct measurement of heat loss from the body [8].

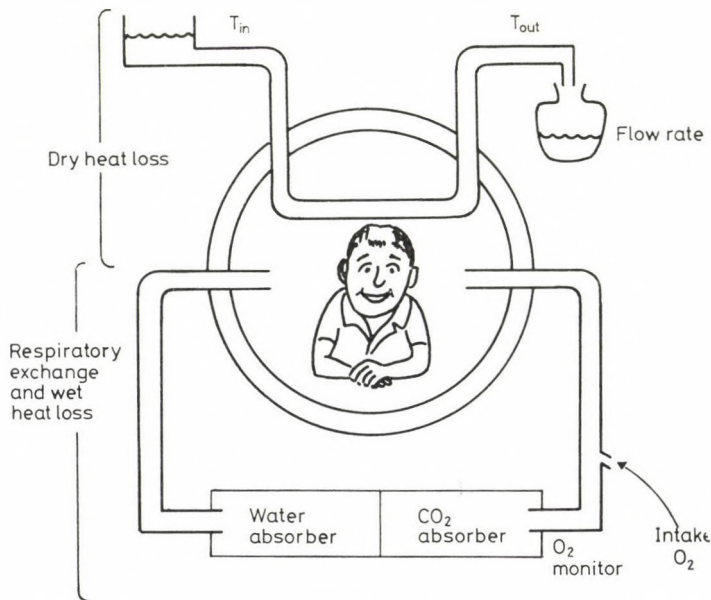
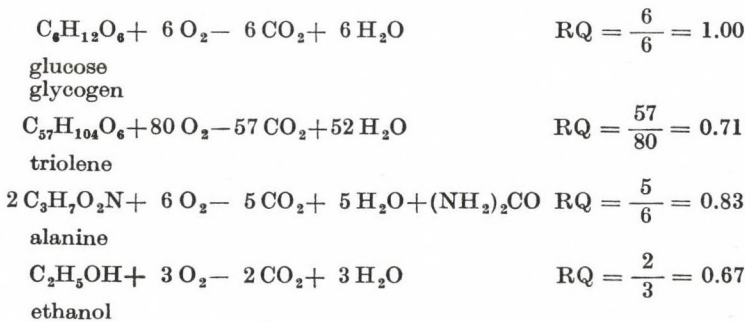


FIG. 1. One method of direct calorimetry (after D. W. Wilmore 1980.)

In clinical practice, however these technique are rarely employed to determine heat production, rather indirect calorimety is the method preferred.

Indirect Calorimetry

In aerobic metabolism oxygen consumed and carbon dioxide produced are related to the release of energy from the body. The relationship between energy release and the quantity of these two gases is stoichiometric for any particular reaction, although the gas exchange for all foodstuffs is not the same. Combustion reactions of various nutrients with the corresponding respiratory quotients (RQ) can be seen below:



The heat generated by these reactions can be directly measured in a bomb calorimeter or the amount of oxygen consumed and carbon dioxide produced can be quantitated relating gas volumes to heat production [6]. Measurement of gas exchange is the basis of the technique of indirect calorimetry [24]. In 1903 Atwater and Benedict and their group applied the up-to-date technique of direct and indirect calorimetry to demonstrate the validity of the law of conservation of energy for the human organism by using carbon dioxide production as a measure of gaseous exchange and later using oxygen consumption (Benedict and Milner in 1907). In their famous experiments they showed that the energy intake balanced the energy expenditure within 0.1% [14].

Actual energy expenditure can be measured either by a closed-circuit or open-circuit technique [6, 13, 18].

The closed circuit technique utilizes a displacement spirometer with carbon dioxide absorber. The tank is filled with oxygen and the patient breathes from the spirometer through a mouthpiece or a face mask. The volume decreasing in the spirometer over a measured period of time is recorded and it represents oxygen utilization. Oxygen consumption is converted to calory expenditure (Fig. 2).

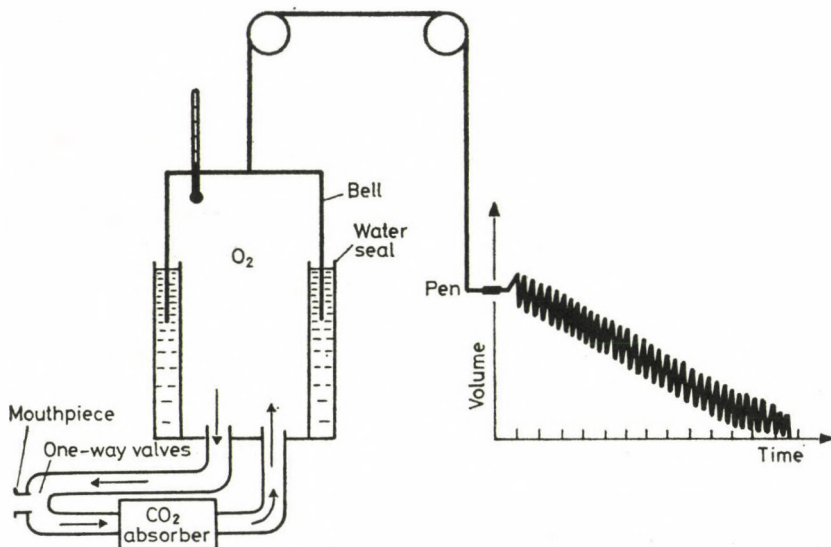


FIG. 2. Measurement of oxygen consumption with spirometer (closed system)

In the open-circuit technique, the patient breathes room air or air-oxygen mixture and the expired gases are either collected in a Douglas bag or Tissot spirometer over a measured period of time for later analysis or immediately analysed by an automatic gas analyser (Fig. 3) [19].

Figure 4 shows the portable apparatus of C. G. Douglas from 1911 for determination of total respiratory exchange in man [9]. After collection of expired air over a definite period, volume and concentration of gases are determined.

Correction have to be made to standard temperature and barometric pressure and dry gas so all measurements are equated with 0°C , 760 mm Hg barometric pressure and dry gas.

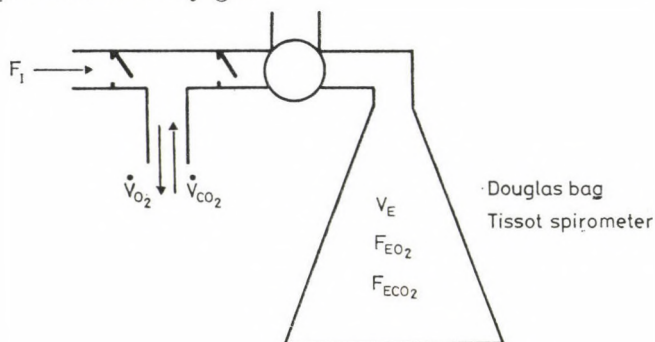


FIG. 3. Measurement of oxygen consumption and carbon dioxide production with open circuit technique

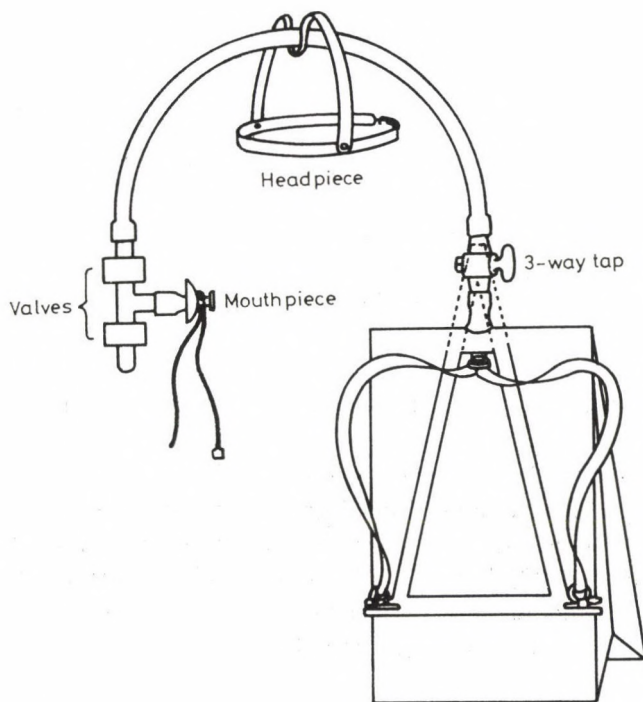


FIG. 4. A portable apparatus for the determination of the total respiratory exchange in man (after C. G. Douglas 1911)

$$\dot{V}_E \text{ STPD} = \dot{V}_E \text{ ATPS} \times (\text{BP} - \text{P H}_2\text{O}) / 760 \times 273 / 273 + \text{T}$$

$$\dot{V}_{\text{O}_2} = \dot{V}_E \text{ STPD} \times F_{\text{O}_2} \left(\frac{1 - F_{\text{EO}_2} - F_{\text{ECO}_2}}{1 - F_{\text{I}_2}} - F_{\text{EO}_2} \right)$$

$$\dot{V}_{\text{CO}_2} = \dot{V}_E \text{ STPD} \times F_{\text{ECO}_2} \text{ RQ} = \dot{V}_{\text{CO}_2} / \dot{V}_{\text{O}_2}$$

where STPD = standard temperature, barometric pressure and dry gas; ATPS = ambient temperature and pressure; saturated; F_I = inspiratory fraction; F_E = expiratory fraction; RQ = respiratory quotient; \dot{V} = volume per minute; \dot{V}_E = expiratory flow and BP = barometric pressure.

The volumes measured per unit time may then be converted to energy equivalents by Weir equation [26].

Energy expenditure = $3.941 \dot{V}_{\text{O}_2} + 1.106 \dot{V}_{\text{CO}_2} - 2.17 \text{ N}$, where N = = nitrogen.

In positive nitrogen balance the cumbersome nitrogen correction can be avoided. It makes only a small error of less than 2%. The abbreviated Weir formula is introduced.

The accuracy of conventional indirect calorimetry is limited. Skin respiration is neglected. Numerous complex metabolic pathways are reduced to a few simple biochemical reactions of synthesis and combustion. The composition of combustion mixture is rather assumed than exactly known. Calorimetric measurements are disturbed by changes in body gas stores in unsteady states, temporary hypo- or hyperventilation [7, 16]. Because the summated effects of these inaccuracies is relatively small, indirect calorimetry is widely applied and the abbreviated Weir formula is generally accepted as a reliable method for determination of energy expenditure.

Clinical Study on Closed Technique Indirect Calorimetry

General anaesthetics are known to interfere with the metabolism of the patients. Experimental and clinical data have proved that the previously used inhalational agents and morphine derivatives may decrease the body metabolism up to 30% [22, 23, 25]. In our study we attempted to assess the effect of isoflurane anaesthesia on the metabolism and the correlation of calculated and measured energy expenditure.

Patients and Methods

At the Department of Anaesthesiology, Texas Tech University HSC., Lubbock, Texas 10 otherwise healthy non-premedicated young male and female orthopaedic patients were anaesthetized with isoflurane-nitrous oxide.

For facilitation of endotracheal intubation 5 mg/kg thiobarbiturate and 1 mg/kg succinylcholine were given.

The relaxed patients were mechanically ventilated with oxygen-nitrous oxide (5 l : 10 l/min) in a semiclosed breathing circuit. After 30 minutes of

TABLE I

Blood gases under isoflurane anaesthesia

pH	7.44±0.02
pCO ₂ (torr)	37.2±3.45
pO ₂ (torr)	130.5±29.5
BE (mval)	-1.1±1.13
St. bic. (mval)	22.8±1.30
F ₁₀₂ (%)	31.6±5.8
t (°C)	37.1±0.3

(± SEM)

equilibrium of the inhaled gas mixture the breathing circuit was closed and different concentrations of isoflurane were given (Fig. 5). At stable inspired oxygen content, body temperature and blood gases, oxygen consumption and carbon dioxide production were measured by monitoring the minute ventilation and the composition of the inhaled and exhaled gas mixture with a respiratory mass spectrometer (Table I, Fig. 6).

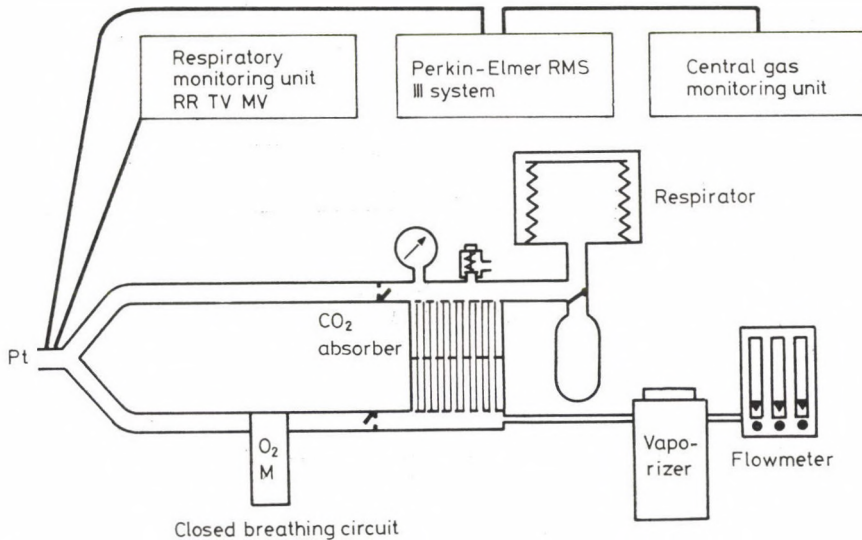


FIG. 5. Closed circuit anaesthesia system. Pt = patient; M = monitor; RR = respiratory rate; TV = tidal volume; MV = minute ventilation; RMS = respiratory mass spectrometer

Results

Figures 7 and 8 show a dose-related decrease in oxygen consumption and carbon dioxide production under isoflurane anaesthesia.

The metabolic data demonstrate an about 14% increase in total energy expenditure measured as compared to the calculated values by the Brody-Kleiber formula (Table II).

Discussion

It has been proved that general anaesthesia reduces total body oxygen uptake and carbon dioxide production by 15–30% when compared to predicted values on standard charts or equations [3, 15]. In our study we found some increase in total energy expenditure in spite of the reducing effect of anaesthetics. It appears that the interference of surgical intervention in the

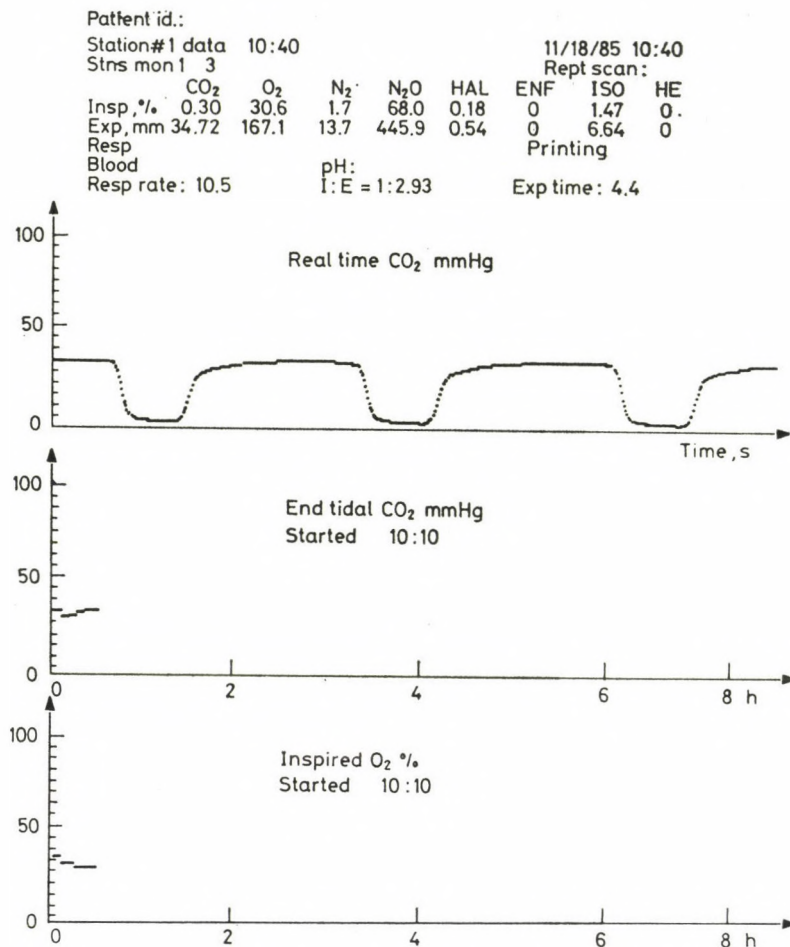


FIG. 6. Inspiratory and expiratory gas contents under anaesthesia. Capnogram, trends of end tidal CO₂ and inspired O₂

TABLE II

Metabolic data of 10 patients under isoflurane anaesthesia

	Measured	Calculated	Δ %
V _{O₂} (ml/kg/min)	3.64 ± 0.45	3.21 ± 0.16	13%
V _{CO₂} (ml/kg/min)	3.97 ± 0.57	3.53 ± 0.19	12%
R _Q		0.91	
TEE (kcal/24 h)	1908 ± 35	1676 ± 42	14%

(± SEM; Brody-Kleiber formula: V_{O₂} = 10 kg 3–4 ml/min)

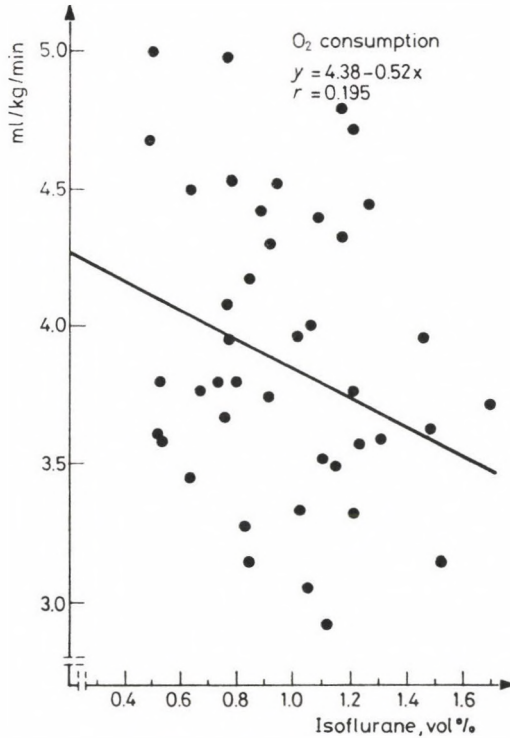


FIG. 7. Changes of oxygen consumption under isoflurane anaesthesia

metabolic processes may start immediately under surgical intervention and the classical clinical sign of post-aggression reaction is only a late reflection of the metabolic disturbances [17]. The non-invasive method of direct monitoring of oxygen consumption and carbon dioxide production with closed anaesthesia circuit reveals developing metabolic problems [20].

Clinical Study on Open Technique Indirect Calorimetry

It is a difficult task to estimate the energy expenditure in sepsis. The extent to which expenditure of energy increases, varies markedly with the nature and degree of injury [2, 4]. In absence of actual measurements under routine clinical conditions, it is nevertheless feasible to estimate energy expenditure. The normal predicted value for basal metabolic rate (BMR) may be obtained from standard tables or formulas. The most frequently used one is the Harris-Benedict equation.

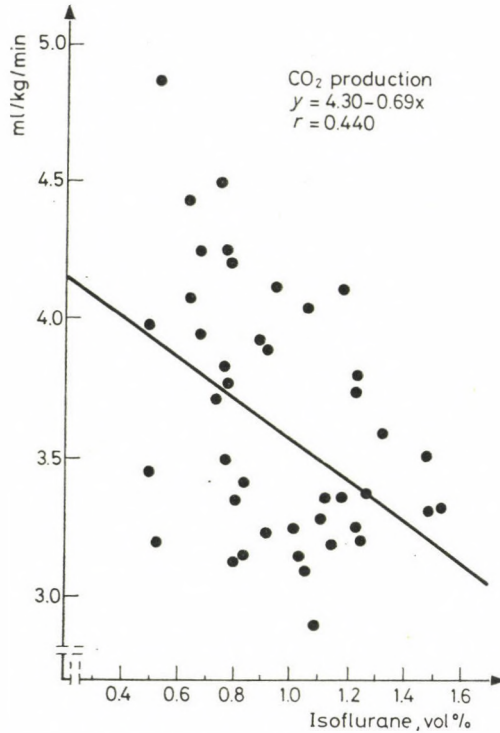


FIG. 8. Changes of carbon dioxide production under isoflurane anaesthesia

$$BEE_{\text{male}} = 66.4230 + 13.7516 W + 5.0033 H - 6.7750 A$$

$$BEE_{\text{female}} = 655.0955 + 9.6534 W + 1.8496 H - 4.6756 A$$

where BEE = basic energy expenditure; W = weight (kg), H = height (cm), and A = age (yr).

The expected increases due to injury or sepsis may be estimated from the figures of Kinney, one of the best estimates available for predicting caloric expenditure in critically ill patients [10, 16] (Fig. 9).

Patients and Methods

In a clinical study we have chosen the Harris-Benedict formula for determination of BEE. For calculation of total energy expenditure we applied the well known activity factors and clinical correction factors and specific dynamic effect of food as modifying factor [1, 10, 16, 21].

$$TEE = [(100 + af)/100] \times [(100 + cf)/100] \times BEE + SDA$$

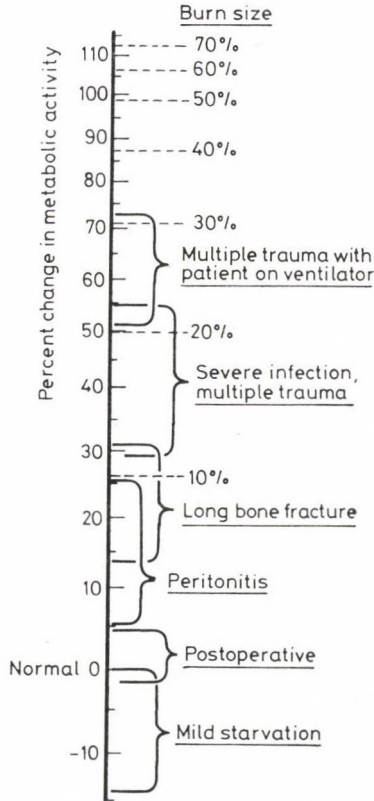


FIG. 9. An estimate of energy requirement for critically ill patients (after J. M. Kinney 1980)

where TEE = total energy expenditure; af = activity factor [%]; cf = clinical correction factor [%] and SDA = specific dynamic action of nutrients.

In 25 septic surgical patients on respirator the total energy expenditure was calculated by using the Harris-Benedict formula and clinical correction factor. The patients refrained from physical activity and were not fed par enterally. Then we measured continuously the 24-hour energy expenditure by indirect calorimetry.

For this purpose a relatively inexpensive metabolic device was designed and tested in collaboration with the Research and Development Unit of Erasmus University Hospital Workshop in Rotterdam [11].

The device was primarily constructed for application in mechanically ventilated patients (Fig. 10). In the inspired and expired gas mixture oxygen concentrations were automatically analysed by paramagnetic oxymeter (Taylor Servomex OA 273). Infrared type capnograph (Mijnhardt UG 51) served for carbon dioxide analysis. Each minute the computed VO_2 and VCO_2

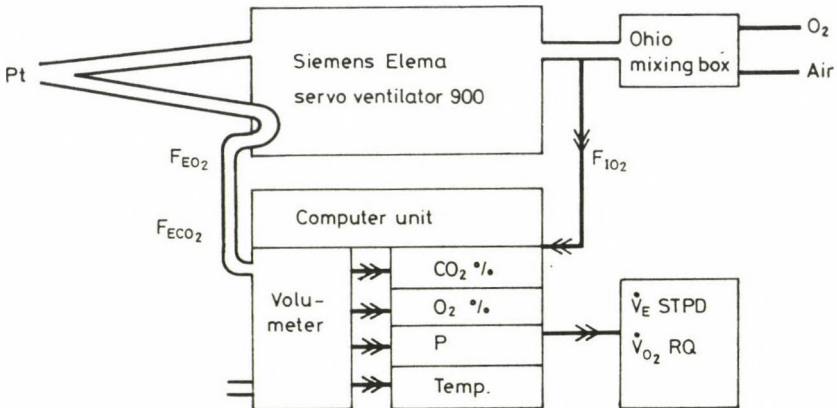


FIG. 10. Diagram of open circuit calorimetry for patients on respirator

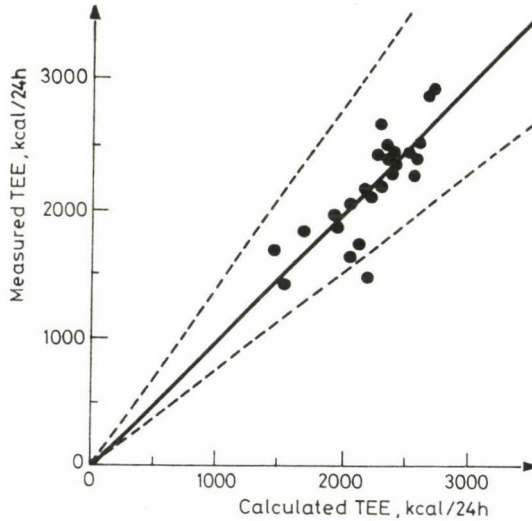


FIG. 11. Calculated TEE compared to measured TEE in 25 septic patients

values were sent automatically to a remote computer and stored. Artifacts due to ventilatory disconnections were removed automatically by an algorithm.

Results

In the septic patients the application of the Harris-Benedict formula combined with careful judgment of the clinical condition led to an average difference between calculated and continuously measured total energy expenditure of $8.9 \pm 9.6\%$. One can see a relatively good correlation between the data ($r = 0.82$) (Fig. 11).

Conclusions

The usefulness of calculation energy expenditure is challenged by several authors, because the use of BEE with a correction factor obviously has its clinical limitation, over- and underestimates of caloric needs according to literary data, may occur by 10 to 60% [4, 5, 12].

It seems, with the time it is likely that definitive guidelines will become available against which groups of patients should have energy expenditure measured rather than calculated from predictive equations. Until that time the more accurate way is to measure energy expenditure.

If equipment is not available, however, the rational use of predictive equation is far better than ignoring the problem.

*

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Indirekte kalorimetrische Methoden der Bestimmung der Energieverwertung

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Nach Besprechung der kurzen Geschichte und der Entwicklung der kalorimetrischen Methoden der Bestimmung der Energieverwertung, werden das Meßprinzip der indirekten Kalorimetrie sowie im Rahmen von zwei klinischen Studien die praktische Ausführung der geschlossenen und offenen Methode dargestellt.

Die Sauerstoffverwertung und Kohlendioxidproduktion des in zehn geschlossenen Narkotisierungssystemen mit Isofluran-Stickstoffoxydul narkotisierten und operierten Patienten haben sich linear mit der Konzentration des Narkosemittels verringert. Die mittels indirekter Kalorimetrie gemessene durchschnittliche Energieverwertung der Patienten übertrafen die mit der Brody-Kleiber-Gleichung gerechneten Werte um 14%. Die Beobachtungen führten zur Folgerung, daß die durch den Operationsstreß bedingte Stoffwechselantwort bedeutender als die stoffwechsellverringende Wirkung des Narkosemittels ist.

In der Folge werden die mit der Bestimmung der Energieverwertung der künstlich beatmeten septischen Patienten verbundenen Schwierigkeiten analysiert. Die mit der, den klinischen Verhältnissen angepaßten Harris-Benedict-Gleichung ausgerechnete Energieverwertung von 25 septischen Patienten wurde mit den Daten der kontinuierlichen indirekten Kalorimetrie verglichen. Die gerechneten und gemessenen Werte korrelierten gut miteinander ($r = 0,82$). Insofern kein indirektes kalorimetrisches Meßgerät zur Verfügung steht, kann die adaptierte Harris-Benedict-Gleichung auch in der klinischen Praxis eine vorteilhafte Anwendung finden.

Определение потребления энергии методом непрямой колориметрии

Э. ДАРДАИ

Автор обсуждает краткую историю и формирование calorimetрических методов определения потребления энергии. Демонстрирует измерительный принцип прямой и непрямой calorиметрии, в двух клинических исследованиях практическое осуществление закрытого и открытого методов.

Потребление кислорода и выделение углекислого газа прооперированными больными (10), получившими изофлуран-нитрогеноксидул в наркозных системах закрытого контура, линейно уменьшалось с увеличением концентрации наркотического средства. Среднее потребление энергии больными, определенное непрямым калориметрией, на 14% превысило значение, высчитанное с помощью уравнения Броди-Клейбера. На основании полученных результатов, автор приходит к выводу, что вызванная хирургическим стрессом реакция обмена веществ превышает действие наркотического средства, понижающего обмен веществ.

Автор анализирует проблемы, связанные с определением потребления энергии септическими больными, находящимися на искусственном дыхании. Высчитанное с помощью адаптированного к клиническим условиям уравнения Харриса-Бенедикта потребление энергии у 25 больных, он сравнил с данными непрерывного измерения методом непрямого калориметрии. Расчетные и измеренные значения хорошо коррелировали друг с другом ($r = 0,82$). С точки зрения клинической практики, адаптированное уравнение Харриса-Бенедикта может вполне применяться, если нет возможности пользоваться методом непрямого калориметрии.

Fentanyl-Midazolam-Flumazenil Anaesthesia during induced abortion

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A new anaesthetic method (fentanyl-midazolam-flumazenil) was compared with recently administered (pethidine-diazepam-ketamine) anaesthesia in two groups of 25 women, each undergoing termination of pregnancy. No significant difference was found between the two groups in the quality of anaesthesia. Recovery was assessed by means of the Aldrete score and a visual analogue scale. The recovery time was significantly shorter in patients who received midazolam-flumazenil. In the ketamine group, 36% of the patients complained of unpleasant dreams. The recovery in the midazolam group was comfortable.

Introduction

Termination of pregnancy by suction under general anaesthesia within the first 12 weeks of gestation is a common ambulatory gynaecological intervention. This is a minor surgical procedure and the length of the patient's hospitalization depends mainly on recovery from the anaesthesia employed. Ideally, the technique should include rapid, smooth induction and maintenance of an appropriate level of anaesthesia without increasing blood loss or provoking cardiorespiratory instability. The recovery should be fast and complications, such as nausea, vomiting and anaphylactoid reactions should be absent [11]. Our study of intravenous anaesthetic techniques for short surgical procedures was undertaken to compare midazolam with thiopental or methohexital [3, 9, 11].

Midazolam, a short-acting water-soluble benzodiazepine is finding an increasing use in anaesthesia for patients undergoing various types of outpatient surgical procedures. Midazolam affects the cardiovascular system minimally, even in patients with already compromised coronary perfusion. Another advantage of this new i.v. induction agent is its amnesic effect [5, 10].

Flumazenil, an imidazobenzodiazepine, is a benzodiazepine antagonist which specifically blocks the central effects of agents acting through the benzodiazepine receptor by competitive inhibition [6, 8].

In the present study we evaluated recovery after fentanyl-midazolam-flumazenil anaesthesia [12] in comparison with pethidine-diazepam-ketamine

anaesthesia and attempted to determine whether the new method (fentanyl-midazolam-flumazenil) is suitable for anaesthesia in outpatients' abortion. In recent years the pethidine-diazepam-ketamine anaesthesia has been generally administered in our department for anaesthesia in abortion (in 10,803 cases).

Methods

Fifty patients (ASA 1-2) with a pregnancy of less than 12 weeks underwent abortion. Patients were consecutive, but those with neurological diseases, known allergy to benzodiazepine or, who were receiving treatment with psychotropic drugs, were not studied. The study was conducted in accordance with the Helsinki II Declaration. The patients were randomly assigned to two groups in order to receive either pethidine-diazepam-ketamine (ketamine group), or fentanyl-midazolam-flumazenil (midazolam group).

Ketamine group: Anaesthesia was induced with 0.15 mg/kg diazepam intravenously, together with 1 mg/kg pethidine, +0.008 mg/kg atropine. After this 1.25 mg/kg ketamine was administered. If necessary, supplementary doses of 0.25 mg/kg ketamine were injected.

Midazolam group: Anaesthesia was induced with 0.3 mg/kg midazolam intravenously, together with 1.5 µg/kg max. 0.15 mg fentanyl + 0.008 mg/kg atropine.

A further dose of 0.15 mg/kg midazolam was administered if the eyelash reflex was still present 3 minutes after the initial dose. Where necessary, supplementary doses of 0.15 mg/kg midazolam or 1 µg/kg, max. 0.05 mg fentanyl, or both, were injected.

Immediately after the termination of anaesthesia patients received 0.4 mg flumazenil i.v. within 60 seconds.

The patients were breathing spontaneously. Oxygen, nitrous oxide or other inhalation anaesthetic agents were not administered. Postoperatively, the patients remained in the operating theatre for 10 minutes and were then transferred to the gynaecological department.

The overall quality of anaesthesia was graded on a 10 cm visual analogue scale by the operating obstetrician (very good, excellent = 10; poor = 0). The obstetricians did not know the type of anaesthesia. Recovery was assessed by means of the postanesthesia recovery score, described by Aldrete [1].

The postanesthesia subjective sedation measured by 10 cm visual analogue scales, marked 0-10. (Quite alert = 0, extremely tired = 10 [7].)

Blood gas analysis was performed in all cases, prior to the induction of anaesthesia, 90 and 180 min after surgery. Blood pressure, heart and respiratory rate were measured every 15 minutes.

All patients were visited postoperatively by one of the anaesthetists before they were discharged. Patients were asked if the same type of recovery

would be acceptable on a future occasion. Statistical analysis was carried out using Student's *t*-test. Values of $p < 0.05$ were considered statistically significant.

Results

The main findings of the study are summarized in Table I, and dosage requirements of anaesthetic agents are shown in Table II.

No statistically significant difference was found between the two groups concerning patients' weights and duration of anesthesia.

The new anaesthetic method (midazolam group) compares favourably with the recently administered method (ketamine group) as regards overall quality of anaesthesia. Assessment score is measured by a visual analogue scale. The postanaesthetic recovery score showed evidence of more rapid recovery in the midazolam group. The difference between the two study groups was significant at 5 min and 10 min after surgery (Table III).

Results of subjective expression of postoperative sedation (measured by visual analogue scale) are summarized in Fig. 1. All patients in the midazolam group were awake 5 min after administration of flumazenil. In the ketamine group the mean recovery time was 31.2 ± 6.8 min.

TABLE I
Comparison of the two study groups. The values are mean \pm SD

	Ketamine group	Midazolam group
No. of patients	25	25
Age (yr)	24.2 \pm 9.8	25.6 \pm 10.1
Weight (kg)	59.8 \pm 15.2	61.4 \pm 16.3
Height (cm)	165.4 \pm 25.3	164.2 \pm 26.8
Duration of anaesthesia (min)	11.9 \pm 9.2	13.1 \pm 10.1
Assessment score (cm)	7.7 \pm 2.1	7.6 \pm 2.3
Recovery time (min)*	31.2 \pm 6.8	4.5 \pm 0.5

* Indicates statistically significant differences between the groups ($p < 0.005$)

TABLE II
Total dose (mg) requirements of anaesthetic agents. Median (range)

	Ketamine group		Midazolam group	
Pethidine	55.3	(25.0-75.0)	Fentanyl	0.125 (0.1-0.15)
Diazepam	15.2	(10.0-20.0)	Midazolam	25.5 (22.5-40.0)
Ketamine	65.3	(50.0-87.5)	Flumazenil	0.4
Atropine	0.5	(0.4-0.6)	Atropine	0.5 (0.4-0.6)

TABLE III

The postanaesthetic recovery of the patients measured with the Aldrete scoring system. The time is the period from the administration of the antagonist—the end of surgery

	5' *		10' *		40'	
	ketamine	midazolam	ketamine	midazolam	ketamine	midazolam
Muscle activity	0	2	0.02	2	2	2
Respiration	1.08	2	2	2	2	2
Circulation	2	2	2	2	2	2
Consciousness	0.6	2	1.12	2	2	2
Skin colour	1.92	2	2	2	2	2
Total-score	5.60	10	7.14	10	10	10

* Indicates statistically significant differences between the groups ($p < 0.005$)

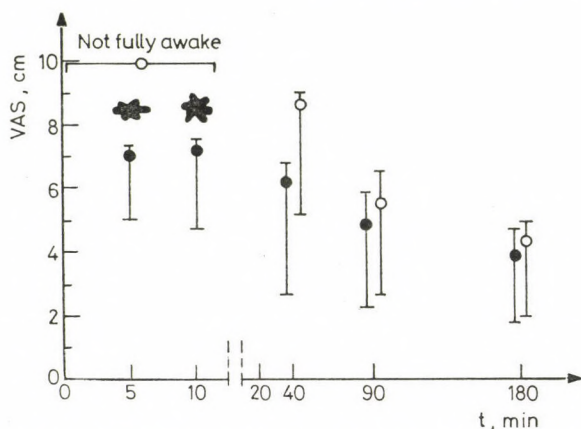


FIG. 1. Postanaesthetic sedation on a 10 cm visual analogue scale (VAS). ○ Values in ketamine group; ● Values in midazolam group; Median (interquartile range). * indicates statistically significant differences between the groups ($p < 0.005$)

This investigation at 5 and 10 min in the ketamine group was impossible, because the patients were not fully awake and could not do the assessment.

The difference between the two groups was significant at 40 min after surgery, but at 90 and 180 min the difference did not reach statistical significance.

In the midazolam group 92%, in the ketamine group 64% would be satisfied with the same type of recovery on a future occasion.

In the ketamine group 36% of the patients complained of unpleasant dreams. In both groups all values of blood gas, blood pressure, heart rate and respiration rate were within normal limits. No serious complications were noted during the study, only two patients in each group vomited slightly. In neither group was any complaint of awareness during anaesthesia.

Discussion

An ideal intravenous anaesthetic agent for outpatient anaesthesia should have a fast onset and short-term action. It should be rapidly metabolized into pharmacologically inactive and nontoxic metabolites. There should be no cumulation after repeated doses. Cardiorespiratory stability, good local tissue tolerance and lack of allergic phenomena should be assured. Midazolam fulfils some of these criteria [2, 4, 11].

This study was undertaken to investigate recovery after two types of intravenous anaesthesia for the termination of pregnancy.

Fentanyl-midazolam-flumazenil anaesthesia was new to our department. The recovery time is shorter after fentanyl-midazolam-flumazenil anaesthesia than pethidine-diazepam-ketamine anaesthesia, but the differences in subjective sedation values at 90 and 180 min are not significant.

In the ketamine group, 36% of the patients complained of unpleasant dreams. The recovery in the midazolam group was comfortable. All patients were discharged 6 hours after surgery.

Results demonstrate that fentanyl-midazolam-flumazenil anaesthesia is suitable for anaesthesia in abortion. The recovery period after this anaesthesia is short and pleasant.

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Fentanyl-Midazolam-Flumazenil Narkose bei Schwangerschaftunterbrüchen

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Die Autoren haben bei 25 Schwangerschaftunterbrüchen Fentanyl-Midazolam-Flumazenil Narkose angewandt. Zur Vergleichsbasis diente eine Krankengruppe mit ähnlicher Stärke, wo die Narkose das früher routinemässig gebrauchte Verfahren (Pethidin-Diazepam-Ketamin) war. Das neue Verfahren ist zur Sicherung der ambulanten Narkose bei Schwangerschaftunterbruch geeignet. Zwischen den beiden gab es keine signifikante Abweichung die Qualität der Anästhesie betreffend. Zur Charakterisierung der Erwachensperiode werden der Aldrete-Erwachenswert, die Komaeinteilung nach Steward und eine visuelle Analogskala angewandt. Die Erwachensperiode war in der Fentanyl-Midazolam-Flumazenil Gruppe signifikant kürzer.

Фентанил-мидазолам-флумазениловая анестезия при прерывании беременности

ХАМАР, О., ГАРАМВЭЛДИ, ДЬ.

Авторы применяли фентанил-мидазолам-флумазениловый наркоз при прерывании 25 беременностей. Основой для сравнения послужила группа беременных сходного числа, где использовали ранее рутинно применяемый наркоз (петидин-диазепам-кетамин). Установлено, что новый подход годный для обеспечения амбулаторно наркоза для прерывания беременности. Между двумя группами не было значительной разницы в отношении качества анестезии. Для характеристики периода пробуждения использовали оценку пробуждения по Альдретэ, шкалу комы по Стюарда и одну визуальную аналогичную шкалу. Период пробуждения был значительно короче в группе фентанил-мидазолам-флумазелина.

Measuring Blood Loss during Transurethral Resections

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Blood loss was measured in 70 patients during the transurethral resection for bladder neck adenoma and prostatic tumour on the basis of the haemoglobin content of the irrigation fluid, and the factors influencing blood loss were assessed. In 20 patients an irrigation fluid of body temperature was used. Their investigations have not proved the irrigation fluid of a higher temperature to be of a bleeding-inducing effect. It was stated that the absolute amount of bleeding was directly proportional to the weight of the resected tissue and the time of resection. These data revealed that a blood loss/1g of resected material/1 min of resection time does not increase with a larger resection weight or during a longer operation.

In the recent one or two years, it has been witnessed all over the world but also in Hungary, that transurethral resection has been given preference over open surgery in prostatic operations. In addition to its efficacy, it is more 'convenient' for the patient and it imposes a smaller risk on elderly people affected in their cardiorespiratory function [1]. Even despite its less drastic nature, the intervention can be accompanied by well-circumscribed complications. Intraoperative blood loss is considered as one of them. Its empirical assessment is uncertain, it may lead to 'unexpected hypoxia', circulatory failure. Several methods are known from the literature, which aim at the accurate measuring of blood loss [2, 3]. Contradictory opinions exist also concerning the individual factors which theoretically can be related with blood loss. These are the mode of anaesthesia, duration of operation the amount of resected material, tissue structure of the prostate, intraoperative hypertension, temperature of the irrigation fluid and experience of the operating surgeon [3, 4].

Material and Methods

During our work at the Department of Urology, Albert Szent-Györgyi University Medical School, Szeged, blood loss during transurethral prostatic resections of 70 patients was measured, and the circumstances supposed to be influential were assessed, i.e. the amount of the resected material, the time of resection, the histological picture and the temperature of the irrigation fluid.

Without exception, our operations were made by an Iglesias resectoscope ensuring continuous irrigation under spinal and epidural anaesthesia. The irrigation fluid was water, filtered, sterilized tap water and a 1.5% glycin solution. In 50 patients an irrigation fluid of a temperature of 21–23 °C was used, while in 20 patients the fluid of 36.5 °C was supplied by the medico-technological water-preparatory and water-providing equipment. Duration of the intervention from introduction of the resectoscope up to the insertion of the urethral catheter was measured. After accurate measurement of the resected specimen, it was subjected to histological examination.

The amount of blood mingled in the irrigation fluid collected during operation can be determined on the basis of the so-called indicator dilution principle [3]. Haemoglobin itself may most simply be used as an indicator substance [2]. If the initial, i.e. preoperative concentration of the indicator substance (in the given case Hb) in the blood (I_0) or in the irrigation fluid (I_d) is known, as also the volume of the irrigation fluid (Y), the volume of the lost blood (X) can be calculated according to the formula as follows.

$$X \cdot I_0 = (X + Y) I_d$$

$$X = \frac{Y \cdot I_d}{I_0 - I_d}$$

where X = blood loss (l); I_0 = Hb concentration of blood (g/l); I_d = Hb concentration of irrigation fluid (g/l) and Y = amount of irrigation fluid (l).

Concentration is given in g/l, and volume in l, while the amount of blood loss is obtained in l.

The irrigation fluid collected intraoperatively without loss, its total amount was determined in a graduate with an accuracy of 0.05 l, and after mixing and haemolization by saponin (adding 3 drops of 2% saponin to 10 ml), Hb was determined by the cyanmethaemoglobin method in a way that, depending on its Hb content, an adequate dilution was made by distilled water in an end-volume of 10 ml, so that the sample contain a concentrated Drabkin's transformation solution in 0.2 ml of blood volume. [The transformation solution was made by 'Human' (Vaccine-producing Company), i.e. 'HAEMISOL' 100 μ l each of r. I and II solutions.] Upon measuring dilution had to be adjusted to be between 0.1 and 1.2 g/l in the Hb end-concentration which corresponded at 546 nm to 0.064 and 0.774 E., resp. Calculation was made on the basis of the molar unit of Hb, its layer thickness as well as the degree of dilution ($U_{1cm}^{546} \times 1.55 \times A = \text{g/l}$, where A is the degree of dilution. The necessary dilution was, in general, 2–6 times greater. The Hb concentration was assessed on the day prior to the operation also in the form of cyanmethaemoglobin by routine haematological diagnostic methods, by the Drabkin's transformation reagent. The photometric measuring was made by the Boehringer/Clinicon 4010 computer photometer.

Results

The amount of irrigation fluid ranged between 6.5 and 39.0 and the Hb concentrations measured in it between 0.135 and 3.87 g/l. During the 70 operations the average amount of resected material was 27.3 g with extreme values of 14 to 80 g. Resection time averaged 60.9 min in the range of 11 to 120 min. Blood loss ranged from 12 to 1128 ml, with an average of 285 ml per patient. There was a blood loss of 10.43 ml for 1 g of resected material and one of 4.67 ml for 1 min resection time (Table I).

TABLE I
The parameters of 70 prostatic TURs

	Average	Range	Blood loss
Amount of resected material (g)	27.3	14-80	10.43 g/l
Resection time (min)	60.9	11-120	4.67 ml/min
Blood loss (ml)	285	12-1128	—

If calculations were made for a resected material over 30 g, an average blood loss of 341 ml and 7.18 ml/g was obtained. In cases of resection time over 60 min, the average blood loss was 388 ml and 3.82 ml per minute.

The values seen below have been obtained as the resection blood losses of benign and malignant prostatic processes: In adenomas the blood loss per g was 11.8 ml, the blood loss per min 5.4 ml, while in tumours these values were 5.1 and 2.6 ml (Table II).

An irrigation fluid of body temperature was used in 20 patients with the blood losses as follows: Average blood loss was 262 ml, 10.8 ml/g of resected material and 4.8 ml/min (Table III).

TABLE II
Blood loss and histology of prostatic TURs

	mg/l	ml/min	No. of patients
Benign	11.8	5.1	56
Malignant	5.4	2.6	14

TABLE III
Blood loss on using an irrigation fluid of body temperature

	ml	ml/g	ml/min	No. of patients
Average blood loss	262	10.8	4.8	20

Discussion

In Desmond's report prostatic resections of 25–125 g were followed by blood losses of less than 300 ml in 79% and 300–2100 ml in 21% of the patients [2].

Freedman et al. observed a blood loss of 3.7 ml/g and 8.4 ml/min, on an average 605 ml during their operations [3]. Heathcote reported these data to be 7 ml/g and 4.63 ml/min [4]. Pompeius found the blood loss/g to be 15,1 ml and one per min to be 8.6 ml [5]. Abrams et al. reported an average blood loss of 185 ml and one of 60 ml at their benign and one of 60 ml at their malignant prostatic resections [1].

The determination of blood loss occurring during TUR according to the haemoglobin content of the irrigation fluid, is much simpler and more useful as any other method recommended for this purpose, i.e. calculation from the amount of potassium dissolved from the erythrocytes haemolysed in the irrigation fluid [3]. According to Drabkin, measuring of Hb in the form of cyanohaemoglobin, is a generally accepted, sensitive, well-reproducible procedure. The advantage of our version is that it fits well into the routine haematological laboratory method, and the same reagents and standards can be employed. The required measuring time of our laboratory is 10–12 min. Desmond has recommended the use of another method based also on the measuring of Hb [2], but he described his procedure for a special photometer, and his dilution-calculation is rather laborious.

In agreement with the experience of others, essentially different results were obtained at resections of bladder neck adenoma and prostatic carcinoma. Less than half of the tumour resections were accompanied by blood loss as compared to adenomas. The literary data attribute this to their different tissue structure and vascularization [1].

Our experiences with an irrigation fluid of body temperature have not confirmed the bleeding-enhancing effect of higher temperature, at the same time the unpleasant consequences of the cooling effect of the fluid can be omitted.

Based on our data, it can be stated that the observed blood loss and the amount of resected material as well as the resection time are closely correlated and directly proportional to each other. Increase of resection weight and prolongation of operation time do not alter this relationship, it remains linear. Concerning blood loss, our findings did not support the widely accepted view of urologists that only a prostate of a size resectable within an hour should be resected [5].

The transurethral resections of the prostate are always accompanied by bleeding. The amount of this can be subjectively judged by the continuous monitoring of the operated region, from the discolouring of the several litres

of irrigation fluid and, indirectly from the patient's circulatory parameters. Inaccuracies due to the subjectivity of these methods and the compensating mechanisms of the organism can be eliminated by the objective data of the above laboratory method. The importance of the exact determination of blood loss available in a matter of minutes may be of paramount importance in our practice of operating on elderly people.

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Messung des Blutverlustes anlässlich transurethraler Resektionen

J. OSZLÁNCZI und M. SZABÓ

Im Laufe der transurethralen Resektion des Blasenhalssadenoms und des Prostatumors wurden bei 70 Patienten anhand des Hämoglobingehalts der operativen Spülflüssigkeit der Blutverlust gemessen und die beeinflussenden Faktoren bewertet. Bei 20 Patienten kam eine Spülflüssigkeit mit Körpertemperatur zur Anwendung. Die Blutung steigernde Wirkung von Spülflüssigkeiten mit höherer Temperatur haben die Untersuchungen nicht bewiesen. Die absolute Menge der Blutung ist mit dem Gewicht des resezierten Gewebes und der Resektionszeit proportional. Die Ergebnisse sprechen dafür, daß der auf 1 g Resekat und 1 min Resektionszeit fallende Blutverlust weder im Falle eines größeren Resektionsgewichts noch im Laufe einer längeren Operationsdauer ansteigt.

Об определении кровопотерь в связи с трансуретральными резекциями

Й. ОСЛАНЦИ и М. САБО

Во время трансуретральной резекции аденомы пузырно-шеечной аденомы и опухоли простаты авторы определили у 70 больных кровопотерю на основании содержания гемоглобина в хирургической промывающей жидкости. Они оценивают влияющие на это факторы. У 20 больных применялась промывная жидкость, имеющая температуру тела. Результаты исследования не подтвердили усиливающее кровотечение действие промывной жидкости более высокой температуры. Было установлено, что абсолютное количество потерянной крови находится в прямой пропорции с весом резецированной ткани и продолжительностью времени резекции. Полученные данные подтверждают, что кровопотеря, приходящаяся на 1 г удаленной ткани и на 1 мин времени резекции, не увеличивается с увеличением веса резецированной ткани, или при увеличении продолжительности операции.

Vitamin B₁₂ Absorption in Some Selected Pathological States of the Gastrointestinal Tract

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The absorption of vitamin B₁₂ in selected pathological states of the gastrointestinal tract was studied. Schilling test was performed with 37 kBq (1 μCi) of ⁵⁷Co-labelled vitamin B₁₂ as an analysis of urinary radioactivity. No increase in cobalamin absorption was present after exogenous IF had been administered to patients after resection of the upper part of the stomach and total gastrectomy. This suggests that there is another factor likely to affect vitamin B₁₂ absorption.

It is well known, mainly from animal experiments, that the stomach plays an important role in absorption of vitamin B₁₂ (cobalamin) [4, 5]. However, the significance of its particular parts in this process has not adequately been studied. Therefore, the objective of the present study was to compare the vitamin B₁₂ absorption in patients who have undergone a variety of gastric resection (which can be compared with the conditions of experiments on animals) with the absorption in healthy subjects and patients with pernicious anaemia.

Materials and Methods

Experiments were carried out in years 1982–1986. Forty-three female and male test subjects participated in the experiment. First group — 27 male patients, aged 28–62 years ($\bar{x} = 48.7$), after gastric surgery. Second group — 9 patients (5 males and 4 females), aged 45–71 ($\bar{x} = 54.1$), with pernicious anaemia (group *n*). Third group — 7 healthy subjects, aged 29–34 years ($\bar{x} = 32.6$), free of gastrointestinal disorders during clinical observation (control group *k*). No patient had a history of diabetes or pancreatic, or thyroid disease, nor any evidence of hepatic or renal dysfunction.

The previously operated patients were divided into four subgroups (Fig. 1):

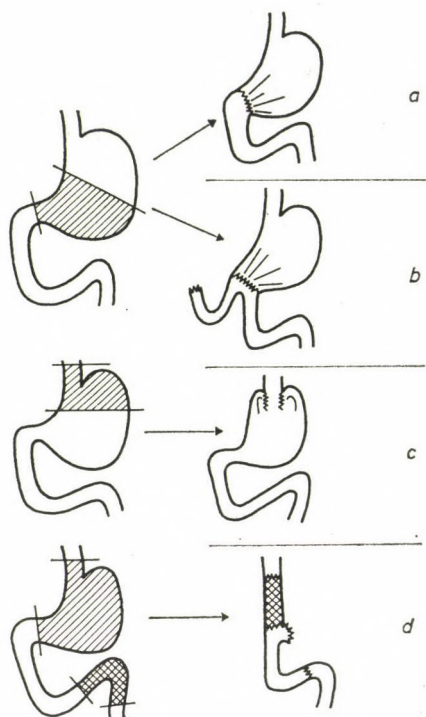


FIG. 1. Schematic presentation of surgical procedures and postoperative state in four groups of patients (*a* — gastroduodenoanastomosis, *b* — gastroenteroanastomosis, *c* — upper resection, *d* — oesophagojejunostomy)

a — 9 male subjects, 28–68 years old ($\bar{x} = 45.3$), after partial excision of the distal part of the stomach; natural food transit through the duodenum was maintained (Haberer's or Rydygier's procedure): the mean postoperative time was 31.8 months (14–58).

b — 9 male patients, 33–62 years old ($\bar{x} = 47.8$), after partial gastrectomy and Reichel–Poly or Hoffmeister–Finsterer gastroenterostomy the passage of food through the duodenum being eliminated; the mean postoperative time was 24.7 months (15–36).

c — 5 male subjects, aged 41–57 ($\bar{x} = 51.2$), after cardiectomy and resection of the upper segment of the stomach, the food passage through the duodenum being maintained (Garlock's method); the mean postoperative time was 21.2 months (7–37).

d — 4 male patients, aged 27–52 ($\bar{x} = 55.3$), after total gastrectomy performed with Henley's procedure (oesophagus-isoperistaltic small intestinal lamella-duodenum); the mean postoperative time was 38.5 months (12–67).

The operations in groups *a* and *b* were made to gastric or duodenal ulceration, and in groups *c* and *d* for oesophageal or gastric neoplastic

disease. The patients complained of no ailments and there were recurrences resulting in surgery.

All subjects gave their informed consent after full explanation of the experimental procedures involved. Besides vitamin B₁₂ the subjects were given no drugs.

The oral administration of 37 kBq (1 μ Ci) of ⁵⁷Co-labelled vitamin B₁₂ was followed by i.m. injection of 1000 μ g of non-radioactive vitamin B₁₂ 1 h later ('washing dose'). The tests were done with and without 60 mg IF Polfa given by the oral route. 24-h urine samples were stored at +4 °C and the urinary radioactivity was measured 72 h after the test and expressed as a percentage of the oral dose [3]. All measurements were done in duplicate with a scintillation detector, Packard 5360.

Statistical analysis was performed with Student's *t*-test for paired or unpaired observations.

Results

The mean values of the 24-h Schilling test in the groups examined are shown in Table I. The values obtained in groups *a* and *b* were high and similar to the controls. In group *c* there were borderline values (Fig. 2) which were significantly lower than those in groups *a*, *b* and *k* ($p < 0.01$, < 0.01 and < 0.05 , respectively). In the patients after total gastrectomy (*d*) and with pernicious anaemia (*n*) Schilling tests yielded similar results, significantly lower than in groups *a*, *b* and *c* ($p < 0.001$, < 0.001 , < 0.05 , < 0.001 , < 0.001 , < 0.01 , respectively).

After the examination with addition of intrinsic factor (IF) in groups *a*, *b*, *c* and *k*, the test values were similar to the results obtained without IF. Administration of IF-bound B₁₂ in group *d* resulted in normal absorption of cobalamin ($p < 0.05$), the results being borderline and similar to the ones obtained in group *c* both prior to and after administration of IF. These values

TABLE I

The mean values of 24-h vitamin B₁₂ urinary excretion in percentage of oral dose of 37 kBq (1 μ Ci) of ⁵⁷Co-B₁₂ with and without 60 mg IF Polfa (for groups examined see test)

Group	⁵⁷ Co-B ₁₂ ^a	24-h Schilling test ⁵⁷ Co-B ₁₂ + IF
<i>a</i>	22.4 ± 1.5	23.0 ± 1.3
<i>b</i>	22.3 ± 1.6	22.6 ± 1.3
<i>c</i>	12.4 ± 2.8	8.6 ± 1.3
<i>d</i>	2.4 ± 0.2	10.6 ± 1.6
<i>n</i>	1.8 ± 0.5	25.4 ± 4.3
<i>k</i>	25.9 ± 2.0	25.7 ± 1.7

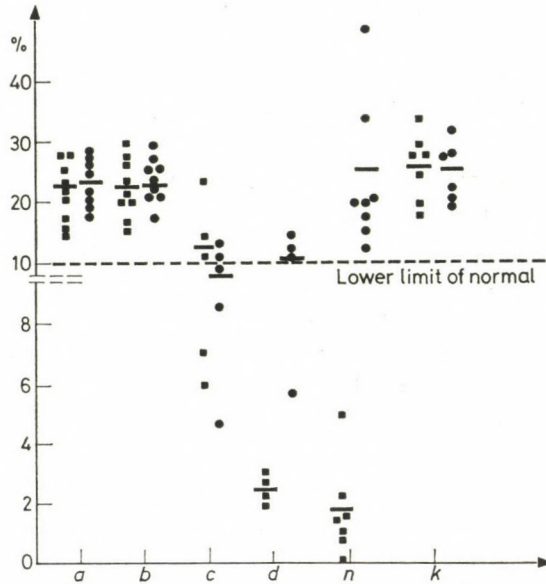


FIG. 2. The values of 24-h urinary excretion in percentage of oral dose of 37 kBq (1 μ Ci) of ⁵⁷Co-B₁₂ without (■) and with (●) 6á mg IF Polfa in the groups examined

were significantly lower than those obtained in groups *a*, *b* and *k* ($p < 0.001$ for respective comparisons). Due to administration of the vitamin B₁₂-IF complex, the patients in group *n* had a normal Schilling test ($p < 0.002$) the values of which were not different from the results obtained in groups *c* and *d* ($p < 0.02$, < 0.05 , respectively).

No correlation between the volume of diuresis, the amount of excreted creatinine and the amount of excreted ⁵⁷Co-B₁₂ was found in the groups examined.

In the course of investigations the patients developed no side effects resulting from administration of the preparations.

Discussion

As expected, resection of the distal part of the stomach caused no reduction in vitamin B₁₂ absorption, since it did not affect the rate of IF secretion by the cells of the cardia and fundus of the stomach. The absorption test values resembled the previously obtained values [2] in healthy humans. The effect of pepsin deficiency and change of the gastric pH on the results obtained in previously operated patients can be excluded since in the Schilling

test [3] free ⁵⁷Co-B₁₂ is utilized, which results in 'eliminating' of the gastric phase of absorption [1, 5].

Low vitamin B₁₂ absorption values obtained in patients after total gastrectomy and in patients with pernicious anaemia were due to lack of Castle's intrinsic factor which is secreted by the parietal cells of the fundus and cardia [5]. Presumably, since part of these cells was not removed in patients after resection of the upper segment of the stomach, the test values appeared to be borderline. It is noteworthy that no increase in cobalamin absorption was present after exogenous IF had been administered to patients in this group.

However, administration of IF-bound ⁵⁷Co-B₁₂ to the patients after total gastrectomy significantly increased vitamin B₁₂ absorption, but also only the borderline values. The possibility of low activity of the IF preparation (Polfa) should be rejected, for the examination with addition of IF from the same batch of preparation in patients with pernicious anaemia revealed normal absorption of cobalamin, similar to the absorption in both the controls and the patients after excision of the distal part of the stomach. It should also be excluded that the activity of natural intrinsic factor secreted in the stomach is competitive in relation to the IF preparation, as the test values in patients after resection of the distal segment of the stomach and in the control group before as well as after the test with addition of IF did not show substantial differences.

Our findings suggest that there is another factor likely to affect cobalamin absorption. Presumably, it may be secreted by the cells of the cardia, since in the patients after resection of the upper part the stomach and total gastrectomy this part of the alimentary tract had been removed. It should also be emphasized that isolated lack of this factor will not result in such a pronounced malabsorption of vitamin B₁₂ as in the case of the deficiency of Castle's intrinsic factor.

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Vitamin-B₁₂-Absorption in einigen ausgewählten pathologischen Zuständen des Magen-Darmtrakts

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In einigen ausgewählten pathologischen Zuständen des Magen-Darmtrakts wurde die Vitamin B₁₂-Absorption untersucht.

Zwecks Untersuchung der Radioaktivität des Harns wurden mit, mit 37 KBq (1 μCi) ⁵⁷Co markiertem Vitamin-B₁₂ Schilling-Tests vorgenommen. Bei Patienten, bei denen der obere Teil des Magens reseziert oder Totalgastrektomie durchgeführt wurde, erhöhte sich bei der Zufuhr von exogenem IF die Kobalamin-Absorption nicht. Dies läßt darauf folgern, die Vitamin-B₁₂-Absorption wahrscheinlich unter dem Einfluß eines anderen Faktors steht.

Всасывание витамина В₁₂ при некоторых выбранных патологических состояниях желудочно-кишечного тракта

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Авторы изучали всасывание витамина, В₁₂ при некоторых патологических состояниях желудочно-кишечного тракта.

С целью определения радиоактивности мочи выполняли тест Шиллинга с витамином В₁₂, меченным изотопом кобальта (⁵⁷Co, 37 KBq (1 μCi)). Всасывание кобаламина не возросло при экзогенном дозировании 11 у больных, у которых произвели резекцию верхней части желудка, или сделали тотальную гастректомию. Это наводит на мысль, что, вероятно, другой фактор оказывает влияние на всасывание витамина В₁₂.

Data on the Pathophysiology and Clinical Aspects of the Mechanical Obstruction of the Small Intestine

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A brief overview is given of the relevant physiology of the small intestine, and the pathomechanism of the clinical picture, based on a material of 423 patients with mechanical obstruction of the small intestine. The various forms of the mechanical obstruction of the small intestine are reviewed, with special regard to strangulation and adhesive obstruction. The possible forms of treatment are dealt with, with an emphasis on the importance of an early surgical intervention and of a careful after-treatment with a view to reducing the still high morbidity rate.

Ileus is, currently too, one of the most severe and most complicated acute abdominal clinical pictures, imposing a serious task on the practising physician. It essentially lies in the mechanical or functional obstruction of the passage of intestinal contents. Its typing and classification, too, are in general made accordingly. Based on them, the following three large groups can be differentiated:

1. *Mechanical ileus*. It includes all forms of obstructions where obstruction is the result of a pathological process in the intestinal lumen or outside it.

2. *Neural obstruction*. Apart from some rare cases of spastic obstruction, which may be due to lead or nicotine poisoning, in general, the paralytic or adynamic obstruction belongs in this group. This is, however, in almost all cases, consequential to some other abdominal disease.

3. *Vascular obstructions* make up the third large group produced by the embolism and thrombosis of the mesenterial vessels.

This simple classification, too, may suggest that it is practically impossible to treat obstruction in depth in the scope of a single report, since the inducing causes are different as also is the pathomechanism, to some extent. The fact should also be considered that the functions of the small and large intestines do also differ. Moreover, the function of the latter is also different in the right or left colon. Let alone that—while the right colon—together with the small intestine—develops from the embryonal midgut, the left colon and the rectum do from the embryonal rectum.

Therefore, but also for other causes, it is necessary to differentiate the various types of obstructions, even if the pathophysiological processes may be identical or may overlap at certain points.

In this report one of the most frequent and most dangerous forms of obstruction, the mechanical obstruction of the small intestine is dealt with, with special concern to the pathophysiological processes and the clinical aspects.

Undoubtedly, the surgeon of today cannot claim the simplified opinion as his own, according to which his only task would be to rapidly eliminate as soon as possible the cause of obstruction, but this is not too much in itself. He should be aware of the physiology of bowel movement in order to understand the pathophysiology of ileus and to recognize, prevent or effectively treat it on its onset.

It is important to emphasize that intestinal obstruction is not a circumscribed clinical picture but a group of symptoms. This may map out further tasks to be reviewed later.

Here are some data on the physiology of small intestinal function which may contribute to the understanding of the lately known pathophysiological processes. It is well known that, in the small intestine, besides the transport of fluids and nutriments their digestion also occurs. Transport is performed by the external longitudinal and internal orbicular muscles. Both types of muscle have a basic tone implying delicate contractions in time and space. This tone sometimes decreases, the other time increases, leading finally to peristalsis, two forms of which are known: the transporting and the mixing types. The contraction always evokes an action potential which can be measured electrophysiologically [10]. Contraction occurs only when a slow intestinal rhythm is overridden by an impulse of higher frequency. The cellular membrane is depolarized on excitation, with an energy supplied by the splitting of ATP into ADP and phosphate [10]. Splitting occurs by fermentation in the presence of Na^+ and K^+ . In absence of the latter intestinal paralysis may occur. The frequency rate varies by intestinal segments: it is 15–20/min in the duodenum, 8–10/min in the ileum, while 5/min in the colon. It also belongs to the basic physiology of the small intestine that its function is relatively independent of the luminal contents, as does also the fact that its stretching may induce strong peristaltic activity. Concerning undisturbed function, neither the large number nor the role of chemo-, presso- and tension receptors, which are capable of responding in a similar way both to vagal and to sympathetic impulses, can be ignored [6]. These, as well as the endothelium performing the varied function of the intestinal wall, belong to the defence mechanism of the intestine, that is to the intestinal barrier.

From the surgical point of view, some important reflexes still deserve to be mentioned. These include

1. The so-called *intestinal reflex*. Here, vagal and sympathetic nervous excitement is of importance through acetylcholine or noradrenaline release. Stimulation of the former nerve leads to enhancement of muscular tone and to acceleration of motility, while that of the latter results in reflex atony and sphincteric hypotony.

2. *Gastroileal reflex*. Following nutriment intake it results in antral distension, and simultaneously with gastric peristalsis, in increased ileal peristaltic activity. This reflex can be shortcircuited by dissecting the antrum or a small intestinal segment [10].

3. *Jejuna gastric inhibitory reflex*. It contains in the delay of the emptying of the stomach by the stretching of the jejunal wall. Most probably, it is about a vagovagal reflex.

4. *Intestinointestinal inhibitory reflex*. It implies that the exaggerated stretching of this intestinal segment may result in the inhibition of the motility and tone of the adjacent intestinal segment. Its importance lies in the fact that the obstruction or paralysis of a small intestinal segment may lead to the decreased motility of the adjacent intestinal one. Treating by probe, or decompression, this reflex can be short-circuited.

5. *Anorectal inhibitory reflex*. Its essence is that the weak stretching of the anorectal region leads to the inhibited motility of the gastrointestinal system. The reflex must be transmitted by the sympathetic fibres. This inhibitory reflex is contradicted by the well-known fact from surgery that dilatation of the sphincter performed on termination of certain operations results in general in early and easy defecation.

Only those aspects of the pathophysiology of the mechanical obstruction of the small intestine are discussed which refer to the latest experimental clinical observations and which are important therapeutically.

Following obstruction, stasis of the intestinal contents over the barrier is increased, while it results in distension of the intestinal loops. At the same time, viscerovisceral reflexes are elicited from the site of obstruction, as a result of which increased peristaltic activity is induced for overcoming the barrier. Due to distension, the intestinal wall is becoming oedematous, its circulation deteriorating with the onset of mural anoxia. Absorption is reduced, however fluid secretion of the stomach, intestine, pancreas and liver remain unchanged, moreover it may increase, which further increases the congestive intestinal contents. Due to additional distension of the intestinal loops, the circulatory disorders aggravate and capillary permeability is enhanced. The accumulated fluid and gas reduces the length of the obstructed intestine by 20–30%, its weight increasing by about 30–40%. In the meantime, distension increases, the intraluminal pressure reaches the value of about 40 mm Hg of the diastolic pressure, resulting in further deterioration of circulation, increasing of capillary permeability, then obstruction of the vessels and necrosis and perforation

of the intestinal wall. During this time, resorption completely stops, with an increase in transudation, and the so-called ileal vicious circle develops followed by ileal shock.

The nutritional disorder of the ileal loops enables the entering of the various toxic substances into the abdominal cavity, which gives rise to peritonitis, and through peritoneal resorption of the toxins, leads to a further deterioration in the patient's state and anoxaemia of the vital organs.

The above-described pathomechanism is followed by partly known pathophysiological changes. The contents of the intestinal loops above the obstruction are hardly or not at all absorbed but are discharged by repeated vomiting. This, in turn, leads to severe fluid and electrolyte loss, then dehydration. Depending on whether gastric or pancreatic fluid is lost in a larger amount, acidosis or alkalosis may develop. In obstruction of the small intestine, in general, Na-loss predominates, therefore there is a predisposition to acidosis. Sodium decrease entails, in turn, an adequate amount of extracellular water loss.

Vomiting in ileus may, however, also cause a considerable potassium deficiency manifesting in muscular weakness, bodily and mental asthenia and hypotonia. The obviously two most important, closely connected factors in the metabolic transport of the organism are water and salt. The former, as a function of salt transport may cause severe disorders already by its 10% deficiency. Hyposalaemia is of similar importance, too, 20–25% of which may already lead to death.

As a consequence, the rapidity of the course of ileus, mainly of strangulation obstruction increases in direct proportion to the height of the obstruction. The higher is the obstruction, the greater and the more severe is the fluid and electrolyte loss. Experiments have unanimously revealed that in a high strangulation obstruction of the small intestine, the plasma potassium and sodium levels decrease in about 50%, while the protein level in 40–45% relatively soon after it has developed [20].

Besides these humoral factors, intoxication processes are assumed to also play an important role. Currently, it is also subject to discussion to what extent the protein catabolites and various bacterial toxins derived from the absorption of the congestive-putrescent intestinal contents play a role in causing death due to ileus. No doubt that, as soon as the metabolism of the intestinal wall is impaired, absorption of the produced toxins commences. The current view is—supported both by clinical as well as experimental observations—that the shock due to obstruction is first of all an endotoxic one [4, 9, 10, 22]. The endotoxin itself is the macromolecular component of the Gram-negative bacterial wall which is released on decomposition of the bacterium. It is chemically composed of polysaccharides, lipids and peptides. Of them, lipid is the toxic component [18].

The endotoxin enters the greater circulation by two routes:

1. From the intestinal lumen, through the damaged intestinal wall, via the portal system, and the inferior vena cava.
2. Through the lymphatic system, via the thoracic duct and the superior vena cava.

It has been unanimously proved by our earlier experiments that there are toxic substances in the circulation of the animal with ileus, because similar to the general and ileal mucosa changes in the animal with obstruction the same finding was observed in the intact one in their crossed circulation [13]. It has currently been also verified that the presence of bacteria is indispensable to the production of toxins and that neither the living tissue nor the secretion of the mucosa are responsible for toxin production [10].

It is also known that in mechanical obstruction bacterial hyperplasia increases multiply which means that the intestinal bacteria multiply at a speed of 10^8 within some hours [10]. Their presence is also proved by the fact that if the intestinal content anterior to the obstruction is aspirated in time and an antibiotic inhibiting their propagation into the intestine is administered, the endotoxic shock can be prevented.

It is debated whether the toxins penetrate the intestinal wall and when do they do so. The fact that, in obstruction causing severe progressive peritonitis, toxins can already be detected in the fluid of the abdominal cavity, moreover, in the peritoneal fluid also the so-called toxic lethal factor has been shown to be present, that means that penetration is certain but its time is questionable [1].

Besides the primary role of the toxin theory, also the observations should be considered according to which distension and obstruction and the mutual effect of these two factors have an important role in the pathophysiology of ileus [8, 19]. The statement is based on the evidence that if in the affected intestine pressure is 20 mm Hg or over it, blood perfusion considerably decreases and the distribution of blood between the aerobic mucosa and the muscular layer changes. Normally, this result is 2 to 1, while on the previous increase of pressure this relation is going to be 1 to 4 in favour of the muscular layer [23]. This latter finding is supported by the so-called 'nervous reflex theory'. According to it, this disorder in blood distribution is due to the irritation of the peritoneum and the affected intestinal segment.

In the obstructed ileal segment, as also proved by histological examinations, an inflammatory process, too, can occur. That is why it is plausible that in intestinal obstruction and peritonitis the catabolites and inductors of the inflammatory chain can also be demonstrated. Here, it is primarily about histamine, bradykinin and serotonin, as the products of mast cells and of various granulocytes. However, also the catabolytes of the arachidonic acid cycle, like prostacyclin and leukotrien, and anaphylatoxin, the catabolyte of

the humoral defence chain of the complement system, can be found [4, 6, 10, 23].

Naturally, in the meantime, also the organism mobilizes its warding off, defence mechanism. Here belong the mesothelial cells of the peritoneum, the specific and nonspecific antibodies, the phagocytosing cells of the RES, with special regard to the RES cells of the liver [10]. As long as the filter capacity of the liver functions adequately, no endotoxaemia occurs.

The above-described pathophysiological progresses slower or faster but irresistibly, depending on the type of obstruction, e.g. in strangulation obstruction more rapidly, and terminate in sepsis. In the first hours of endotoxaemia, temperature increases with an elevated pulse rate and vasodilatation; blood pressure is reduced. Partly as a result of the latter, the RES cells of the liver are damaged. The toxic impairment of the vascular endothelial cells of the renal cortex leads to vasoconstriction, oliguria then anuria. In this pathological process the role of the lung deserves special attention. Besides the well-known defence mechanism, as a filter organ, it collects the mobilized cells from the abdominal cavity, like the micro- and macrophages [6]. From this point of view the intestinal system and the lung should be looked upon as a unified, coherent system. The lung, however, responds already very early to the functional disorders of the intestine. Still, before the typical picture of the so-called septic shock lung can be visualized on the X-ray, ultrastructural changes can already be verified by electro-optic methods when the patient is still in a compensated state [6]. Finally, the direct and indirect endotoxin effect produces oedema and congestion in the intraalveolar septa, smooth muscle spasm which will lead to impaired gas exchange, metabolic acidosis then complete pulmonary insufficiency.

Although, in the recent years, several new results have been produced on the pathomechanism of ileus, the exact course of the pathological processes is

TABLE I
Age distribution and mortality (No. of cases: 423)

Age (years)	10-20		21-30		31-40		41-50	
No. of cases	18		47		87		106	
	R	D	R	D	R	D	R	D
	18	—	44	3	81	6	97	9
			6,4		6,9		8,5	

R = recovered; D = died

still not fully clarified. Therefore, our view may be correct if we do not attribute death due to obstruction to a single pathophysiological change, because it probably occurs as a result of the above coefficients, but these require to be supplemented yet.

Clinical Material

The symptomatology and diagnostics of the mechanical obstruction of the small intestine are not dealt with here, because they are well known, but we wish to report on the distribution, mortality of the clinical material, some differential diagnostically important clinical pictures and the up-to-date therapy.

During a period of 10 years (1977–1987) in our previous workplace, as well as during one of 5 years 1985–1989, at the 3rd Department of Surgery, our current one, 423 operations were carried out because of mechanical obstruction of the small intestine (the 23 obstructions due to ileal tumours are excluded from the material).

The age distribution of the 423 cases as well as the mortality are shown in Table 1.

The overall mortality rate is 15.6%, being not at all a low figure. If this 15.6% is compared with the mortality data of patients operated for the same disease at my previous workplace, the 2nd Department of Surgery during the period 1950 and 1970, the following results were achieved: between 1950 and 1960 the mortality rate was 27.4%. In the period between 1960 and 1970 it was 18%, i.e. during these two decades the average mortality rate was 22.8% (276 cases). Comparing this to the 15.6%, the improvement—which is primarily the result of up-to-date anaesthesia and intensive therapy—is by no means considerable but is not acceptable at all.

The type distribution of obstructions is illustrated in Fig. 1.

51-60		61-70		71-80		81-90		91-	
79		33		25		16		12	
R	D	R	D	R	D	R	D	R	D
64	15	21	12	19	6	10	6	3	9
	19		36		24		38		75
Total mortality: 66 (15.6%)									

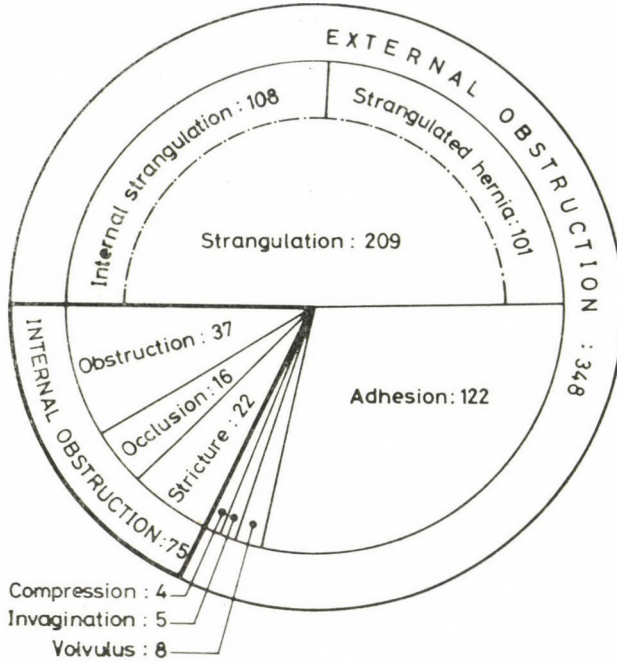


FIG. 1

Most patients belong to the group of strangulation obstructions (209) being partly the frequent consequence of previous abdominal operations. It is primarily caused by fibrous, string-like bands developing as a result of omental adhesions and inflammatory changes. It often occurs after pelvic, mainly gynaecological operations. Another frequent form is the occlusion due to a strangulated hernia. An essential difference, as opposed to the simpler forms of obstruction, is that the mesenterium of the intestinal loop is also herniated with it and so the damage of the intestinal wall is much sooner to occur here. This form of obstruction is also called destructive ileus. If compression occurs abruptly and involves a larger segment of the mesenterium a reflex shock may ensue. In view of these, it is evident that strangulation ileus is one of the most severe forms of intestinal obstruction. The distribution and mortality rate of internal strangulation obstruction (108 cases) is demonstrated in Table 2. As seen, it occurs most frequently after gynaecological operations.

The obstructions are often caused by intraabdominal adhesions. These are due to those endogenous and exogenous factors which give rise to adhesions while producing the colloid-chemical changes of the cover cells of the peritoneum. Although these processes are partly known, the adhesions are consequences of intra-abdominal surgery which are most difficult to influence. It is a clinical observation that adhesions involving the whole abdominal cavity

cause obstruction less frequently, while minor adhesions often lead to obstruction of the lumen through kinking of the intestine. To prevent formation of newer adhesions, there is unfortunately not much to do during operation, because this largely depends on constitution, and the individual congenital constitutional traits. Therefore, a certain percentage of adhesions is inherent in the clinical picture and cannot be influenced surgically.

The distribution and mortality rate of adhesive obstruction are shown in Table 3.

The intraluminal obstructions, i.e. the internal occlusions do not belong to the frequent cases (see Table 3, Fig. 1). The lumen can be obstructed internally by gallstone, tumour, intestinal parasites, various swallowed foreign bodies.

In giving rise to gallstone ileus it is not the size of the stone which is important but rather the colicky contraction due to its irritating effect. That is why gallstone ileus is a combination of mechanical and spastic obstructions.

Due to the oedema of the intestinal wall, inflammation rarely produces a passage disorder, it is much more due to the scarred obstruction of the affected intestinal segment. Our material includes 22 cases (see Table 3, Fig. 1.)

TABLE 2

Distribution and mortality of internal strangulation ileus (No. of cases: 108)

Following a previous abdominal operation	No. of cases, %		Mortality, %	
	97	89.8	25	25.8
1. Gynaecological operation	31	31.9	7	22.6
2. Appendectomy	21	21.6	4	19
3. Gynaecological operation + appendectomy	7	7.2	1	
4. Gallbladder operation	13	13.4	3	23
5. Gastric operation	9	9.3	3	
6. Other abdominal operation	16	16.5	7	43.7
NO ABDOMINAL OPERATION	11	11.2	2	18.2
Total	108		27	25

TABLE 3

Distribution and mortality of adhesive ileus

Following a previous abdominal operation	No. of cases, %		Mortality, %	
1. Gynaecological operation	42	34.5	4	9.5
2. Gallbladder operation	9	7.4	3	33.3
3. Gastric operation	12	9.8	3	25
4. Colonic operation	23	18.8	6	26
5. Appendectomy	15	12.3	2	13.3
6. Other abdominal operation	21	17.2	4	19
Total	122		22	18

The inducing cause was primarily Crohn's disease and inflammation of the Meckel's diverticulum.

Compression may rarely lead to ileal obstruction. Namely, while the anatomical conditions of the abdominal cavity are intact, i.e. the excursive movement of the intestines is not inhibited by any immobile structure, the external pressure causes obstruction only occasionally. There is a different situation on the rapid growth of intra-abdominal tumours which usually produce chronic inflammation causing adhesions. Namely, it is primarily not the size of the tumour which is decisive in giving rise to obstruction, but the pathological immobility due to adhesions. Invagination is, in Hungary relatively rare mainly in adults (see Table 3, Fig. 1). Among its three forms referring to the small intestine the most frequent one is the ileocaecal invagination. The pathological course of this specific form of obstruction is twofold: on the one hand it is strangulation, while on the other obstructive with the corresponding clinical picture, i.e. a mixture of strangulation and obstructive ileus. Volvulus (Table 3, Fig. 1) is also rare in Hungary. It consists in torsion of the mesenterium of the small intestine, which can be partial, complete (360°) or multiple. The more complete torsion is, the more intense are the symptoms, the more dangerous it is, because, due to compression of the vascular trunk, intestinal necrosis is faster to follow.

From a differential diagnostic point of view the first and foremost problem is the differentiation of the mechanical and the primary paralytic obstruction. The paralytic obstruction is actually never a primary one, in general it is associated with an underlying disease, as an early reflex complication, or as a later sequel. There is no problem in the early phase of mechanical ileus, it appears rather in its late stage of secondary paralysis. Accurate history-taking may help as also the careful inspection of the abdomen, the auscultation finding and last but not least the X-ray. Recently, the use of sonography has been increasingly gaining ground in diagnosing mechanical obstruction of the small intestine [16]. Naturally, other abdominal clinical pictures, too, may be considered in the differentiation. The most frequent of them include the perforation of the cavital systems, pancreatitis, acute cholecystitis, uretero-, nephrolithiasis, etc. The aspects of differentiation can be, to some extent, determined by the history.

It is often problematic for the surgeon which form of mechanical obstruction he encounters. First of all, the two most frequent forms, i.e. strangulation and adhesive, are important to differentiate, because the adhesive obstruction can resolve due to conservative treatment.

Strangulation ileus is to be considered if there is a rapid succession of symptoms; prolonged, periodically presenting intensive abdominal pain, nausea, vomiting, tachycardia, abdominal tenderness and resistance, muscular rigidity, leucocytosis and finally shock. In adhesive ileus, the obstruction is often

present in the pelvis, i.e. the lower segment of the small intestine and so the complaints are milder at the beginning, the pain is less intense, the circulatory failure starts later and it responds well to decompression. In spite of this, to be more objective concerning practice, it should not be left untold that laparotomy is often performed by the surgeon only establishing the fact of ileus without knowing its cause. This latter is, however, less important, what is decisive is to perform the operation as soon as possible. The mechanical ileus of the small intestine can be treated conservatively and surgically.

By conservative treatment first of all aspiration is implied of which various forms are known. Its advantage is that in certain forms of ileus the obstruction can be solved also without operation. It should, however, be emphasized that aspiration cannot be regarded as a causal treatment, because the inducing cause persists even in the cases where the intestinal passage disorder could be eliminated by aspiration. Its aim is to relieve the intestine, and to remove the congestive toxic fluid, allowing the distended intestines to regain their tone and to restore their peristaltic activity. The amount of the removed fluid—together with the amount of urine—partly provide information on the extent of loss and this allows an aimed fluid therapy to be started. Prior to the aspiration treatment, it is, however, suitable, besides the thorough physical examination, to take an X-ray and to decide on the question of indication for surgery. Namely, due to decompression, the symptoms characterizing ileus can be modified or they disappear, which incurs the danger of making the objective assessment of the situation more difficult [2, 11, 24]. Therefore, the aspiration treatment can only be looked upon as preparation for surgery. Postoperatively, it is advisable to carry on until bowel movement is restored and the patient has passed stools, even if the probe—mainly in old patients—may cause respiratory problems.

Another crucial point of the treatment is fluid and electrolyte replacement. Since the date of the surgical intervention is not indifferent, the lengthy and complicated laboratory tests should be omitted. It is enough to roughly correct the intravascular volume preoperatively. The fine correction of the overall volume should be made in the postoperative phase. Besides the fluid and electrolyte replacement, it is important to prevent hypoxia, if necessary, to support cardiac and adrenal cortical function, to administer antibiotics to ward off bacterial toxicosis. Improvement can be assessed from the clinical picture (pulse rate, shock-index, blood pressure, central venous pressure, the amount of urine), from some generally used rapid laboratory tests (haematocrit serum electrolytes, total protein, R_N, specific urinary weight). As soon as the patient's circulation is normalized, with partial normalization of his salt and electrolyte balance, he should be operated on.

The technical part of the operation is not going to be discussed here, but some general aspects should be pointed out. These are as follows:

— Exploration should be made possibly from median laparotomy, because this allows the best view and in case of need it can be extended or be supplemented by auxiliary incision.

— Exploration through the previous incision should be avoided, because as a result of an adhesion to the operative scar, intestinal injury may often occur.

— Attempt should be made to shorten operation time and to eliminate the obstruction by the simplest method. The distended intestinal loops and adhesions often make the accurate finding of the site of obstruction difficult.

— The substantial part of the operation depends on the cause of occlusion. Without giving the details, this can be transection of the segment, resection of the necrosed tumorous intestinal segment causing stenosis in volvulus, though there are differing views on this question, retorsion and fixation or resection on necrosis, in invagination, disinvagination or resection. The solution of occlusion by a foreign body is its removal by enterotomy. In gallstone ileus it is particularly important to carefully explore the intestinal segment distal to the obstruction, because of the stones in the lower segment. In certain cases a bypassing anastomosis or an ileostomy can be constructed. There are presently controversial views concerning enterotomy for decompression and aspiration. In our opinion, if it is not necessary to open the intestine, the aimed puncture by needle is not advisable, instead the intestinal contents should be milked into the colon.

— On termination of the operation it is advised to lavage and carefully cleanse the abdominal cavity by an antibiotic, mainly if peritonitis already persists. If intestinal opening and resection have not been made and there is no evidence of peritonitis, it is superfluous to drain the abdominal cavity, it will probably do more harm than good.

There is only a limited number of surgical diseases which would require such careful postoperative treatment than does ileus. The therapy started already in the preoperative phase should be continued. Of them the most important one is the accurate correction of the change in the fluid-electrolyte balance and the clarification of the acid-base relations. A further task is to prevent shock, to replace the plasma proteins responsible for the colloid-osmotic pressure, to secure the caloric requirement, to induce bowel movement if possible, already on the first postoperative day, if no intestinal resection has been made. Undoubtedly, the mortality rate of the mechanical small bowel ileus, as compared to the previous decades, has considerably decreased, but it ranges between 10 and 30% even today [3, 12, 15, 24, 25]. In our own material it was 15.6%. The decrease in the mortality rate can be primarily attributed to the complex therapy based on the pathophysiology of the clinical picture learned recently, to the use of broad-spectrum antibiotics, to the

up-to-date anaesthesia and to intensive therapy, but not or only to a small extent, to surgical technique.

The main task for further reducing the mortality rate of ileus is that the patient should be admitted and subjected to operation as soon as possible [24]. It can be proved statistically that if clinical admission occurs in the first 24 hours, the mortality rate is 10–15%. On the 2nd and 3rd days, however, it is 20 to 30% and after the 3rd day it ranges between 35–40%. Data on the delayed surgical intervention: if operation is made only by the end of the first 24 hours after admission, the mortality rate is 20–25%. Between the 2nd and 3rd days it is 25 to 35%, while after the 3rd day it is 55 to 60%. Regarding that the mechanical small bowel ileus—first of all strangulation and adhesive—are in general consequential to some intra-abdominal operation and the question arises what the surgeon's tasks are to reduce the number of obstructions. These are as follows: atraumatic surgical technique, prevention of the intestines from dehydration, the omission or careful use of intestinal clamps and the avoidance of en masse ligations. Although the role of glovepowder, mostly in giving rise to adhesive occlusion is known, it must still be stressed. Namely, there was a high percentage of crystals and foreign body granulomas shown by the polarization microscope as evidence of contamination by powder [9]. During abdominal operations injury of the intestinal serosa is not rare, which is generally sutured. The current view is, if it is only about a serosal injury, it is needless to be sutured, because if tissular blood supply is good, these defects heal without adhesions [7, 24]. Any attempts at a drug therapy inhibiting adhesions have so far been unsuccessful.

Finally, it should be repeatedly stressed that we wished to treat the subject primarily from the clinician's point of view—without aiming at completion—by summarizing the latest experimental and clinical results on the research of mechanical small bowel ileus of a still high mortality rate in the hope of further improving the results of healing work.

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Daten zur Pathophysiologie und zum Klinikum des mechanischen Dünndarmileus

M. IHÁSZ und A. BÁLIT

Anhand von 423 Fällen mit mechanischem Dünndarmileus werden die diesbezügliche Physiologie des Dünndarms sowie der Pathomechanismus des Krankheitsbildes überblickt. Erläutert werden die verschiedenen Formen des mechanischen Dünndarmileus, mit besonderer Rücksicht auf den Strangulations- und den Adhäsionsileus. Im Rahmen der Besprechung der möglichen therapeutischen Formationen werden — im Interesse der Herabsetzung der noch immer hohen Mortalität — die Wichtigkeit des Früheingriffs und der sorgfältigen Nachbehandlung betont.

Данные к патофизиологии и клинике механического илеуса тонкой кишки

М. ИХАС, А. БАЛИНГ

На основании анализа материала 423 механических илеусов тонкого кишечника авторы дают краткий обзор физиологии и патологического механизма заболевания. Описывают различные формы механического илеуса тонкого кишечника, обращая особое внимание на странгуляционную и адгезивную формы. Занимаются возможными способами лечения, подчеркивая важность раннего хирургического вмешательства и заботливого послеоперационного ухода, в интересах снижения все еще высокой летальности.

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Diagnostic Value of Foil Thermography in Urological Diseases

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(Received: October 1, 1989)

Authors summarize their experience of 8 years with foil thermography. Based on a total of 1113 examinations, they assess the diagnostic value of this method in some andrological and urological diseases. They found foil thermography to be an independent, but not the exclusive procedure in diagnosing varicocele. In addition, this method has proved to be highly valuable also in differentiating the inflammatory and tumorous processes of the testicles. They point out that thermography is very useful for outpatient practice, due to its inexpensiveness, simplicity and rapid applicability.

Introduction

In the past 10 years we have been witnessing the advance of non-invasive methods in the field of medical diagnosis. A particularly obvious progress can be traced in nuclear medicine, in ultrasonographic diagnosis and in NMR tomography still not introduced in Hungary. In the middle of the 70s and at the beginning of the 80s, similar hopes were centered in infrared diagnosis. The results of foil thermography and telethermovision studies are often difficult to interpret and their diagnostic value does not achieve that of the above imaging procedures [7, 8, 9, 10, 11, 12, 13, 19, 20]. Still it has been accepted in several fields, e.g., in technique, biotechnology, pathophysiological and pharmacological studies [1, 16, 17].

From the point of view of practical application, foil thermography has been more extensively used, regarding that—contrary to telethermography—it does not require considerable supplies of equipment. It can be rapidly mastered and is easy to use [2, 3, 4, 5, 6, 14, 15]. This has been the basis for our starting, in 1981, to deal with this investigative procedure.

We wish to report on our 8-year experience and results.

Physical and Physiological Principles

Regarding that the infrared investigation procedure is still little known, it seems to be necessary to outline some basic, partly physical, partly physiological aspects.

Definition of Medical Thermography

Medical thermography is an examination procedure which measures the self-emanating infrared radiation of the human body, produces the thermogram of the examined surface and draws diagnostic conclusions from the disorders of heat distribution and the differences in temperature.

Physical Principles

The theses of classic thermodynamics also apply to living objects. The elements of a closed system aim at achieving a state of heat equilibrium. In the human organism the routes of heat transfer towards the environment include evaporation, conduction, flow and radiation. The emission coefficient of the human skin (0.99) approaches that of a black body, the value of which is 1 [10, 17].

Physiological Bases

The temperature of the human body depends on the thermic relations of the environment, the intracorporeal metabolic processes (metabolism), the blood supply, the skin's own blood supply and, on the heat conductivity of the various tissues. For studying the temperature of the human body surface, the interval between 25 and 40 °C is sufficient. The corresponding wavelength ranges between 3 and 5 μm [10, 17].

Methods and Patients

Foil thermography was performed by Bayer foils with a difference in temperature of 1 °C in the interval between the ranges of 31 and 35 °C. In some cases semi-rigid foils were also used. In accordance with the literature scrotal examinations were carried out in two positions and colour photographs were taken on the cases of interest [16].

At foil thermography the examination of the genitals was made by comparing the two sides. The operative finding and the histological results, and in inflammatory cases, the clinical course of the process were regarded as bases for assessing the diagnostic value of the method.

TABLE I
Data of foil thermography

Diseases	Foil thermography	
	No. of patients	No. of examinations
Varicocele	100	328
Sterility	32	56
Retained testis	168	336
Hydrocele	65	65
Epididymo-orchitis	102	308
Testicular tumour	10	20
Total	477	1113

Parallel examinations were performed also with an AGA 680 infrared camera, and the results were compared. These data are published in a subsequent report.

In the clinical cases presented in Table 1, 1113 examinations were carried out in a total of 477 patients.

In the case of varicocele, an answer was sought to the following questions: (i) What is the difference in temperature between the two sides? (ii) Is the Palomo's operation made by us (i.e., the high retroperitoneal ligation and resection of the spermatic vein) suitable for elimination of the difference between temperature of the two sides? (iii) How much time is needed to eliminate the difference in temperature? (iv) Can subclinical varicocele be diagnosed in the patients presenting with sterility?

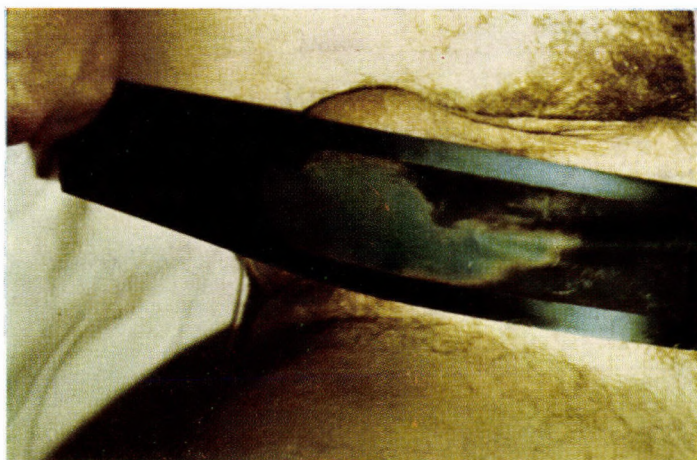


FIG. 1. Typical foil-thermographic picture of varicocele of the left side

Results

1. The examination of varicocele revealed that there was a heat difference of at least 1.5 °C between the two sides (Fig. 1), but in 36 cases this exceeded even 2 °C.

2. In 7 cases the so-called Palomo's operation (high retroperitoneal ligation of the spermatic vein) was not effective, therefore no second intervention was required.

3. The postoperative control examinations of patients operated because of varicocele (at 2, 4 and 8 weeks then at 3–6 months) showed that the difference in temperature disappeared between the two sides during 8–12 weeks.

4. Subclinical varicocele could be detected by foil thermography in 8 cases which revealed the actual cause of subfertility (Fig. 2). The foil thermography of hydrocele showed unequivocally lower temperatures in non-inflammatory changes (non-reactive hydrocele) than on the contralateral side, while in reactive hydrocele, the band-like scan in the cold zone of the more bulky epididymis and testicle occasionally of even a higher temperature was notable.

Similarly uniform and well differentiable were the scans of the testicular and epididymal inflammations. There was an at least 1–1.5 °C difference between the two sides. This corresponded, also in the literature, to a temperature difference accepted as of pathophysiological value. Normalization of the process could similarly be well followed up.

Although far-reaching conclusions cannot be drawn from our 10 cases, the differential diagnosis of the tumours showed that in the case of a larger, more compact scrotum being painless on palpation and displaying inflammatory symptoms, the thermograph of the scrotum was visualized as a colder area

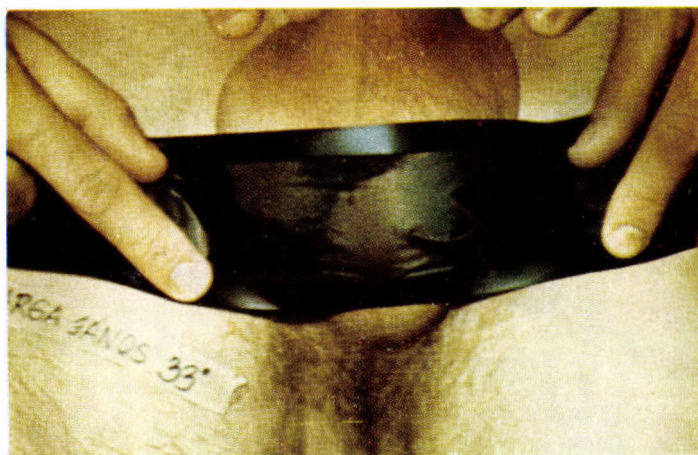


FIG. 2. Subclinical varicocele

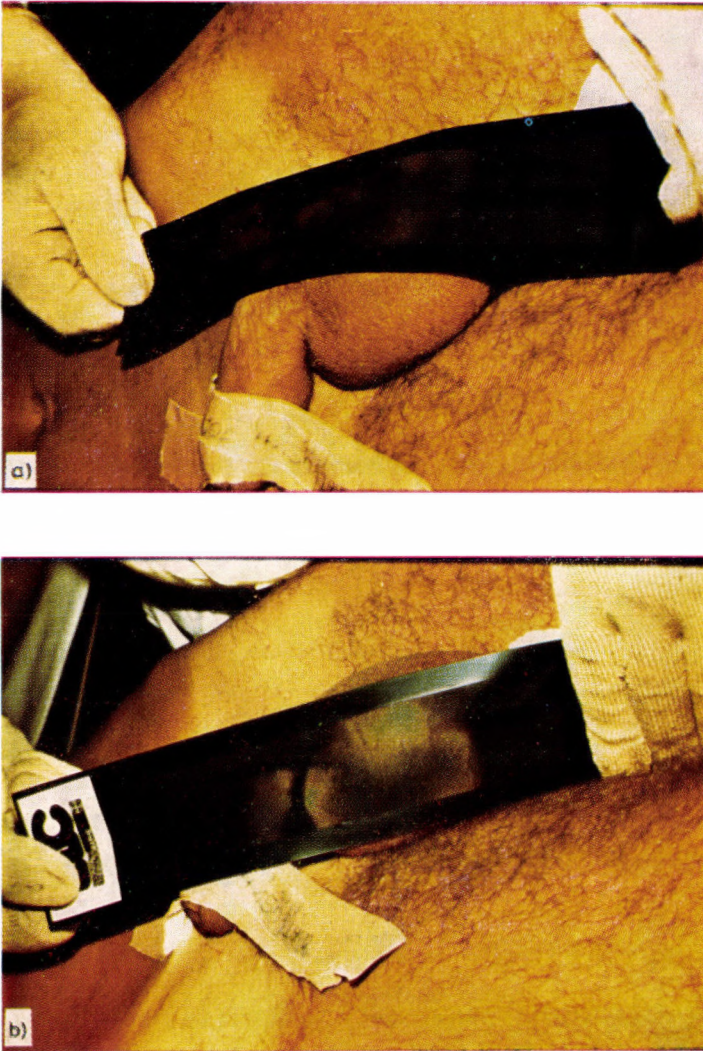


FIG. 3a. The colder tumorous side; b. Thermogram of the unaffected side

than on the contralateral side (Figs 3a, b). The operative and histological findings verified the thermographic diagnosis (Fig. 4).

In cases of retained testicle, in 168 children, it proved to be useful for the detection of the empty cavity. This helped in diagnosis even despite that it was more difficult to examine the inguinal region, particularly under the age of one year than at later ages, because of the relative bulky fat pad. Foil thermography also aids in the follow-up examinations of operated children, primarily in assessing the circulatory relations, size and temperature of

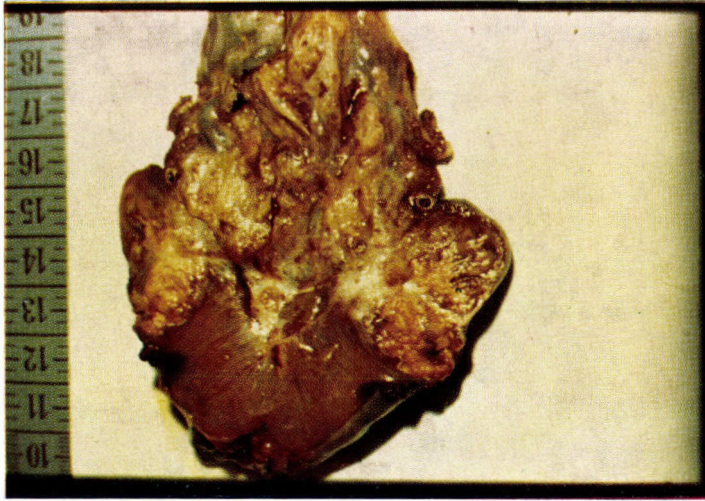


Fig. 4. Macroscopic picture of a removed testicular tumour

the testis fixed in the scrotum. The advantage of the examination is that it offers a possibility even for comparison with the contralateral side.

The examination of undescended testis has led to telethermographic studies, regarding that in this clinical picture the two procedures were used in combination, being compared with each other. Telethermovision has the advantage that it enables examination of temperature differences below 1 °C.

Besides the cases of undescended testis, the detection of lower temperature differences is also beneficial at the examination of varicocele and at postoperative controls.

Discussion

In the examined clinical picture, foil thermography was found to be a rapid and non-invasive diagnostic tool. In concert with the literature, it can be considered an independent but not exclusively diagnostic, procedure in detection of varicocele, even in the so-called subclinical forms [2]. The questions raised by us were answered unambiguously by the results of operations and follow-up. The pathological change due to varicocele lies essentially in the higher temperature of the affected side; this was, on average, 1.5–2.5 degrees. One of the causes—even if not a fundamental one—of the spermatological lesion due to varicocele is higher temperature. This seems to be verified by our 11 cases where 6 to 9 months after Palomo's operation the patient's partner became pregnant. Palomo's operation proved to be suitable for solving varicocele in 93% of the cases [2, 4]. The cases not improving were solved by

Narrath's operation 6 months later. Control examinations showed that the temperature difference disappeared between the two sides, by the latest within three months. After this time it is not worth waiting for improvement. Detection of subclinical varicocele, being more difficult to diagnose by physical examinations, is of particular value in proving subfertility. Therefore, this method is also considered beneficial for andrological practice. Its differential diagnostic value at the examination of inflammatory and tumorous diseases of the testicle should be pointed out. This question is of great importance since it is known what a great role the time factor plays in curing testicular tumours. In our practice, after thermographies all our patients with a suspicion of testicular tumour could be referred to exploration within 24 hours.

By this statement we wish not to diminish the importance of scrotal ultrasonography in examining cases with a suspicion of testicular tumour. We believe that the two methods usefully complement each other. Foil thermography is of similar importance in cases of undescended testis in the follow-up of operated children in assessing the circulatory relations and size of the testis fixed in the scrotum. Another advantage is that the relations of the operated side can be compared with the unaffected contralateral one. It is also useful because of its relatively low costs and the easy way it can be mastered. It does not need any preparation or special conditions. At the same time, on assessing the examination, it should be considered that it can be documented only by preparing slides. There are marked limitations of spatial diagnosis. Based on our experience and on the literature, one can only rely on the results of foil thermograms down to a depth of at most 2-3 cm.

Foil thermography appeared to be an ideal method for outpatient practice in the above-mentioned clinical pictures for its simplicity and rapid applicability. Probably for reasons motivated by different attitudes, it is still not extensively used.

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Diagnostischer Wert der Platten-Thermographie bei urologischen Krankheitsbildern

M. GERVAIN, Zs. ÓRI und Z. ТОБАК

Nach Zusammenfassung der sich auf die Plattenthermographie beziehenden 8jährigen Erfahrungen wird anhand der 1113 durchgeführten Untersuchungen der diagnostische Wert der Methode in einigen andrologischen und urologischen Krankheitsbildern bestimmt. Bei der Diagnostizierung der Varikozele hat sich die Platten-Thermographie als eine souveräne, aber nicht als die einzige Methode erwiesen. Als äußerst wertvoll hat sich das Verfahren auch zur Differenzierung der entzündlichen und tumorösen Prozesse der Hoden erwiesen. Die billige, einfache und rasch anwendbare Platten-Thermographie kann auch in der ambulanten Praxis eine nützliche Anwendung finden.

Диагностическая ценность пластиночной термографии при урологических заболеваниях

М. ГЕРВАИН, Ж. ЁРИ и З. ТОБАК

Авторы обобщают 8-летний опыт применения пластиночной термографии. На основании результатов выполненных ими 1113 исследований они определили диагностическую ценность метода при некоторых андрологических и урологических заболеваниях. Они считают, что пластиночная термография при диагностировании варикоцеле является суверенным, но не единственным методом. Метод оказался ценным при дифференциальном диагнозе патологического процесса в яичках (воспалительный или опухолевый). Авторы обращают внимание на то, что пластиночная термография очень полезна и в амбулаторной практике из-за своей дешевизны, простоты и быстроты применения.

Ultrasonography in the Preoperative Diagnosis of Chronic Pancreatitis Causing Severe Obstruction, an Indication for Surgery

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It is pointed out that some cases of chronic pancreatitis causing severe obstruction may clinically simulate tumour. This can occasionally be confirmed by other examinations (e.g. ERCP) or by macroscopic inspection at surgery, and palpation. With the passive symptomatological treatment applied in these cases, the patients' condition keeps on deteriorating, reinforcing the suspicion of tumour. Sonography performed by a high-resolution equipment may raise, as an alternative to the tumour, the prevalence of chronic pancreatitis. Of 169 documented cases 7 were found to be of this condition. The strict criteria of establishing diagnosis are reviewed, supported by figures and case reports.

Introduction

The absolute number of chronic pancreatitis and pancreatic tumours has recently increased the world over [1, 2, 3, 4, 5, 6, 7, 8]. By the extensive use of up-to-date non-invasive procedures, there has been a great advance in their detection, and the possibilities of their examination.

The diagnostic attempts have primarily been focussed on the early detection and verification of pancreatic tumour. The results have so far been disappointing. According to the data of Baumel and Deixonne, the rate of resectability of pancreatic tumours in establishing their diagnosis is only 25%, with a 5-year survival of mere 1% and an average life expectancy of not even 6 months from the diagnosis [2]. According to Moossa [14], at the time of operation, 90% of the patients are incurable. Based on the assessments of the Mayo Clinic, the early detection of one single case of pancreatic tumour at the complaint-free stage would require the screening of over 10,000 people [15].

In a part of chronic pancreatitis cases, however, in addition to symptomatological treatment, also surgical intervention, may improve the patient's condition. Particularly promising are, in this respect, the decompressive operations eliminating the obstruction of the pancreatic duct, which, by ensuring the flow of pancreatic juice, may provide dramatic improvement [8].

In this report, we attempt to point out the potentialities of ultrasonography in the preoperative diagnosis of chronic pancreatitis giving rise to obstruction and in indication for surgery, with special regard to the severe cases clinically simulating tumour.

Patients and Method

The total number of chronic pancreatitis and pancreatic tumours involving the actually documented cases was 169 in the period between August 1, 1983 and August 1, 1988. Pancreatitis was considered to be verified if, beside the characteristic clinical picture, ultrasonography and ERCP were equally positive. Pancreatic tumours were, however, regarded as documented if equally confirmed by the histological study. In a part of the cases, the tumour could only be verified histologically at autopsy.

Hundred-and-forty-one of the 169 actually documented cases were found to be chronic pancreatitis and 28 to be pancreatic tumours. The incidence rate of chronic pancreatitis was, as a result, five times that of pancreatic tumours. Regarding that in a part of the diseases found clinically to be pancreatitis ERCP had not been performed for various reasons, the rate of pancreatitis cases had actually been still higher.

Ultrasonography was carried out by a Siemens Sonoline SL-2 equipment, using a 3.5 MHz transducer.

The ERCP studies were made by JFB-3 and JF1T10 Olympus duodenoscopes, while X-ray visualization by amplified, focussed images using a spotfilm camera.

Surgical decompression was carried out by the so-called double plastic operation in cases where the change was restricted to the common orifice of the pancreatic duct. In addition to the plastic operation of the papilla of Vater, that of the orifice of the Wirsungion duct was also performed, followed by removal with a Fogarty's catheter of stones of various size. Thus flow of the pancreatic juice became free.

Results

In our material 7 out of 169 patients were found where, due to clinical symptoms and/or after the individual examinations, pancreatic tumour had been suspected, but a high probability of chronic pancreatitis had been diagnosed by ultrasonography. In two of them the clinical picture, in another two the clinical picture along with surgery, while in one the clinical picture, ERCP and surgery together had raised the suspicion of pancreatic tumour.

In all cases, excruciating pain and cachexia were the major symptoms. In three cases obstructive jaundice, while in two, fresh diabetes were associated with the disease. None of the patients had cytological or histological findings indicative of tumour. Based on a sonographic scan characteristic of chronic pancreatitis (Table 1 and Figs 1 to 8A, B), the diagnosis of tumour was revised, and a decompressive operation made for eliminating the obstruction to the pancreatic flow. Postoperatively, the patients' pain ceased, they gained considerably in body weight, with a marked improvement in their general condition and revival of their spirits. Two patients have been under our observation for 5 years, one for 4, further two for 3 years, while one patient each for two years and one year. In this period transitory deterioration occurred in 4 patients due to an acute exacerbation. Apart from this, they have been in a permanently satisfactory condition. So far none of them have proved to have tumour.

TABLE I
Sonographic criteria of chronic pancreatitis

PANCREAS	
Size	entirely enlarged (Figs 1B, 2A, 4A, 5A, 7A)
Contour	occasionally irregular (Figs 2B, 3, 7, 8)
Structure	inhomogeneous (Figs 1B, 2A, B, 3) mostly reduced echogenicity (Figs 1B, 2A, B) calcification in the parenchyma which may be of various degree and localization (Figs 2A, B, 3, 7B, 8A, B) presence of cysts in the parenchyma (Figs 1A, 3, 4) (absence of cysts in some cases)
PANCREATIC DUCT	
Lumen	its AP diameter is larger than normal (up to 3 mm) (Figs 4, 5A, B, 7A)
Calibre	fluctuating (Figs 4, 5A, B)
Length of visualization	larger than normal (Figs 4, 5A, B, 7A)
Lumen of visualization	not echofree but contains calcium (stone) (Figs 5A, B, 7A)
BILE DUCT	
Lumen	larger than normal (C/P like 0.8) [17] (Fig 6B). Dilatation is not necessarily associated with the increase in bilirubin level, in some cases it may even be absent
THE LIVER	
Structure	homogeneous, with no solid circumscribed change (Fig. 6B)*

* Note: It is an important condition of diagnosing chronic pancreatitis that there should be no evidence of metastasis in either the liver, on the lymph nodes as not in the vessels either. Other distant metastases should be excluded preoperatively.

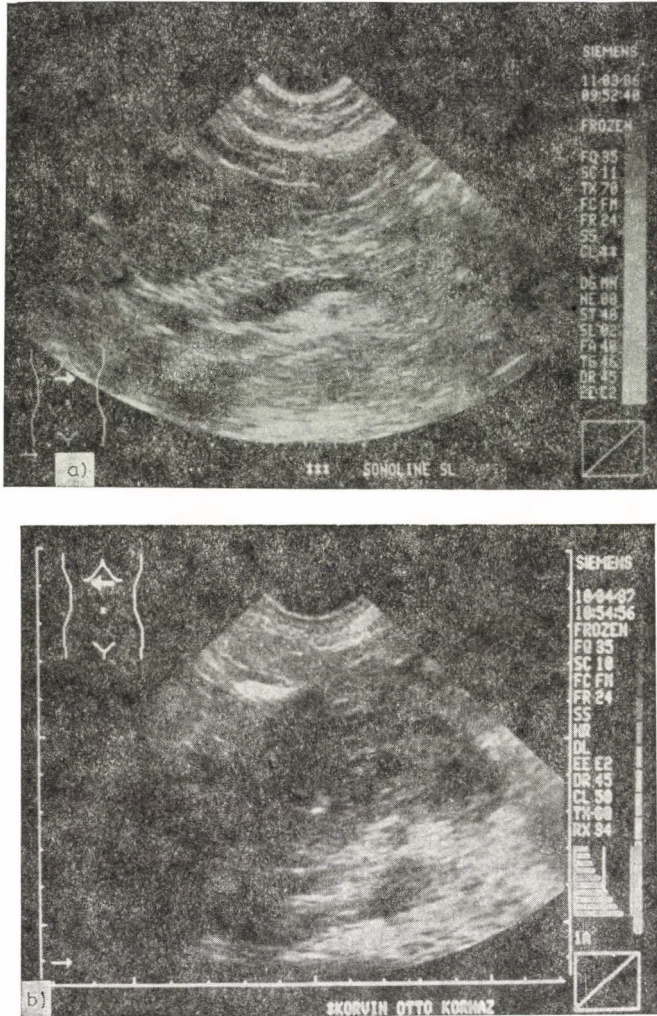


FIG. 1A. Pancreas of normal size and structure. The pancreatic duct has been visualized at a short segment and is of normal lumen. B. The entire pancreas is enlarged and of inhomogeneous structure

One of our characteristic cases will in the following be enlarged on. M. J., a male patient, aged 53, was admitted in 1984 because of an excruciating epigastric pain, a marked loss in weight and a prostrated general condition. The patient had had a history of transurethral resection for bladder papilloma as well as chronic recurrent pancreatitis. The clinical picture raised the suspicion of pancreatic tumour. In the meantime, also diabetes developed. The patient's condition further deteriorated and the patient and his physician could only be convinced, after repeated ultrasonographies (Fig. 7A, B) and the time

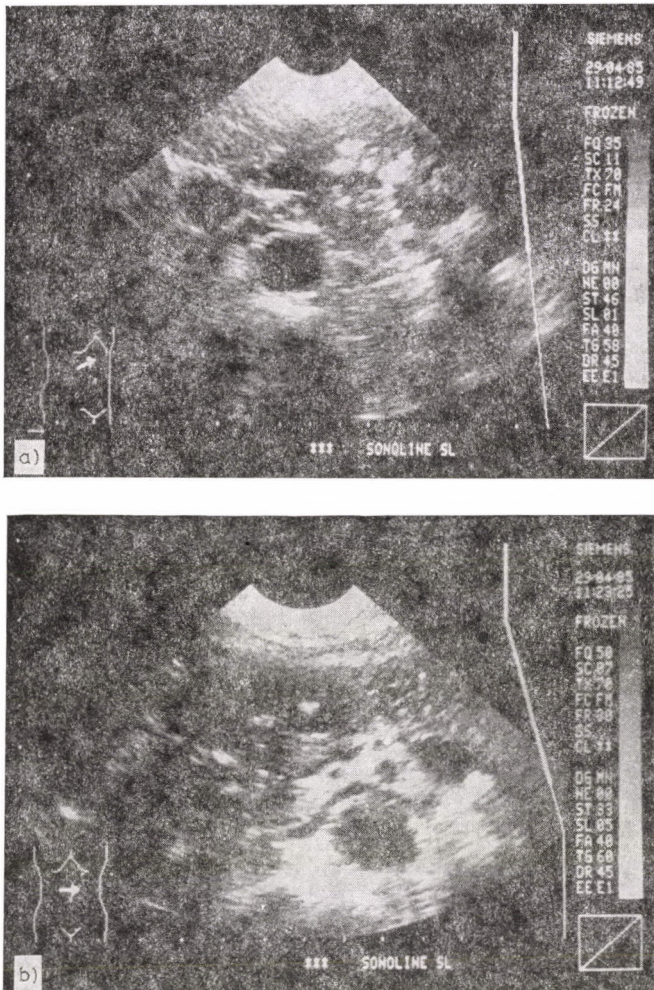


FIG. 2A. Calcification in the pancreatic parenchyma. B. In some cases, there is acoustic shadow behind the calcification and so the extension and border of the pancreas cannot be visualized in some places

having elapsed since then, that it was not a tumour. Then ERCP was performed. It disclosed the distal stenosis of the bile duct. The bile duct could not be filled, however the calcification corresponding to the parenchyma could be detected. Subsequently, a decompressive operation was made in 1985. Surgery revealed the stenosis of the distal segment of both the bile and the pancreatic ducts, beside an enlarged solid pancreas corresponding to chronic pancreatitis, Cholecystectomy and Roux's hepaticojejunostomy were performed then plastic operations of the papilla of Vater and the Wirsungian duct were carried out from a transverse duodenostomy. Then, one pea-sized and several small stones

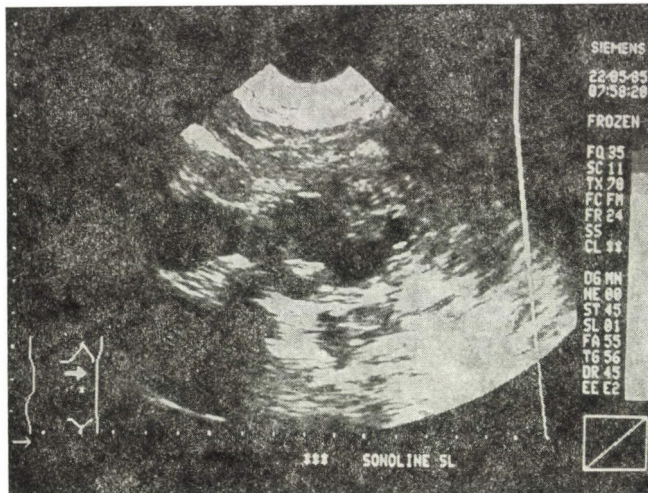


FIG. 3. Cystic masses of various size in the parenchyma

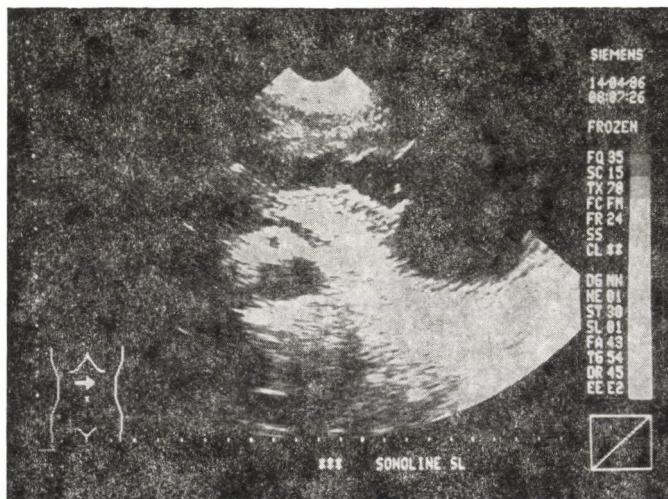


FIG. 4. The pancreatic duct is dilated, visualized along a long segment, showing fluctuations in calibre

were removed from the pancreatic duct. There was a dramatic postoperative improvement. The patient became free of pain and gained more than 10 kg. Ultrasonographies performed at various times after the operation (Fig. 8A, B) revealed no sign of obstruction and enlargement of the pancreas was reduced. Inhomogeneity of the pancreatic parenchyma and calcification were the only signs of the previous chronic pancreatitis. The patient has so far been in a good general condition, free of pain, consulting a doctor now and then only to have his diabetes controlled.

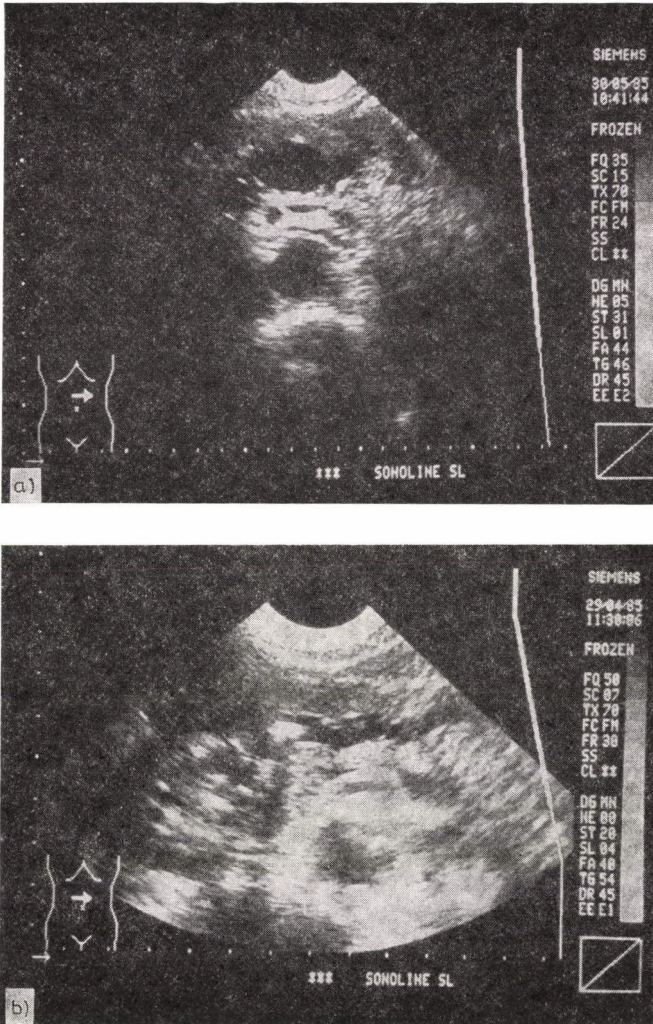


FIG. 5. Stones in the pancreatic duct. A. The stones in the pancreatic duct are small. B. The stones in the pancreatic duct are large with an acoustic shadow behind the largest one

Discussion

A moderate chronic pancreatitis does often not cause morphological changes demonstrable by sonography [11, 12, 13]. Unambiguous ultrasonographic signs do not appear in semi-severe cases either [16]. Severe chronic pancreatitis may produce a variety of ultrasonographic changes, however, the individual signs are not specific, so it is difficult to differentiate chronic pancreatitis from a

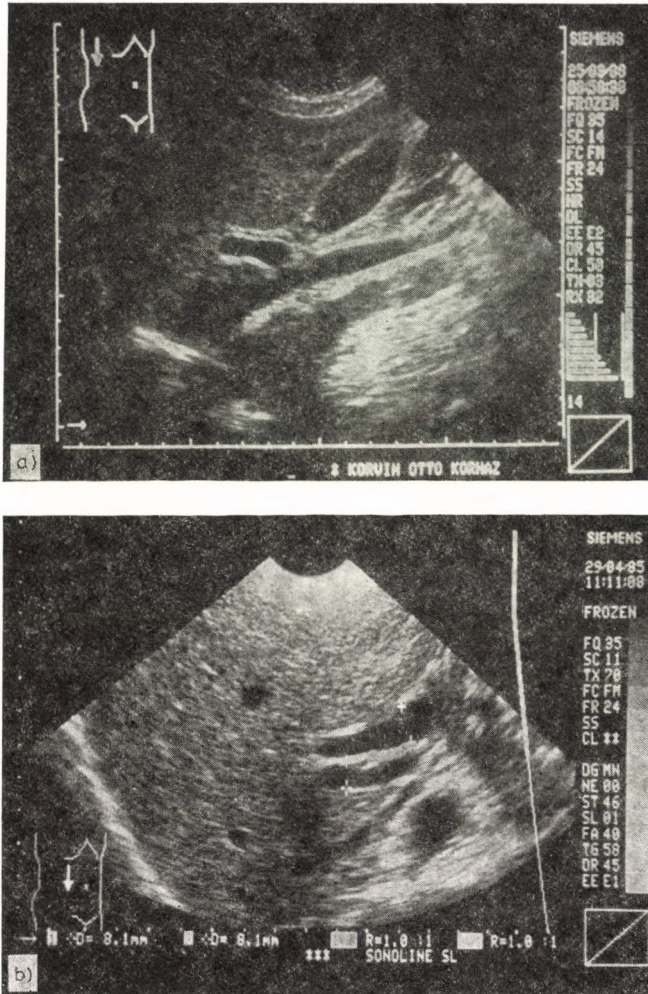


FIG. 6A. Bile duct of normal calibre. B. Bile duct dilated due to a pancreatic process

pancreatic tumour [9, 13]. Difficulties are still enhanced by the fact that reactive pancreatitis may develop around the tumour with concurrence of both diseases [8]. There are advanced severe cases of pancreatitis where the clinical, ERCP, moreover surgical pictures simulate an inoperable tumour although this is not the case. The severe state is largely due to the obstruction of flow of the pancreatic juice and its sequelae [8]. The clinical picture is characterized by excruciating pain, a marked loss in weight, deteriorated condition sometimes with development of obstructive jaundice. The overall picture is so impressive that the physician tends to become passive in treating the patient. He usually does not attempt to confirm the diagnosis cytologically or

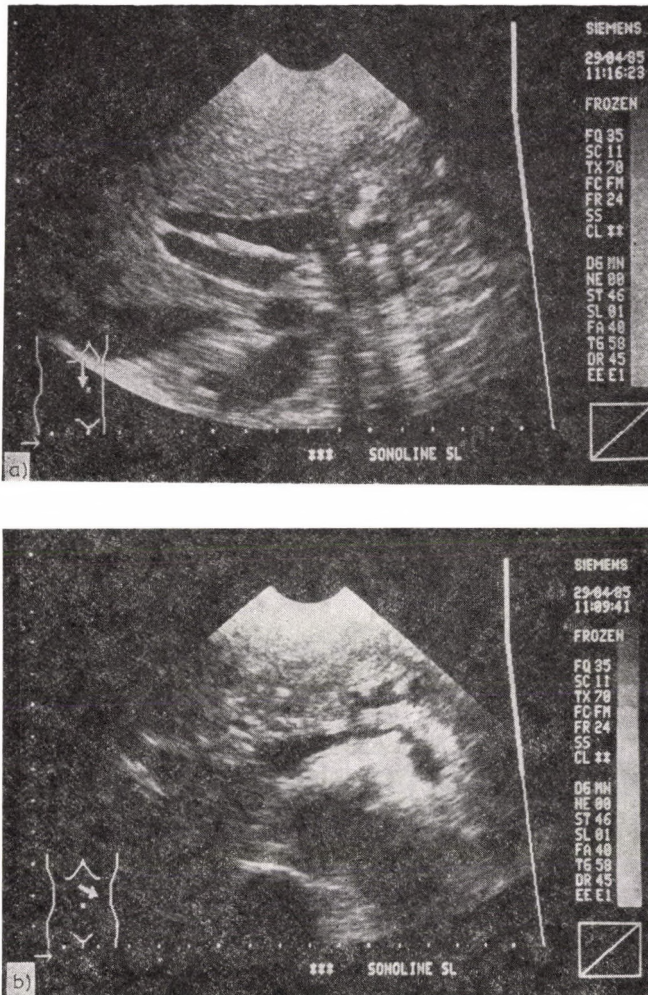


FIG. 7. Sonographic scan of MJ., a male patient, aged 53, characteristic of chronic pancreatitis. **A.** The pancreas is enlarged, inhomogeneous, with calcification in the parenchyma. The bile duct is dilated, the liver is homogeneous in structure. **B.** The pancreatic duct is dilated, visualized along a long segment and of a tortuous course, containing stones

histologically, or if he still does, he assesses the negative tumour finding to be a false-negative one and deems only a symptomatic treatment possible. Sometimes ERCP is also regarded by the patient as a superfluously strainful procedure and in these cases the examination is not made. Ultrasonography is, however, performed in the case of any disease involving the pancreas. The responsibility of the ultrasonographer is therefore great. His attempt to make the right diagnosis is useful for the patient if his primary

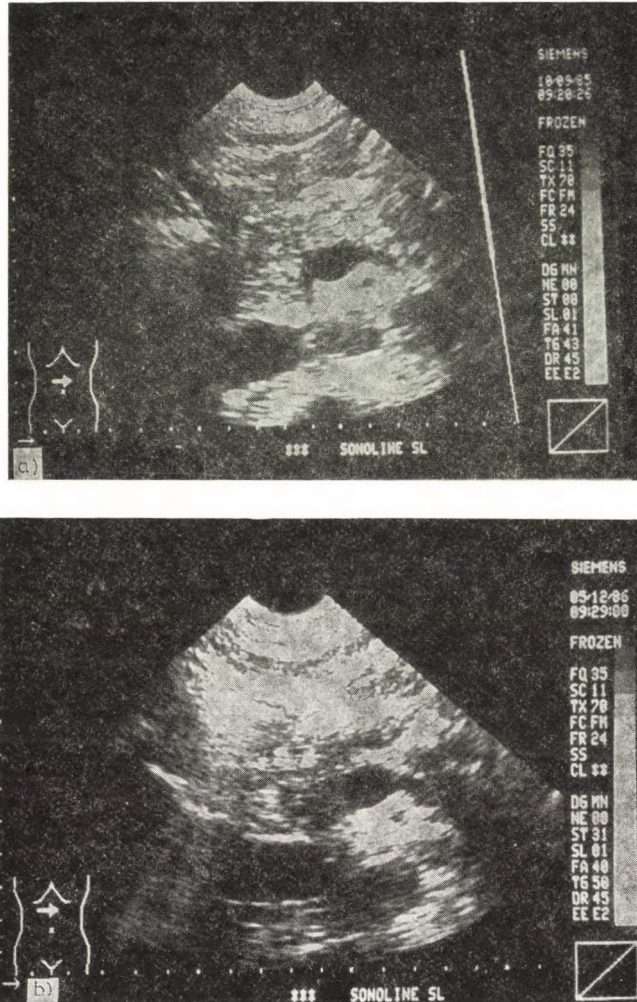


FIG. 8. Sonographic scan of MJ., a 53-year-old male patient, following a decompressive operation. *A.* Half-a-year postoperatively, there is no evidence of obstruction, the enlargement and inhomogeneity of the pancreatic parenchyma are essentially reduced with no stones detectable in the pancreatic duct of normal calibre, but with persisting calcification in the parenchyma. *B.* Ultrasonographic picture of a patient of good general condition with no evidence of progression not even one-and-a-half year after operation

aim is not to detect or exclude tumour but to verify chronic pancreatitis and the consequential obstruction.

Is this actually possible? Since it is well known that ultrasonography is not suitable for the histological differentiation of changes [9, 17] and so, as already pointed out, it is generally not effective in differentiating chronic pancreatitis from pancreatic tumour. Still, the ultrasonographic picture is so specific in these severe progressive cases simulating tumour that critically

assessing the individual signs by a high-resolution equipment, the experienced examiner may prove with a high probability the chronic pancreatitis as well as the mechanical obstruction of the pancreatic and bile ducts and can also, with high probability reject the diagnosis of tumour.

Another important condition in diagnosing chronic pancreatitis is that there be no evidence of metastasis whether in the liver or in the lymph node as not in the vessels either. (Prior to operation, distant metastases of other localizations should also be excluded.)

Based on a characteristic picture, the suspicion of tumour changes into that of pancreatitis, while the physician's positive attitude to an active one. Ultrasonography can be followed by ERCP and/or biopsy under sonographic control. The diagnosis is not one of chronic pancreatitis if cytology discloses tumour. Ultrasonographic diagnosis is reinforced by the confirmation of chronic pancreatitis by ERCP. With a characteristic clinical and ultrasonographic diagnosis, if cytology does not reveal tumour, and there is no evidence of distant metastases, a decompressive operation can be indicated even without ERCP. In our cases other imaging procedures did not provide additional data substantiating indication for surgery and thus these are not regarded as strictly obligatory. In the time to come the determination of the individual tumour markers in the serum may offer new possibilities in differential diagnosis.

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Ultraschalluntersuchung bei der präoperativen Diagnostik und der Erstellung der Operationsindikation bei schweren, Obstruktion verursachenden chronischen Pankreatitiden

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Die schweren, Obstruktion verursachenden Pankreatitiden können in einigen Fällen einen Tumor nachahmen. Diese Tatsache unterstützen fallweise auch sonstige Untersuchungen (z.B. ERCP) oder intraoperative makroskopische Inspektion und Palpation. Der Zustand des Patienten verschlechtert sich nebst der in diesen Fällen eingesetzten passiven, symptomatologischen Behandlung zusehends, welcher Umstand den Tumorverdacht weiter verstärkt. Die Ultraschalluntersuchung, durchgeführt mit einem Gerät mit großem Auflösungsvermögen, kann unter Umständen auf die Möglichkeit einer chronischen Pankreatitis hinweisen. In 7 der 169 mit Sicherheit verifizierten Fällen waren solche Krankheitsbilder zu beobachten. Abschließend werden mit Abbildungen und Falldarstellungen unterstützt, auch die strengen Kriterien der Diagnostizierung erläutert.

Значение ультразвукового исследования для предоперационной диагностики хронических панкреатитов, вызывающих тяжелую обструкцию, и для установления показаний к операции

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Авторы обращают внимание на то, что некоторые случаи хронического панкреатита, вызывающие тяжелую обструкцию, клинически могут имитировать опухоль. Иногда это подтверждается с помощью других исследований (например, ERCP), а также макроскопическим наблюдением и прощупыванием во время операции. Состояние больного во время применяемого при этом пассивного симптоматического лечения продолжает ухудшаться, подкрепляя подозрение относительно наличия опухоли. Ультразвуковое исследование, выполненное аппаратом с большой разрешающей способностью, может вызвать сомнение в наличии опухоли, а не хронического панкреатита. Авторы выявили семь таких больных среди 169, у которых была диагностирована опухоль. Они знакомят с строгими критериями постановки диагноза, подкрепляя это рисунками и описанием собственных наблюдений.

Local Recurrences Following Colorectal Operations

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In about 15–20% of patients operated for colorectal tumours local recurrences develop mainly in the first postoperative year. This large number can only be reduced by adequately radical operations taking into account the patient's age, tumour site and the tumour-biological factors. Indispensable factors are the organized care and regular control of the operated patients with an emphasis, beside CEA test on US and CT studies. In local recurrences attempt should be made at removal of the tumour by an additional operation which is implementable in 20–30% of cases. For palliative treatment first of all radiotherapy can be applied for pain relief.

Colorectal carcinoma is the most frequent malignant tumour of the alimentary canal. According to the data of Deucher [2], in the FRG on average yearly 25,000 fresh cases of colorectal tumour are to be reckoned with. If taken for granted that in Hungary similar aetiological factors are at play, this number can be estimated at 4000 per year.

Prognosis of colorectal tumours is relatively favourable because of the early symptoms, the widely available diagnostic tools and the favourable anatomical conditions for radical surgery, the 5-year survival rate can be estimated at 50–70%. Following curative operations in about 15–20% of patients local-regional recurrences appear [1]. In the majority, 80% of cases, these occur in the first two postoperative years [23]. In another group of the same magnitude died within 5 years, beside local recurrence there is also distant metastasis formation.

Local recurrences can, in about one-third of patients, be removed by a further operation. The patients' life can be prolonged, that is, 30% of them survives 5 year after the second intervention.

A total of 174 patients were operated for colorectal tumours at the 2nd Department of Surgery, Semmelweis University Medical School in the period between January 1, 1983 and December 31, 1988.

The intervention was assumed to be curative in 115 cases, that means that there was no evidence of macroscopic tumour residue. The patients were controlled at 3 monthly intervals in the first two postoperative years. Beside

TABLE 1
Colorectal tumour operations between 1983-1988

Curative operations	115
Palliative operations	31
Inoperable	28
Total	174

physical examination, CEA test, US and, depending on the previous operation, rectoscopy and irrigoscopy were performed.

In the study period 23 patients were admitted because of local recurrence (in 3 cases the primary operation had been made at our clinic). In 80% of patients local pain, in 10 increasing passage disorder were the major symptoms. In two instances a repeatedly increased CEA titre called for clinical admission and examination. In one of them anastomosis recurrence could be removed by resection. Recurrences appeared in the majority of cases within one year (Fig. 1), primarily after sigmoid and rectal tumour operations (Table 2). The

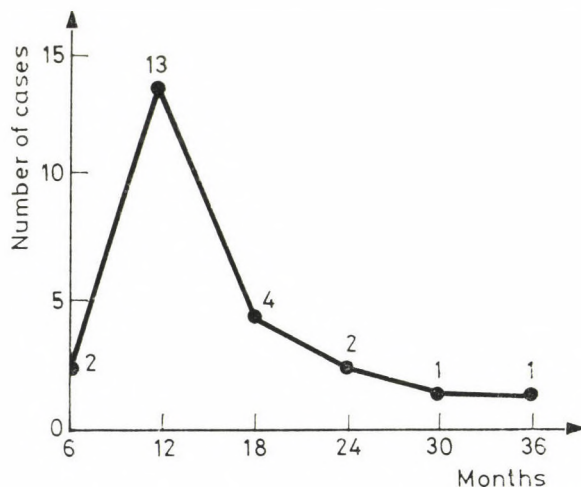


FIG. 1. Time of appearance of local recurrences

TABLE 2
Site of primary tumour in local recurrences

Rectum	14
Sigma	6
Transverse colon	1
Ascending colon	2
Total	23

primary tumour was adenocarcinoma in 20 cases. Grading was made only in some cases therefore this fact could not be assessed. Anterior resections were carried out during the first operation in 5 patients.

The pathohistological examination showed that the distal safety zone was less than 2 cm in one patient and between 3–4 cm in 4 patients. In concert with literary data, the recurrence occurred in stage Dukes C (Table 3). A further

TABLE 3

Stage of primary tumour in local recurrences

Dukes A	3
Dukes B	5
Dukes C	15
Total	23

attempt was made in patients but the recurrence could be removed only in 3 cases (1 abdominoperineal rectal extirpation, 1 Hartmann's operation, 1 re-resection). In the other patient only irradiation or symptomatological treatment were applied (Table 4). Of the three patients with recurrence after

TABLE 4

Therapeutic possibilities in local recurrences

Removal of recurrences	3
Radiotherapy	5
Inoperable at surgery	5
Symptomatic treatment	10
Total	23

surgical removal, one patient died 10 months and one 16 months after the second operation. One patient has survived: here one year passed after a further intervention.

Discussion

Local recurrence is logically associated with the first surgical intervention in so far as it has not been of adequate radicality or the process has already been inoperable because of the dimensions of the tumour not detectable macroscopically. According to the order of preference of causes, however, tumour-biological or surgical causes can be given priority. Recurrences ap-

pearing in anastomosis or regionally may largely be ascribed to surgical, while lymphatic recurrence (in the case of an adequate primary operation) rather to tumour-biological causes.

Tumour-biological Factors

1. *Typing.* WHO classification of colorectal tumours was made by Morson and Sobin [17] in 1976. Accordingly adenocarcinoma, epithelioma, dedifferentiated and non-classifiable tumours can be distinguished among the malignant epithelial tumours. This sequence means a prognostic sequence as well. Most frequent is adenocarcinoma of an incidence rate of about 80%, its highly differentiated forms the papillary carcinoma is of relatively favourable prognosis. Mucin formation, in particular, its intercellular form is a considerable menace to prognosis. According to Donnes' data [1], the 5-year survival rate of adenocarcinoma, being in 50% mucinous, is 25%, while with non-differentiated tumours the patients did not have a 5-year survival.

2. *Grading.* Adenocarcinoma and mucinous adenocarcinoma can be divided on the basis of their cytological and histological patterns into three grades. The prognosis of highly differentiated tumours (Grade I, G1) is significantly better. According to Mentges' data [15], local recurrences appear in 21% of patients in grade G1, 28% in G2 and 51% in G3.

DNA ploidy is of a similar prognostic importance in so far as the survival of diploid tumour is better than that of non- or tetraploid ones [18].

Staging

Based on the classical but currently still used Dukes' staging, the frequency rate of local recurrences in stage A can be estimated at 3%, in stage B at 14% and in stage C at 25%. Also TNM classification shows similar results [10] in so far that, while in case of pT₁NoMo tumours the ratio of local recurrences is 1.6%, in that of pT₃NoMo tumours it is 25–37% [21].

Tumour Localization

Dommes [1] published the overall statistics of several authors. According to this, the higher is the frequency of local recurrence, the more distal the primary tumour is localized. In intraperitoneal rectal carcinoma this amounts to 5–8%, while in the case of infraperitoneal rectum to 15–30%. This is likely to be associated with the radicality of operations of the small pelvis. This is also indicated by the fact that, in females, after rectal tumour operations the rate of local recurrences is much higher, i.e., 25%, than in males (15%). This can perhaps be attributed to the possible sparing of the vagina.

Recurrences Due to Surgical Causes

In tumours growing circularly, intramural tumour invasion can be noted as a result of obstruction of the lymphatics. This averages 1 or 2 cm but also a retrograde invasion of 7 cm, has already been described. This is of importance in low anterior resection, because, in other segments of the colon, the distal resection distance can be extended as required. The *in vivo* measured 5 cm safety zone has earlier been generally accepted [6]. *In vitro* this corresponds to 3 cm [5]. With the extensive use of circular intestinal staplers, there has been an increase in the number of low anterior resections with a decrease in the rate of abdominoperineal rectal extirpations [7]. In surveying 50 rectal carcinoma specimens, Williams found no intramural invasion in 76%, 1 cm in 14% and 2 cm in 4% on a stretched specimen. In 6% of the studied cases, resection was not curative, it was made by transection of the tumour (cit. 1).

In differentiated tumours, Kiene [12] leaves a safety zone of 2 cm, although he performs intraoperative histological study in dubious cases. There is a general tendency to accept a 3 cm safety zone as satisfactory [2]. In our opinion, in view of the above-mentioned tumour-biological factors, and of the patient's age, a distance between 3 and 5 cm should be chosen individually.

The number of local recurrences attributable to surgical causes may be reduced by dissection in rectal operations along the Waldeyer's or Deno-willier's fasciae. Intraoperative laceration of the tumour may result in dissemination and tumour cell implantation in the small pelvis.

Although not improving the results of 5-year survival, the number of recurrences may essentially decrease due to preoperative irradiation therapy [25].

Diagnosis of Local Recurrences

Early detection can be expected only of regular control examinations. In the first two postoperative years a 4 yearly control is recommended. In addition to clinical and routine examinations, CEA tests [19], US and US-controlled fine-needle biopsy as well as CT [3, 4, 8] are also of importance.

The sensitivity of these examinations is around 70–80% [20]. In the higher colonic segment double contrast irrigoscopy and colonoscopy are recommended for the early detection of recurrences. CT is indispensable in detecting local recurrences after extraluminal recurrences or rectal extirpations. It indicates invasion to the adjacent organs or possible inoperability. CEA test is extremely useful, the repeatedly elevated CEA titres may be an early sign of local recurrence. It may indicate the 'second look' operation [1] after Dukes C stage tumour operations.

Therapy

In about 20–30% of patients operated for local recurrence, a curative intervention can be repeatedly performed [9]. This means an abdomino-perineal rectum extirpation in rectal tumours. Resection can be made only rarely in recurrences in a higher segment. It is only rarely possible to make radical removal of a recurrence in the small pelvis after rectum extirpations. Following curative operations 20 to 30% of the patients survive the first 5 years [21].

Preternatural anus belongs to the palliative interventions solving the passage disorder and rarely palliative tumour removal is also possible.

The primary aim of palliative irradiation therapy is to alleviate pain. The efficacy of the procedure is relatively good, pain is decreased in 60–70% of patients, about 40% becomes temporarily complaint-free. According to the data of Arnott, the effect is dose-dependent, 72% of his patients treated by 55 Gy have become free of complaints (cit. 24).

Despite the large number of new compounds, chemotherapy has so far not yielded essential therapeutic results.

There is a possibility for reducing pain by insertion of an indwelling epidural cannula without the detrimental effect of narcotics administered systemically [22].

Procedures Recommended for Prevention of Local Recurrence

Our most important task is to reduce the number of local recurrences, since therapeutic results are modest even on early detection. For this purpose the following principles have to be observed.

1. 'No touch isolation' operative technique.
2. High ligation of the inferior mesenteric artery with removal of the lymph nodes.
3. Removal of perirectal adipose tissue along the fasciae.
4. Intraoperative lavage of rectal stump with a cytotoxic solution.
5. Individual determination of the distal safety zone in view of the patient's age, sex, the histological type of tumour, its degree of differentiation and its stage.
6. Extensive use of perioperative neoadjuvant therapy.

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Lokalrezidive nach Dick- und Mastdarmtumor-Operationen

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Bei 15–20% der wegen eines Dick- oder Mastdarmtumors operierten Patienten entwickelt sich, größtenteils im Laufe des ersten postoperativen Jahres ein Lokalrezidiv. Diese hohe Zahl kann mit einer das Alter des Patienten, die Lokalisation des Tumors und die tumorbiologischen Faktoren berücksichtigenden, mit der nötigen Radikalität durchgeführten Operation herabgesetzt werden. Unerlässlich sind die organisierte Betreuung und die regelmäßige Kontrolluntersuchung der Patienten; im Rahmen der letzterwähnten sind vor allem die CEA-Bestimmung sowie die US- und CT-Untersuchun-

gen von Bedeutung. Im Falle eines Lokalrezidivs muß die Entfernung des Tumors mit einer erneuten Operation versucht werden, welches Vorhaben in etwa 20–30% der Fälle realisiert werden kann. Als palliative Behandlung kommt zur Schmerzlinderung in erster Linie die Strahlentherapie in Frage.

Местные рецидивы после удаления опухолей толстой и прямой кишки

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У 15–20% больных, оперированных по поводу опухоли толстой и прямой кишки, наблюдались местные рецидивы, главным образом в первый год после операции. Этот высокий процент можно снизить только с помощью соответствующей радикальной операции, принимая во внимание возраст больного, местонахождение опухоли и туморбиологические факторы. Современны необходимы организованное патронирование больных и проведение регулярных контрольных обследований, при которых наряду с определением СЕА имеют значение также ультразвуковое исследование и компьютерная томография. В случае локального рецидива следует сделать попытку удаления опухоли с помощью повторной операции, что выполнимо в 20–30% случаев. В качестве паллиативного лечения речь может идти в первую очередь о болеутоляющей лучевой терапии.

Experience with Stapling Dixon's Anastomosis

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The techniques of Dixon anastomosis by end-to-side EEA stapler is reviewed, applied successfully in 48 cases. Results are compared with those of 125 Dixon's operations previously performed by the authors manually. In their opinion, the process reviewed is rapid, reliable and safe and so it can be recommended for use.

It has been forty-three years ago that the colonic surgeon of the Mayo Clinic, C. F. Dixon, performed his first successful rectosigmoid resection preserving the sphincteric musculature only from an abdominal exposure (hence the term: anterior resection).

During the classical Dixon's operation the anastomosis is placed underneath the peritoneal fold and is created by two-layer suturing. After the original report, successful attempts have been made also by one-layer sutures [11, 16]. The end-to-side anastomosis was beneficially modified side-to-end [5, 18] but also end-to-side [7]. Creation of an orifice in the above ways (even in any forms) is not easy to perform technically and requires great skills and experience. The frequency rate of suture insufficiency was around 5–8% [4, 6, 8].

The construction of Dixon's anastomosis was largely facilitated and its safety improved by the various kinds of stapling devices. First of all, the Soviet KC stapler (or SPTU M-249) creating one-layer sutures, then the American EEA stapler making a double-layer of sutures, have been manufactured.

Both types (the so-called suture guns) create, according to the original directions, end-to-end anastomoses. Both the KC (or SPTU M-249) [6, 10] as well as the EEA stapler [1, 9, 12, 13, 14, 15, 17, 20] were used with benefit on a large patient material. A great advantage of the EEA stapler over the KC (or SPTU M-240) stapler is that it is simpler to use, it produces safe two-layer sutures, its disposable parts required for creation of the sutures and anastomosis do not become damaged due to sterilization. The use of the EEA stapler may facilitate the attempt of physicians concerned with the surgical management of rectal tumour to preserve the sphincter musculature and to prevent them from making a compromise at the expense of radicality for technical reasons.

Aspects of Surgical Techniques

The usual way of using the EEA stapler is to introduce it transanally following intestinal resection. Being knotted by approximation of the two ends of the device, one pursestring suture each is made by the pursestring-stapler attached to the device at the proximal and distal intestinal ends.

This method has several limitations. The pursestring suture made by a factory-made device is not safe (by a straight needle and Prolene-00 suture), very often the circular suture must be completed manually. The second problem is that the distal intestinal segment is always wider than the proximal one and therefore, while creating the anastomosis by approximation of the two ends of the stapler, the distal pursestring suture is subjected to great tension and so some small part of the lower stump may easily slip from it (where the suture is cutting through), which leads to suture insufficiency.

To overcome and solve the above technical difficulties numerous modifications have been put forward [1, 12, 14, 19] of which the modifications of Adloff [2] and Wiest [21], the end-to-side method, seems to be the most favourable so we have tried this.

Material and Method

Our patients are prepared for operation with the conventional mechanical method and medication. For antibiotic, cephalosporin (Rocephin), having recently been administered in one dose not long before operation, is applied [3], combined with metronidazole. The patient lies in the lithotomy position. After the usual mobilization the rectum is sutured transversely 3–5 cm underneath the tumour by UKL-60 or TA-55 staplers, then it is transected. Sub-



FIG. 1

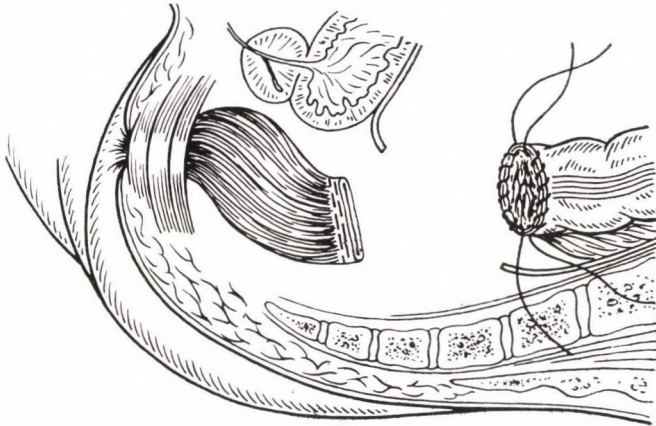


FIG. 2

sequent manipulation is facilitated if the two lateral edges of the row of suture made by the device is elevated by a long instrument or supporting thread. So the distal intestinal segment remains close through the operation (Fig. 1).

The transverse sutures made by the stapler should not be secured by manual sutures. After selecting the adequate height, the proximal intestinal segment is resected transversely (in protection of an intestinal staple and a 00-Prolene pursestring suture taking a bite of all layers, is made) (Fig. 2).

The assistant performs Recamier's dilatation then passes the EEA stapler transanally without its head, the shank supporting the head being maximally twisted. (The preliminary antibiotic lavage of the distal stump prior to this manipulation is recommended) [7]. Care should be taken that the 'spit' not be caught on or damage the rectal mucosa (this manipulation can be made without damage in protection of the Thiemann's catheter passed over the guide previously introduced through the distal stump into the abdominal cavity [21]. The shank of the stapling gun is introduced in a way that it should reach the closed rectal stump on the ventral wall distal to the transverse stapled suture. The guide makes the intestine to 'bulge' here, in this region a small 2-3 mm auxiliary incision is made by a scalpel touching only the musculature of the intestinal wall and the guide being pierced through it. In this way the mucosa will not retreat and it can be avoided to place pursestring sutures into the distal stump. Another advantage of this method is that the anastomosis can be created fairly deeply. The operation is facilitated by the assistant's exertion of pressure on the perineum to promote thereby the transabdominal removal of the distal stump [2]. The device is further introduced up to the point where the 31 mm disposable polyethylene inlay containing the row of staples reaches the blind end of the lower stump. Then the head portion is wound on the guide pierced through the stump and the

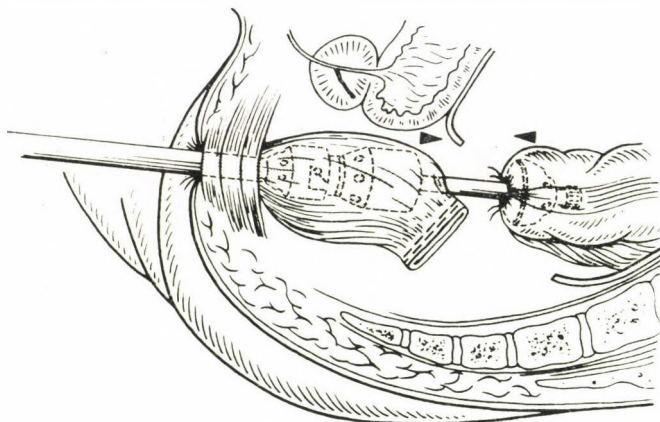


FIG. 3

proximal intestine is pulled onto it by clamps in three places or a soft Pean's forceps (prior to this its end sutured with pursestring sutures is dilated by corntongs. The pursestring suture is knotted checking whether it is complete, Fig. 3.)

The stapler is closed, taking care that it does not pinch the interpositum. With the suturing completed, the stapler is slightly opened and removed by a moderately rotating and pulling movement (the two severed intestinal rings are removed from the stapler in all cases, then checked for completeness and sent for histology). No manual securing sutures are placed on the anastomosis. Transanally, under manual control, a soft, thick rubber drain is introduced 10 cm over the anastomosis which is left there for 2-3 days, while passage starts. (It is recommended to lavage the drain daily by sodium chloride or an

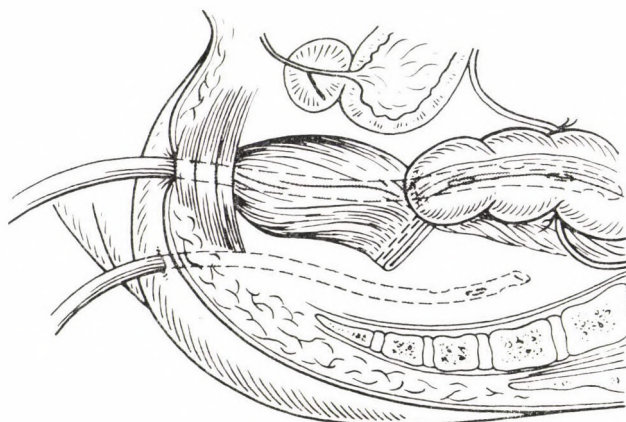


FIG. 4

antibiotic solution [18]. Some authors retain the intraluminal drain for 5–6 days.) In protection of his finger passed into the rectum, the assistant makes a small dermal incision 2–3 cm adjacent to the anal orifice through which he introduces a rubber drain in the sulcus of the sacrum (from the direction of the abdomen), draining thereby the presacral cavity, the site of the anastomosis intraperitoneally towards the perineum (Fig. 4).

The two rows of staples are placed in a way not to cross one another but it does not count as an error and implies no suture insufficiency if they still do.

The operation is terminated in the conventional way, without creating a relieving solution (a preternatural anus). In aftercare also the routine procedure is adopted. The sacral drain is removed after starting of passage. The above method has been used in 48 cases from 1984 onwards, operating in 46 of them for tumour and in two cases for constrictive diverticular sigmoiditis.

All of our patients treated this way recovered. In two of them minor fistula formation occurred in the anastomosis which closed after subsequent relieving. There were no other operative complications. Postoperative strictures were not revealed during check-ups either clinically or endoscopically. Recurrences appeared in two cases after three or two years, respectively.

Discussion

A total of 125 Dixon's operations have been made in our department between 1956 and 1979 with the traditional manual suturing, which we have reported elsewhere [18]. Comparing the two operative techniques our experience is summarized as follows.

1. It is essentially easier to create anastomosis by end-to-side EEA stapler than by manual suturing and it is simpler to perform technically than any other stapled anastomosis.

2. There is a considerable cut in the duration of the operation.

3. The safety of the stapled anastomosis is fairly good.

4. It is practically unnecessary to make a preternatural anus.

5. It makes possible the creation of a very distal anastomosis which is hardly implementable manually or by other mechanical ways with the observance of radicality.

6. Regarding sterility, it is also very advantageous. The distal intestinal segment remains closed throughout the operation. It is, however, to be borne in mind that stapled suturing should be made by a surgeon who can construct the same anastomosis also manually because it may be needed due to any technical reasons or errors.

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Erfahrungen mit der maschinellen Dixon-Anastomose

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Erläutert wird die technische Ausführung der mit der EEA-Nähmaschine durchgeführten End-zu-Seit-Anastomose, die in 48 Fällen eine erfolgreiche Anwendung fand. Die Ergebnisse werden mit den Erfahrungen der früher manuell durchgeführten 125 Dixon-Eingriffen verglichen. Angesichts ihrer Vorteile — zuverlässlich, rasch, sicher — wird die Anwendung der beschriebenen Methode aufrichtig empfohlen.

Наш опыт создания анастомоза диксона с помощью машины

И. КЁВЕШ, И. БЕСНЯК и Л. МОЛНАР

Авторы знакомят с техникой создания анастомоза Диксона способом «*end-to-side*» с помощью швейной машины ЕЕА. Этот метод они применяли в 48 случаях. Сравнивают результаты, полученные с помощью нового метода, с результатами ранее произведенных ручным способом 125 операций Диксона. По их мнению, описанный метод является надежным, быстрым, поэтому можно рекомендовать его применение.

Diagnosis and Therapy of Metastatic and Recurrent Colorectal Tumours

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A total of 77 patients were treated for recurrent and metastatic colorectal tumours. The follow-up protocols after elective operations are reviewed, making a distinction between interventions for colonic or rectal tumours. The diagnostic and therapeutical principles applied in the cases of the individual recurrences and metastases (i.e., anastomosis recurrence, metachronous tumours, local recurrence, liver, lung, lymph node and bone metastases) and the results are discussed in detail. The authors' attitude favouring a more active than the hitherto applied surgical management of the recurrences and metastases of colorectal tumours is presented.

In Hungary 40% of patients with rectal tumours treated surgically survives 5 years postoperatively [5, 16, 27, 33].

Recovery and survival essentially depend on the stage the tumour is operated at. The probability of recovery is 90% in stage Dukes A, 60% in Dukes B and 35% in that of Dukes C [11, 12, 13, 16].

Unfortunately, next to 20% of patients in need of surgery is currently referred to operation being inoperable and 70–80% of operable patients are already in stages Dukes B–C.

This grim statistics could be basically improved in two ways: (i) The patients should be operated at the earliest stage possible and (ii) recurrence and metastasis should be detected in time by a close follow-up and aftercare of the operated patients and solved possibly by new surgical interventions.

In the present paper we were concerned with the latter issue. Attempt has been made to answer this question based on the conclusions drawn from the management of 77 recurrent colorectal tumours and metastases observed and treated surgically.

Tables 1 and 2 show when and which kind of secondary tumorous manifestations were encountered.

The tables clearly reveal that recurrences are most likely to appear in the first two years, after the 3rd year they occur much less frequently [1, 2, 3, 6, 8, 11, 12, 13]. In primary tumours of distal localization (i.e. distal to the rectosigmoid junction) first of all local recurrences can be expected with

TABLE 1

Temporary appearance of recurrences and metastases

	COLON		RECTUM	
	No.	%	No.	%
1 year	13	38.0	12	31.0
2 years	10	31.0	18	42.0
3 years	6	15.0	6	14.0
4 years	3	8.0	2	5.0
5 years	2	5.0	3	6.0
	35		42	

TABLE 2

Localization of recurrences and metastases (%)

	COLON (35)	RECTUM (42)	
		Resection	Extirpation
Anastomosis	10.0%	5.0%	—
Anastomosis + distant metastasis	5.0%	2.0%	—
Local recurrence	8.0%	12.0%	30.0%
Local recurrence + distant metastasis	8.0%	4.0%	—
Solitary distant metastasis	8.0%	2.0%	8.0%

distant metastasis formation being only secondary [16, 18, 22]. In primary tumours of a higher localization rather the appearance of distant metastases has to be reckoned with [16, 19, 21]. The enumerated facts support our view to discuss patients with colorectal tumour in two separate groups because, for the above reasons, these are not comparable in all aspects.

So, for example, it is worth drawing a distinction in the follow-up of patients concerning the examinations performed at the individual check-ups —although follow-up time and the pace of control are equal—whether the previous intervention has been made because of a colonic or rectal tumour. So the question arises when and what kind of control examinations should be carried out for detecting recurrences and metastases.

Laboratory Tests

The CEA test is of prime importance. It is worth to perform in the first year in patients operated for tumours of both the colon and the rectum at every second then every third month [6, 27, 28, 31, 35]. In our material the CEA test values were falsely high in 60.7% in recurrences and metastases

(there were no recurrences and metastases and falsely low values were found in 15.6% of the cases). With an elevated serum CEA (over 10ng/ml) the patients are subjected to a detailed check-up even if being completely free of complaints clinically. If there is no verifiable or documentable recurrence or metastasis, literary data suggest exploration [17, 18, 20]. It is due to the fact that exploration still reveals in 90% recurrences which can be largely solved by operation. We ourselves have not performed operations for such indication. Serum gamma-GT and Haemocult test, too, may be valuable supplementary data for liver involvement and detection of occult bleeding.

Ultrasonography (US)

Ultrasonography includes the examination of the liver, retroperitoneum, the kidneys and the pelvis. This is important primarily in the early detection of liver metastasis, in that of ureteral compression and in verifying the involvement of the retroperitoneal lymph nodes. It is to be performed in all patients operated on the colon or the rectum at every half year. Figure 1 shows the sonographic scan of a typical solitary liver metastasis.

X-rays, Endoscopy

The aim of irrigoscopy and colonoscopy is (i) to control the operative region by early(!) detection of local recurrence in the operative region; (ii) to detect early the so-called metachronous tumours occurring in 3-5% of cases



FIG. 1. Ultrasonographic picture of a liver metastasis



FIG. 2. Irrigoscopic picture of a metachronous colonic tumour

and (iii) to detect in due time, and possibly solve by endoscopy, the pre-cancerous states (polyps) arising in 8–10% of cases [16, 33, 36].

Three, 12, 24 and 36 months offer a colonic tumour, routine irrigoscopy and, if its results is uncertain, colonoscopy, is performed.

Following rectal surgery, it should be distinguished whether resection or extirpation has been made. (i) Following rectal resection, rectoscopy is worth performing at three monthly intervals in the first two years, in all cases com-

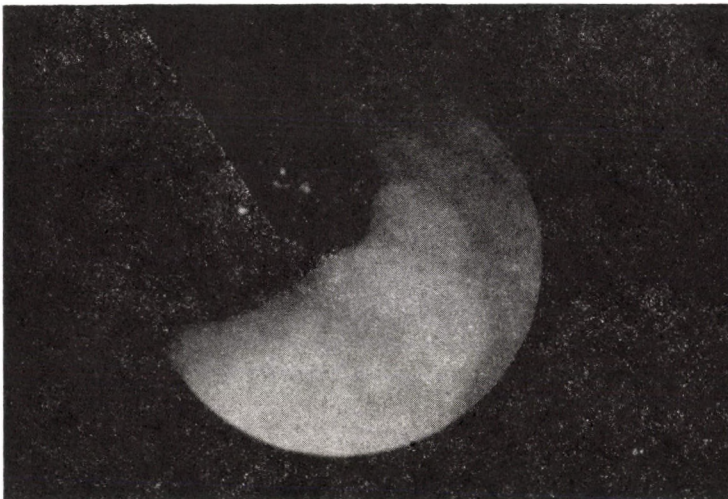


FIG. 3. Colonoscopic picture of an anastomosis recurrence

pleted by endoscopy. (iii) Three, 12, 24 and 36 months after rectal extirpation it suffices to perform irrigoscopy.

Figure 2 demonstrates the irrigoscopic picture of a metachronous tumour, while Fig. 3 the colonoscopic picture of an anastomosis.

Computed Tomography (CT)

It is advisable to use it primarily for studying the small pelvis and the liver, since after operations of the distal colonic segment (rectum, distal segment of the colon) local recurrences are frequent, it is first of all performed after such operations at six-month intervals in the first two years. If necessary the examination can be supplemented by aimed aspiration cytological sampling [10, 11]. Figure 4 shows the CT scan of a local recurrence following Dixon's operation.

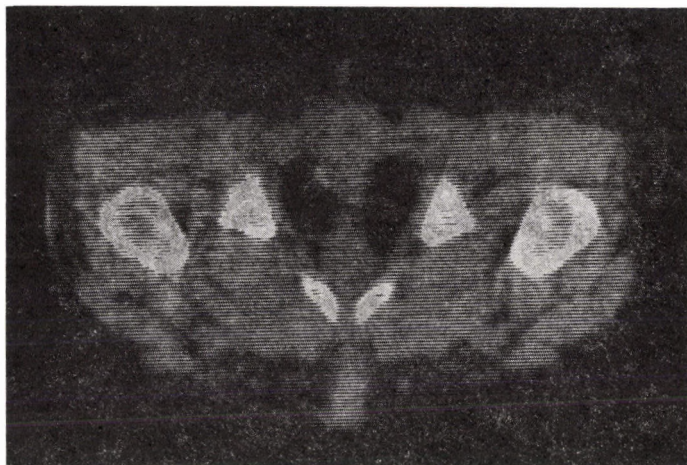


FIG. 4. CT scan of a local recurrence in the small pelvis

The MR examination is of a similar value but more favourable from the point of view of radiation exposure and imaging.

Chest X-ray

Knowing the very slow doubling time (over 200 days) of pulmonary metastases of colorectal tumours, their control at half-yearly intervals seems to be sufficient. In Fig. 5 the roentgenogram of a solitary operated pulmonary metastasis is presented.



FIG. 5. Solitary lung metastasis

Bone X-ray and Scintigraphy

Bone metastases should be reckoned with in 5–6% of the cases following rectal operations, while in 1% after operations of colonic tumours. No routine control is performed and examination is recommended only in case of complaints. Since the majority of metastases involves the bones of the pelvis and vertebrae these may require to be examined. Figure 6 shows the CT scan of a pelvic metastasis.

After the above review the treatment principles and methods, applied in our practice in the case of individual recurrences and the types of metastases, are presented.

In case of an intraluminal tumorous manifestation—if it is localized distally to the operative region (anastomosis)—it is considered to be a metachronous tumour and is treated according to the prerequisites of the primary operation. If the recurrence appears in the region of the previous operation (anastomosis) and arises in the higher colonic segment, resection is attempted or if it is not possible for local or other causes, then some local or palliative solution (first of all bypass) is sought. If the recurrence is observed following

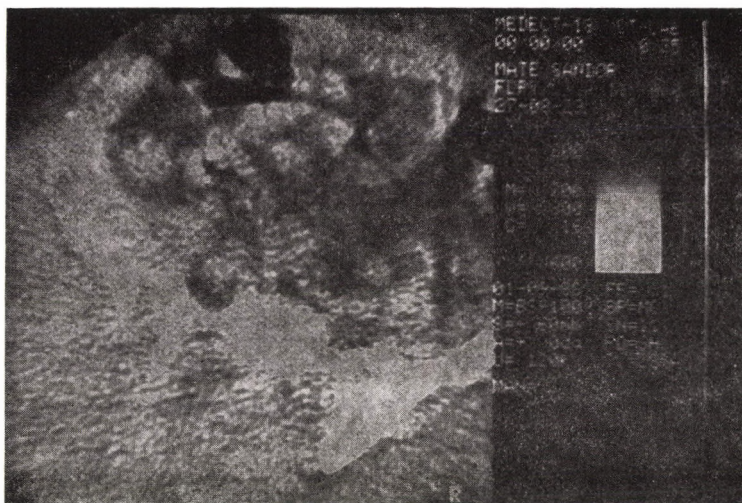


FIG. 6 CT scan of a bone destruction

rectal resection the only radical solution seems to be extirpation of the rectum. One should be, however, aware of the fact that after either Dixon's or another type of rectal resection, the majority of local recurrences is not a local recurrence but the invasion into the intestine of an extraintestinal manifestation in the pelvis, and so there is only a rare possibility of a curative solution. Should such a recurrence be inoperable not due to a local cause but because of a multiple distant metastasis or the patient's poor tolerance for the operation, a cryodestruction or Ra-needle implantation may spare the patient, in his remaining time, from the inconveniences caused by preternatural anus.

Perineal Recurrences

They are frequent (30%) following extirpation of the rectum performed primarily abdominoperineally or abdominosacrally, but occur at an almost similar rate after rectal resection [15, 29, 32, 34, 35, 36]. If recurrences appear after rectal extirpation, the only satisfying solution is surgical removal attempted from perineal or a newer abdomino-perineal incision ('iceberg tumour'). If it is not possible to remove the recurrence for the environmental condition, local Ra-needle implantation and irradiation may alleviate pains and check tumour growth.

Metastases in Distant Organs

In retroperitoneal lymph node metastases, since the haematogenic invasion of colorectal tumours frequently occurs, there is no question of surgical reintervention. Adjuvant chemotherapy cannot be considered.

Liver Metastases

In their presence, if the underlying disease has been controlled at least for half a year (i. e., the patient is locally tumour-free) with no evidence of other metastasis formation, the surgical solution may be considered. Even in the case of (multiple) metastases, resection involving one lobe, is performed. Although the number of such cases is not high, successful results have been reported from abroad and home: its 5-year survival rate has been about 20% [12, 25]. In metastases involving both lobes, results can be expected of chemotherapy administered via a Porth-A-Cath implanted indirectly into the hepatic artery. Figure 7 shows an implanted catheter.

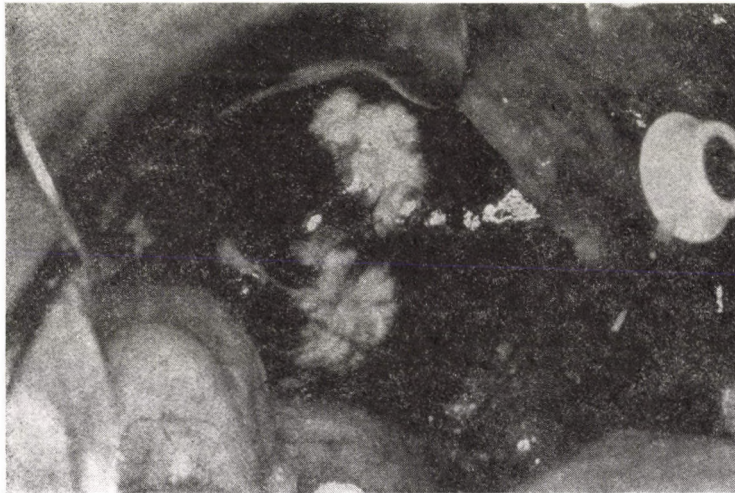


FIG. 7. Implanted Porth-A-Cath

Lung Metastases

Being a locally controlled tumour and solitary metastasis, resection is made. A limited number of unilateral metastases is still worth operating on by atypical resection of lobectomy. A metastasis solved only by pulmonectomy

is considered to be inoperable. Some surgeons would operate also a small number of bilateral metastasis, in one or two sessions. We have so far not made such an operation.

Bone Metastases

In these cases there is no plausible surgical solution. Irradiation and calcitonin treatment may alleviate pain and check growth of metastases.

Finally, for the sake of completeness, it is worth mentioning that is the symptomatological treatment of inoperable patients suffering from incurable pain, the methods beneficial in the alleviation of pain, such as permanent anaesthesia by lumbosacral phenol or ethanol, or analgesia with morphine via an epidural indwelling cannula, alcohol blockage of the coeliac ganglia may render the rest of the patient's days endurable.

In summary, our present view is that we have to adopt a more active attitude in treating recurrences and metastases developing after rectal or colonic tumour operations, because currently there are no better procedures or more successful ways of treatment [1-4, 7, 9, 14, 23, 24, 30, 37-39].

In tumours of the colon, radical intervention was successfully performed (from the point of view of surgical technique) in 25% for treating recurrences and metastases, while in case of rectal tumours only in 10%.

Even if with modest results, knowing the large number of colorectal tumours, they represent the recovery of several patients, the prolongation and durability of their lives.

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Diagnostik und Therapie metastatischer und rezidiver kolorektaler Tumoren

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Wegen rezidiver bzw. metastatischer kolorektaler Tumoren wurden 77 Patienten behandelt. Erläutert wird das nach der elektiven Operation angewandte "Follow-up"-Protokoll, dementsprechend differenziert, an der Eingriff wegen eines Kolon- oder eines Rektumtumors stattfand. Die bei den einzelnen Rezidiv- bzw. Metastaseformen (Anastomosenzidiv, metachroner Tumor, lokales Rezidiv, Leber-, Lungen-, Lymphknoten-, Knochenmetastase) diagnostischen und therapeutischen Prinzipien, sowie die erzielten Ergebnisse finden eine ausführliche Besprechung. Betont wird die Notwendigkeit der im Vergleich zu der bisherigen aktiveren chirurgischen Behandlung der Rezidive und Metastasen der kolorektalen Tumoren.

Диагностика и терапия метастатических и рецидивирующих колоректальных опухолей

И. КЁВЕШ, И. БЕСНЯК, Л. МОЛНАР

Авторы лечили 77 больных по поводу рецидивирующих или метастатических колоректальных опухолей. Они знакомят с протоколами, фиксирующими состояние больных после операции, демонстрируя по отдельности протоколы с вмешательством на ободочной и прямой кишке. Подробно обсуждают диагностические и лечебные принципы и результаты в случаях отдельных видов рецидивов и метастазов (рецидив анастомоза, метакронная опухоль, локальный рецидив, метастазы в печень, легкие, лимфатические узлы, кости). Авторы являются сторонниками более активного хирургического лечения рецидивов и метастазов колоректальных опухолей, чем это было принято до сих пор.

Experimental Study of Parenteral Nutrition and of the Exocrine Function of the Pancreas

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The effect of parenteral nutrition on the pancreatic secretion was studied under experimental conditions.

Experiments were carried out in 24 mongrel dogs. In all animals pancreatic fistulas were created for collection of pancreatic juice. Subsequently, in three groups (6 dogs in each) parenteral nutrition via a catheter enterostomy was applied in three different segments of their small bowels, while collecting the pancreatic juice. Group IV served as control where no parenteral nutriment was administered.

The amount, pH, protein and enzyme levels of the pancreatic juice secreted during 4 hours were studied in all groups.

The experiments revealed that parenteral nutrition at the initial segment of the jejunum enhanced pancreatic secretion, while this was not experienced in the other groups. The effect is assumed to be humoral, rather with a secretin-like stimulation.

Based on the experimental results, the authors call attention to the fact that, during treatment of acute pancreatitis, if a feeding enterostomy is constructed for calorie intake, it should not be performed within the first metre of the jejunum.

An important part of the therapy of acute pancreatitis is the deprivation of oral nutriment and fluid ('O' diet). However, in severe cases, the insufficiency of parenteral nutrition may lead to a catastrophic catabolism. According to the data of Pollock reported in 1959, in severe forms of the disease, the patients' daily loss of weight even reached 1 kg, being fatal in most of the cases [10].

According to our present knowledge, the most often applied and most effective method of calory intake in acute pancreatitis is parenteral nutrition and hyperalimentation [1, 3, 12]. This can be ensured by administering various carbohydrate, fat and protein preparations [13]. The protracted course, the difficulties imposed by prolonged parenteral nutrition and the inavailability and costs of the preparations have created a need for seeking for other methods.

For ensuring sufficient calory intake parenteral nutrition by jejunostomy is suggested and used by several authors in treating acute necrotic pancreatitis [6, 7, 8, 11]. According to the opposing views of Hollender et al., however, no enterostomy is to be made [4]. In Dürr's opinion, this method of nutrition in acute pancreatitis is still in the experimental phase [2].

These controversies have prompted us to study in animal experiments the effect of parenteral nutrition through jejunostomy on exocrine pancreatic function. To be more precise, we were curious about whether parenteral nutrition does not increase pancreatic secretion which would be a non-desired effect in the management of acute pancreatitis.

Material and Method

The experiments were carried out in collaboration with the Institute of Experimental Surgery of Debrecen University Medical School. In the experiments 24 mongrel dogs were used independent of their age, sex and weight. In the animals median laparotomies were performed under hexobarbital-Na anaesthesia (VEB Arzneimittelwerk, Dresden). The large pancreatic duct was dissected out prior to entering the duodenum to be found with adequate expertise 4–5 cm distally to the papilla of Vater. The pancreatic duct was opened introducing a thin plastic cannula at a length of 0.5 cm then, placing sutures under the duct, the cannula was fixed. The pancreatic juice obtained through the cannula was collected.

Catheter enterostomy was made according to Marwedel in three of the four groups of 6 experimental animals each (Table 1). In group I, a catheter jejunostomy was constructed at the initial segment of the jejunum, 40 cm from the duodenojejunal junction, in the second group 1 m more distally, while in the third 1 m preceding the caecum. In group IV, the controls, no enterostomy was made.

In the first three groups, an amount of 200 ml each of a parenteral nutriment containing 400 ml milk and a package of Biosorbin MCT (Pfrimmer + Co Pharmazeutische Werke Erlangen GmbH) was administered via catheter jejunostomy, and pancreatic juice collected for 4 hours through a pancreatic fistula. Milk was applied as a solvent, because it is used in clinical practice in prolonged parenteral nutrition for enhancing calory and protein intake. Group IV served as control where pancreatic juice was collected for 4 hours without parenteral nutrition.

TABLE 1

Experimental groups

- I. Pancreatic fistula + catheter jejunostomy at the initial segment of the jejunum (in 6 experimental animals)
- II. Pancreatic fistula + catheter jejunostomy 1 m more distally (in 6 experimental animals)
- III. Pancreatic fistula + catheter ileostomy 1 m in front of the caecum (in 6 experimental animals)
- IV. Pancreatic fistula (in 6 experimental animals)

Then the amount, pH, protein as well as the amylase, lipase and trypsin contents of the collected pancreatic juice were determined, drawing conclusions as to the exocrine function of the pancreas.

Results

The experimental results were demonstrated graphically, differentiating the earlier defined four groups (Fig. 1). The column chart shows the amount of pancreatic juice secreted during 4 hours, presenting the concentrations of the various substances studied in the juice as well as the pH of the juice under the individual columns.

No pancreatic juice was obtained in one experimental animal each of all groups because of slipping or obstruction of the cannula, so these were not evaluated. Five experimental animals each per group were examined.

Comparing the amount of pancreatic juice secreted during 4 hours in the first group to that in the controls a three-fold rise was noted as compared to the controls. In the animals of groups II and III, the amount of collected fluid equalled that of the controls.

The values of the studied enzymes were found to show a great scatter, but regarding the average values, no characteristic peaks or decreases were observed. pH values ranged between 7.4 and 7.8, while as to total protein, a gradual decrease was noted in groups I to IV.

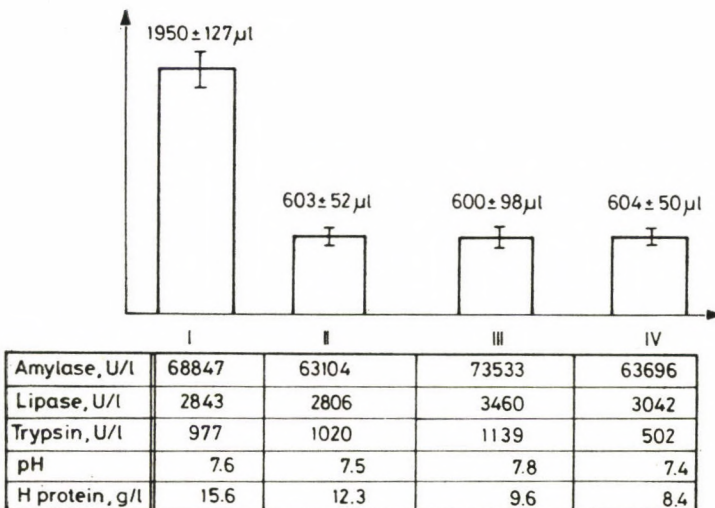


FIG. 1. Examination of pancreatic juice in dogs during nutrition via catheter enterostomy

The overall results of the experiments showed that at the initial segment of the jejunum, as a result of parenteral nutrition (group I) the secreted amount of pancreatic juice as compared to the controls, essentially increased, while it remained unchanged in groups II and III. The enzyme levels of the juice in the individual groups were approximately similar, without a specific change.

Discussion

In acute pancreatitis, a generally accepted part of treatment is oral nutriment- and fluid deprivation and gastric suction which are bound to inhibit the humoral effect, playing a role in pancreatic juice secretion. The importance of the caloric requirement of the organism is, however, also known from the point of view of the recovery of these patients [10], which is ensured by parenteral and enteral nutrition.

Our experiments in dogs under anaesthesia revealed that, due to enteral nutrition in the uppermost segment of the jejunum, exocrine pancreas stimulation occurs which is not felt due to the parenteral nutrition 1 m more distally. Explanation for the phenomenon has been sought theoretically in the regulation of pancreatic juice secretion.

Regulation of the secretion of pancreatic juice is based, according to our current knowledge, on the equilibrium of stimulatory and inhibitory factors. This is exerted by the autonomous nervous system and hormonal effects. Pancreozymin, the secretin playing a role in the hormonal stimulation in man and the generally used experimental animals (such as dog), can be found in the upper segment of the small intestine, in the highest concentrations in the duodenum [5]. Release of these hormones is effected by the entrance into the duodenum of the acid gastric content. Wang and Grossman found in their dog experiments that the intestinal perfusion of the various substances, primarily of amino acids, induced stimulation of enzyme secretion which is assumed to be the consequence of the aforementioned hormonal effect [14]. Of the proteins, in intact form, casein alone is of stimulating effect [9]. The similar perfusion of fatty acids is also stimulatory, but dextrose is ineffective [5].

In view of the data enumerated above, it is probable that, due to casein, and the various amino acids being present in the parenteral nutriment, the stimulation of the exocrine pancreas occurred humorally which, however did not come about in the more distal part of the jejunum and the ileum. The increased secretion corresponds rather to a secretin-like effect, because first of all the amount of secreted pancreatic juice increased while its enzyme level did not change.

In our opinion, what is to be profited from the experiments for clinical practice is that a jejunostomy for parenteral nutrition should not be made

within the upper 1 m which, regarding absorption, is no serious drawback for the patient, while may have a considerable advantage by the absence of pancreatic stimulation.

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Experimentelle Untersuchung der enteralen Ernährung und der exokrinen Pankreasfunktion

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Untersucht wurde die Einwirkung der enteralen Sondenernährung auf die Pankreassekretion unter experimentellen Verhältnissen.

Die Versuche fanden bei 24 Mischlingshunden statt. Zur Sammlung des Pankreassaftes wurde bei sämtlichen Tieren eine Pankreasfistel angelegt. Des weiteren kam bei den in drei Gruppen (je 6 Hunde) eingeteilten Tieren durch eine, an drei verschiedenen Dünndarmabschnitten angelegte Katheterenterostomie eine Sondenernährung angewandt und der Pankreassaft gesammelt. Gruppe IV, die keine Sondenernährung erhielt, diente als Kontrolle.

In sämtlichen Gruppen wurden folgende Parameter untersucht: Menge, pH, Einweiß- und Enzymgehalt des im Verlauf von 4 Stunden ausgeschiedenen Pankreassaftes.

Die Experimente wiesen darauf hin, daß durch die am Initialabschnitt des Jejunums angewandte Sondenernährung die Pankreassekretion gesteigert wurde, während diese Erscheinung bei den anderen zwei Gruppen nicht zu beobachten war. Hierbei handelt es

sich wahrscheinlich um eine humorale Wirkung, es dürfte eher eine sekretinartige Stimulation angenommen werden.

Anhand der Versuchsergebnisse wird darauf hingewiesen, daß falls im Laufe der Behandlung der akuten nekrotischen Pankreatitis zwecks Kalorisierung eine Ernährungs-Enterostomie angelegt wird, dies keineswegs innerhalb des ersten Meters des Jejunums geschehen soll.

Экспериментальное исследование энтерального питания и экзокринной деятельности поджелудочной железы

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В экспериментальных условиях авторы исследовали влияние питания через энтеральный зонд на панкреатическую секрецию.

Эксперименты были выполнены на 24 беспородных собаках. Для сбора панкреатического сока у всех животных была создана фистула поджелудочной железы. В дальнейшем в трех группах животных (по 6 собак) применяли питающую энтеростомию в трех разных участках тонкой кишки, собирая при этом панкреатический сок. 4-я группа служила контролем, когда не получала питание через зонд.

Во всех группах определяли выделенное за 4 часа количество панкреатического сока, pH, содержание белков и энзимов в нем.

Результаты экспериментов показали, что питание через зонд, введенный в начальный участок тощей кишки, усиливало секрецию поджелудочной железы, тогда как в двух других группах этого не отмечалось. Вероятно, это гуморальное воздействие, скорее всего, можно предположить секретин-подобную стимуляцию.

Основываясь на результатах экспериментов, авторы обращают внимание на то, что если при лечении острого некротического панкреатита создают с целью калоризации питающую энтеростомию, то ее не надо делать на протяжении первого метра тощей кишки.

Surface pH and Morphological Changes of the Liver in the Recirculation Phase of Experimental Liver Transplantation

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Measurement of the surface pH of the liver in the recirculation phase of liver transplantation is an indicator of tissue perfusion. In the recirculation phase there is a close correlation between arterial blood and the surface pH of the liver. The surface pH of the liver and EM study together can be of prognostic importance in establishing the viability of the transplanted liver.

During liver transplantation a need emerges for determining the viability of the organ to be transplanted [5]. Attempts were made to define its viability and function already during organ preservation, prior to transplantation. Therefore, the K^+ and pH values of the renal surface were examined with simultaneous histological studies [4, 5]. Surface pH was measured for determining viability in other organs (heart, small intestine) and tissue (muscle) [1, 4].

There has been a long search for signs in the liver, on the basis of which the function and viability of the preserved liver can be assessed during transplantation [7, 8, 12, 14]. Concerning the liver, beside changes due to preservation, during reperfusion cellular damage, structural and metabolic disorders, Ca^{++} ion cellular influx and marked cellular edema were observed [2, 3, 9, 10].

Our experiment was carried out for studying (*i*) how surface pH of the liver changes during preservation of the liver and recirculation; (*ii*) how surface pH and the pH of arterial blood are correlated; (*iii*) whether conclusions can be drawn from the degree of change of surface pH, and whether there is a simultaneous change in the ultrastructure of the liver indicating reduced viability.

Material and Method

The experiments were carried out in 15 female mongrel dogs weighing 15.6 ± 3.9 . Transplantation was performed according to Starzl's method [15]. The donor's liver was preserved by 2000 ml of 4 °C Ringer's lactate of a pH of 7.4. The time elapsing from the start of precooling to that of complete recirculation was 187 ± 22 mi. The venovenous bypass was maintained in the recipient animal by a PEMCO (Cleveland, Ohio) heart pump during the anhepatic phase [11].

Surface pH of the liver was measured at half-hour intervals for a period of three hours. An OP 211/1 digital pH recorder (RADELKIS) and an OP 801 P surface electrode were used. After calibration the surface electrode was placed on the convexity of the liver over the regions of the right and left lobes. The pH readings were taken after 30 seconds. (There was no significant difference between the two lobes of the same liver.) Values measured after laparotomy served as the initial values and in three animals a sham-operation of a duration equal to that of the transplantation and continuous pH monitoring were made.

The pH values of the blood of the femoral artery and the hepatic vein were registered at the same intervals as on recording surface pH. Blood was obtained by puncturing of the hepatic vein.

In the recirculation phase sample was obtained for EM study at half, one- and two-hour intervals. Glutaraldehyde fixation was applied. The recirculation phase was calculated from the restoration of the arterial and venous afferent circulation of the liver. The venous and arterial anastomoses were sutured by running 4/0, 5/0 and 6/0 NOVAFIL (Davis-Geck) sutures.

On the basis of SEM-values, significance analysis was made by the Student's 2-sample t-test, p being significant if $p < 0.05$.

Results

The pH measured on the liver surface during precooling and cooling decreased from the control value (7.42 ± 0.19) significantly with an insignificant subsequent change during preservation (Fig. 1).

In the first half hour following recirculation surface pH further decreases with a subsequent elevation. In the 2nd and 3rd hours of recirculation surface pH of the liver increased to a value of 7.19 ± 0.12 (Fig. 2).

(In the 10 animals not included in the experimental series, with a bad systemic circulation and the implanted liver having become spotty and hard, the surface pH did not reach a value of pH 7 in the 2nd and 3rd hours of recirculation.)

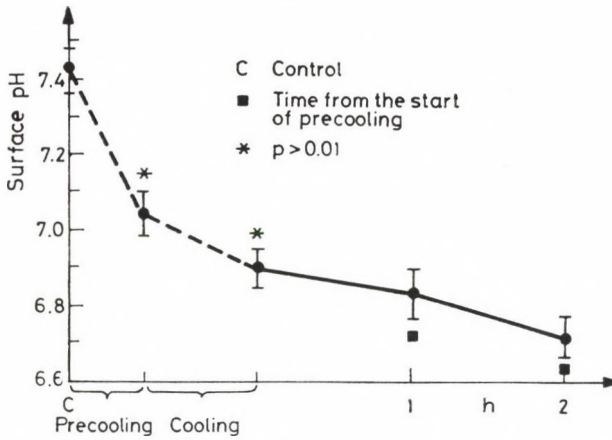


FIG. 1. Liver surface pH during liver preservation

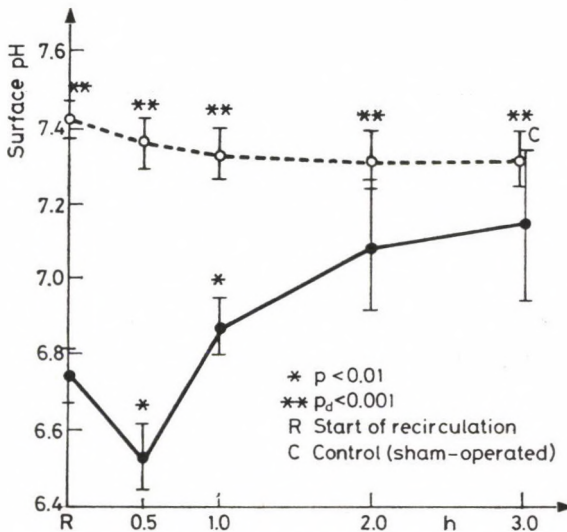


FIG. 2. Liver surface pH during recirculation

At the end of the first hours after starting recirculation, the surface pH increased significantly ($p < 0.01$) and, at the same time, it differed significantly in all the values from the controls ($p < 0.001$). During this time rectal temperature did not change significantly ($p > 0.05$), with a mean of 33–34 °C (Fig. 3).

According to determinations from the blood of the femoral artery and hepatic vein, the pH values were shown to decrease significantly following the anhepatic phase ($p < 0.05$). The arterial pH stabilized at the value of 7.18 ± 0.08 in the

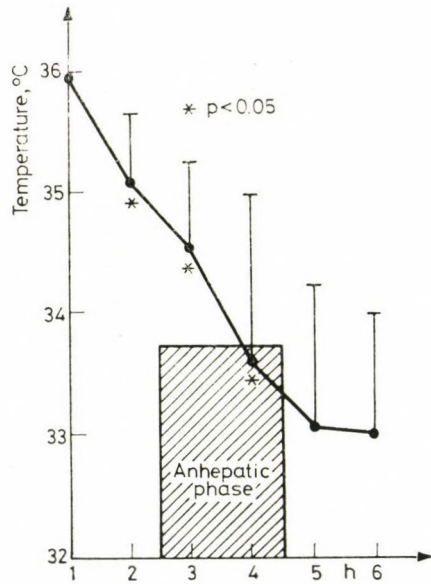


FIG. 3. Body temperature (rectal) during experimental liver transplantation

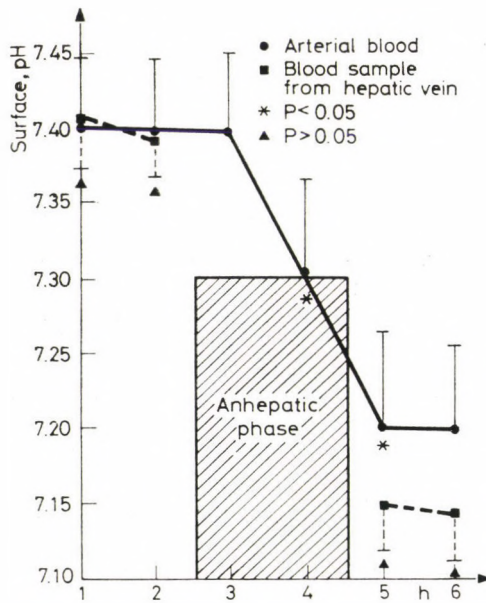


FIG. 4. pH changes during experimental liver transplantation in the arterial and hepatic venous blood

recirculation phase (Fig. 4). The pH of the hepatic venous blood also decreased significantly by the starting of the recirculation phase: 7.14 ± 0.06 ($p < 0.05$).

It is noteworthy that, in the recirculation phase, the pH values of the arterial and hepatic venous blood did not differ significantly.

The samples taken from the intact liver were considered as reference for EM studies. The ultrastructure of the intact dog liver is shown in Fig. 5.

The samples obtained during recirculation displayed the changes as follows: the lobulate structure was found to be intact. Electron microscopy revealed enlarged mitochondria in the cytoplasm of the hepatic cells. The amount of glycogen was considerably reduced with an absence of the characteristic rosette formation. The amount of rough endoplasmic reticulum diminished as well (Fig. 6). Adjacent to the hepatic cells lymphocytes and Kupffer cells could be seen. There were no permanent changes in the organelles of the liver cells (Fig. 7). In between the liver cells parts of leukocytes could be observed with an intact structure of mitochondria (Fig. 8). The chromatin substance of the nucleus of the liver cell was found to be aggregated around the nuclear membrane. The plasma contained regular organelles. The amount of rough endoplasmic reticulum was reduced (Fig. 9).

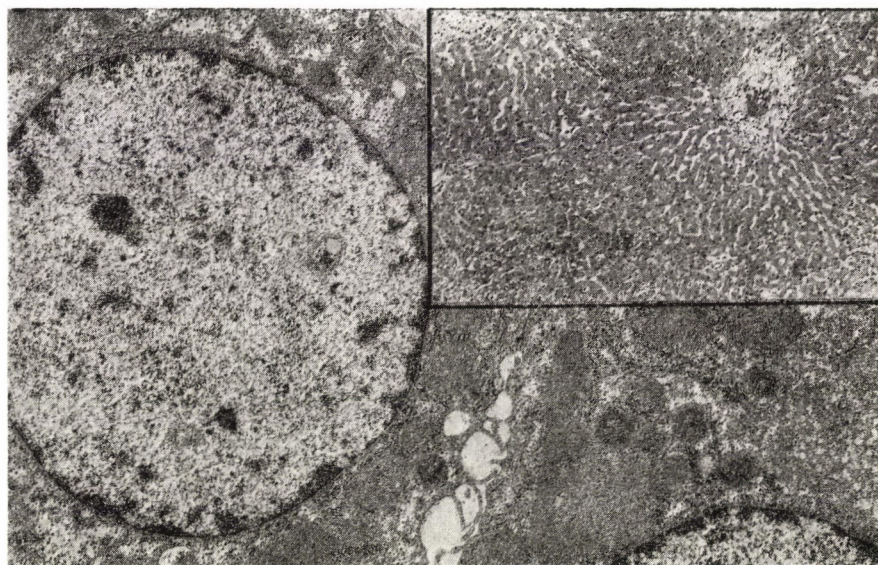


FIG. 5. Intact dog liver. Portion of a liver cell with a regular nucleus and intracytoplasmic organelles. The Disse's spaces are somewhat dilated containing simple and compound nuclear bodies intranuclearly. Basic magnification: $\times 4000$. Final magnification: $\times 13,200$

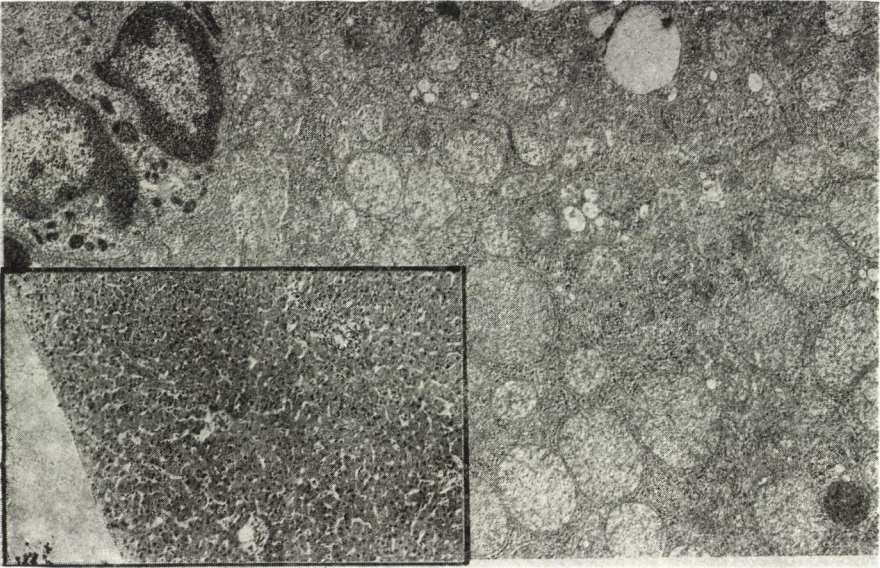


FIG. 6. A recirculation phase of 60 min in transplanted dog's liver. Adjacent to a partly unidentified cell debris, a part of a leukocyte can be seen in the slightly dilated sinusoids. The endothelial cell processes are swollen. The cytoplasm of the liver cell contains enlarged mitochondria. The matrix is pale. The amount of glycogen is considerable reduced. The characteristic rosette formation is absent. The amount of rough endoplasmic reticulum is equally reduced. Basic magnification: $\times 4000$. Final magnification: $\times 13,200$

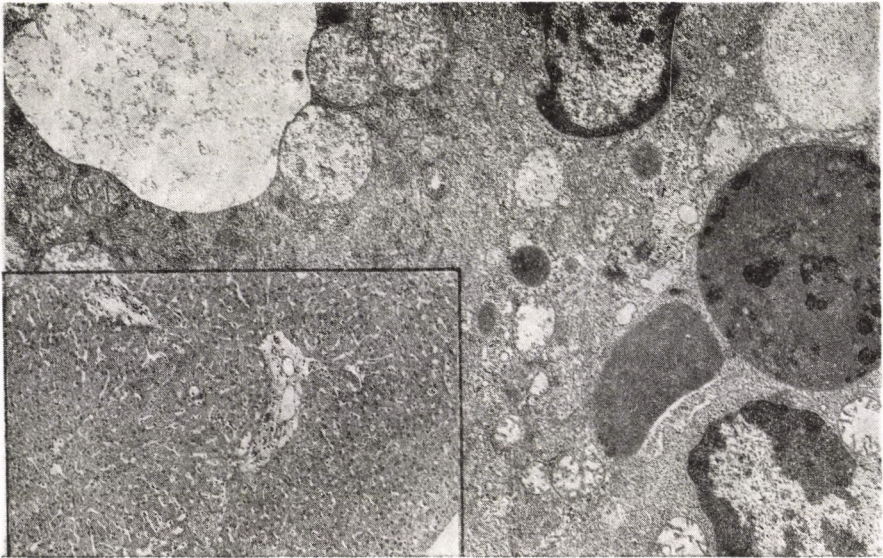


FIG. 7. A recirculation phase of 60 min. Adjacent to the liver cell a lymphocyte and detail of a Kupffer's cell can be noted. There are no permanent changes in the organelles of the cells. Basic magnification: $\times 40000$; Final magnification: $\times 13,200$

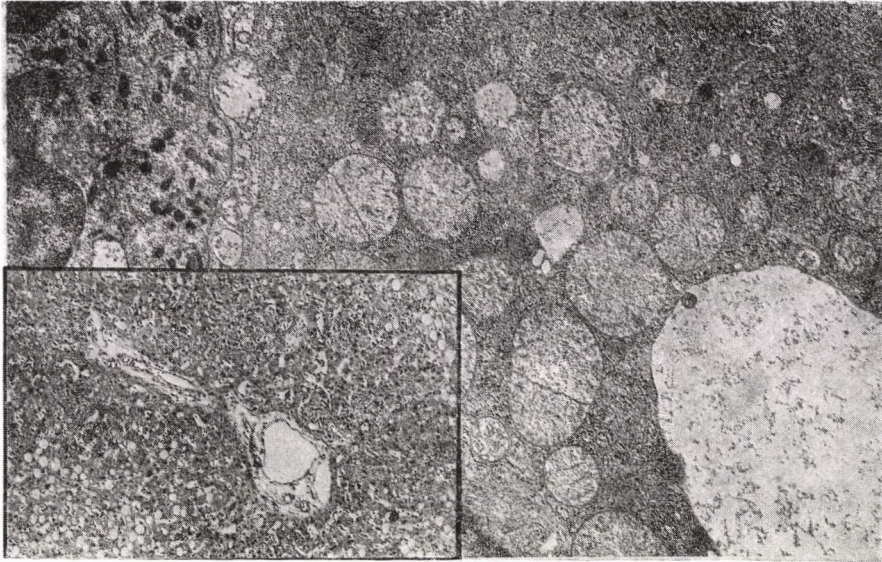


FIG. 8. The structure of the mitochondria is intact. In between the liver cells part of a leukocyte is seen. Basic magnification: $\times 4000$; Final magnification: $\times 13,200$

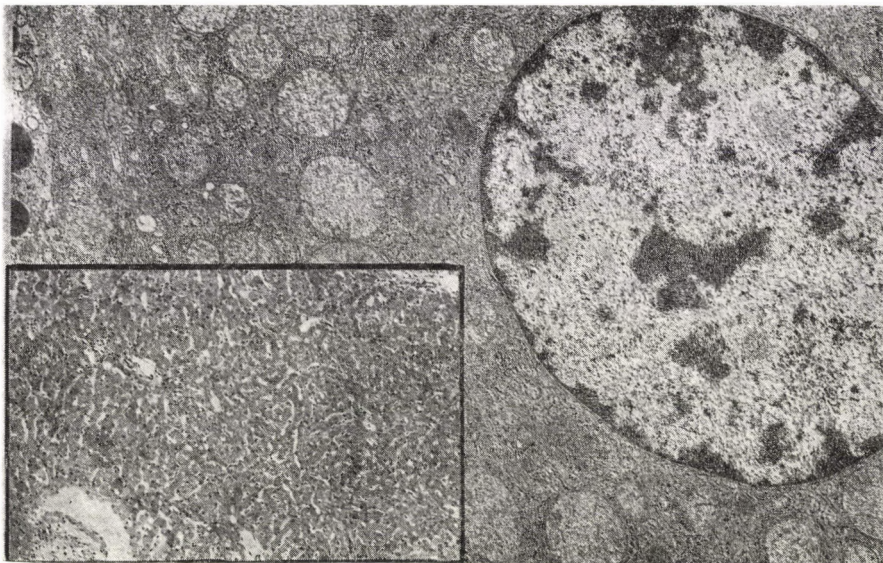


FIG. 9. The chromatin substance of the nucleus of the liver cells is aggregated at the inner aspect of the nuclear membrane. The cytoplasm contains regular organells. The amount of rough endoplasmic reticulum is diminished. Basic magnification: $\times 4000$; Final magnification: $\times 13,200$

Discussion

Data obtained during recirculation were compared with those of Couch and Middleton [4]. These were gained by recording surface pH by the passive warming of liver tissue having been precooled for one hour (Fig. 10).

The surface pH of nonviable liver having been warmed passively differed significantly from that of the recirculated liver, tissue and organ surface pH seems to be a reliable indicator of metabolic activity, particularly of the anaerobic metabolism. Surface pH values indicate, in this sense, also the perfusion of a tissue or organ where the pH is recorded. For example in the intact kidney, surface pH is immediately reduced at compression of the renal artery and it returns to normal values as soon as circulation is restored [5]. In haemorrhagic shock pH of the muscle surface decreases with an increase in the lactic acid concentration of the blood [1].

Anaerobiosis, the accumulation of lactate and pyruvate, i.e., precursors of the ischaemic necrosis of the organ, can be detected within 60 minutes already on reducing or stopping the perfusion of the liver. Hypothermia considerably reduces the accumulation of lactate and pyruvate, i.e., it slows down anaerobic metabolism. Liver surface pH, i.e., the rate of change of hydrogen ion concentration is a good indicator of glycogenolysis, of anaerobic glycolysis and lactate acidosis, resulting from the ischaemia due to the insufficiency of organ perfusion.

Liver surface pH was found not to be correlated with body temperature (Fig. 11). The regression between the values of arterial blood and liver surface

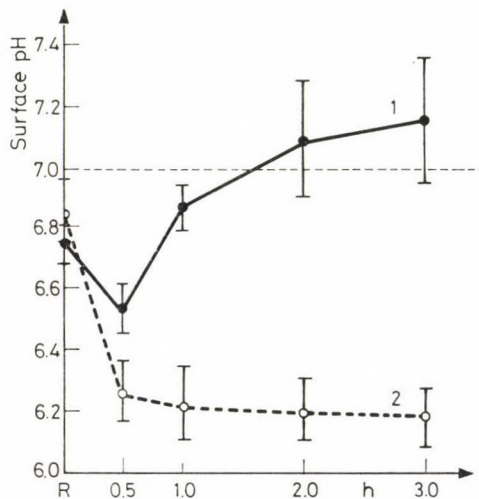


Fig. 10. Liver surface pH during recirculation in liver transplantation and during warming after one hour of cooling at 5 °C. (The latter is based on the data of Couch and Middleton [4])

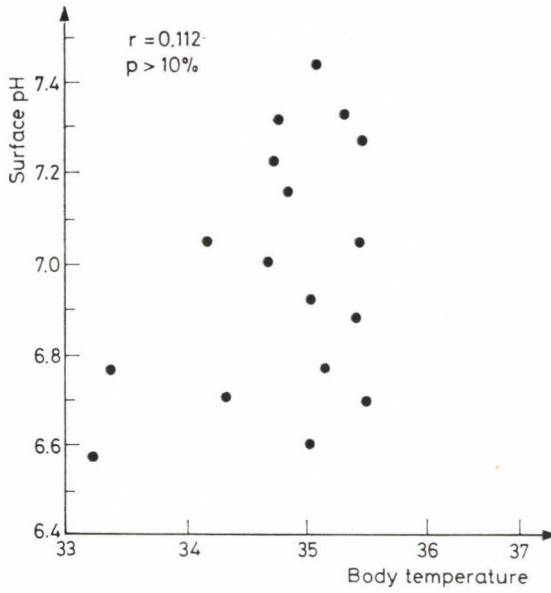


FIG. 11. Regression between surface pH and body temperature in reirculation of liver transplantation

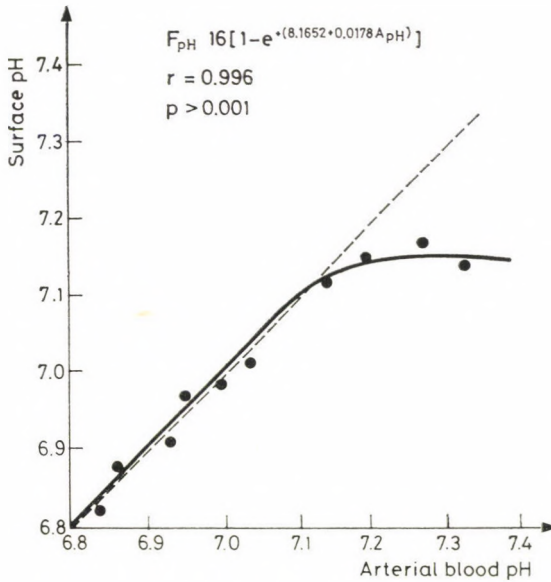


FIG. 12. Regression between arterial blood and liver surface pH in the reirculation phase of liver transplantation

pH corresponds, however, to a so-called saturation curve. A line can be adjusted to the ascending phase of the curve which can be characterized by the regression equation of

$$F_{\text{pH}} = 16/1 - e^{(8 \cdot 1652 + 0 \cdot 0178A_{\text{pH}})}$$

It appears that in the recirculation phase the increase of arterial pH does not induce that of the liver surface pH over a certain value (Fig. 12). The relationship is based on mathematical analysis so far-reaching conclusions are not to be drawn from it. Nevertheless, the insignificant difference between the pH values of the hepatic venous blood and those of the arterial blood indicates that the surface pH in an adequately preserved and recirculated liver is a good indicator of liver cell function between the means of the two values.

The EM studies revealed no irreversible cellular change. Forty-eight hours after liver transplantation in dog, light microscopy disclosed status of the central venule, interstitial edema and swelling of Kupffer cells. Electron-microscopically, lymphoid cells, granulocytes were found to be present in the vicinity of the sinusoidal endothelium and the minor portal veins. The hepatocytes around the central veins were necrotic. The peripheral liver cells contained lipofuscin granules and swollen mitochondria. Glycogen and rough endoplasmic reticulum were missing [8, 14].

Our own investigations revealed in the early phase of recirculation the enlargement of mitochondria with a decrease in the amount of glycogen and of the rough endoplasmic reticulum. A crucial point was that no cellular necrosis with irreversible ultrastructural changes was found to occur.

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pH- und morphologische Änderungen der Leberoberfläche in der Rezirkulationsphase der experimentellen Lebertransplantation

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Die Ergebnisse der pH-Messung der Leberoberfläche stellen in der Rezirkulationsphase der Lebertransplantation die Indikatoren der Gewebepерfusion dar. In der Rezirkulationsphase kann zwischen den pH-Werten des arteriellen Blutes und der Leberoberfläche eine enge Korrelation nachgewiesen werden. Der pH-Wert der Leberoberfläche und die Ergebnisse der elektronenmikroskopischen Untersuchung können bei der Bestimmung der Lebensfähigkeit der transplantierten Leber von prognostischer Bedeutung sein.

Значение рН на поверхности печени и морфологические изменения в фазе рециркуляции при экспериментальной трансплантации печени

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Измерение значений рН на поверхности печени в фазе рециркуляции после трансплантации печени является индикатором тканевой перфузии. В стадии рециркуляции выявилась тесная корреляция между значением рН артериальной крови и рН поверхности печени. рН поверхности печени и исследование ЕМ вместе могут иметь прогностическое значение при установлении жизнеспособности трансплантированной печени.

Aspects of Diagnosis and Therapy of Gallstone Ileus

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The clinical experience with 14 gallstone ileus patients operated within a time period of 17 years is analysed with a survey of the relevant literature. For surgical solution enterolithotomy is recommended. The difficulties of early diagnosis are pointed out with an emphasis, in case of gallstone, on cholecystectomy for prevention of gallstone ileus.

Gallstone ileus is a mechanical ileus in which one or several stones cause obstruction in the alimentary canal. Of the acute intestinal obstructions, the incidence rate of gallstone ileus is 1–6%, according to the authors' data [1, 4, 10, 12, 20, 27]. The most frequent complication of gallstone ileus is acute cholecystitis the development of which can be expected in 50%. A further complication associated with acute cholecystitis is biliodigestive fistula formation in 1–2% [2, 13, 16, 24, 30, 31]. In bilioenteral fistula, gallstone ileus occurs in approximately every 10th case [1]. According to data of the literature, 0.2 to 8% of gallstone operations is made for solving a gallstone ileus [4, 10, 30].

Gallstone ileus occurs most often in elderly patients with other severe persisting diseases. It is characterized by a late and often uncertain, preoperative diagnosis which, together with an incriminating history may be responsible for the high morbidity and mortality.

In this report the clinical symptoms of gallstone ileus, the difficulties of preoperative diagnosis, the importance of aggravating associated diseases as well as the possibilities of treatment are discussed in view of our own material.

Case Report

In the period between 1971 and 1988, 14 patients with a diagnosis of gallstone ileus were operated. During this time 505 operations were made because of intestinal obstruction, with a ratio of 2.77 of gallstone ileus among the mechanical ileus cases. During the same period 3473 operations were carried out for cholelithiasis, so the incidence rate of gallstone causing intestinal obstruction was 0.4%.

All our patients were females, with an average age of 74 (66–86 years). Six patients had a history of known cholelithiasis, 9 patients had, prior to their ileus, undergone an abdominal operation. The leading clinical symptoms included vomiting in 13 cases, abdominal pain in 12 cases, intestinal distension in 11 cases. On admission, at physical examination exaggerated borborygmi and succussion were found in five patients each. Icterus and fever did not occur in any of the patients. Laboratory tests revealed a moderate dehydration and electrolyte disturbance, with marked hypokalaemia in 3 patients ($\text{SeK}^+ \leq 3 \text{ mmol/l}$), and a leukocytosis over 10.0 G in 6 cases. Plain abdominal X-ray showed a picture of fluctuating small-bowel ileus changing in time, with transitory regression and later progression. X-ray revealed pneumobilia in two patients, but dystopic gallstone could be visualized in none of the cases.

On average, 4.5 days (1–7) elapsed between the appearance of symptoms and the operation, during which time after admission, the patient was kept on a zero diet, with a duodenal tube being introduced. Through this the gastroduodenal contents were aspirated, and attempts were made at arresting the subileic state by giving enemas and purgative. During this time the disorders of electrolyte, protein and water metabolism also normalized. Preoperatively, gallstone ileus was diagnosed in two cases. In further six instances gallstone was assumed to be the disease underlying mechanical ileus, however, this could only be verified intraoperatively.

The gallstone giving rise to obstruction can most often be found in the ileum. This has also been proved by our own cases, in 12 patients the stone was localized at the ileojejunal junction in 9 cases while in the more aboral ileal segment in 3 cases. In further two, the gallstone became lodged at the initial segment of the jejunum. More than one stone was not found on scrutinizing the digestive tract. Biliodigestive fistula between the gallbladder and the duodenum could be proven intraoperatively in two patients. In 12 patients the pericholecystic adhesions and the inflammatory conglomerate were indicative of tumour, but its clarification would have meant the marked extension of the operation, so considering the frailty of the elderly patients, we declined from this attempt.

The operation was enterolithotomy in every case made from an enterotomy proximal to the impaction. Relaparotomy was not performed because of a second ileus due to a residual stone. Suppuration of the wound was observed in 5 cases, associated in one of them, with deep vein thrombosis, pneumonia and skin necrosis due to Syncumar. Four patients were lost, this constituting a lethality of 28.5%. The cause of death was severe pneumonia associated with heart failure. Autopsy disclosed the cholecysto-duodenal fistula in all four patients without any evidence of peritonitis indicative of intestinal suture insufficiency.

Postoperative care ranged from 3 to 158 days on average 30.3 days.

Discussion

Gallstone ileus is in general a disease affecting elderly people occurring most often between 67 and 75 years of age. The female-male ratio is 9–10 to 1 (11.29). The youngest patient with gallstone ileus was aged 13 [11]. Cholecystitis calculosa is often part of the patient's history. Intermittent ileus causes rapid deterioration in the patient's otherwise poor general condition, associated, in particular, with cardiac decompensation, chronic obstructive bronchitis, hypertension, diabetes mellitus, atherosclerosis, renal and hepatic insufficiency. Regarding that with advancing age the number and severity of accompanying diseases are increasing, the fact, that this patient group is more at risk, is understandable [15, 18]. Several aggravating associated diseases also occurred in 85% of our patients. The initial symptoms of gallstone ileus are poor. Clinical course is characterized by fluctuation. This circumstance often results in postponing the date of the required operation. In general, the usual picture of mechanical ileus is seen with exaggerated borborygmi and succussion can be induced on the physical examination of the abdomen. Sometimes the patients have a history of repeated subileic events. These are due to the fact that, passing in the digestive tract, the gallstone may temporarily cause obstruction up to the final impaction or spontaneous discharge, contributing by all these to a prolonged and varying clinical picture, rendering preoperative diagnosis difficult.

Passing aborally in the alimentary canal, the gallstone may increase because of superposed intestinal contents [12, 28]. Consequently, it may occur that a gallstone of a relatively small diameter—passing even through the papilla of Vater, currently grown in size—causes complete ileus in the more distal segment of the small bowel. As a result, the time from the onset of symptoms and the operation is variable and may range up to several days. In our cases this averaged 4.5 days (1–7 days) [10]. Considering the time having elapsed from the patient's admission to the operation, it was found, on average, to be 1.8 days (0–6 days) [14, 31]. In preoperative diagnosis US, endoscopy, plain X-ray and contrast studies were of help. US may reveal the presence of stones in the gallbladder, informing about the wall thickness and size of the gallbladder and gallstones of dystopic position. By endoscopy, in a fortunate case, even a biliodigestive fistula may be diagnosed, moreover gallstones just about to pass from the duodenum were also described during endoscopy [12, 22]. In most cases, however, it may help only in differential diagnosis. Of the X-ray studies, the plain roentgenogram is the method of choice. According to the literature, a dystopic gallstone can be detected by it in 10% of the cases [4]. It succeeded in non of our cases. The biliodigestive fistula is proved by the presence of aerobilia. There are controversial data on its occurrence. Some found it only exceptionally while others in 80% [6, 17].

We noted air in the bile duct in 14% of the cases. The complete Rigler's triad (aerobilia, dystopic gallstone and the roentgenographic picture of small bowel ileus) rarely occurs [21]. In ambiguous cases repeat plain X-ray or, if necessary, some gulps of gastrographin, may yield the expected diagnosis, including even the detection of the biliodigestive fistula. Gallstone ileus was diagnosed preoperatively in two out of 14 cases, while in additional 6 cases there was a strong suspicion of its causing the mechanical ileus. A preoperative diagnosis of a confidence level of 4–88% has been reported in the literature [8, 23, 31]. Obstruction occurs most frequently in the distal ileal segment. Gallstones causing ileus are encountered less frequently in the jejunum, duodenum, stomach and colon [22, 26]. The incidence rate of multiple stones is estimated at 3 to 16%, we have not found more than one stone in the digestive tract [7, 8, 23, 25, 27]. Of the biliodigestive fistulas, the cholecystoduodenal one occurs the most often but cholecysto- (cholecho-) gastric and cholecystocolonic fistula are also frequently encountered. These can be clarified pre-, intra or postoperatively. Considering our very frail, aged patients of a limited endurance, the verification of fistulas is not regarded as an indispensable requirement intraoperatively, since if there are no more stones left in the gallbladder, spontaneous healing of the fistula can also be expected. This possibility is excluded by the presence of a stone in the gallbladder. In two of our patients the fistula could be found and localized intraoperatively, both of them being cholecystoduodenal ones. Autopsy of the four lost patients revealed also a cholecystoduodenal fistula.

The possibilities of surgical treatment are as follows:

- enterolithotomy;
- enterolithotomy + cholecystectomy in one session, biliary duct revision by management of the biliodigestive fistula;
- enterolithotomy + cholecystectomy performed at an elected date and management of fistula.

The most important task of surgical treatment is to eliminate the cause of ileus [4, 10]. Impaction of the stone may give rise, after some time, to decubitus, ulcer or perforation in the intestinal mucosa. In such cases resection of the involved intestinal segment may also be necessary. Our cases were confined to enterolithotomies without intestinal resection. After removal of the (found) stone it is an important task to carefully check the entire intestinal segment, because in 3–16% of the cases the multiple stones can be expected to occur [4, 7, 8, 23, 25]. Stones overlooked may cause ileus recurrences in 2–10% of cases [1, 10] in which the operative risk is much higher. Among our cases no ileus recurrence was noted [11, 23, 25, 29].

If there are residual stones in the gallbladder after a gallstone ileus operation, this may induce further complications, like recurrent ileus, mechani-

cal ileus, cholangitis, pancreatitis and malignant degeneration of the gallbladder. Due to the possibility of these complications, it is recommended to perform cholecystectomy. A precondition of this is that the patient's general state should allow his or her exposure to an increased risk. There are controversial opinions about the time of the second operation. Some authors perform the definitive operation after solving the ileus and adequately preparing the patient without discharging him or her from hospital. Others claim this time to be 4 to 6 months after the first operation.

For the extension of the operation absolute indications are a biliocaeliac fistula, gangrene and carcinoma of the gallbladder and the presence of stone in the biliodigestive fistula.

In our opinion, the type of operation should be adjusted to the individual. Progressive ileus, peritonitis, severe associated diseases, advanced age and the consequential short life expectancy are justifications for stopping the ileus only by enterolithotomy. Our patients were always subjected to this operation. Four patients were lost, this constitutes a lethality of 28.5%. In the literature the lethality of gallstone ileus is assumed to be 5–30% in the case of an early operation [4, 5, 9, 18, 25]. With the advancing of time this is bound to rise and lethality of late operations may even amount to 70–100% [3, 4, 6, 17, 30].

Operative results can be improved by an early diagnosis. Extension of the operation is basically determined by the patient's general condition and each case should be judged individually. The best prophylaxis of gallstone ileus is the removal of a calculous gallbladder in due time.

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Gesichtspunkte zur Diagnostizierung und Behandlung des Gallenstein-Ileus

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Im Zusammenhang mit 14, im Verlauf von 17 Jahren operierten, an Gallenstein-Ileus leidenden Patienten werden im Spiegel der einschlägigen Literatur die klinischen Erfahrungen analysiert. Als Operationsmethode der Wahl wird die Enterolithotomie empfohlen. Nach Erläuterung der Schwierigkeiten der Frühdiagnose, wird im Falle eines Gallensteines die Notwendigkeit der Cholezystektomie Gallenstein-Ileus-Prophylaxe betont.

Точки зрения на диагностику и лечение желчных камней илеуса

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Авторы анализируют свой клинический опыт в связи с прооперированными за 17 лет 14 больными, страдавшими желчнокаменной болезнью и илеусом. Дают краткий обзор литературы, относящейся к этому вопросу. В качестве хирургического вмешательства они рекомендуют энтеролитотомию. Подчеркивают трудности постановки раннего диагноза, рекомендуют при наличии желчных камней холецистэктомию для профилактики желчных камней-илеуса.

Effect of Bacterial Endotoxin on Placentation of Rats

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The effect of bacterial endotoxin on placentation in rats was studied on 160 CFY pregnant rats. Based on this experiment, it was concluded that (i) the endotoxin (1 mg/animal i.p.) inhibited placentation (in 90% of animal). (ii) The endotoxin-induced fetopathy almost exclusively resulted in abortion. (iii) The fetuses reacted to endotoxin with relatively the same degrees of susceptibility. (iv) The growth of surviving fetuses seemed to be undisturbed. (v) Endotoxin-induced damages in mothers first of all depend on the individual susceptibility of these pregnant animals and (vi) the endotoxin tolerance induced by radio-detoxified endotoxin (TOLERIN) significantly protects both the mothers and the fetuses against endotoxin challenge.

It has long been known that bacterial endotoxins may induce fetal death, fetal absorption, abortion and malformations in experimental animals, particularly in endotoxin-sensitive species (golden hamster, swine), but also in human studies [9, 10, 11, 13, 14, 18, 19, 22, 24, 25, 26].

The majority of earlier investigations were focussed on placental changes in the third trimester of pregnancy [9, 11, 12]. Only a few reports have been concerned with the effect and consequences of bacterial endotoxaemia during placentation [2, 9]. It is also known that numerous effects of endotoxin cannot be prevented or warded off by small doses of endotoxin administered parenterally [3, 5, 6, 7, 9, 16, 17]. This phenomenon is called endotoxin tolerance. Beside its useful (endotoxin tolerance-inducing) effect, bacterial endotoxin has several unwanted and dangerous (toxic, fever-producing) side-effects. That is why endotoxin-detoxification has long been the primary aim of research workers by retaining its beneficial effects. For this purpose a bacterial endotoxin preparation, TOLERIN, detoxified by ⁶⁰Co-gamma by Bertók et al. [4, 5, 8] has been in use in our laboratory for almost 15 years. Its clinical tests are currently underway. This preparation has also been applied in our experiment.

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In these experiments an answer has been sought to the questions as follows:

1. What is the effect of endotoxaemia on placentation?
2. What forms of fetal damage are resulted?
3. How do surviving fetuses develop?
4. What kind of maternal impairment is induced in relation to, or simultaneously with, fetal damage?
5. How can all these harmful effects be prevented by the previous induction of endotoxin tolerance?

Material and Methods

In the experiment female CFY rats (LATI, Gödöllő) of an average weight of 210 g were used. Based on vaginal smear tests, the females in proestrus were kept together with males, then, after repeated vaginal smear tests the 'sperm-positive' females were included into the experiment, a total of 160 animals divided into 4 equal groups. The day of seminal examination was the first day of pregnancy. The animals were kept on granulated rat food and tap-water *ad lib*.

Treatment: Each animal of group I was administered a 1.0 ml physiological saline solution i.p. on the 12th day of her pregnancy. Group II received 0.2 mg TOLERIN/animal endotoxin i.p. on day 10, group III 0.5 mg/animal endotoxin i.p. on the 12th, while group IV equal amounts of TOLERIN as group II, on the 10th day, then toxic endotoxin on day 12, similar to group III.

Endotoxin: LPS (*E. coli* 089)P₂ 87061601 (OSSKI). The endotoxin was prepared from a fermentor culture of an *E. coli* 089 strain by using the warm phenol-water method of Westphal et al. [28].

TOLERIN: RD-LPS (P₂: 150 KGy) 87061601 (OSSKI).

Time of observation: From the administration of TOLERIN (from the 10th day of pregnancy) up to the 15th day following parturition. The animals were kept under standard laboratory conditions during the experiment, then from the 19th day of their pregnancy they were separated from each other. After the inoculations, the animals were continuously monitored for 48 hours, and the dead were immediately dissected. The visible changes were recorded. The uteri containing the small embryos arranged like a string of beads were fixed in 4% neutral formalin for histological study. Following paraffin-embedding they were stained with heamatoxylin-eosin. The offspring was weighed on the 15th day after birth and their sex was determined.

Results

The experimental results were summarized in two tables. These reveal that in group I, including animals given a physiological saline solution, and in group II given only radiodetoxified endotoxin, no maternal deaths occurred. There was no change in the animals' behaviour and 38 and 37 animals, respectively, delivered the fetuses.

In group III treated only with endotoxin, within 48 hours of their endotoxin exposure, 21 animals died and four of the survived animals gave birth to fetuses. In group IV, pretreated with TOLERIN, 13 animals died following endotoxin administration and subsequently 13 animals produced offspring.

TABLE 1

Group	No. of animals (sperm-positive)	Treatment		Deaths* within 48 hours after endotoxin challenge	Parturition
		TOLERIN on 10th day	endotoxin on 12th day		
		of pregnancy			
I	40	—	—	—	38
II	40	+	—	—	37
III	40	—	+	21	4
IV	40	+	+	13	13

* No other deaths occurred

Pathological examination of animals died as a result of endotoxin challenge, disclosed typical organic changes characteristic of endotoxin shock, i.e., pulmonary edema, pulmonary haemorrhage, thymus bleeding, congestive enlargement of the liver, intestinal edema, segmental intestinal bleeding, thin colonic contents, mesenterial lymph node swelling and haemorrhage and swelling of the Peyer's plaques. Histology disclosed the following changes in the developing placenta: extensive necrosis in between the cells of both the chorionic and the trophoblastic layers, similar to those in the decidua. The invasion of fetal capillaries was moderate, with sporadic fibrin thrombi in the sinuses, on the maternal side of the labyrinthine layer.

In group III one of the 21 died animals was proved at dissection to be non-pregnant.

Discussion

It can be made probable from the data of groups I and III and from the literature [1, 15, 20, 21, 27] that pregnancy occurs in at least 90% of sperm-positive female rats. Consequently, in our experiment pregnant rats were supposed to be found at least in this proportion in groups III and IV. (This

TABLE II

Group	No. of newborn	Mean litter no. (min. and max. litter nos)	Sex ratio Male : female	Mean weight, g at 15 days
I	278	7.3 (2-14)	1.1 : 1	37.1
II	265	7.2 (2-14)	1.1 : 1	36.1
III	27	6.75(3-10)	0.9 : 1	36.7
IV	92	7.1 (2-11)	1 : 1	36.6

empirical fact is important because a 10-day pregnancy in rat cannot be safely established by non-invasive methods.) At the same time, data of group II show that TOLERIN in the applied dose does not have a permanent toxic effect either on the mother or the fetus [9].

The endotoxin administered during placentation killed a considerable part of the mothers in group III (a total of 21 animals died, but on dissection one was found not to be pregnant). Four of the surviving animals littered, much less than they were supposed to do. So it can be concluded that endotoxin killed a considerable part of the fetuses in the period of placentation. In summary, half of the mothers died, the other half survived endotoxin exposure and about one-fifth of the survivors gave birth to healthy fetuses, while four-fifths aborted.

The data of group IV revealed that preliminary induction of endotoxin tolerance afforded the mothers some protection against endotoxaemia (only 13 died of 40). At the same time the extra protection for the mother implied also an extra protection for the fetus.

In summary, two-thirds of the mothers died, two-thirds survived endotoxaemia, and half of the survivors produced healthy fetuses, while the other half aborted.

Changes disclosed by the pathological and histological studies of the died animals corresponded to the changes induced by edotoxaemia already described by us in the literature [9, 10, 12, 13, 18, 19].

Comparing the four groups, there was no difference concerning litter number and the average weight of the fetuses measured at their age of two weeks at a 5% concordance level. Concerning the sex rate, there was only one thing to be noted, namely that it shifted towards females in group III. However, this information was obtained on the basis of 4 litters and so it cannot be considered specific for the group.

In conclusion, a certain amount of endotoxin exerts its effect during placentation in a way that, due to a single applied dose, a considerable part of the mothers (about half of them in our experiment) died, some survived but aborted, while some survived and produced healthy fetuses. Apparently, in this process, the mother's individual sensitivity is predominant, therefore

the 'all but none' law seems to be valid, i.e., if the mother and her fetuses survive endotoxin exposure in the period of placentation then practically all fetuses are born healthy. This means that the fetuses of a mother respond with the same degree of individual sensitivity to endotoxin. The development of the viable fetuses up to the 15th day after parturition shows that a single endotoxin exposure does not cause a notable difference in growth.

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Untersuchung der Wirkung in der der Periode der Plazentation ausgelösten bakteriellen Endotoxämie bei der Ratte

GY. SZÓCS, TERÉZ CSORDÁS und L. BERTÓK

Untersucht wurde die Wirkung des bakteriellen Endotoxins in der Periode der Plazentation bei der Ratte. Die Experimente führten zu folgenden Feststellungen: 1. Im Falle einer, mit der i.p. Gabe von 1 mg/Tier Dosis Endotoxin ausgelösten Endotoxämie ist die Plazentation in bedeutendem Maße (bis zu 90%) gehemmt. 2. Die sich entwickelnde Fruchtschädigung ist fast ausschließlich eine Fehlgeburt. 3. Die Früchte reagieren mit einer relativ identischen individuellen Empfindlichkeit auf das Endotoxin. 4. Die Entwicklung der überlebenden Früchte scheint ungestört zu sein. 5. Die Grundlage der mütterlichen Schädigung ist die individuelle Endotoxinempfindlichkeit des Muttertiers. Ein Teil der trächtigen Rattenweibchen geht ein, ein Teil bleibt am Leben, bei ihnen kommt es aber zu einer Fehlgeburt, während einige Tiere gesunde Früchte auf die Welt bringen. Die vorangehende Auslösung der Endotoxintoleranz mittels TOLERIN (strahlendetoxyziertes Endotoxin) bot einem bedeutenden Anteil der Mütter und auch der Früchte einen Schutz gegenüber den katastrophalen Folgen.

Исследование в экспериментах на крысах эффекта бактериальной эндотоксемии, вызванной в период плацентации

Д. СЕЧ, Т. ЧОРДАШ и Л. БЕРТОК

В экспериментах на крысах авторы изучали действие бактериального эндотоксина в период формирования плаценты. Результаты экспериментов показали, что: 1) эндотоксемия, вызванная интраперитонеальным введением 1 мг эндотоксина, значительно (примерно в 90%) тормозит развитие плаценты. 2) Во всех случаях без исключения повреждение плода приводит к выкидышу. 3) Плоды примерно с одинаковой чувствительностью реагируют на эндотоксин. 4) В основе повреждения материнского организма лежит индивидуальная чувствительность к эндотоксину. Часть матерей погибает, другая часть остается в живых, но у них происходит выкидыш, несколько животных донашивает и рождает здоровых детенышей. 5) Предварительное выявление толерантности к эндотоксину с помощью ТОЛЕРИНА (детоксцированный облучением эндотоксин) спасло от гибели значительную часть как матерей, так и плодов.

Pulmonary Metastasis of Colorectal Tumours

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A total of 21 metastases manifesting only in the lungs were observed during the follow-up of 510 colorectal tumour patients. The general aspects of the surgical solution of pulmonary metastases are reviewed and, based on the data of the patients operated by the authors and that of the literature, the possibilities and expected results of the surgical treatment of pulmonary metastases of colorectal tumours patients are discussed in detail.

The surgical solution of metastases is suggested in carefully selected cases.

Assessment and management of metastases are one of the most difficult and also most debated fields of tumour therapy. The initial fundamental principle that in a secondary tumorous manifestation there is practically no possibility for curative treatment, is still valid.

Similar to metastases manifesting in other sites of the organism, the assessment of lung metastases, too, is affected by numerous factors. Malignant extrapulmonary tumours metastasize during their natural course in 35–45% in the lung [6, 15, 20]. The highly extensive pulmonary capillary network and the similarly rich lymphatic network, being also connected with the cervical and abdominal lymphatic systems, predispose to metastasis formation.

The majority of lung metastases is haematogenous (of caval type), the smaller part is due to lymphogenous invasion [15, 23]. Direct local invasion is essentially less frequent, in some cases—very rarely—also transpleural or bronchial invasion, may occur [15].

Based on pathological data, the frequency of pulmonary metastases, depending on the site and morphological type, is as follows: testicular, melanoma, chorionic carcinoma, bone tumours, breast, cephalocervical, kidney, colon [2, 10].

Solitary, nodular metastases, the multiple nodular miliary form, reticular and mixed types of metastases can be differentiated [2, 11, 15]. The haematogenous lung metastases appear on the X-ray as solitary or multiple circular densities. Lymphangitis carcinomatosa can be visualized as a reticular density characteristic of interstitial processes.

They occur in the inferior lobe in 37% of lung metastases, while in the superior lobe in 21% [6, 14].

The biological course of metastasis formation is well known in pathology [14, 15, 20]. The biological behaviour of metastases, the aggressivity of the tumour, the degree of malignancy can be made more plausible by several parameters which can, at the same time, be of use in selecting the method and course of treatment and assessing its effectivity [2, 5, 8, 9, 11]. The changes in size of the tumour or metastasis can be most simply characterized by the temporary changes of their volume, which are expressed by the following parameters.

1. *Doubling time (DT)*. It means the time period expressed in days, during which the volume of the examined tumour doubles;
2. *Halving time (HT)*. It is the reverse of the above.
3. *Stationary phase*. It indicates the time period during which the size of the tumour does not change.

Based on comparative X-rays and ultrasonograms, six types can be differentiated depending on whether metastases grow or diminish or possibly remain unchanged [11, 12, 13].

Type I. Growth of the metastasis is continuous;

Type II. Permanent growth stops in some metastases, a stationary phase ensues, occasionally with regression (but it is less than 50% of the volume of metastasis);

Type III. The metastasis decreases in size, this exceeding even 50% of the original volume;

Type IV. Concurrence of types II and III in the same patient;

Type V. All metastases disappear;

Type VI. Adjacent to the growth of one metastasis, the diminishing of the other can be noted [11, 12, 13].

It is known how the pulmonary metastases of tumour of various origin respond to the currently used combined chemotherapy, i.e. to which group they can be classified [11].

Table 1 clearly shows that colorectal carcinomas, bone sarcomas, tumours of the soft parts, melanomas, metastases of renal origin, metastases of thyroid cancers can only be moderately influenced by chemotherapy while those of breast cancer respond well, and testicular metastases fairly well, to medication [11, 12, 13].

In lung metastases responding poorly or hardly at all to adjuvant therapy, only surgical treatment can be expected to help. It is also necessary to remove the residues of metastases responding well and showing considerable regression, because they give rise, after suspension of chemotherapy, to new metastases [12, 13, 22].

TABLE I

Tumour	Type of change in size						Total
	I	II	III	IV	V	VI	
Colorectal	9	6	—	—	—	—	15
Osteosarcoma	12	—	—	1	—	—	13
Soft part sarcoma	18	9	1	—	—	—	28
Malignant melanoma	14	6	—	1	—	—	21
Mammary	22	42	32	8	11	1	116
Testicular	2	9	14	5	44	11	85
Renal	28	12	4	—	—	1	45
Thyroid	24	3	—	—	—	—	27
Total	129	87	51	15	55	13	350

Based on empirical experience, a crucial point in selecting patients for surgery is to know their so-called doubling time (DT). Metastases of a DT of 40 days or less grow very rapidly, then, according to the 40-day increase of the DT index, rapid, moderately rapid, slow and very slow growth rhythm can be established. The degree of malignancy of metastases of a very rapid DT index (of 40 days) is high therefore, they mostly cannot be surgically solved [11, 14, 17]. In general, those metastases are appropriate for surgery which have a DT index of over 40 days.

An important factor is the time elapsed from the development of the primary tumour to the appearance of metastases, i.e. the so-called 'free interval'. The longer it is the better results can be expected [11, 14, 17, 23].

In summary, theoretically those lung metastases are operable with relatively promising results which (i) appear after a long free interval, (ii) their doubling time is long, at least over 40 days, (iii) there is a possibility of adjuvant treatment and (iv) they are solitary or appear in small number.

It is to be noted that the influence of the absolute number of removed metastases on the outcome is only secondary. According to some authors, there is no significant difference between the number of removed metastases and the results in survival rate [7, 8, 14, 17, 18, 21, 25].

Naturally, there are also preconditions for metastasectomy:

1. The primary tumour should be controlled (without any recurrence).
2. Metastasis should be present only in the organ to be operated (in our case, only in the lung).
3. The patient's cardiopulmonary condition should enable thoracotomy.

In patients previously operated for tumour, the actual possibility should also be entertained that the circular density appearing in the lung is not necessarily a metastasis! The circular pulmonary opacities in patients of a

history of tumour are actually metastases with a 70% probability but, particularly in case of a longer free interval it could be a second primary tumour, i.e., bronchus carcinoma. However, also benign clinical pictures, like hamartochondroma, cyst, tuberculoma, etc., may also occur [10]. Transthoracal needle biopsy can help in differentiating them.

Based on the above principles, surgical interventions are performed in an ever increasing number even in pulmonary metastases all over the world. To get a clearer insight, Table 2 gives a summary of the ever accumulating data from home and abroad [4, 5, 14, 18, 21, 23, 26, 28].

It reveals the primary causes of lung metastases to be operated on — according to their order of frequency — to be as follows: cephalocervical in 17.6%, colorectal in 13.8%, hypernephroma in 11.8%, mammary in 11.1%, gynaecological in 9.9%, testicular in 7.6%, osteosarcoma in 6.2%, synovial sarcoma in 3.8% and occult in 4.9%.

As already mentioned, survival is basically defined by doubling time, the free interval and the number of metastases. The postoperative survival of metastases of a DT below 40 days is 15–20 months that over 40 days is, on

TABLE 2

Primary tumour	1	2	3	4	5	6	7	8	9	n	%
Mammary	34	10	3	28	9	1	30	27	2	144	11.1
Gynaecological	17	2	3	17	9	—	63	17	2	130	9.9
Testicular	32	5	9	7	14	—	—	6	28	100	7.7
Hypernephroma	32	15	7	34	28	2	27	9	—	154	11.8
Wilms + bladder tumour	7	—	2	—	5	—	—	—	1	15	1.1
Cephalocervical	7	—	18	—	—	4	38	151	1	229	17.6
Lung, heart, thymus	12	—	—	—	—	—	—	27	—	39	3.0
Gastric	1	—	—	—	2	1	—	5	—	9	0.6
Liver, bile pancreas	2	2	—	—	2	1	—	3	1	11	1.1
Thyroid	3	3	—	—	—	—	—	—	1	7	0.55
Melanoma	8	7	3	8	9	—	—	5	0	42	3.1
Colorectal	16	11	13	20	35	3	51	25	7	180	13.8
Osteogenic sarcoma	28	2	15	28	4	14	9	2	—	78	6.02
Synovial	14	—	—	—	6	—	—	—	1	21	3.8
Malignant fibrous histiocytoma	10	—	—	—	8	—	—	—	7	25	1.3
Rhabdomyosarcoma, leiomyosarcoma, liposarcoma, Ewing, other	18	—	—	—	8	—	—	—	3	29	1.8
Occult	—	8	14	15	11	3	—	—	2	53	4.09
Total	253	65	87	157	142	35	228	277	56	1300	100.0

1. Vogt-Moykopf I, 2. Csekeő-Kulka, 3 Van de Wal, 4. Swoboda, 5. Wilkins, 6. Salsari, 7. Moun-tain, 8. Cahan, 9. Own

average, 44 months [3, 7, 24, 25, 26]. Survival after a solitary metastasis averages 27 months, that after multiple ones 19 months [3, 7, 24, 25, 26].

Since the frequency of colorectal tumours shows an ever increasing tendency in Hungary, it is worth dealing with the treatment of the lung metastases of patients suffering from this basic disease.

Material

In the past 10 years a total of 510 patients were operated because of colorectal tumours.

In postoperative follow-up pulmonary metastases were observed in 36 cases (6.8%). In 22 of them metastasis involved only the lung, in 14 cases the pulmonary manifestation represented part of an excessive tumour metastasis.

In 15 patients—because of their poor general condition, advanced age, etc.—operation could not be considered; they received chemotherapy (5-FU + Adriamycin). Based on the radiological follow-up, by which the results of drug treatment can be estimated, 9 patients were classified as type I and 6 as type II [11] (see Table 1). These patients could not essentially be brought into remission by adjuvant therapy. The free interval of these patients averaged 23.5 months (min. 7, max. 36). On average, 15.8 months elapsed from the appearance of lung metastasis to death (min. 6, max. 30).

Three patients were operated. In one case the lung operation preceded that of the tumour of the colon, in one instance, in synchronously occurring tumours, first the colonic operation was performed followed, 5 months later, by removal of the pulmonary metastasis. In 5 patients following colonic tumour operation pulmonary metastasectomy was made after a free interval of 14, 16, 34, 37 and 72 months. In one case 3, on one occasion 2, and in 4 cases solitary unilateral metastases were operated. In one patient one unilateral metastasis and 2 metastases from the contralateral side were removed in one session.

Presently, all 7 patients are alive. The patients operated following a free interval of 14, 34, 37 and 72 months are tumour-free 8, 15, 1 and 39 months postoperatively. Our patient operated after a free interval of 16 months has been surviving for 12 months with a contralateral multiple pulmonary metastasis. The patient with the synchronous tumour has been surviving 12 months after metastasectomy with a contralateral multiple metastasis, while the patient operated in a sequence of metastasectomy and colonic resection, has now been surviving for 20 months also with contralateral multiple pulmonary metastases.

Discussion

The surgical solution of the pulmonary metastases of patients operated for colorectal tumour involves several problems. The tumorous recurrence or metastasis following remission appears in the majority of cases as a part of dissemination and so offers no possibility for curative reintervention [3, 16]. Based on overall statistics, it can be stated that during the pulmonary manifestation of colorectal tumour patients, altogether 8% undergoes operation, in 64% these are partial phenomena of an excessive dissemination, in the remaining cases other conditions of thoracotomy are not present [4, 16, 27].

The pulmonary metastasis is due, in two-thirds of colorectal tumours, to sigmoid and rectal, in one-third to primary tumours localized in other regions of the colon [3, 4].

Based on reports, in cases where the tumour-free interval is shorter than two years, the survival time following metastasectomy is 19–28 months, while where this exceeds two years, it is 30–48 months [3, 4, 7, 23, 24]. Independent of all parameters, a 2-year survival after metastasis operations of colorectal origin can be expected in 70% and a 5-year one in 25% [3, 7, 23, 24].

Since pulmonary metastases are not necessarily associated with clinical symptoms (dyspnoea, cyanosis, sputum)—the so-called general symptoms (lack of appetite, anaemia, loss of weight) are more frequent—control plays the major role in the early detection of metastases [2, 5]. Considering the slow doubling time, a half yearly check-up seems to be sufficient.

In screening of metastatic patients, CEA tests may also be of help. Elevated values were found in all of the observed 35 patients.

If in a patient operated for colonic tumour the control reveals a pulmonary density of densities, our tasks are summarized as follows:

1. The patient is subjected to a detailed examination finding out whether the pulmonary metastasis is part of the dissemination or of solitary localization.

2. It should be checked whether there is no local primary tumour recurrence.

3. Some authors perform a second-look laparotomy to exclude dissemination [26].

4. If metastasis is only confined to the lung and the primary tumour is controlled:

- a. Chest X-ray and CT for defining the number and site of metastasis.
- b. Bronchoscopy, due to peripheral localization, is negative in most cases.
- c. Transthoracic needle biopsy can offer a preoperative proof in assessment of the metastasis—the primary lung tumour—(its performance is not essential).

If, in view of what has been said, the metastasis can be removed, as far as surgical technique is concerned, and the patient's cardiorespiratory state and endurance make it possible, the operation is indicated. Some authors operated only after an observation period of 4–6 weeks, screening thereby the metastatic cases of a DT index below 40 days, that is of a very rapid growth since their surgical treatment is not too promising [23, 24].

The question of what kind of operation is to be performed and from what kind of exploration can be outlined on the basis of data of a large patient material.

Resection should by all means be economical, i.e., a lung portion as small as possible should be removed (atypical resection, segmental resection, lobectomy). We believe that a metastasis removable only by pneumonectomy can be described as inoperable. Our view is supported by the observation that, in cases of pulmonary metastases believed to be unilateral by CT, MR and plain X-ray there is already a not yet detected contralateral metastasis simultaneously with the operation (!!!) in 20–25% [23, 24]. The metastasis having actually proved to be unilateral but assumed to be solitary appears to be multiple in a similar proportion during exploration [23, 24, 25]. Some authors consider it important to remove also the primary lymphatics and lymph nodes belonging to the metastasis [10, 20], although the secondary lymphogenic invasion of metastases is inconsiderable [20]. These factors account for the attempt to prevent simultaneous bilateral exploration (from transverse sternotomy or longitudinal sternotomy) the so-called 'secondary inoperability', i.e., not even the undetected metastases remain [23, 24, 25]. Since the pulmonary

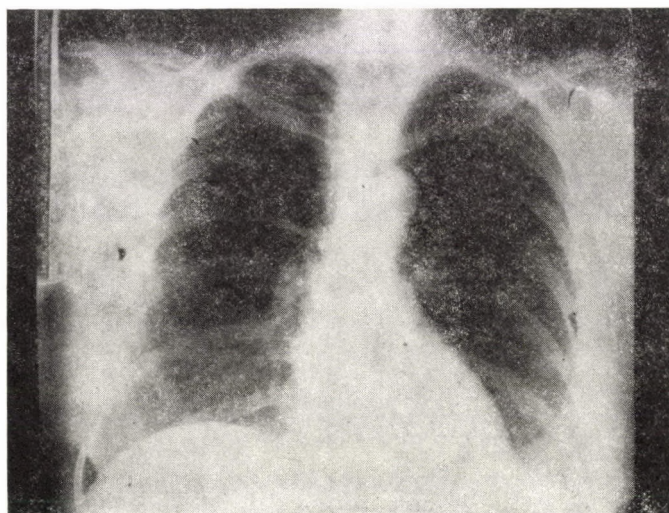
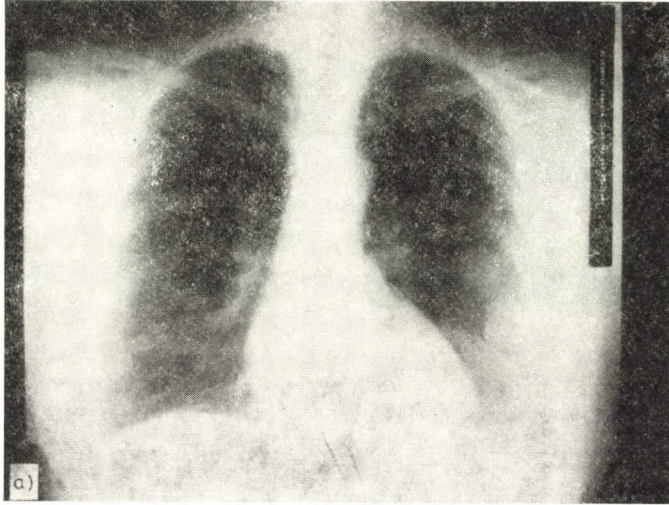


FIG. 1

metastases of colorectal tumour patients hardly respond to adjuvant treatment (chemotherapy), the supplementary drug treatment is not generally accepted even after surgical metastasectomy [23, 24, 25].



FIGS 2a, b

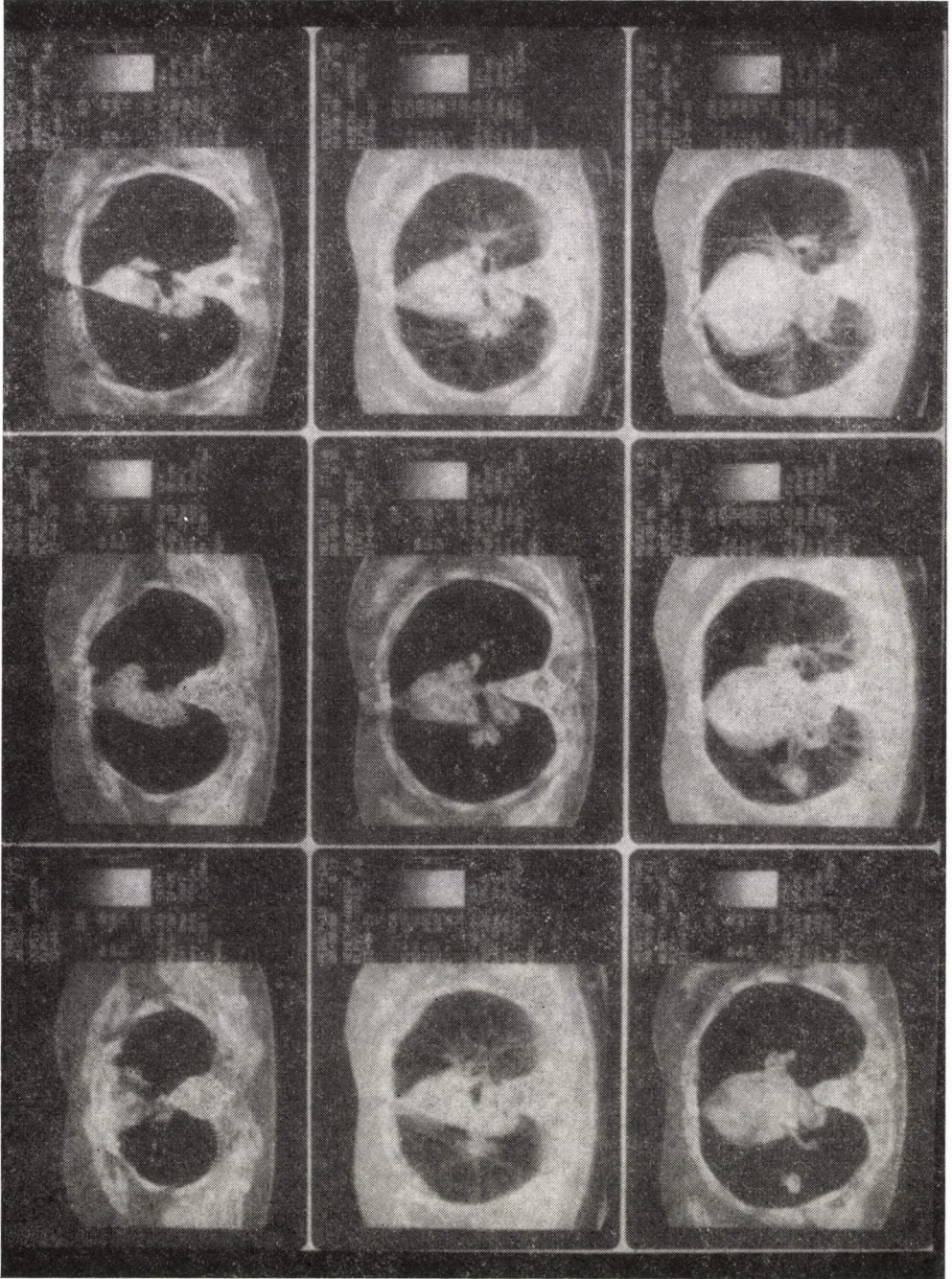


Fig. 3



FIG. 4

In the case of synchronous occurrence, the surgical solution of the primary tumour should be given preference. After 2–3 months, if there is no further dissemination, also pulmonary metastasectomy can be performed. For illustration, the documents of the history of one of our patients is reviewed.

X-ray taken 37 months following right hemicolectomy (Fig. 1): a left double and an uncertain right solitary metastasis were assumed. There was no evidence of dissemination elsewhere. He received chemotherapy in six series (5-FU+Adriamycin). Despite treatment, the left metastases, though very slowly, kept on growing, the uncertain right opacity seemed to be no metastasis. At this time, i.e., 8 months after the first positive roentgenogram, a second one followed (Fig. 2a, b). Then surgical solution was decided upon and for assessing the obscure contralateral opacity CT was performed with negative result. This is shown in Fig. 3. In view of the above, exploration was made from median sternotomy during which 2, 1–15 cm metastases were removed from the left inferior lobe, but, despite the negative CT, a metastasis, 1 cm in diameter, was found in the right inferior lobe as well. Healing was uneventful. Figure 4 was taken directly in the postoperative state. Histology verified an adenocarcinoma metastasis.

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Über die pulmonalen Metastasen kolorektaler Tumoren

I. KÖVES, GY. LISZKA, I. BESZNYÁK und L. TÓTH

Im Laufe der Follow-up-Untersuchung von 510, an einem kolorektalen Tumor leidenden Patienten war in 21 Fällen, eine sich nur in der Lunge manifestierte Metastase zu beobachten. Nach Überblickung der allgemeinen Fragen der chirurgischen Lösung der pulmonalen Metastase werden anhand der Daten der eigenen operierten 8 Patienten und der Literatur die Möglichkeiten der chirurgischen Behandlung und die voraussichtlichen Ergebnisse der chirurgischen Behandlung der pulmonalen Metastasen der an kolorektalem Tumor leidenden Patienten überblickt. In sorgfältig ausgewählten Fällen wird die chirurgische Lösung der Metastasen empfohlen.

О легочных метастазах коло ректальных опухолей

И. КЕВЕШ, ДЬ. ЛИСКА, И. БЕСНЯК, Л. ТОТ

В связи с наблюдением за 510 больными с колоректальной опухолью авторы только в 21 случае отметили проявившиеся в легких метастазы. Они рассматривают общие вопросы, связанные с хирургическим разрешением легочных метастазов, и подробно обсуждают, основываясь на данных 8 оперированных ими больных и литературных данных, возможности оперативного лечения пульмональных метастазов у больных с колоректальными опухолями, а также ожидаемые результаты.

A Case of Funicular Schwannoma

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(Received: March 30, 1979)

A case of schwannoma in a 55-year-old male patient is reviewed.

The diagnostic difficulties are pointed out in view of the literature. Currently, it is still difficult to form a diagnosis without operation either by physical examination or by other diagnostic procedures. That is the authors' point in reviewing their case. The castrated patient has been well and free of complaints for 5 years after operation with no recurrence.

The tumours of the peripheral neurones are called schwannomas after their origin from the Schwann cells. Neurilemmoma is also a synonymous term. In general, it is a benign, solid, encapsulated tumour of regular surface, being rubber-like on palpation. Its cut surface is homogeneous and pale in colour. Microscopically, there are cells arranged in a palisadic pattern with characteristic cigarette-like nuclei arranged parallelly. The cells of malignant schwannoma are markedly atypical. In the presence of mesenchymal cells it is termed neurofibroma [1].

Schwannoma is most often intracranial, originating primarily in the vestibular region. Of 304 schwannoma patients, Gupta et al. [6] found a change in 150 cases in the cephalocervical region. It frequently occurs also in the orbital and nasal cavities. In a part of the cases it is not solid, but can appear simultaneously in several peripheral nerves (Recklinghausen's neurofibromatosis).

Schwannoma develops in the urogenital tract very rarely. That is why we consider our case worth to be presented.

Case Report

The 55-year-old male patient was admitted in February 1984, because of a mass having persisted for half a year, palpable in the scrotum. Physical examination revealed both testicles to be intact. Directly above the left testicle a hard egg-sized node, 6 by 4 by 3 cm, was palpated. Changes were disclosed neither by additional physical examinations nor by the laboratory results (tumour markers) nor by urography. Exploration was decided upon.

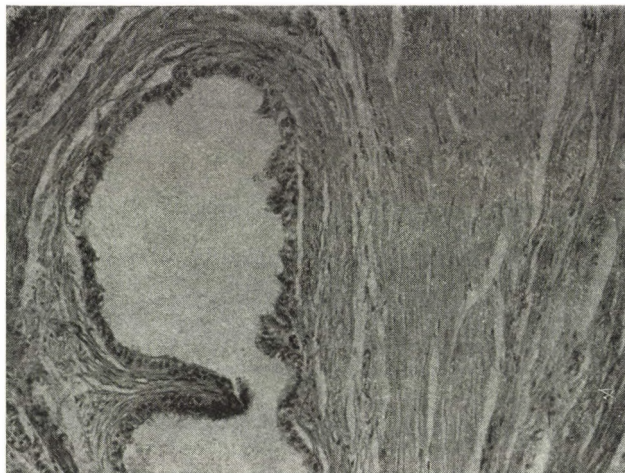


FIG. 1

Cutting on the tumour, the cut surface appeared to be malignant, therefore castration was performed. The histological study revealed no change in the testicle. In the sections prepared from the tumour, longitudinal and cross-sections of peripheral neural fibres arranged in bundles were seen. The cells were found to correspond to mature Schwann cells. Neither necrosis and haemorrhage nor mitoses occurred (Fig. 1).

The patient is in a good condition 5 years postoperatively, he is free of complaints without any recurrences.

Hard nodes in or associated with the testicle always raise the possibility of malignant tumours [7] which may occur in all age groups [13]. Ultrasonography has recently improved the possibility of their diagnosis, but a final, precise diagnosis can be expected solely of exploration [16].

The urologist rarely encounters schwannoma. Retroperitoneal schwannomas were reported by Miller [10], Niforsi et al. [11], scrotal ones by Doldurov [5], penile by Marsidi and Winter [14], paravesical ones by Rössler and juxta-adrenal schwannomas by Denes et al. [3] and Oliver et al. [12]. Shoda et al. [15] operated a retroperitoneal tumour of 260 g in a male patient, aged 40, having raised the suspicion of an adrenal tumour based on ultrasonography, CT and angiography. Histology revealed it to be a schwannoma.

One similar case, published by Corredera-Zambrene [2] has been found in the literature of the recent ten years.

The treatment of benign schwannoma is surgical, the disease does not require any aftercare [2]. This happened also in our case. In the malignant form of the disease, results can be expected of radiotherapy [8].

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Darstellung eines Falles mit «Funikulus-Schwannom»

I. ROMICS und K. SIMON

Im dargestellten fall handelt es sich um einen 55 jährigen Patienten, der an einem seltenen Krankheitsbild, dem «Funikulus-Schwannom» litt.

Im Spiegel der Literaturdaten werden die diagnostischen Schwierigkeiten erläutert. Ohne Operation ist die Diagnostizierung sowohl mit physikalischer als auch mit sonstigen diagnostischen Verfahren schwierig. Deshalb schien die Darstellung des Falles interessant zu sein. Der kastrierte Patient befindet sich 5 Jahre nach der Operation in gutem Allgemeinzustand, er ist beschwerdefrei, auf ein Rezidiv weisende Zeichen meldeten sich nicht.

Случай шванномы семенного канатика

И. РОМИЧ и К. ШИМОН

Авторы описывают случай редко встречающейся шванномы у 55-летнего мужчины.

На основании данных литературы указывают на диагностические трудности этого заболевания. Как физикальным обследованием, так и другими диагностическими методами и сегодня еще трудно поставить диагноз без проведения операции. Поэтому авторы считают полезным ознакомить с собственным наблюдением. Кастрированный больной спустя пять лет после операции хорошо себя чувствует, рецидива нет.

EMASH

The European Medical Association for Smoking or Health (EMASH) has been established, presided over by Professor Paul Freoun (Bordeaux, France). The objectives of the Association include promotion of an activity for the prevention and stopping of smoking, dissemination and exchange of information on the deleterious effect of smoking and on its prevention, the support and propagation of non-smoking behaviour and, first of all, transformation of the public attitude on smoking exemplified by physicians and health workers.

The foundation of EMASH has emerged from the realization that smoking, being the most important health risk which *can be avoided*, has its own impacts on both West and East. Physicians and health workers in all countries of Europe are equally concerned with avoiding it. Propagation of the successful methods, a favourable influencing of the social and governmental attitudes towards the smoking epidemic by a mutual attempt, can be more successful by having information on, and helping, each other.

As a first step EMASH calls upon joining the Smoking or Health Charter of Physicians or Health Workers. The Charter is going to be sent to every physician by the National Committee on Health Protection.

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Evaluation of Preoperative Hospitalization Duration in Skin Flora

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The skin microbial flora of 18 patients was evaluated during prolonged preoperative hospital stay. Five cultures for bacteria and fungi were obtained on different days: on admission one, three and seven days after admission and after skin disinfection with povidone-iodine solution. There was no change in the mean bacterial count from the admission day to seven days after admission. All but one culture obtained following skin disinfection were negative. Pathogenic bacteria were isolated in only one of each of the following culture day: admission, three and seven days after admission. All cultures were negative for yeasts. The findings suggest that the higher rate of wound sepsis observed in patients with long preoperative hospitalization may not be due to bacterial flora change.

Postoperative wound infection rate is dependent on several factors, including the age and associated illness of the patient, duration of operation and contamination of wound at operation [2, 7]. Higher wound infection rate has also been reported in patients with long preoperative hospital stay [2, 4, 6]. Some authors have suggested that the increase of wound infection rate in this group of patients is due to an invasion of the patient's skin by pathogenic bacteria during hospital stay [2, 6]. Others have interpreted that this increase might be related to the type of illness, age of the patient and the presence of associated disease that require longer preoperative preparation and evaluation [4, 7].

The influence of preoperative hospital duration on skin flora has not yet been evaluated. Only a few clinical studies have addressed this issue [2, 4]. The objective of the present study is to evaluate the skin microbial flora during prolonged preoperative hospitalization and to determine the efficacy of skin disinfection at the end of this period.

Material and Methods

A total of 18 patients of either sex was subjected to five abdominal skin cultures on different days. Culture 1 was obtained on the admission day, culture 2, one day after admission; culture 3, three days after admission; culture 4,

seven days after admission; culture 5, seven days after admission, following skin disinfection for 5 minutes with povidone-iodine solution and rinsing with sterile normal saline solution. All patients were admitted to a general surgical ward and were on preoperative preparation with iodine for thyroidectomy. No patient received antibiotics, steroids or immunosuppressive drugs during the hospitalization period or the previous week.

All culture samples were obtained from the epigastrium skin at the midline. For each sample, a skin area was delineated by a sterile glass cylinder of 4 cm in diameter that was firmly pressed to the skin with a sterilized gloved hand. Two millilitres of sterile 0.1% Triton X-100 with 0.1% sodium sulphite was poured into the cylinder and the delineated skin scrubbed with moderate pressure for one minute employing a small pestle. The wash fluid was then aspirated, diluted in triplicate and cultured in blood agar, MacConkey Agar and Blood agar with phenyl-ethylic alcohol. After 48 hours of aerobic incubation at 37 °C, the bacteria were identified and counted. Identification was made by usual biochemical methods. Cultures for yeasts in Sabouraud medium were also made and incubated at 37 °C for 96 hours. The data were submitted to statistical analysis employing regression analysis.

Results

The mean bacterial counts of the skin samples obtained from the admission day to seven days after admission are shown in Table 1. There was no change in the number of bacteria during the seven days of hospitalization.

TABLE 1
Mean bacterial count of abdominal skin during hospitalization

Bacterial Count	Hospitalization Time				
	day 0	day 1	day 3	day 7	after skin disinfection
Mean	238.5	120.1	86.1	170.1	0.5*
S.D.	338.0	268.3	255.3	530.0	2.4

* Indicates that this value is significantly different from the values on the left columns, $p < 0.01$.

All cultures obtained following skin disinfection were negative, except one that grew ten colonies of *Staphylococcus epidermidis*. All Sabouraud cultures were negative for yeasts.

The bacteria identified from the skin cultures during patient hospitalization are shown in Table 2. The predominant bacteria isolated were *Staphylococcus epidermidis*, *Micrococcus* sp. and *Corynebacterium* sp. Pathogenic bacteria

TABLE 2
Number of positive cultures per bacteria isolated from abdominal skin during hospitalization

Bacteria	Hospitalization time				
	day 0	day 1	day 3	day 7	after skin disinfection
<i>S. epidermidis</i>	18	18	18	18	1
<i>Micrococcus sp.</i>	12	13	13	14	—
<i>Corynebacterium sp.</i>	6	4	3	5	—
<i>S. aureus</i>	1	—	1	—	—
<i>E. coli</i>	—	—	—	1	—
Others	4	5	3	7	—

were isolated only in three cultures: one on the admission day, one three days after admission and one seven days after admission, preceding skin disinfection with povidone-iodine.

Discussion

Selection of an adequate method to determine skin flora is very important. Selwyn and Ellis [9] have demonstrated that the excision biopsy procedures have given the highest possible yield. The second best method was the cylinder-scrub technique which was employed in the present study, that gives an about 15% bacterial yield when performed consistently by the same investigator [9]. All the other possible methods, apart from rigorous standardized swabbing, give very poor results for quantitative determinations [8].

Several authors have reported a high wound infection rate in patients with prolonged preoperative hospital stay [2, 6]. Jepsen et al. and Cruse and Foord have suggested that this elevated infection rate may be due to a colonization of the patient's skin during the hospitalization by pathogenic bacteria [2, 6]. Based on this assumption it has been recommended always to bring preoperative hospital stay to a minimum [2].

Another explanation for the relationship between high wound infection rate and prolonged preoperative hospitalization could be the age and the diseases of these patients that require long preoperative preparation and evaluation and might render them more susceptible to wound infection. This is exemplified by patients that are subjected to colorectal operations and need a long preoperative hospital stay for bowel preparation. Hasselgren et al. [4, 5] reported that 85% of their patients with wound sepsis after prolonged preoperative hospitalization had three or more other factors associated with high infection rate. No patient had prolonged preoperative hospitalization as the only factor associated with high infection rate. In addition, they noted

that high age, long operative procedures, potentially contaminated and contaminated operations and treatment with steroids were significantly more common in patients with prolonged preoperative hospitalization. It has also been observed that there was no difference in wound infection rate when the same surgical procedure was performed after different days of hospital admission [5].

In the present study, it was demonstrated that there is no change in mean bacterial count or the bacterial flora of the skin during hospitalization from the admission to seven days after admission. In addition, skin disinfection with a potent antiseptic solution is effective in removing all bacteria from the operative site of most patients. Therefore, possible changes in skin bacterial flora during hospitalization would be effectively treated by adequate preoperative skin preparation. These findings support the concept that the higher rate of wound sepsis observed in patients with long preoperative hospitalization may not be due to bacterial flora change.

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Über die Wirkung der präoperativen Hospitalisationszeit auf die Hautflora

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Die Mikrobenflora der Haut von 18 Patienten wurde im Laufe einer langen präoperativen Hospitalisationszeit untersucht. An verschiedenen Tagen, bei der Aufnahme sowie 1, 3 und 7 Tage nach der Aufnahme wurden nach einer Desinfektion mit einer Povidon-Jod-Lösung 5 Bakterien- und Pilzzüchtungen vorgenommen. Betreffs der

durchschnittlichen Bakterienzahl gab es keine Differenzen zwischen dem Aufnahmetag und dem 7. Tag. Nach der Hautdesinfektion waren sämtliche Züchtungen, mit einer Ausnahme — negativ. Pathogene Bakterien waren in Einzelfällen nur an einem der in der Folge angeführten Tagen — am Aufnahmetag, sowie 3 bzw. 7 Tage nach der Aufnahme — zu isolieren. Hefepilze ließen sich nicht vorfinden. All dies weist darauf hin, daß die höhere Häufigkeitsproportion der Sepsis bei den seit langer Zeit hospitalisierten Patienten nicht mit der Änderung der Bakteriumflora zusammenhängt.

Влияние времени госпитализации перед операцией на кожную флору

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Была исследована микробная флора кожи 18 больных в период длительного нахождения в больнице перед операцией. Произвели посевы культур 5 видов бактерий и грибов в разные дни: после приема в стационар, через один, три и семь дней после приема, и после обработки кожи обеззараживающим раствором повидонйода. Между средним числом бактерий разницы не наблюдалось с первого дня и до седьмого после приема. Все культуры, за исключением одной, после обеззараживания кожи были негативными. В одиночных случаях были выделены и патогенные бактерии в один из следующих дней: при приеме, а также спустя три и семь дней после приема. Дрожжевые бактерии обнаружены не были. Все эти результаты указывают на то, что у больных с большой давностью госпитализации более высокая частота встречаемости сепсиса не связана с изменением бактериальной флоры.

Oxygen-derived free radical reactions in Experimental Acute Pancreatitis of the Dog

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Acute edematous and necrotic pancreatitis have been induced in dogs with retrogradely intraductal injections of 5% hydrogen peroxide solution and sunflower-oil. The process of disease could be followed daily by a zipper sutured into the abdominal wound. In this manner the temporal changes of markers of oxygen-derived free radicals (concentrations of malondialdehyde and reduced glutathione of the excised pancreas tissue and abdominal exudate, as well as the superoxide dismutase content of the tissue) could be controlled. Light microscopic analysis was also done. In edematous pancreatitis reversible membrane lesions, in the necrotic form the irreversible damage of membranes and cells could be seen. The results obtained suggest the role of oxygen-derived free radicals in experimental acute pancreatitis.

Introduction

Recently the incidence of acute pancreatitis shows an upward tendency, e.g. in the haemorrhagic-necrotic form the mortality rate may reach 85% [16]. In the majority of cases, effective causal therapy is not available. Improvement can only be expected from increasing pathological and pathophysiological knowledge of the disease. This purpose has not yet been reached despite the new achievements in this field of research.

The pathomechanism of acute pancreatitis is not exactly clear yet [1, 13, 18–19, 30, 37, 40, 42].

Recently, the cytotoxic effect of oxygen-derived free radicals and their possible role in cellular and tissue damage have been described and investigated extensively [4, 8–9, 20–21, 27]. Firstly, Sanfey et al. [34–36], later Guice et al. [14] have presumed that oxygen-derived free radicals play a role in the forming of acute pancreatitis because allopurinol and endogenous scavengers (superoxide dismutase and catalase) had favourable effects. Allopurinol decreases the hypoxanthine-xanthine transformation and thus the accumulation of free radicals. Superoxide dismutase and catalase are also able to scavenge the oxygen-derived free radicals.

Nevertheless, there is no direct evidence whether and how the free radicals play a role in the development of acute pancreatitis. It seems to be obvious that oxygen-derived free radicals can attack various membrane structures of

the cell, activating the digestive enzymes and lysosomal hydrolases and causing a severe increase of membrane permeability, leading to subsequent irreversible membrane lesions.

Until now, studies have attempted to prove the aetiological role of oxygen-derived free radicals only indirectly from the side of therapeutic effects. In our present study we examined [1] whether acute pancreatitis may be produced through intraductally injected hydrogen peroxide which behaves as oxygen-derived free radical, and [2] what pathological events appear in comparison to the previously described edematous and necrotizing pancreatitis induced by sunflower-oil [8, 17, 24].

Materials and Methods

Experimental Induction of Acute Pancreatitis

Twenty-two female mongrel dogs weighing between 11 and 30 kg (mean weight: 17.4 kg) were used. After Droperidol (1.5 mg/kg), Fentanyl (0.03 mg/kg), Atropin (0.025 mg/kg) premedication, the animals were narcotized with sodium-hexobarbital (20–40 mg/kg). Endotracheal ventilation was maintained by a mixture of $N_2O:O_2$ in a ratio 3:1, if necessary by 0.5–1% of halothane. Under sterile conditions through a midline upper abdominal incision 1 g of pancreas tissue was excised for biochemical examinations. Then, in the angle of the duodenum and pancreas the duct of Santorini (which is the main pancreatic duct of the dog) was prepared. The duct was ligated at the side of the bowel, then cannulated and within half a minute either a solution of 5% hydrogen peroxide or sunflower-oil or saline was retrogradely injected and finally the duct was ligated.

As to the retrograde injection, it should be noted that the proposed pressure of 30 to 37 mm Hg [6–7, 10–11, 29] was insufficient to fill up the ductal system. More than 120 mm Hg had to be applied. This observation is identical with experience of others [2–3, 12, 25].

The dogs were divided into four experimental groups depending on the material injected: Group I (5 animals): 0.35 ml/kg sunflower-oil; Group II (8 animals): 0.5 ml/kg sunflower-oil; Group III (5 animals): 0.4 ml/kg 5% solution of H_2O_2 ; Group IV (4 animals): 0.6 ml/kg saline; the latter served as control group.

At the end of the operation a sterile zipper was sutured into the laparotomy wound (Fig. 1). Around the zipper penicillin powder was scattered and sterile small towel was fixed to the skin in order to prevent wound infection.

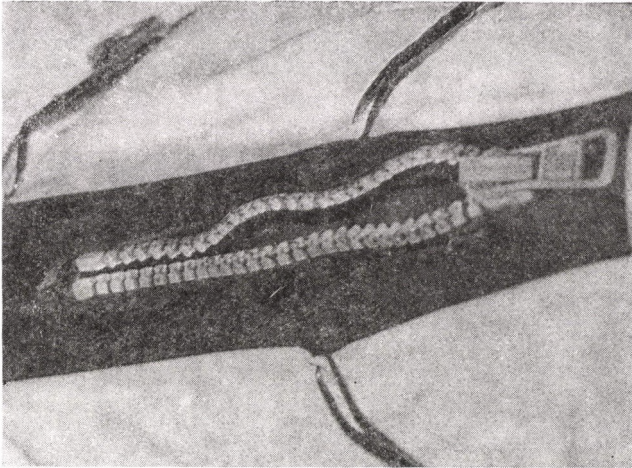


FIG. 1. Zipper sutured into the laparotomy wound

Observation of the Course of the Disease

Blood samples were drawn preoperatively, at the end of operation and 3 hours after injection. If a sufficient amount of the exudate was formed during the operation, then samples were also obtained from it. On each postoperative day the zipper was reopened under sterile conditions in a short intravenous narcosis. Inspection, excision of the pancreas and obtaining of exudate and blood samples were done. Only infusion, analgetics and penicillin were given to the dogs.

The fate of the dogs was mostly followed for 7 days. If they remained in good general condition, the zipper was excised and the abdominal wall was closed. If a grave infection of the abdominal cavity was observed, they were sacrificed.

The following laboratory determinations were made from the tissue and blood samples:

From the blood samples: amylase by the Phadebas method [5]; thio-barbituric acid (TBA) reactive materials, mainly malondialdehyde (MDA) by the method of Placer [28]; reduced glutathione (GSH) by the modified Sedlak method [38].

From tissues: MDA and GSH. Moreover, superoxide dismutase (SOD) by the method of Misra and Fridovich [23].

From exudate: amylase, MDA and GSH.

A part of the tissues were embedded in paraffin, stained with haematoxylin-eosin for light microscopic examinations. Paired *t*-test was used for statistical analysis.

Results

Morphological Alterations

Through the applied methods we were able to induce pancreatitis which was characteristic of the whole group.

In Group III, on the first day after the operation a medium-degree edematous pancreatitis could already be observed with scattered peripancreatic adipose tissue necrosis and significant production of exudate. Whereas in Group I edema of high degree and many small focal necroses were found. Animals of Group III survived and one animal died in Group I on the third day.

The most severe alterations were found in Group II. Already, at the end of the operation a significant edema developed in the area of the pancreas and on the next day a mass of bloody exudate and extensive adipose tissue and parenchymal necrosis were found. Seven out of eight animals died on the 2nd-3rd day after operation.

It is noteworthy that in control Group IV, only mild edema developed and occasionally a little exudate occurred; all the animals survived.

Table 1 summarizes both the severity of pancreatitis and the extensiveness of the necrotic area in all the groups.

TABLE 1

	Scale of severity	Area of necrosis
Group I	+++	30-35
Group II	++++	90-95
Group III	++	2-5
Group IV	+	0

+ only mild edematous signs; ++ severe edema, moderate accumulation of leucocytes; +++ numerous necrotic cells; ++++ total necrosis

Biochemical Examinations (Figs 2-4)

The blood amylase level acutely increased in all cases, to the greatest extent in Group III, moderately in Group IV. The earliest maximal increase was found in Group II (3 hours after the operation). From the 2nd-3rd day the amylase content began to return to the original level in all groups. Amylase concentration of exudates was always higher than that of the blood. The increase and decrease of blood amylase level show no correlation with the

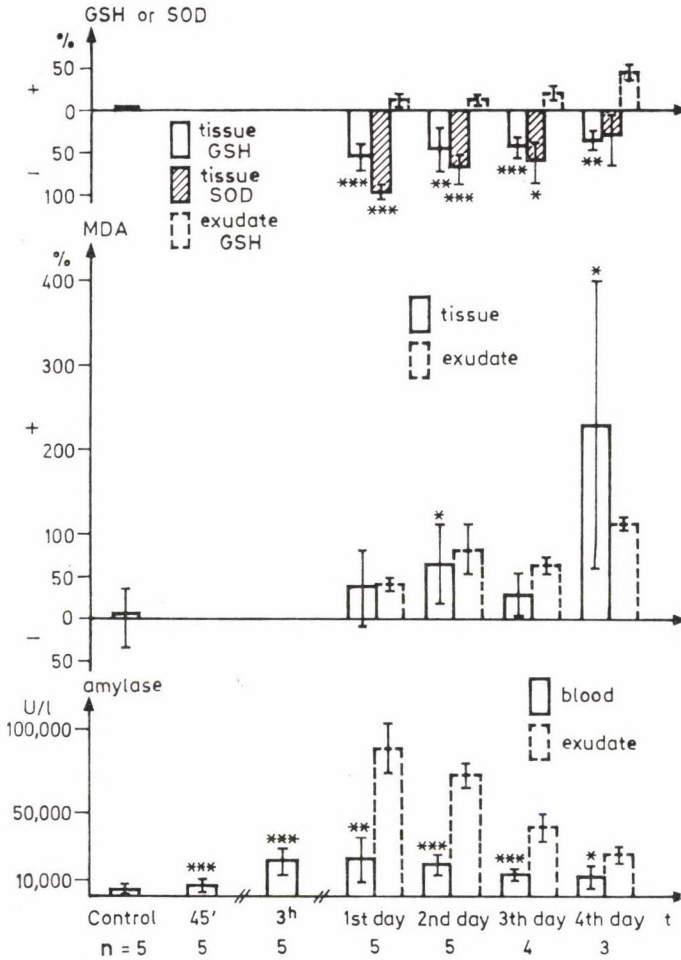


FIG. 2. Changes of biochemical parameters in Group I. Alterations of tissue GSH, SOD and MDA contents in comparison to the normal, expressed in per cent deviation. The MDA and GSH content of the exudate cannot be compared to normal values for lack of data, for this reason 1.0 OD/g value was considered to be 100% at the representation. n = number of cases; * - 0.02 < p < 0.05; ** - 0.01 < p < 0.02; *** - 0.001 < p < 0.01

severity of inflammation. After some days nearly normal levels could be found in some cases despite the severe alterations described [39].

The contents of MDA and GSH did not change in the blood.

The tissue MDA increased especially in Group II but not in Group IV. In Groups I and III, it remained at a relatively higher level. The decrease of tissue GSH and SOD was temporary in Group III and considerable in Group II. In Group I the GSH and SOD contents increased again, but did

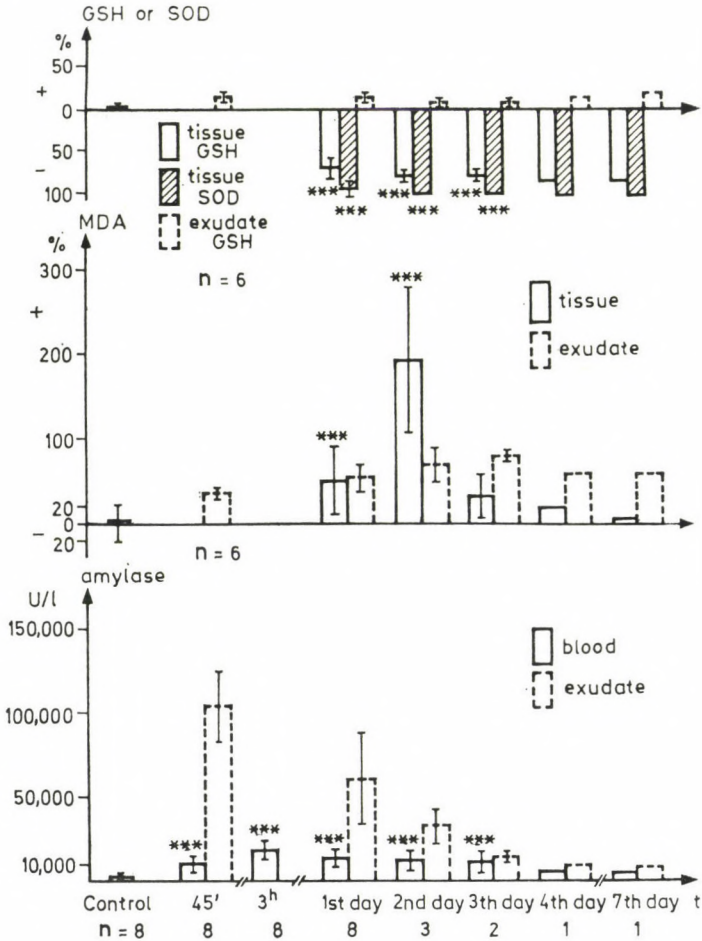


FIG. 3. Changes of biochemical parameters in Group II (For Explanation see Fig. 2)

not reach the original level. In Group IV these parameters did not change significantly.

The changes in the MDA content of the exudate showed parallelism with that in the tissue, but they were always less. The highest levels were found in Groups I and III. The GSH concentration of the exudate was low in all cases. We cannot refer to the presence or alteration of SOD, because the massive occurrence of blood and cellular debris in the exudate made the measurements uncertain.

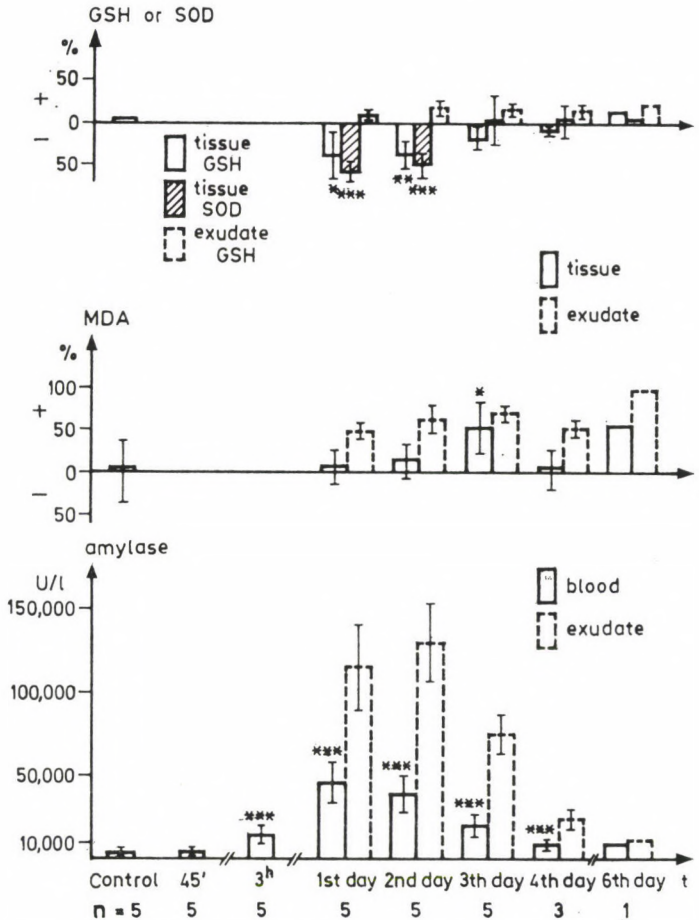


FIG. 4. Changes of biochemical parameters in Group III (For explanation see Fig. 2)

Discussion

On the basis of literary data and our original work, it can be suggested that the free oxygen radicals play some role in the pathomechanism of acute pancreatitis, which seems to be important and/or they can unfavourably influence the induced tissue damage processes. For methodological reasons, our experiments could not provide direct evidence whether the production of free radicals had been the primary cause of pathological alterations, we only succeeded in verifying that the applied H_2O_2 , which also appears as oxygen-derived free radical, is suitable for inducing pancreatitis. On the other hand, the results verify that the MDA, which is one of the degradation products of

polyunsaturated fatty acids formed from the membrane system, shows a regular increase in the course of experimental inflammation. At the same time, the level of SOD, which is a ubiquitous scavenger enzyme and the concentration of GSH which is also an available scavenger thiol compound, decrease. The data refer to the possible role of oxygen-derived free radicals.

The daily changes of tissue biochemical markers require explanation. In the case of acute pancreatitis induced by H_2O_2 solution a moderate gradual increase of the MDA content can be noted. To understand the events, it has to be taken into account that a part of the MDA is shifted to the exudate. On the other hand, a "healing phase" follows the acute processes with a decrease in edema and an improvement of local blood-flow. GSH temporarily diminishes, then returns to the initial level. The level of SOD shows similar alterations. These data indicate that temporary membrane damages occur, nevertheless, the locally available and "transported" scavenger compounds are able to mitigate the aggression of peroxidative materials which behave as "free radicals".

In the case of pancreatitis induced by sunflower-oil, probably different events are observable. Damage of cellular elements and membrane systems is very profound; lower sunflower-oil doses cause similar pancreatitis seen after H_2O_2 injection, MDA increases, however, more perpetually, GSH and SOD hardly decrease. Applying higher doses, the rise of MDA is very significant. From the third day on an apparent decrease can be found, which has an alternative explanation. A few of the animals perished, thus pathognomonic measurable data were not available. Moreover, the process of necrosis in the surviving animals is advanced, accordingly a "characteristic" structural material excised from the pancreatic tissue from which MDA would have been originated, is not present any more because of the total necrosis. Increased diminution of GSH and nearly complete disappearance of SOD are unambiguous.

All these indirect data suggest that in the course of acute pancreatitis the oxygen-derived free radicals may play a certain role. The pathomechanism is not completely clear [15, 22, 26, 32, 41]. In severe cases, where extensive microcirculatory disorders have to be reckoned with, the explanation is relatively easy. In ischaemic-hypoxic tissues univalent reduction of molecular oxygen continuously induces the production of free radicals, which — attacking the lipid structures of membranes — inhibit DNA synthesis, inactivate the SH groups of membrane-bound enzymes, and damage the lysosome releasing enzymes which commit "cellular suicide" (lipases, hydrolases, proteases, beta-glucuronidase, etc.). Explanation is more difficult in cases of edematous pancreatitis, where probably no durable blood-flow disorder is present, although the acute edema may limit the microcirculation in circumscribed areas and can produce local hypoxia. Perhaps this can explain the changes of biochemical markers of tissues excised in a random way. Since not only the local enzyme-

system, but also other defensive compounds in the microcirculatory system are available for tissue protection, the reversal of the decrease of the GSH and SOD contents can gain a real explanation. On the other hand, mainly at the boundaries of the inflammatory or necrotized tissue and the intact or healing areas, the infiltration of leukocytes has to be taken into account by which the presence of radical reactions is evident [31]. This theory has been confirmed by Guice and Sanfey [14, 36], i.e. the application of some scavengers (SOD, catalase, allopurinol) had protective effects. At any rate, the pathogenetic role of free radicals is not completely clarified. Controversies exist in the evaluation of scavenger effect. It seems to be without doubt that the scavenger compounds reduce the edema formation but hardly alter other features of severe pancreatitis [33]. To reconcile the divergences and to extend our findings, further experiments with artificial scavengers are going on.

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Charakterisierung der experimentellen akuten Pankreatitis im Spiegel der Reaktionen der freien Sauerstoff-Wurzeln

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Bei Hunden wurde durch retrograde Injizierung einer 5%igen Hydrogenperoxyd-Lösung und Speiseöl akute ödematöse und nekrotische Pankreatitis herbeigeführt. Mit Hilfe eines in die laparotomische Öffnung eingenähten Reißverschlusses wurde der Krankheitsverlauf täglich registriert. Kontrolliert wurden die chronologischen Änderungen der Marker der Reaktionen der freien Sauerstoff-Wurzeln, Malondialdehyd- und Glutathionkonzentration des exzidierten Pankreasgewebes und des Bauchhöhlenexsudats sowie der Superoxyd-Dismutase-Gehalt in den Geweben, außerdem fand auch lichtmikroskopische Analyse statt. Bei ödematöser Pankreatitis läßt sich eine reversible Membranläsion beobachten, bei den nekrotischen Formen weist die Änderung der biochemischen Marker auf eine definitive, irreversible Membran- und Zellschädigung. Die ermittelten Ergebnisse scheinen die akzessorische Rolle der freien Sauerstoffwurzeln bei experimenteller akuter Pankreatitis zu verwahrscheinlichen.

Характеристика экспериментального острого панкреатита в зеркале свободных кислородных радикалов

Д. КЕЛЕМЕН и Б. ТЁРЁК

Авторы вызывали у собак острый отечный и некротический панкреатит ретроградным интрадуктальным введением 5% раствора перекиси водорода и растительного масла. Вшитая после лапаратомии в отверстие молния позволяла ежедневно проследивать течение болезни. При этом контролировали изменения во времени маркеров свободных кислородных радикалов (концентрация малондиальдегида и глутатиона в эксцидированной панкреатической ткани и в экссудате брюшной полости, в также содержание суперокисной димутазы в тканях), делали также анализ под световым микроскопом. При отечном панкреатите наблюдается обратимое повреждение мембраны, при некротической форме изменение биохимических маркеров указывает на дефинитивное необратимое повреждение мембраны, или же клетки. Полученные результаты позволяют думать о добавочной роли, которую играют свободные кислородные радикалы в экспериментальном остром панкреатите.

Preserved Tendon Grafts in Reconstructive Hand Surgery: a Review

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The authors discuss the use of tendon grafts, primarily in flexor tendon repair, a problem not yet satisfactorily resolved. Criteria for successful non-autogenous tendon grafts are presented, with interest focussing on the immunologic antigenicity of the grafts and the physiologic properties and processes of tendon regeneration. Methods for preserving tendon grafts, including freeze-drying and the use of various chemical agents, are compared and recommended, as well as methods for managing tendon grafting procedures. Questions remaining to be answered in the area of preserved tendon grafts are raised, with suggestions for some answers and avenues for future research. Possibilities for wider clinical applications of the procedure are supported and discussed as well.

Restoration of the flexor tendon system after tendon injury within the digital sheath still remains a major problem in hand surgery. For digits that are classified pre-operatively as being in poor condition [5], that is, badly scarred, having residual joint stiffness, or with severe bone and soft tissue damage [7], the outcome after repair is disappointing; this applies as well to reconstruction for salvage of a failed flexor tendon repair. Single-stage reconstructive techniques are lacking for the treatment of these injuries, and the most widespread method available and accepted is a staged flexor tendon reconstruction [6, 7, 11–14, 16, 37, 38, 40, 41, 53].

There are numerous methods described in the literature for staged flexor tendon reconstruction, all of which require the use of a free graft that is usually a free autologous tendon graft; an obvious consequence of using autogenous tendon as a transplant is loss of function in the donor unit. Fortunately, there are various sources for tendon grafting that are not critical for function, and their use does not significantly affect the donor site.

The palmaris longus and plantaris tendon are often utilized, although not consistently [20, 43]. The extensor tendon of the third toe or the extensor indicis proprius are also available. Nevertheless, the most notable disadvantage of these tendon grafts is the mechanical difference between these tendons and the flexor tendons [19, 31]. In addition, the supply of expandable autogenous tendons is limited, and their utilization involves prolonged operating time.

Solutions to the problems mentioned have involved two main approaches: 1) the use of artificial tendons to replace damaged flexor tendons; and 2) the use of homo- or heterograft, with or without preservation.

Synthetic tendon prostheses have expanded the scope of tendon surgery. The active gliding prosthesis developed by Hunter and Jaeger is a suitable method for flexor tendon reconstruction, but still requires a tendon graft in a second stage [22–24]. There have been other promising attempts to develop permanent tendon implants [27], but more detailed studies are necessary for wider clinical applications. Further studies of synthetic implants have involved experimenting with new materials similar to tendon tissue; however, despite a few encouraging results, no such material is currently available [18].

The other approach to replacing a severely damaged tendon involves the use of some type of homo- or heterologous tendon graft. The concept of applying non-autogenous tendon graft has persisted in the literature since 1882 [4]. In the last 30 years, there have been many reports about the application of various forms of homo- or heterograft. These have been mainly experimental, but there are a few reports of clinical applications of these grafts as well [1–3, 8, 10, 17, 21, 25, 26, 28–31, 34, 36–38, 42, 44, 45, 48–52].

Any non-autogenous tendon graft used in reconstructive hand surgery must satisfy the criteria established by McMaster and colleagues [31]: the applied graft should be neither antigenic nor carcinogenic; it should be easily incorporated by the host and should function for the lifetime of the host; it must simulate the mechanical properties of the original part; and it should be easily stored and implantable.

A primary question in transplanting homologous or heterologous tendon graft concerns the immunologic antigenicity of these tendons. Tendon tissue is a relatively hypocellular structure [13, 32] containing mostly mature collagen. Although there is little doubt that soluble collagen may be species-specific and possess an antigenic character, most data prove that insoluble mature collagen is not antigenic [31, 37, 38, 48]. Peacock and co-workers indicated that collagen can be considered a freely transplantable material, and that transplantation is possible without significant immunologic reactions [35]. Several authors have described lymphocyte infiltration and enlargement of regional lymph nodes, caused by the donor cells, but the antigenicity of these cells does not appear great enough to induce a second-set rejection [29, 38, 48–52]. Moreover, the antigenicity of donor cells may be reduced by immunoreactive management [33, 49].

Another consideration is the incorporation of a non-autogenic tendon graft by the host. There is no doubt that a homo- or heterologous tendon graft may serve only as a trellis for tendon regeneration [3, 37, 38]. There appears to be little consensus about the fate of a fresh homograft: Ashley and others [1–3] have suggested that fresh homografts undergo necrosis and fragmenta-

tion, while Peacock and his followers have used unpreserved human grafts one day following a patient's death, with successful results [17, 21, 36, 38].

Descriptions of other properties and outcomes of transplanting non-autologous graft are similar throughout the literature, and there are few significant differences noted in reports of tendon grafts preserved by various methods [2, 8, 10, 29, 34, 48, 49, 51].

After one week, the grafts appear edematous and thickened, and microscopically reveal infiltration by polymorphonuclear leukocytes and lymphocytes. The nuclei of the grafted segments disappear or their staining is paler. Collagen structure seems almost normal. After three weeks, leukocyte and lymphocyte infiltration decrease, fibroblastic activity originating from the surrounding tissue increases, and capillary proliferation can be seen, especially at the tendon junctions.

The collagen fibres of the grafted tendon appear to be continuous with the fibres of the host tendon, and some tenocyte-like cells are present in the grafted tendon. After three months, the grafted tendon is microscopically and macroscopically similar to the normal tendon, except that the amount of tenocytes is less than in normal tendon, and focal infiltration of lymphocytes is still present. After six months and one year, the appearance of grafted and normal tendon is very similar, and microscopically almost indistinguishable [51].

The previously described healing process in a non-autogenous tendon graft is very similar to an autologous graft [39, 40], except that the former seems slower and is accompanied by a decreasing infiltration of leukocytes [29, 51]. Re-cellularization takes place from both ends of the graft and the surrounding tissue as well. It is not clear whether the original collagen structure of the graft remains intact or is rebuilt, partially or totally, by the host [28, 29, 37, 38, 40, 46, 47].

Transplantation of a non-autogenous tendon graft can be carried out either with or without preservation. Although Peacock described successful transplantation of homologous composite tendon grafts stored at 4 °C, this method has numerous disadvantages. Harvesting of the grafts must be done in the operating room, under the same conditions as any other operative procedure, and the risk of contamination is higher than with the use of other preservation methods.

A freezing-drying technique will eliminate most of these disadvantages: storing a freeze-dried graft is quite simple; storage time is unlimited; and utilization of these grafts is relatively easy [8, 42, 52]. The main disadvantage is the high cost of this procedure.

There are various ways of preserving tendon grafts using chemical agents. One of the most common methods of preservation is the use of a mercurial solution, Cialit [25, 26]. Other authors prefer the use of beta-proprilacton

[28, 46, 48, 51]. Additional experimental methods have been described, such as preservation in alcohol, formalin vapour, and other materials [1, 10, 45]. Recently, preservation of a tendon graft with the chemical agent glutaraldehyde meets almost all the criteria mentioned above [9, 31, 49, 50]. The use of X-ray irradiation has similar effects, but is not as inexpensive [23, 45, 46].

All preservation methods utilizing chemical agents provide good sterility, ease of storage, and are inexpensive. In addition, some agents have the added advantage of diminishing transplant antigenicity. Currently, it is unclear whether the focal lymphocyte infiltration is caused by the antigenicity of the graft, or is a late result of the preservation method used.

Preserved grafts must also fulfil certain mechanical criteria [43]. Recent studies have shown that the tensile strength of grafts preserved in glutaraldehyde or freeze-dried is similar to that of autogenous tendon grafts [31, 52]. Unfortunately, the anastomosis between the host and the preserved graft was found to be weaker in the first three weeks than with the use of an autograft; however, greater similarities subsequently appeared [52]. This suggests that when using preserved grafts in clinical application, more intensive postoperative physiotherapy might positively affect the tensile strength of such preserved grafts.

In addition, all of the experimental data and some clinical observation have indicated that a preserved graft can function in the host, similarly to an autograft, although with the preserved graft, scar formation around the tendon anastomoses is greater than with the autograft [2, 10, 31, 42, 50–52].

Although there have been numerous encouraging experimental attempts to use preserved tendon grafts, clinical applications have remained limited, predominantly to Europe and Asia. Iselin, Jozsa, Liu, and Salamon [25, 26, 28, 30] have reported the clinical use of preserved tendon graft, with good results comparable to the transplantation of autologous tendon. Peacock, Furlow, and Hueston have also described good results, using homologous composite tendon grafts for salvage of badly damaged digits. The latter results are especially promising, as the methods used assure the transplantation of an intact gliding surface as well, and provide the possibility for a one-stage reconstruction [11, 29, 50].

Impediments for general clinical use of the technique are socio-ethical in some parts of the world [9], but using heterologous grafts, as is done in other medical procedures [15], might obviate socio-ethical objections.

Although further experimental studies are necessary, it appears that the homologous graft is a useful procedure. Grafts can be taken from fresh cadavers, maintaining the criteria mentioned above. Although most of the preservation methods provide simultaneous sterilization, it is not recommended that donors with histories of hepatitis, syphilis, AIDS, or cancer be used. With

some preservation methods, such as beta-propiolacton or Merthiolate, routine bacteriologic cultures must be done later.

It seems most unlikely that a tendon prosthesis will be found to meet all the criteria described. Still, all available information establishes that the use of a homologous tendon graft can be clinically applicable and may be a useful substitute for an autograft [25, 29, 37, 41, 49–51]. A tendon homograft is applicable not only for flexor tendon reconstruction, but for other areas of reconstructive hand surgery such as ligaments or pulleys [9].

In summary, the authors believe that the tendon homograft is a useful technique, comparable to others, in reconstructive hand surgery of selected cases. Through its use, the arsenal of the hand surgeon is enlarged. Further investigations are necessary to provide answers to questions that remain: for example, whether a heterograft can be found that can promote the development of a "bioprosthesis". This would indeed be applicable to a large range of clinical problems that currently exist in reconstructive hand surgery.

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Verwendungsmöglichkeiten der konservierten Sehne in der Handchirurgie. Literarischer Überblick

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Die Verwendungsmöglichkeiten der konservierten Sehne werden mit besonderer Rücksicht auf die Wiederherstellung der Beugungssehne — auf ein bis heute noch nicht definitiv gelöstes Gebiet — überblickt. Beschrieben werden die gegenüber dem Konservin gestellten Anforderungen, besonders die Fragen der Antigenezität und es wird auch der Prozeß der Sehnenregeneration im Falle einer konservierten Sehne beschrieben. Die verschiedenen Konservierungsverfahren — Lyophilisation, verschiedene chemische Methoden — werden verglichen und die Kriterien der Behandlung der Konservsehnen besprochen. Im Rahmen der Erläuterung der Verwendungsmöglichkeiten der Konservsehnen, werden zahlreiche, weitere Forschungen beanspruchenden Fragen berührt. Für die Zukunft wird eine weitläufigere Anwendung der Konservsehnen empfohlen.

Возможности применения консервированного сухожилия в хирургии

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Авторы рассматривают возможности применения консервированного сухожилия, особенно в области восстановления сгибающего сухожилия — в области, проблемы которой нельзя считать полностью разрешенными. Знакомят с требованиями, предъявляемыми к консервированному сухожилию, выдвигая на первый план вопросы антигенности, и описывают процесс регенерации в случае консервированного сухожилия. Сравнивают различные методы консервирования, как, например, высушивание в замороженном виде, и различные химические методики, обсуждают критерии обработки консервированных сухожилий. Затрагивают вопросы возможности использования консервированных сухожилий, а также поднимают многие вопросы, которые требуют проведения дальнейших исследований. Авторы рекомендуют в будущем более широко применять консервированные сухожилия.

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“Second-Look” Operations in Patients with Colorectal Tumour

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The diagnostic problems of metastases and recurrences in colorectal tumour patients are reviewed. The question and indications of relaparotomies are discussed in detail. The results of relaparotomies made for tumorous and nontumorous indications at the Department of Surgery of the National Cancer Institute are reported.

In tumour surgery recovery is verified only by the time factor. There may be a possibility of recurrence or metastasis formation even after the seemingly most radical operation. The attending physician thus cannot be sure about recovery for years. It is well known that metastasis and recurrence appear in 80% of the cases within a period of two years [4, 11, 22], as also that recurrences can be found in 15 to 50% of the cases following seemingly curative operations [3, 6, 19, 20, 24]. There are controversial opinions as to the second operation: according to the various authors operability is estimated at 8 to 60% [2, 7, 8, 9, 13, 18, 24].

Solution to the question how recurrence or metastasis formation can be detected as early as possible has been sought for years. The patient's recovery or the prolongation of his survival can only be secured by the early detection and removal of recurrences or metastases. A procedure was developed by Gilbertsen and Wagensteen as early as in 1948, which was called second-look programme. Some time after radical operations made because of colorectal tumour according to a schedule, a second operation was also made. Thus 10% of relaparotomized patients could be cured. Based on this, the introduction of the second-look programme into tumour surgery was suggested. This proposal has caused many debates, and second-look operations performed according to a programme have not become extensively used in tumour surgery for various reasons.

Solutions are invariably being sought by oncology for the early detection of recurrences and metastases. In this field some progress has been made by learning about and regularly examining tumour markers. It was established that the elevation of the CEA value may call attention to the presence of a

recurrence or metastasis. In such a case the patient must be thoroughly examined and in the case of tumour operation can be indicated [21]. Difficulties may occur if the CEA value is increased, however, the result of the examination is negative. The question is whether it suffices to observe the patient very carefully or the relaparotomy should also be performed [17, 20]. The confidence level of CEA tests is, according to various authors, 50 to 70%. This can partly be attributed to the diversity of examination methods and partly to the fact that it is not sure that such an amount of antigens is aromatized by the metastasis that it would be detectable.

In view of this single information, it is difficult to recommend an operation. The position of the attending physician is facilitated also by computed tomography (CT), sonography (US) and the endoscopic examinations.

Recurrences and metastases, could be detected by CT also in relatively early cases. Naturally, neither this examination is 100% safe. False-positive results can be particularly found in assessing lymph node metastases. In rectal carcinoma, the appearance of local recurrence is estimated at 12 to 18% by the literature [10]. On suspicion of recurrence based on the clinical symptoms, the recurrent tumour is in general large, reaching a diameter of 3 cm. Already an even smaller, that is 1.5 cm tumour, can be detected by CT. By this method the tumour recurrence, when invasion into the neighbouring organs is still not verifiable, is estimated as being of a degree of severity of 1. In a 2/a-degree of severity, this can already be detected and in degree 2/b the tumour invades also the bony wall of the pelvis. In degree 3 local recurrences are also associated with distant metastases [16]. On the basis of the literature, CT is indicated within three months of the operation for establishing the status [23]. Control examinations must be performed more frequently mostly in the first two years, because about 70% of local recurrences appear during this time [12]. According to our present knowledge, CEA tests are more sensitive for local recurrences than CT.

Often it is not enough to perform CT for establishing a safe diagnosis, but it is also necessary to carry out needle-biopsy under sonographic control. The diagnostic value of this method is fairly good in liver metastases, its sensitivity and specificity range between 88 to 89 and 93 to 94%, respectively [1, 5, 14].

By CT studies, first of all intraabdominal metastases can be detected. Concerning the patient's control, they are to be preferred to X-rays because they do not expose the patient to radiation. According to overall data of the literature, the confidence level of the method ranges between wide limits, i.e. 75 to 90%. This is due to the fact that diagnostic possibilities are not equally good in the individual abdominal regions. The best results can be achieved in the metastases of the lumbar chain of retroperitoneal lymph nodes, while in the iliac regions these values are by about 10% more modest [15].

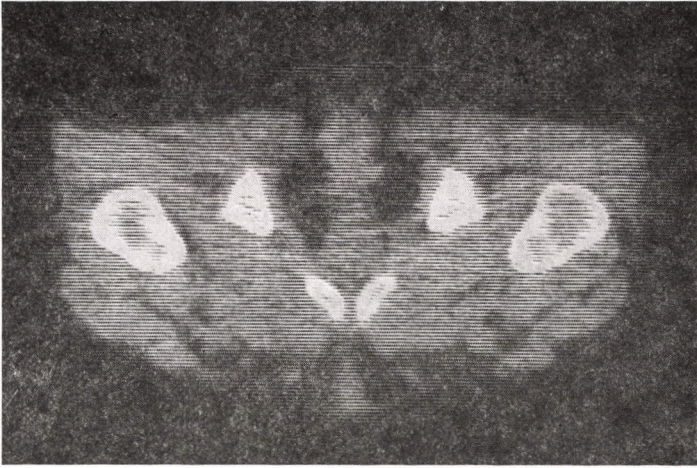


FIG. 1. CT scan of local (sacral) recurrence

Diagnostic problems arise because the enlarged lymph node detected by the examination is not always a metastasis.

The same is true to the opposite: small metastases, still not changing the size of lymph nodes can be assessed to be negative by sonography. The sonographic scan of an enlarged lymph node can also be obtained if the closely arranged lymph nodes of normal size are visualized by the sonograph as an enlarged structure, because the minor lymph nodes are below the resolution capacity of the equipment (Figs 1, 2).

The regular endoscopic examination helps in detecting local recurrences and reoperation can be made. In our department patients having undergone colorectal operations for tumour are regularly controlled at half-year intervals by endoscopic examination.

During endoscopy, either biopsy or cytological study can provide accurate data on the presence of recurrence or metachronous tumour. The value of biopsy and cytology should be emphasized, because the macroscopic picture does not always yield a reliable result due to the anatomical deformation. It would be ideal if all patients operated for tumour could be regularly controlled by CT and sonography.

Special attention should be paid to the questions of the liver metastases of colorectal tumours.

In the case of liver metastasis, further management is determined by whether there is any other tumour propagation in the organism, or where and in what number the changes occur in the liver. For detection of liver metastasis, laboratory tests, CT, sonography, liver scintigraphy and occasionally angiography are of benefit (Figs 3, 4, 5, 6).

In concert with the views of several authors, of the laboratory tests, primarily CEA, alkaline phosphatase and the sonographic liver function tests may raise the suspicion of liver metastases. CT may, however, give a more

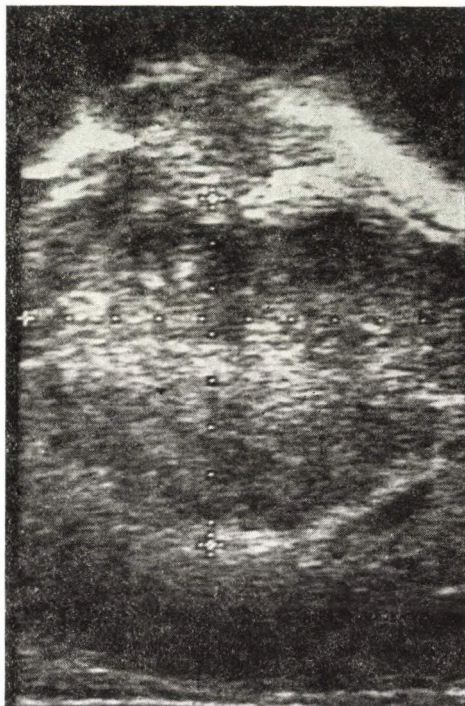


FIG. 2. Sonographic scan of retroperitoneal lymph node

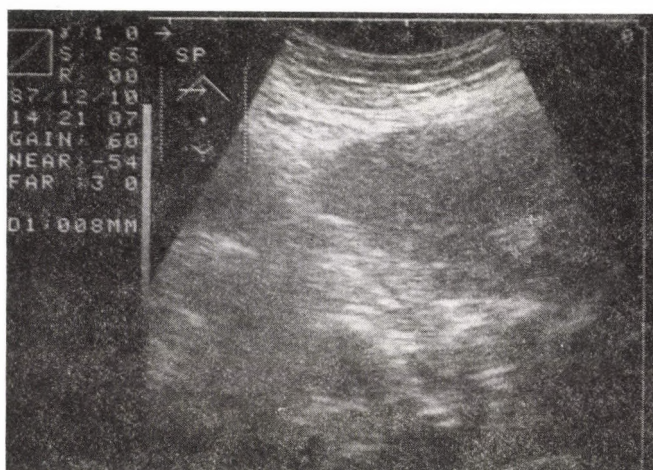


FIG. 3. Sonographic scan of liver metastasis

reliable diagnosis and this can also be promoted by liver scintigraphy. In the case of solitary metastases or those involving one lobe, relaparotomy should be performed. In multiple metastases involving both lobes, actually there is no question of radical operation. In these cases, however, the introduction of a Porth-A-Cath cannula for local chemotherapy can be useful. If tumour metastases occur also elsewhere (the retroperitoneum or lymph nodes, etc.), then even the introduction of the cannula seems to be superfluous.

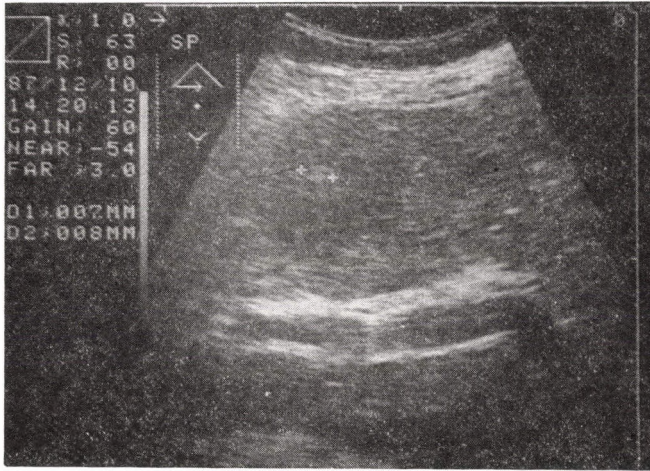


FIG. 4. Ultrasonogram of liver metastasis

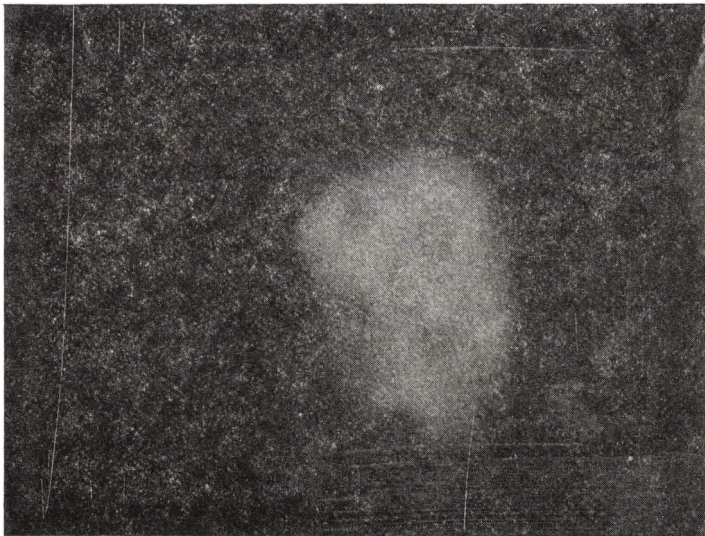


FIG. 5. Scintiscan of liver metastasis (AP view)

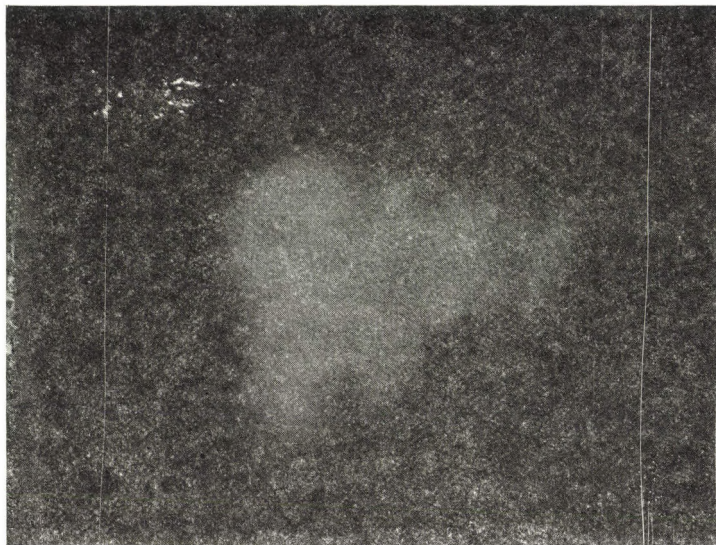


FIG. 6. Scintiscan of liver metastasis (lateral view)

Review of our Own Material

"Second-look" operations in colorectal tumour patients were made at the Department of Surgery of the National Cancer Institute during the 10 years between 1976 and 1986 in 97 cases, with non-tumorous indication in 25 cases (hernia, preternatural anus, obstruction, etc.) and with indication of tumour in 72 cases.

The CEA values of our 72 patients reoperated because of tumour were as follows: they were normal in 10 cases, elevated in the remaining ones, of

TABLE 1
Second-look operation for non-tumorous indication (n = 25)

Time elapsed between the first operation and reoperation	No. of cases	Negative	Operability	Inoperability
Less than				
1 year	12	10	1	1
2 years	4	4	—	—
3 years	4	3	—	1
5 years	4	4	—	—
7 years	1	1	—	—
Total no. of cases	25	22	1	2

In 3 out of the cases operated with non-tumorous indication (12%) tumour was found in 3 cases and they were inoperable. In 15 cases the operation was indicated by abdominal hernia, in 7 cases by preternatural anus and in 3 cases obstruction.

TABLE 2
Second-look operations with tumorous indication (n = 72)

Time elapsed between first operation and reoperation	No. of cases	Operable	Inoperable	Palliative	CEA false-neg.
Less than					
1 year	36±3	13	14	6	4
2 years	8	5	0	3	1
3 years	19±2	11	3	3	4
5 years	9	4	1	4	1
Total no. of cases	72	33	18	16	10

Completely tumour-free state was found on relaparotomy in ±5 cases.

which 5 were false-positive (no tumour was found). In 9 cases after the elevation of the CEA values the patients were examined and considered inoperable in 8 cases (disseminated liver or lung metastasis). In one case the CEA test was false-positive because no kind of tumorous change was detected by the examination (Tables 1, 2).

Discussion

The question of relaparotomy, as stated earlier, is not a matter of debate in the case of positive results. The question is, however, raised by the authors what is to be done in tumour surgery if the test results are uncertain: should a second-look operation be made according to programme? The examination has revealed suspicion of recurrence or metastasis: should relaparotomy be performed? What is to be done if there is a strongly increased CEA value, but clinical results are negative?

Based on our own results, our opinion is as follows. In the case of elevation of CEA values a detailed examination, in that of negative results, either very close observation or exploration should be made. With positive results, or a suspicion of recurrence or metastasis, relaparotomy of the patient should be made. One relaparotomy involves smaller risk for the patient than an occasional residual tumour.

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"Second-look"-Operationen bei an kolorektalem Tumor leidenden Patienten

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Die diagnostischen Probleme der Spätmetastasen und Rezidiven bei kolorektalen Patienten werden erläutert. Eine ausführliche Besprechung finden die Fragen und Indikationen der Relaparotomien. Bekanntgegeben werden die an der Chirurgischen Abteilung des Landesinstituts für Onkologie wegen tumoröser und nicht tumoröser Indikationen durchgeführten Relaparotomien und die ermittelten Ergebnisse.

«Second-Look» операции у больных с коло-ректальными опухолями

Л. МОЛНАР, И. КЁВЕШ, И. БЕСНЯК и ДЬ. ЛИСКА

Авторы знакомят с проблемами диагностики поздних метастазов и рецидивов у больных с коло-ректальными опухолями. Детализируют вопрос релапаротомий и показаний к ним. Приводят результаты, полученные в хирургическом отделении Государственного онкологического института в связи с повторными лапаротомиями, произведенными по поводу опухолей и в связи с другими показаниями.

Thoracic Surgery in the Elderly: Review of 100 Cases

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One hundred cases surgically intervened due to thoracic pathology between 1977 and 1986 were studied. The ages were equal to or higher than 70 years. Mean age was 73.13 years (70–91). In 70 cases a neoplastic aetiology existed (78.57% of primary bronchial carcinoma), while in the other 30 cases the cause was not neoplastic. In these cases with a high operative risk, a detailed systematic study before surgery is recommended, which should be treated in the most conservative possible way. Although the complication rate was higher than the average in other groups ($p < 0.05$), mortality was only 4%, being related, to a greater or lesser extent—, to the surgery ($p < 0.05$). In the cases diagnosed as bronchial carcinoma, a 2-year survival was obtained in 66.4%, 3 years in 49.8% and 5 years in 25.7%, concluding that an age equal to, or higher than, 70 years does not represent any contraindication for thoracic surgery.

Introduction

Surgery continues to represent the therapeutic method most useful for the treatment of bronchial cancer. In recent years, the feared barrier of 70 years, as an age limit to perform a thoracotomy, has been overcome by diverse groups, and we present here the revision of the problem in 100 patients.

It has been calculated in the United States that the life expectancy of one having reached 70 years of age as being 13.1 years, and for those of 80 years as 8.2 years, respectively. From this can be deduced that the most important limiting factor to be considered in these patients, when they are diagnosed as having bronchial carcinoma, is the tumor itself and not the age of the patient [1].

Materials and Methods

We revised the casuistics of the Thoracic Surgery Department of the Hospital Ramón and Cajal in Madrid, finding 100 patients with surgical operation, of ages equal to, or higher than, 70 years, between 1977 and 1986. The average age was 73.13 years with a range between 70 and 91 years. Twenty-six

TABLE 1
Neoplastic series (Group I)

	Cases	%
Bronchial carcinoma	55	78.57
Pulmonary metastasis	6	8.57
Thoracic wall tumours	4	5.71
Mediastinal tumours	3	4.28
Bronchial carcinoid	1	1.42
Condroid hamartoma	1	1.42

TABLE 2
Non-neoplastic series (Group II)

	Cases	%
Pulmonary hydatidosis	10	33.33
Pneumothorax with prolonged leak	7	23.33
Flail chest	5	16.66
Empyema	2	6.66
Interstitial lung disease	1	3.33
Tracheal amiloidosis	1	3.33
Myasthenia gravis	1	3.33
Rib infection	1	3.33
Bullous emphysema	1	3.33
Stab wound	1	3.33

patients were equal to or older than 75 years. There were 85 males and 15 females.

On 70 occasions, surgical intervention was made for an oncological cause (Group I) and in the remaining 30 cases for a non-oncological one (Group II). Among the causes analysed in Group I, the most frequent was bronchial carcinoma in 55 cases (epidermoid in 35, adenocarcinoma in 15 and undifferentiated of giant cells in 5), followed by pulmonary metastasis (3 due to adenocarcinoma of the rectum, 1 to breast cancer, 1 to thyroid gland cancer and 1 to a lower limb osteogenic sarcoma) (Table 1). In Group II pulmonary hydatidosis predominated, followed by spontaneous pneumothorax not resolved by conservative management (Table 2). It should be pointed out that 30 patients (42.85%) from Group I and 10 (33.3%) from Group II had some added pathology, mainly as COPD or gastroduodenal ulcer (Table 3).

The approach most frequently used in Group I was the posterolateral thoracotomy, the same as in Group II, but also in the latter axillar thoracotomy was used in an almost similar proportion (Table 4).

TABLE 3
Added pathology

	Group I		Group II	
	Cases	%	Cases	%
COPD	16	22.85	7	23.33
Gastroduodenal ulcer	7	10	4	13.33
Coronary insufficiency	4	5.71	2	6.66
Arterial hypertension	4	5.71	2	6.66
Cerebral haemorrhage	3	4.28	—	—
Depression	1	1.42	—	—
Dementia	—	—	1	3.33
Ulcerative colitis	1	1.42	—	—
Liver cirrhosis	1	1.42	1	3.33
Intermittent claudication	1	1.42	—	—

TABLE 4
Surgical approach

	Group I		Group II	
	Cases	%	Cases	%
Posterolateral thoracotomy	59	84.28	15	50
Axillary thoracotomy	7	10	13	43.33
Cervicotomy	3	4.28	1	3.33
Median sternotomy	1	1.42	1	3.33

In the cases diagnosed as bronchial carcinoma we performed 22 lobectomies (40%), 15 segmentectomies or wedge resections (27.27%) and 14 pneumonectomies (25.45%). Four patients were only explored after thoracotomy (7.27%). The pulmonary metastases were treated by lobectomy on two occasions and by segmentectomy or wedge resection in the remaining 4 cases. The carcinoid and the hamartoma were treated by wedge resection. Regarding the four tumours of the thoracic wall, two were extracted, being diagnosed as neurofibroma and osteochondroma, respectively. In the other two cases (metastasis of a liver carcinoma and metastasis of a breast cancer) only a biopsy was performed. Of the 3 tumours of the mediastinum, 2 were extracted (neurinoma and thymoma) and in the other case only a biopsy was done (epidermoid carcinoma) (Table 5).

In Group II segmentectomies or wedge resections of the lung predominated, followed by cystopericystectomies for hydatidosis (Table 6).

In all patients we carried out a systematic preoperative study, with a detailed analysis of the respiratory function (spirometry, gasometry, pletismography, determination of postoperative FEV1 with a perfusion scanning with technetium-99) and an additional study of the oncological cases with CT

TABLE 5
Surgical techniques in the neoplastic series

	Cases	%
Pneumonectomies	14	20
Lobectomies	24	34.28
Segmentectomies or wedge resection	21	30
Exploratory thoracotomies	4	5.71
Tumorectomies	4	5.71
Biopsies	3	4.28

TABLE 6
Surgical techniques in the non-neoplastic series

	Cases	%
Segmentectomies or wedge resections	9	30
Cystopericystectomies	6	20
Fixation of flail chest	5	16.66
Decortications	3	10
Exploratory thoracotomies	2	6.66
Lobectomies	1	3.33
Bullectomies	1	3.33
Thymectomies	1	3.33
Rib resection	1	3.33
Biopsies	1	3.33

and/or mediastinal scanning with gallium-67, besides a bone scanning with technetium-99. All patients fulfilled criteria of operability and resectability.

The statistical studies were performed by *t* and *Chi*-analysis, with Yates correction in the latter in cases of statistical significance.

Results

We have registered a higher incidence of postoperative complications in Group I ($p < 0.05$), that is, in 14 patients in Group I we found 18 complications (20%), the most frequent being atelectasia, respiratory insufficiency or auricular fibrillation, a correlation existing between the number of complications and the degree of the surgery performed ($p < 0.05$). On the other hand, in Group II, the appearance of complications was less, finding 6 complications in 5 patients (16.6%) (Table 7). Altogether, the average overall index of complications was significantly higher with respect to a control group integrated by 150 patients operated of diverse ages ($p < 0.01$).

TABLE 7
Complications

	Group I		Group II	
	Cases	%	Cases	%
Atelectasiae	3	4.28	1	3.33
Respiratory insufficiency	3	4.28	1	3.33
Auricular fibrillation	3	4.28	—	—
Wound infection	2	2.85	1	3.33
Pneumothorax	2	2.85	1	3.33
Renal failure	1	1.42	1	3.33
Gastric bleeding	1	1.42	1	3.33
Haemothorax	1	1.42	—	—
Bronchial fistula	1	1.42	—	—
Haemoptysis	1	1.42	—	—

An overall mortality of 4 cases (4%) was registered. Three of them were in Group I and one in Group II. In two, the cause of death was respiratory insufficiency after the performance of a right pneumonectomy and an upper right lobectomy, in both cases due to a bronchial epidermoid cancer. One patient, only explored, diagnosed of bronchial epidermoid carcinoma, died postoperatively due to an haemoptysis. Another case, after a car accident, who needed a fixation of his flail chest, died postoperatively due to renal failure. Mortality was not higher in patients older than 75 years, in comparison with those of ages between 70 and 74 years. In patients treated by segmentectomy or wedge resection, there were no deaths, in comparison to those in whom it was necessary to use a more extensive procedure ($p < 0.05$).

The actual survival in patients operated for carcinoma of the lung over than 70 years was 66.4% at 2 years, 49.8% at 3 years and 25.7% at 5 years (Fig. 1). In lung metastasis we had one survivor at 3 years in a patient operated

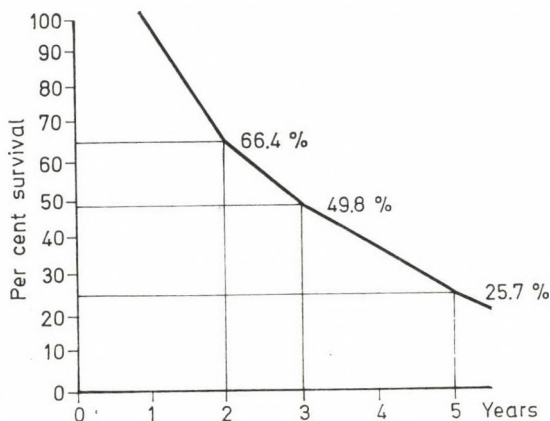


FIG. 1. Actual survival in patients operated for lung cancer over 70 years

for metastasis of a carcinoma of the rectum, while the other two cases of the same aetiology are in good state two years after surgery. The case operated for a thyroid gland carcinoma metastasis lived for 6 years and the one for breast cancer, died 18 months after surgery, while the case with metastasis of an osteogenic sarcoma died 20 months later.

The patient with epidermoid carcinoma of the mediastinum died after 8 months despite a management with chemotherapy and radiotherapy. The case diagnosed as metastatic hepatoma of the chest wall died after 5 months and the patient with breast cancer died after 14 months. The cases operated upon with non-malignant aetiologies had no recurrences, while 4 died due to intercurrent causes.

Discussion

Patients older than 70 years can develop bronchial cancer, especially the epidermoid type, which can grow more slowly than in younger patients. However, on other occasions, it is deduced that the doubling time does not differ from other group of patients [2]. From that we can therefore, conclude that the staging of these tumours should be the most precise, particularly taking into account the high operative risk of these patients, so the number of exploratory thoracotomies must be reduced [3].

Thanks to the improvement, in recent years, of surgical procedures, anaesthetic techniques and intensive care units, the operative risk for these patients has been decreased. Yellin [4], established the possibility of death in the 80s, after a thoracotomy for bronchogenic carcinoma for patients over 70 years inferior to the risk of younger patients in their 60s and 70s.

Gaillard [5] defends that contraindications for the performance of a thoracotomy in a patient over 70 years should be the same as for other groups of patients of whatever age, being the greatest operative risk induced by the degree of cerebral arteriosclerosis, which may on occasions limit in a decisive manner the collaboration of these patients in the postoperative period.

Keagy [6] recommends anticipating complications, the same found by us, which appear more frequently than in younger groups, and can in certain cases compromise the patient's life. For this they advise an early incorporation in the postoperative period and an intensive physiotherapy, which prevent further complications, mostly in patients with frequent added pathologies [7].

The most important complications that can occur in these elderly patients appear in the form of respiratory insufficiency, ventricular arrhythmias, on occasions difficult to control, or congestive cardiac insufficiency, which in our study are related to the degree of the aggressiveness of the surgery. As to complications called minor, which can at times, particularly in these people,

become important, we can refer to the appearance of a prolonged air leakage, postoperative atelectasia or auricular fibrillation [8].

Weiss [9] and Higgins [10] showed arduous defences of the age factor as limiting surgery in patients older than 70 years, based on a high operative mortality, which was nearly 20%.

Since 1980 and as concluded from our own results, which are in agreement with those of Ginsberg [11], the operative mortality is between 4% and 7%, thanks to the increased practice of more conservative procedures [12].

Similar to Kirsh [13], we have found similar results in 5-year survivors as those referring to patients of other ages. Breyer [8] refers to a 27% 5-year survival, which is between 13% for pneumonectomies and 42% for segmentectomies, similar to the 25.2% found by Wapler [14] for the group of the Marie Lanelongue, with 25.9% for lobectomies and 22.2% for pneumonectomies. Roeslin [15] on the other hand, refers to a lower survival and found a 21.3% rate at 5 years for patients of ages ranging between 65 and 69 years, and only 14.6% for those older than 70 years.

These results support the assumption of Thompson [16], who found an average survival of only 7% at the end of the first year, in patients older than 70 years who could not be extirpated of their tumour. In this way, surgery continues nowadays to be the only therapeutic method that can be curative on certain occasions for these patients, although in cases with a higher operative risk, we can obtain acceptable results in both neoplastic and non-neoplastic pathology [17, 18].

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Thoraxchirurgie bei bejahrten Patienten anhand von 100 Fällen

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Untersucht wurden die Daten von 100 Patienten, bei denen in den Jahren zwischen 1977 und 1986 ein thoraxchirurgischer Eingriff stattfand. Die Patienten waren 70 Jahre alt, oder älter (Durchschnittsalter 73,13 Jahre, 70-91 Jahre). In 70% der Fälle wurde der Eingriff wegen einer tumorösen Krankheit vorgenommen (in 78,5% der Fälle primäres Bronchuskarzinom) während in den restlichen 30 Fällen eine nicht tumoröse Krankheit vorlag. In diesen, mit ernstem Operationsrisiko verbundenen Fällen empfiehlt es sich eine ausführliche, systematische Untersuchung durchzuführen und die am konservativste Lösung zu wählen. Obwohl die Proportion der Komplikationen höher, als der Durchschnitt in der übrigen Gruppen lag ($P < 0,05$) betrug die Mortalität vom Maß des chirurgischen Eingriffs abhängig nur 4% ($P < 0,05$). In den Fällen mit Bronchuskarzinom betrug das 2jährige Überleben 66,4%, das 3jährige 49,8% und das 5jährige 25,7%, woraus zu folgern ist, daß das Alter von 70 Jahren oder mehr, keine Kontraindikation eines thoraxchirurgischen Eingriffs bedeutet.

Грудная хирургия у пожилых больных в связи с 100 случаями

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Авторы изучили данные 100 таких больных, которым в период 1977—1986 гг. было произведено хирургическое вмешательство на органах грудной клетки. Возраст больных был старше 70 лет. Средний возраст составлял 73,13 г. (от 70 до 91 г.). В 70% случаев хирургическое вмешательство производилось по поводу опухолевого заболевания (среди них в 78,5% была карцинома бронхов), в остальных 30 случаях заболевание не было опухолевым. В этих случаях с высоким риском в случае хирургического вмешательства рекомендуется серьезное, детальное предоперационное систематическое обследование, причем надо выбирать по возможности наиболее консервативные способы. Хотя процент осложнений был выше среднего по сравнению с другими группами ($P < 0,05$), смертность достигла только 4%, в зависимости от тяжести хирургического вмешательства ($P < 0,05$). Выживание при бронхокарциномах в 66,4% составила 2 года, в 49,8% три года и в 25,7% пять лет, из чего можно сделать вывод, что возраст от 70 лет и старше не является противопоказанием для проведения оперативных вмешательств на органах грудной клетки.

Transvaginal Operation of the Stein-Leventhal Syndrome: Description of a New Operative Technique

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The vaginal operation of the Stein-Leventhal syndrome is presented. The procedure is described. In comparison to the abdominal operation, the new technique has the following advantages: shorter duration of the operation, no scar due to laparotomy, smaller peritoneal wound, and less severe trauma.

More than fifty years ago, Stein and Leventhal [5] recommended the wedge resection of the ovaries as an operative treatment of the syndrome named after them. The technique of wedge resection was repeatedly modified [1, 3]. No attempts have been made so far to operate the Stein-Leventhal syndrome vaginally. We consider the widespread subspecialization as the cause of this operative technical gap in gynaecology. Surgical gynaecology is restricted to a few vaginal operations such as in the case of incontinence and other standard interventions.

Operative Technique

The operation is made under general anaesthesia in the lithotomy position. The vaginal part of the uterus is exposed by a bivalve speculum and grasped by a bullet forceps. The bullet forceps is replaced by two perlon holding sutures traversing sideways from the uterine orifice. Thus traumatization of the cervical canal can be avoided. After the portio is drawn down, the anterior vaginal wall is incised arcuately far upward. This cut has not be excessively wide.

The margins of the vaginal wound are held by sharp clamps, the bladder is separated and the plica vesicouterina is opened. A holding suture is applied to the anterior peritoneal fold. Next a long speculum is inserted into the anterior part. The uterus can now be pressed backward with a long speculum so that both the ovaries appear laterally in the visual field. Simultaneously

the uterine appendages and the pelvis can be inspected. The ovaries are then grasped on the ovarian ligament with a long clamp. They can be exposed without effort after releasing the speculum pressure on the uterus. However, we prefer first to expose the fundus uteri and then to seize the ovarian ligaments with long clamps. Care should be taken not to clamp the Fallopian tube or round ligament.

First the right ovary is exposed. The fundus uteri may slip backward again in this procedure. The ovary can be easily moved almost to the introitus and be surveyed in its full extent. Then the wedge resection from pole to pole can be easily carried out on the fully accessible ovary to the intended extent. The wound edges are approximated with interrupted sutures.

After opening the clamp the ovary retrocedes into the pelvis. The same procedure is carried out on the left ovary. After inspection for bleeding the peritoneal suturing is performed with three interrupted sutures. Finally the vaginal wound is closed with interrupted sutures. After removing the holding sutures a vesical catheter is inserted, a vaginal pack is placed and removed the next day.

Discussion

Arguments raised against the vaginal operation result from the clinical appearance of the disease. Stein–Leventhal syndrome is found mostly in women with menstrual disturbances and sterility in connection with a narrow vagina and an elevated uterus. However, the vagina is generally well supplied with estrogen and has a great dilatability under anaesthesia. The portio can easily be drawn to the introitus in most adolescent patients. Finally the ovaries can easily be drawn downwards also almost to the introitus. This is due to the elasticity of the juvenile tissue. The vaginal approach turns out to be the more suitable one for adipose patients. A variant of the transvaginal approach is the access to the ovaries through the posterior fornix. However, the described operational procedure appears to be the more advantageous one as the ovaries can be brought down as low as possible.

With skill and experience in vaginal operations, the whole operation does not take more than 20 minutes. The follow-up examination after three weeks reveals an absence of scarring because the juvenile tissue has a strong tendency to heal.

The operation of the Stein–Leventhal syndrome vaginally has the following advantages:

- The laparotomy scar is avoided.
- The peritoneal wound is very small and is even covered by the bladder thus reducing the danger of adhesion.

— The duration of the operative procedure is essentially shorter. Due to this the tissues are less traumatized.

— The transvaginal approach for exposing the ovaries is as effective as the abdominal approach.

— The risk of infection is lower.

The prerequisite to this operation is the diagnosis of the Stein–Leventhal syndrome confirmed by laparoscopy and hormonal examinations. Up to date we have had experience with 45 patients. There are no absolute contraindications to the vaginal operation. However, it is the case of a virgin when we have objections to the transvaginal operation. But even in this case we prefer a medical conservative treatment to the abdominal approach [2, 4]. The simplicity of our operative procedure seems to justify the claim that the transvaginal approach of the wedge resection of the ovaries is the operational method of choice in the treatment of the Stein–Leventhal syndrome.

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Transvaginale Operation des Stein–Leventhal-Syndroms: Beschreibung des neuen Operationsverfahrens

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Beschrieben wird die vaginale Operation des STEIN–LEVENTHAL-Syndroms. Die Vorteile der neuen Technik im Vergleich zur abdominalen Operation sind wie folgt: Kürzere Operationsdauer, keine laparoskopische Narbe, kleinerer peritonealer Schnitt und milderer Trauma.

Трансвагинальная операция синдрома Штейн–Левенталья: описание нового оперативного метода

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Авторы описывают в статье вагинальную операцию синдрома Штейна–Левенталья, подробно знакомят с этим способом. Новая техника имеет следующие преимущества по сравнению с брюшной операцией: операционное время короче, отсутствие лапароскопического рубца, меньше размер перитонеального сечения и травма слабее.

Inflammatory Pseudotumour of the Liver

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In view of their own case, authors review the diagnostic and clinical characteristics of the inflammatory "pseudotumours" of the liver. They state that this liver disease is important from the differential diagnostic point of view.

The inflammatory pseudotumours should be basically differentiated from malignant tumours in which the imaging procedures and their repetition are significant.

Authors review their case in connection with 13 cases collected from the literature.

Inflammatory pseudotumours were first described in the lung and the tumour-promoting changes are currently termed "plasmacytic granulomas" [3]. Some cases have been reported in the gastric wall, the ovaries, the pancreas [1], the heart and the thyroid gland.

Inflammatory pseudotumour of the liver was described by Pack and Baker [9]. They pointed out the similarities with changes in the lung. Thirteen cases have been reported so far [8].

Our case may be of interest because of the rarity of the change but decisively of the differential diagnostic problems of the space-reducing processes of the liver.

Case Report

Sz. J., a 74-year-old male patient was admitted to the 3rd Department of Medicine of János Hospital on January 1, 1988. He was admitted for a dull subcostal pain, loss of appetite and subfebrility. He had a history of prostatectomy due to hypertrophy. On physical examination a moderate tenderness under the right costal arch could be observed. His laboratory findings were characterized by an extreme leukocytosis ($30.2 \times 10^3/\text{mm}^3$), a qualitative blood count slightly shifted to the left, a high sedimentation rate (80 mm/h), an elevated blood sugar value (9.2 mmol/l) and moderately increased enzymes (SGOT: 40U, SGPT: 61U, AP: 247U). Abdominal sonography verified (Fig. 1) stone of the gallbladder, and indicated a space-reducing process, 10 cm in dia-

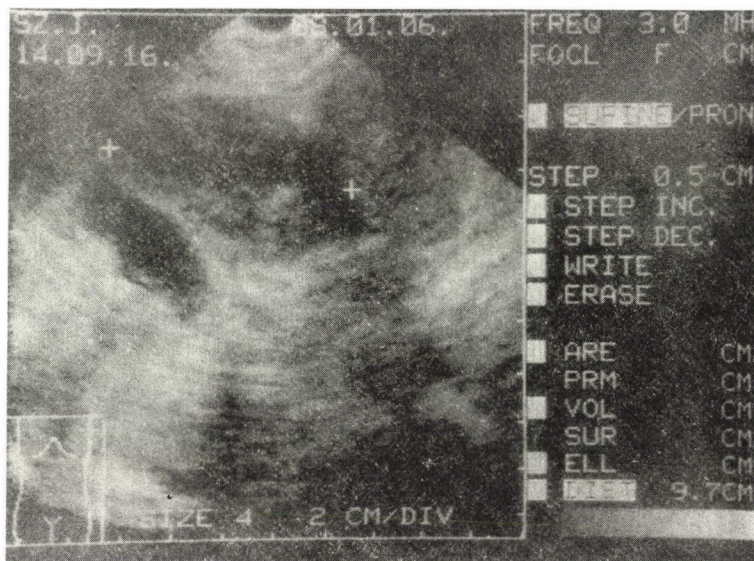


FIG. 1. Sonogram (06, 1, 1988). On the border of the two lobes, anterior to the gallbladder, but mainly in the right lobe, an inhomogeneous region, about 10 cm in diameter containing also not distinctly differentiable cystose parts can be seen. A somewhat larger than normal thick-walled gallbladder with several echodense structures and acoustic shadows

meter, and occasionally of cystous structure. Further examination of the gastrointestinal tract (including X-ray of the stomach, double contrast irri-goscopy and Weber's test) showed negative results, moreover, neither liver scintigraphy, nor the *Echinococcus* complement-binding reaction, as neither the alpha-fetoprotein test revealed any pathological feature. As a result of the initiated combined antibiotic treatment, he became afebrile, his leukocytosis stopped, and his We value decreased to 12 mm/h. The course of his disease was indicative of inflammation. Nevertheless, the CT performed in the mean-time (Fig. 2) did not seem to support this finding. This latter rather indicated malignant liver tumour or haemangioma. For further differentiation digital selective angiography was performed, which excluded with great probability the possibility of haemangioma, echinococcus cyst or abscess and seemed to support the presence of a primary liver process (Fig. 3).

He was transferred as a consequence of this finding to the Department of Surgery for exploration and possible liver resection on February 24. Regarding that the extended liver resection necessary to be performed in the aged patient of a rather poor general condition would have involved a tremendous risk, indication for surgery was reconsidered in view of the patient's totally complaint-free state, his permanent afebrility and the normalized laboratory values. At the beginning of March, i.e. two months after the first examinations, repeat sonography and CT were decided upon. Sonography did not, at

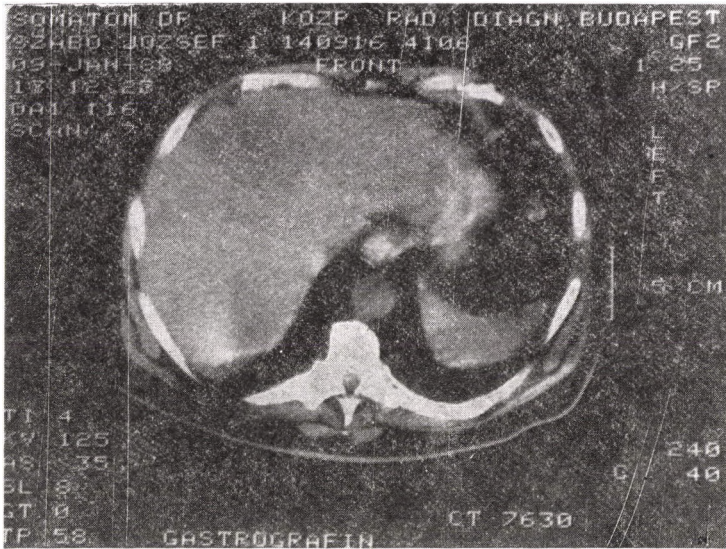


FIG. 2. CT (09, 1, 1988). Following administration of contrast medium, in the hepatic lobe a definite echodensity of the marginal region of an inhomogeneous area, 10 cm in diameter, visualized also by X-rays, appears, with several cystose regions of a diameter of 0.5–3 cm showing no uptake of contrast material. The gallbladder is distended, with a thickened wall

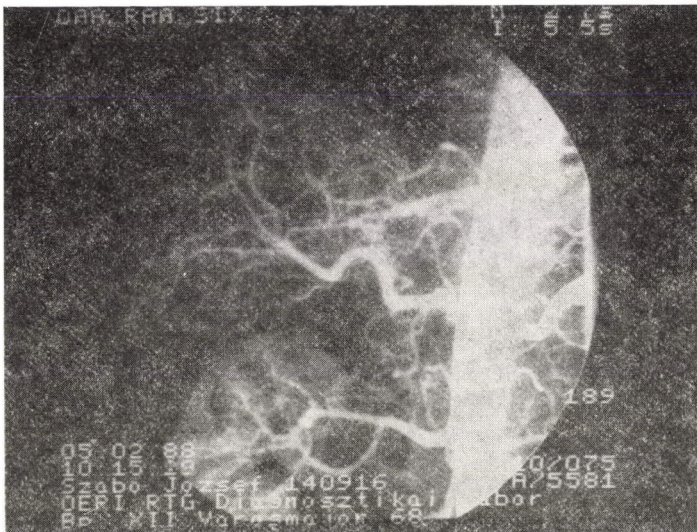


FIG. 3. Abdominal aortography + selective celiac angiography (05, 2, 1988). Varying celiac branches. In the about 4–5 cm region between the two lobes there is an irregular arterial vascular region as well as a protracted parenchymatous phase as compared to the environment

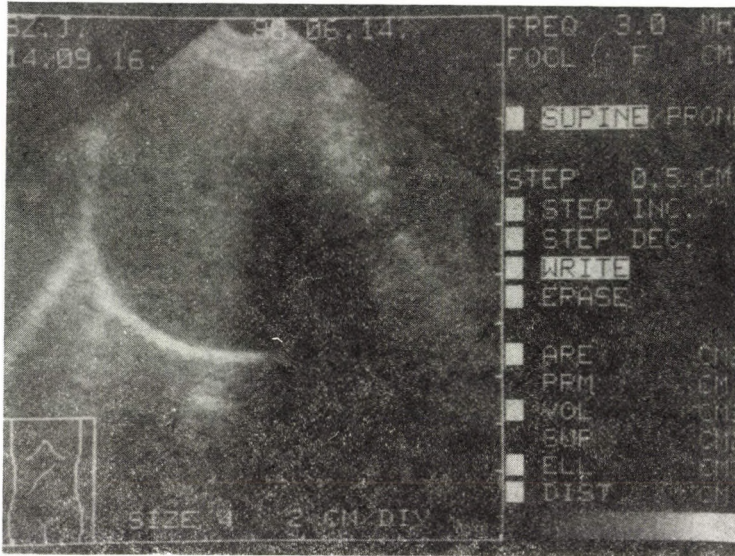


FIG. 4. Sonogram (14, 06, 1988). The change earlier described in the hepar cannot be visualized. The more delicate gallbladder shows signs characteristic of cholelithiasis

that time, disclose the liver change, while only a hypodensity of 1 cm was shown by the CT scan. Subsequent to fixing further control examinations, the patient was discharged. After additional three months, in June, these two examinations were repeatedly made in the complaint-free patient and they revealed no pathological change (Fig. 4).

Discussion

Based on the limited number of reports, inflammatory pseudotumour of the liver is assumed to occur very rarely and it is of interest mainly differential diagnostically, because knowing about and being aware of the change, a superfluous resection can be avoided. An extended liver resection, which would seem to have been necessary to perform because of the localization of the change, would also have incurred great risk for the patient.

In the overwhelming majority of the cases reported in the literature, the macroscopic diagnosis both pre- and postoperatively was malignant liver tumour and diagnosis was not unanimously clarified by the intraoperative histological examination either. Therefore, liver resection, moreover liver transplantation, were also made (Table 1). It seems to be more advisable to wait for the final histological results in doubtful cases. A case similar to ours was reported by Chen [4]. Heneghen's patient [6] was a girl, aged 8 years, in whom the inflammatory pseudotumour produced obstructive jaundice as

TABLE 1
Inflammatory pseudotumours of the liver (1953—1988)

Author	Symptoms	Solitary or multiple	Site	Size, cm	Treatment	Outcome
Pack, Baker, 1953	fever and loss of weight	solitary	r. lobe	25 × 13	lobectomy	recovery
Haith, 1964	fever, icterus, loss of weight	solitary	porta hepatis	3	pancreatoduodenect.	malabsorption
Hertzer, 1971	fever, icterus, loss	solitary	porta hepatis	??	biopsy	port. hepatis hy-pertension
Someren, 1978	fever	solitary	r. lobe	15 × 22	lobectomy	recovered
Painean, 1983	fever, loss of weight, hyperglobulinaemia	solitary	r. lobe	7	lobectomy	recovered
Chen, 1978	fever, loss of weight	solitary	r. lobe	6	marginal excision, biopsy	recovered
Heneghan, 1984	pain, resistance	solitary	r. lobe	??	liver transplantation	recovered
Anthony, Telesighe, 1986, 5 cases	1. pain 2. fever, loss of weight 3. pain 4. intermittent icterus 5. fever, pain, icterus	solitary multiple solitary multiple multiple	r. lobe r. lobe r. lobe ? ?	9 ?? 5 ? ?	lobectomy biopsy marginal biopsy biopsy	recovered recovered recovered recovered recovered
Kessler, 1988	fever, pain	solitary	r. lobe	8	biopsy	recovered
Jakab, 1988	pain, subfebrility	solitary	hilus hepatis	10	conservative	recovered

well as hypertension. Here, extended liver resection followed by liver transplantation were performed. Recently, Anthony [2] reported 5 such cases.

Based on literary data, the inflammatory pseudotumour of the liver is associated with fever, anaemia, loss of weight and manifests as a change raising the suspicion of a tumour detectable by imaging procedures. Its aetiology is unknown. The histological picture is characterized by a lymphocytic, plasmacytic, eosinophilic infiltration. The inflammatory infiltrate can be observed in the stroma and the liver parenchyma [2, 8]. Somerch and Chen [10, 4] also described occlusive phlebitis. Bacterial or fungal pathogens could never be demonstrated, although the symptoms definitely indicate a bacterial origin. In our case, it was probably about a process associated with gallbladder stone and cholecystitis.

Concerning its localization, inflammatory pseudotumour was observed multiply in the right lobe (see table).

Inflammatory pseudotumours of the liver are assumed to occur more frequently as reported in the literature. Their importance lies mainly in their differential diagnosis. As already mentioned, by its detection the unnecessary radical liver resection can be avoided.

It is not easy to recognize a pseudotumour, therefore (i) it is necessary and appropriate to wait even in the case of a clinical picture characteristic of typical liver tumour, i.e. fever, leukocytosis and a high sedimentation rate. (ii) In these patients the easiest and most obvious thing is to repeat sonography preoperatively. A change in the picture, i.e. the reduced size of the "tumour" may raise the suspicion. (iii) It is useful to make histological examination by aimed biopsy. (iv) During the operation if the repeated intraoperative biopsies have not yielded unanimous results, it is more appropriate to wait for the final histological result.

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Entzündlicher Pseudotumor in der Leber

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Anhand eines eigenen Falles werden die diagnostischen und klinischen Eigentümlichkeiten der entzündlichen «Pseudotumoren» der Leber überblickt. Der Krankheit wird eine differentialdiagnostische Bedeutung beigemessen. Die entzündlichen Pseudotumoren müssen von den malignen Tumoren grundlegend differenziert werden. Von differentialdiagnostischem Standpunkt ist den Abbildungsverfahren und ihrer Wiederholung eine differentialdiagnostische Bedeutung beizumessen. Im Zusammenhang mit den aus der Literatur gesammelten 13 Fällen wird der eigene Fall dargestellt.

Воспалительный псевдотумор в печени

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Авторы рассматривают диагностику и клинические особенности воспалительных «псевдотуморов» печени на основании изучения собственного опыта. Они установили, что при этом заболевании имеет значение дифференциальная диагностика.

Воспалительные псевдотуморы в основном надо отграничить от злокачественных опухолей. Важную роль играют методы, дающие изображение, с точки зрения дифференциальной диагностики имеют значение повторные исследования с их помощью.

Авторы описывают собственные наблюдения вместе с 13 случаями, найденными ими в международной литературе.

Changes in Hepatic Blood Flow in Jaundice Due to Hilar Carcinomas, the So-called Klatskin Tumours

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The hepatic circulation of patients with hilar carcinoma and icterus was studied by isotope technique. A marked alternation in blood flow was observed, that is that the ratio of the circulation of the hepatic artery and the portal vein became balanced. By elimination of the icterus, the hepatic circulation normalized. This allowed the conclusion that the change in blood flow must have rather been due to the mechanical icterus and the increased pressure of the bile duct than to the tumorous infiltration and therefore the earliest possible elimination of the icterus is urgently indicated.

Data on the changes in hepatic blood flow observed in mechanical obstruction are contradictory [2, 3, 4, 7, 11, 13, 15].

In our own experiment in dogs, following ligation of the common bile duct, on an average a 39% increase in hepatic venous flow and a decrease of 50% in portal venous flow were observed according to our examinations made by electromagnetic flowmetry [13, 14].

Adenocarcinomas, the so-called Klatskin tumours, being relatively small, but causing rapid obstruction of the hepatic bifurcation may lead to exacerbating ileus [8]. It was assumed that consequently marked changes are produced in the hepatic circulation. Therefore, it was studied how hepatic blood flow changes in Klatskin tumour patients and whether surgical decompression and the resulting desicterization affect the changed liver circulation.

Material and Method

Ten Klatskin tumour patients were included in our examination (Table 1).

The table shows the highest serum bilirubin level prior to performing the drainage. The post-decompression serum bilirubin level was the lowest value obtained by drainage. As demonstrated in the table, none of the patients were

TABLE I

Data of Klatskin tumour patients on the ratio of the hepatic arterial and portal venous flow

No.	Age	Serum bilirubin level before decompression	after decompression	Ratio of hepatic arterial and portal venous flow, %	Mode of decompression
1.	55	376	126	45/55	PTD
2.	80	434	72	55/45	ITD
3.	76	391	40	48/52	internal drainage
4.	72	410	83	40/60	PTD
5.	70*	320	44	54/46 27/63*	PTD
6.	76	398	51	51/49	internal drainage
7.	60	286	74	39/61	PTD
8.	61*	343	68	50/50 29/71*	
9.	79	440	105	61/39	ITD
10.	82	3861	140	50/50	PTD
		376.6	80.3		
	average age: 71.1 years			average: 49.3/50.7 27/63*	

* Flow studies were carried out also 4 weeks after the decompression in the marked patients. PTD = percutaneous hepatic drainage; ITD = intraoperative transhepatic drainage.

freed of their icterus completely, moreover some of them remained massively icteric. For decompression percutaneous transhepatic drainage and palliative, transtumoural endoprosthesis and intraoperative transhepatic drainage were applied. The ratio of the hepatic arterial blood flow and portal venous flow can be determined by radioisotope technique by a gamma-camera computer system. The essence of the method is that the influx into the liver of the radioactive indicator administered intravenously occurs in two phases. The radioactive substance can be first detected by the perfusion of the system of the hepatic artery then by that of the portal vein. Following the abrupt injection of an isotope preparation of high activity, but of low volume the first "hepatic phase" and the second "portal phase" can in general be well differentiated on the time-activity curve (the histogram) recorded over the liver. (As a help, also the changes in the activity of the abdominal aorta can be registered.) The peak on the aortic histogram indicates the influx of active substance. This may provide evidence for determining the boundary between the "hepatic phase" and the "portal phase".

The histogram of hepatic activity reveals the ratio below the region of the "hepatic phase" and the "portal phase" to be identical with the ratio of flow of the hepatic artery and the portal vein.

The method was developed and applied by Biersack [1], Fleming [5] and Sarper [12]. According to their reports, the examination is reliable, the measured values can well be reproduced and the results are in agreement with clinical data and with data obtained by other techniques.

The Examination

The examination was carried out at the Department of Radiology by using a Nuclear Chicago Pho/Gamma II. H.P. gamma-camera with a connected data processing on-line Gamma MB 9100 computer. Placing the patients under the camera detector, technetium-labelled human serum albumin of an activity of 700 MBq (Tc-99m HSA) was administered i.v. in bolus. The volume of the bolus was 0.5 ml.

Using the computer in the frame-mode, data collection was started simultaneously with the administration of the injection by recording 1 s frames at intervals of 60 s.

On evaluation, the regions necessary for recording the time-activity curves (histograms) were marked with the help of a series of pictures projected on the computer screen by using the so-called "region of interest" technique (ROI).

On analysing graphically the activity curves recorded of the region of the liver and the abdominal aorta, the ratio of the perfusion of the hepatic artery and the portal vein was obtained. (There was no program needed for automatic computer analysis available at the time of performing the examination.)

It should be noted that the main source of error of the method was inherent in the imperfection of the bolus technique. If the peak of the curve recorded of the abdominal aorta has flattened, i.e. the radioactive indicator did not reach the site of detection in high concentration, the measured values were less reliable.

It should also be stressed that the examination in this form does not provide information on the absolute degree of hepatic blood flow in terms of ml/min. It is only suitable for assessing the ratio of perfusion of the hepatic artery and of the portal vein. Naturally, the procedure can be combined with an isotope technique suitable for determining the absolute value of the perfusion, however this cannot be solved by one examination, there is a need for two separate isotope diagnostic interventions. This was not performed because for deciding the present issue basically the recording of the ratio of hepatic arterial and portal venous flows was rather needed.

Results

The bilirubin values of our 10 patients suffering from Klatskin tumour, their mode of treatment and the ratio of hepatic arterial and portal venous flows are shown in Table 1.

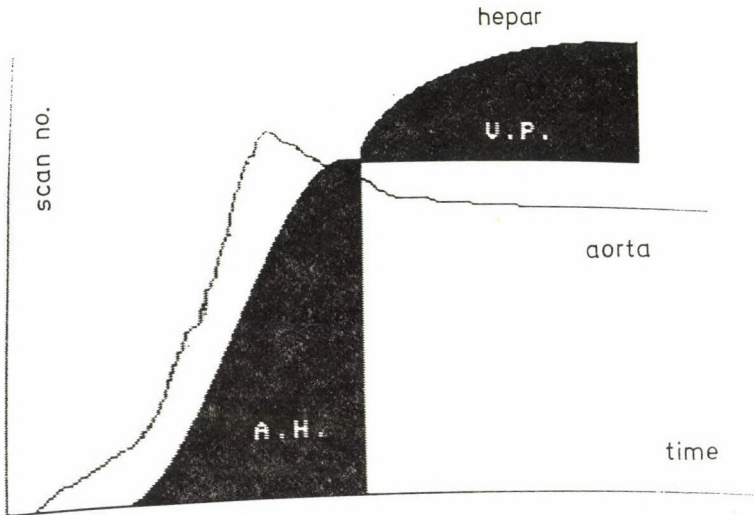


FIG. 1. Hepatic flow measurement of a Klatskin tumour patient before decompression. Serum bilirubin level: 320 mmol/l; the ratio of hepatic arterial (A.H.) and portal venous (V.P.) flows: 54 : 46%

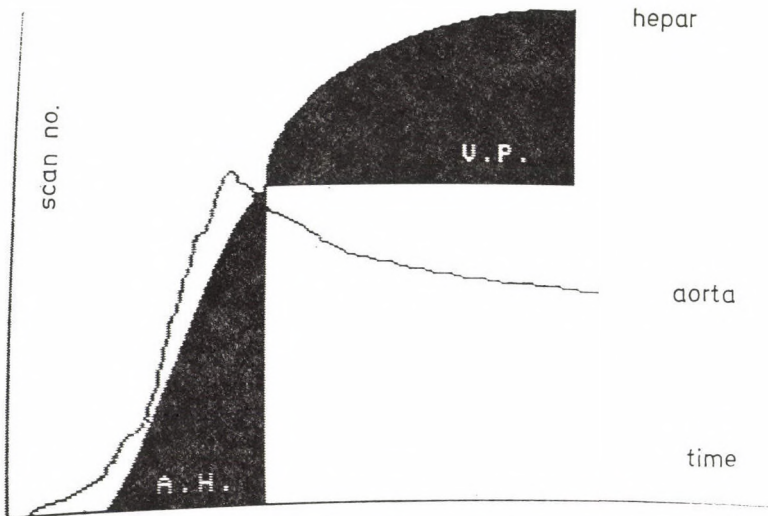


FIG. 2. Hepatic flow measurement of the same Klatskin tumour patient after decompression and desarterization. Serum bilirubin level: 44 mmol/l; the ratio of hepatic arterial (A.H.) and portal venous (V.P.) flows: 27 : 63%

Based on the examination, the ratio of the circulation of the hepatic artery and the portal vein was found to be 50% each in the Klatskin tumour patients. In two patients there was a possibility for repeating the examination in the phase of almost complete desicterization. Figure 1 demonstrates the curve recorded before decompression. (The serum bilirubin value at the time of the examination was 320 mmol/l.) The ratio of hepatic arterial and portal venous blood flows was 54 to 46%. Figure 2 shows the liver circulation study of the same patient 25 days following decompression. The curve to be considered physiological concerning liver circulation, that is the ratio of hepatic arterial and portal venous flows returned to its normal value, i.e. to 27 to 63%.

Discussion

Based on our examinations on hepatic circulation made in Klatskin tumour, icteric patients, it could be established that the ratio of the blood flow of the hepatic artery and the portal vein became identical. Since, with this method the absolute determination of the complete blood flow of the liver was not possible, there seem to be three possibilities to explain this phenomenon:

1. The afferent circulation of the liver did not change. In this case shifting of the flow ratios implies that the flow of the hepatic artery has increased, while that of the portal vein decreased.

2. The total hepatic perfusion was reduced. In this case the flow of the hepatic artery remained unchanged and the flow of the portal vein considerably diminished.

3. Perfusion of the liver increased, while the flow of the portal vein remained unchanged, with a marked increase in the flow of the hepatic artery.

What seems so be decisive is that whichever variation is dominant, portal flow does not change or decreases. Hunt [6] used ^{133}Xe clearance technique in rats with ligation of the common bile duct. He measured hepatic blood flow daily for a week, which decreased on the first day to 50% of the preoperative value, remaining so for the subsequent five days. Bosch [3] proved in dogs that after ligation of the choledochus the portal flow diminished then sinusoidal portal hypertension developed with extensive portal-systemic shunts. It was proved by Mathie [10] by selective flow assessment that arterial hepatic flow was reduced by 36% and portal venous flow by 44% after ligation of the common bile duct. Undoubtedly, these observations modelled chronic biliary obstruction and derive from animal experiments, that is, they cannot be fully adapted to humans.

Doi et al. are assumed to have the most reliable data on humans. They found the flow ratio of the hepatic artery and the portal vein to be 26 to 74%

by using a transit time ultrasonic volume flowmeter. Since they used the most up-to-date method having proved, according to several observations, to be the most reliable ones as well, we have regarded their values as the physiological bases.

In our experiments changes corresponding to the first possibility were observed. After ligation of the common bile duct, with the increased biliary pressure, arterial hepatic flow increased and at the same time portal venous flow diminished, after all the total blood flow of the liver did not change (Fig. 3).

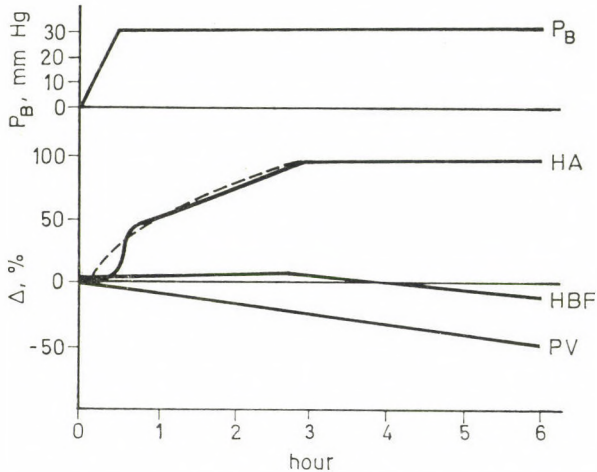


FIG. 3. The effect of the obstruction of the choledochous duct, i.e. of the increased biliary pressure on hepatic circulation in dog. P_B: biliary pressure; HA: change in hepatic arterial flow; HBF: change of total hepatic blood flow; PV: change in portal venous flow in %

As to the changes in circulation in patients with Klatskin tumour, the decrease in portal venous flow is assumed to be the primary one. Nevertheless, the normalization following decompression proves that the alteration is not caused by the tumorous infiltration but by the increased pressure due to obstruction of the bile ducts. This seems to be supported also by clinical observations [9]. As a result, decompression appears to be indicated and urgent not only because of the mechanical obstruction but also of the altered flow.

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Änderungen des Leberkreislaufes bei durch Hilus-Karzinome, sog. Klatskin-Tumoren verursachter Gelbsucht

F. JAKAB, T. HERNÁDI und I. SUGÁR

Der Leberkreislauf der an Hiluskarzinom oder Ikterus leidenden Patienten wurde mit der Isotop-Technik untersucht. Die beobachtete, bedeutende Kreislaufalteration lag darin, daß die Proportion der Zirkulation der A. hepatica/V. portae sich ausglich. Nach Behebung des Ikterus hat sich der Leberkreislauf normalisiert. Daraus wird gefolgert, daß für Kreislaufänderung wahrscheinlich nicht die tumoröse Infiltration, sondern der mechanische Ikterus und die Druckerhöhung in den Gallenwegen verantwortlich sind, weshalb die je frühere Behebung des Ikterus dringend indiziert ist.

Изменения печеночного кровообращения при желтухе, вызванной раком корня легкого (т. н. опухоли Клацкина)

Ф. ЯКАБ, Т. ХЕРНАДИ и И. ШУГАР

С помощью изотопной техники авторы изучали кровообращение в печени у желтушных больных с карциномой корня легких. Они отметили значительное изменение кровообращения, а именно — выравнивание пропорции кровообращения печеночная артерия/портальная вена. С исчезновением желтухи кровообращение печени нормализовалось. На этом основании они делают вывод, что причиной изменения кровообращения является, вероятно, не опухолевая инфильтрация, а механическая желтуха, повышение давления в желчных путях, вследствие чего обоснованным является срочное устранение желтухи.

The Influence of Clinical and Histopathological Characteristics upon Survival in Melanoma Patients

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The clinical and histopathological features of melanoma were selected which may have an effect upon the 5-year-survival of melanoma patients, and serve as prognostic factors. 165 patients with cutaneous malignant melanoma were analysed and followed up for 5 years at least, during the period 1967–1982. The depth of invasion, tumour thickness, the presence of exulceration and the clinicopathological type of the primary tumour related to complexion have been found reliable prognosticators in order to predict further outcome in terms of minimal and possible 5-year-survival calculated by the life table method. The anatomical site of primary tumours gives a clue to the possible lymphatic drainage and, added to other relevant factors mentioned above, is also helpful in the planning of surgical intervention. Considering measurable prognostic factors of a great significance upon survival, rather additional elective lymph node dissection combined with adjuvant treatment than increased local surgery are advised.

The prognosis of cutaneous malignant melanomas is difficult due to the varying clinical appearance, histological picture and the different duration of growth phases (horizontal and vertical) which *per se* are inherent characteristics of each individual melanoma. However, the clinicopathological classification of melanomas [3, 9] — even if not complete — and their microstaging according to depth of invasion [3] and vertical thickness in millimetres [1] have substantially added to predicting further outcome, mainly by proving a rising incidence of occult regional metastases at a certain level of tumour invasion and/or growth [1, 10, 11].

On the other hand, if we summarize the effectiveness of the several treatment modalities directed against melanoma, it is evident that surgery has remained the most important one [2, 6]. Indeed, there is no other treatment which can reduce tumour burden so effectively than does surgical removal. But it should not be concluded that the more radical the operation the better the life expectancy. It is the tactics of surgery that must consciously be altered but always based on the knowledge of factors which help us in setting up risk groups and planning the surgical intervention [7].

The present paper will deal with the main characteristics of both the tumour-bearing patient (age, sex, complexion) and the individual melanoma, and elucidate their effect upon patient survival.

Patients and Methods

A total of 165 melanoma patients have been studied during the period 1967–1982. Male and female ratio was 1:1.32, the average age 51.4 years (extreme values 15 and 92 years, respectively). There was no significant difference between males and females related to incidence of disease and age distribution. Beside sex, age and complexion (clinical factors) the anatomical site of the primary tumour, the depth of invasion, the clinicopathological type of the tumour and the presence of exulceration have been studied related to the 5-year-survival of the patients. Cumulative survival values were determined by the actuarial life table method as described by Cutler and Ederer [4] while \pm SE was calculated by means of the Greenwood-equation [5]. For the assessment of significance in the difference between comparable groups the *Chi*-square test was used. The microstaging of tumours according to depth of invasion was performed in the Pathological Institute of the University Medical School in Pécs.

Results

1. *The overall 5-year-survival* of 165 patients 52 died within 5 years and further 29 patients fell out of "follow-up" in the 2nd and 3rd year following admission. If the latter were also added to the group of those "died within 5 years", a minimal 5-year-survival of 51% was calculated. The life table method, considering also cases lost from follow-up but exposed to risk of death within 5 years, yielded a $52 \pm 6\%$ survival.

2. *Effect of duration of pre-existing pigment naevi upon survival.* We found that survival was more favourable when precursor naevi had existed for longer than 2 years (Table 1).

3. *Effect of sex.* Our patients included 71 males and 94 females. The minimal 5-year-survival did not differ significantly between the two groups (in males: 45%; females: 55%) ($p < 0.3$ N.S.).

4. *Effect of age.* Under 20 years the 5-year-survival was nearly 100% showing that occurrence of melanoma is the rarest in this age group and so the statistical evaluation of a few number of patients is questionable. About one-third of patients in the 3rd decennium survived 5 years, while patients aged between 30–70 years reached a 40–50% survival rate. The high survival rate in the group of aged people (above 70 years) points to the fact that the

TABLE 1

Effect of duration of pre-existing naevi upon the 5-year-survival in MM cases (n = 109)

Duration of "precursor" naevi (yrs)	No.	5-year-survival	
		No.	%
1 year	12	3	25
1-2 yrs	18	7	39
2-5 yrs	64	48	75
>5 yrs	15	14	93.3

TABLE 2

Effect of age upon survival in melanoma patients (n = 165)

Age (yrs)	No. of patients	5-year-survivors	
		No.	%
10-20	3	3	100
20-30	11	4	36
30-40	12	6	50
40-50	38	19	50
50-60	41	15	37
60-70	57	20	54
70-80	21	17	80
80-90	1	—	—
90<	1	—	—
Total	165	84	51

course of melanomas established in advanced age are by far the most favourable (Table 2).

5. *Effect of complexion.* The effect is indirect if incidence of SSM type melanomas was found more frequently ($n = 117$; 70.9%) associated with fair complexion (fair or ginger hairs, white and freckled skin, lightblue eyes) than among those with dark complexion.

6. *Effect of clinicopathological type.* Superficially spreading melanomas (SSM) were associated with a significantly higher ($p < 0.01$) 5-year-survival rate (70%) than nodular melanomas (NM; survival rate: 27%) showing from the beginning a vertical infiltrative growth pattern (Table 3).

7. *Effect of infiltrative growth (Clark's staging).* Superficially spreading melanomas (Depth Clark II-III) produced a significantly ($p < 0.0001$) more favourable 5-year-survival than deeply infiltrating tumours (Clark IV-V). The high grade of significance underlines its role as a valuable and valid prognostic factor (Fig. 1).

TABLE 3

Effect of the clinicopathological type of the primary tumour upon survival
($n = 160^*$)

Clinicopathological type	No. of cases	5-year-survivors	
		No.	%
SSM	93	65	70
LMM	5	3	60
ALM	12	7	58
NM	15	4	27
Other	35	5	14
Total	160	84	52.5
SSM vs NM $p < 0.01$			

* 5 cases with unknown primaries.

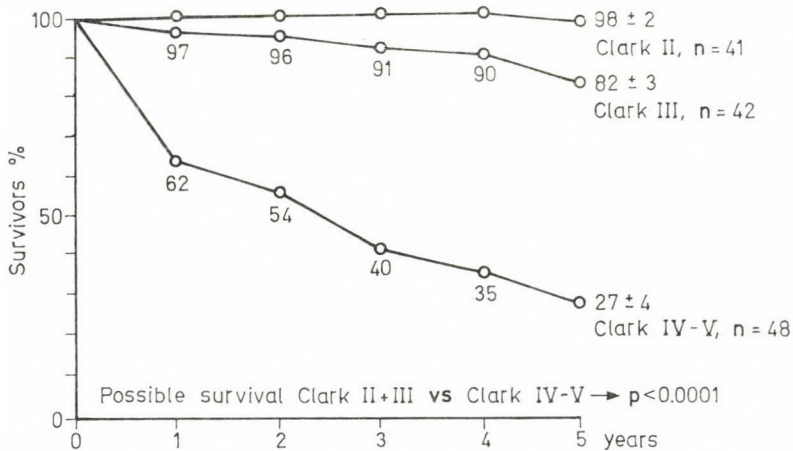


FIG. 1. Melanomas regardless of clinicopathological type, until they infiltrate superficially, the cure rate and survival are favourable (Clark I + II + III). However, when they start infiltrative growth and reach beyond Clark levels IV and V, the 5-year-survival rate will be significantly decreased

8. *Effect of exulceration of the primary tumour.* Among 132 primary tumours satisfactorily documented both clinically and histologically, 47 showed exulceration. Apart from their being either microscopic or macroscopic, exulcerated melanomas had a significantly less favourable life expectancy (5-years survival $32 \pm 4\%$ vs non-exulcerated $80 \pm 6\%$; $p < 0.0005$) than tumours without exulceration. The depth of invasion in the exulcerated tumours was Clark II in 6 cases, Clark III in 21 cases and Clark IV-V in 20 cases.

9. *Effect of the anatomical site.* Melanomas of the extremities are associated with the best 5-year-survival rate ($65 \pm 6\%$) if compared to truncal

TABLE 4
 Mean survival within the follow-up period** and cumulative 5-year-survival according to anatomical location of primaries (n = 160*)

Body region	No.	Mean survival (yrs)	Cumulative 5-year-survival
Upper and lower limbs	63	3.5	65.4 ± 6
Trunk	63	2.5	37 ± 4
Head-neck	17	2.9	51.6 ± 2
Other	22	3.2	54 ± 2

* 5 unknown primaries; ** for 5 years.

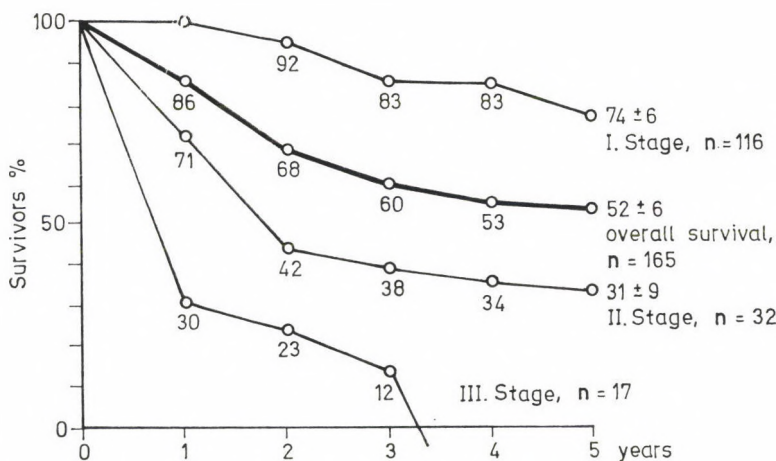


Fig. 2. Cumulative 5-year-survival according to gross clinical stages. Only about one-third of stage II cases reach the 5-year-survival limit following excision and therapeutic regional lymph node dissection, while all cases with distant metastases will die at least after 3 years

melanomas of significantly worsened prognosis ($37 \pm 4\%$; $p < 0.01$). Melanomas of the head and neck region appear in the middle field ($51.6 \pm 2\%$) (Table 4).

10. *Gross clinical staging and 5-year-survival.* In non-localized disease the state of the regional lymph nodes (Stage I vs stage II), as well as the site of distant metastases and the tumour burden they represent will become the most important prognostic factors (Fig. 2).

Discussion

The overall cumulative 5-year-survival of patients depends mainly on their distribution according to clinical stages. The comparison of 5-year-survival rates in stage I patients is more relevant because the chance for cure is

best in this group, and supposing a uniform treatment policy, different survival rates would just point to prognostic factors. Depth of invasion and vertical tumour thickness measurements are best combined for judging the prognosis [11]. In an earlier study we saw a strong correlation between these two prognosticators mainly at Clark level II–V and found that the depth of invasion can be made responsible for the tumour thickness in about 80% [8]. The exulceration of the primary tumour is not independent of infiltrative growth, size and vertical thickness and can be considered a necrosis in the central friable, poorly vascularized tumour tissue. A long pre-existence of pigmented naevi on the base of which melanomas have developed later and associated higher survival rates will underline the fact that the longer the duration of precursor naevi the greater the chance to detect melanoma in its horizontal growth phase. One should be aware that once superficially spreading melanomas started infiltrative growth, it is the depth of invasion that matters in predicting further outcome [7, 8]

The recent TNM-classification of melanoma primary tumours already incorporates tumour thickness and depth of invasion in their pT grading. [12] and gives a new stage grouping according to patients' risk. We believe that the selection of patients at risk of early dissemination will be more precise if more prognostic factors are considered.

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Wirkung der klinischen und histopathologischen Charakteristika auf das Überleben bei an Melanom leidenden Patienten

L. LUKÁCS

In der Arbeit sind jene ausgewählten klinischen und histopathologischen Faktoren des Melanoms zusammengefaßt, die auf das 5jahres Überleben eine Wirkung ausüben können und demzufolge auch als prognostische Faktoren zu bewerten sind. Zwischen 1967 und 1982 erfolgte die Analyse von 165, an malignem Hautmelanom leidenden Patienten, während sich die Follow-up Untersuchungen auf mindestens 5 Jahre erstreckten. Tiefe der Tumorinvasion, Dicke des Primärtumors, eventuelle Exulzeration, ferner der klinikopathologische Typ des Primärtumors in Hinblick auf den Komplex des Patienten waren jene zuverlässigen prognostischen Faktoren, mit denen das weitere Schicksal des Patienten — mit dem, der «life table»-Methode gemäß kalkulierten minimalen und wahrscheinlichen 5jahres Überleben charakterisiert — vorausgesagt werden konnte. Die anatomische Lokalisation des Primärtumors bietet einen guten Stützpunkt zur Beurteilung der möglichen Lymphableitung, deren Kenntnis, mitsamt den oben angeführten Faktoren bei der Planung des chirurgischen Eingriffs ebenfalls eine nützliche Hilfe bietet. Anstatt der Steigerung der Radikalität des lokalen chirurgischen Eingriffs, wird eher die mit elektiver regionaler Lymphknotendissektion und adjuvanter Behandlung kombinierte Exzision empfohlen.

Влияние, оказываемое на выживание больных с меланомой клиническими и гистопатологическими характеристиками

Л. ЛУКАЧ

Автор попытался выделить среди клинических и гистопатологических характеристик меланомы те из них, которые могут оказывать влияние на 5-летнее выживание и, таким образом, могут оцениваться как прогностические факторы. Он провёл анализ данных 165 страдавших меланомой кожи больных в период 1967—1982 гг., состояние которых он контролировал, по крайней мере, в течение пяти лет. Глубина проникновения tumора, толщина первичной опухоли, факт изъязвления, а также клинко-патологический тип первичной опухоли были теми надёжными прогностическими факторами в аспекте комплекса больного, с помощью которых можно предсказать дальнейшую судьбу больного — характеризуя минимальным и вероятностным 5-летним выживанием, вычислительным методом «life table». Анатомическое расположение первичной опухоли даёт хорошую точку опоры для оценки возможного лимфатического оттока, что, вместе с вышеперечисленными факторами, также полезно при планировании хирургического вмешательства. При знании статистически значимо влияющих на выживание прогностических факторов, автор рекомендует в первую очередь иссечение элективного регионального лимфатического узла в комбинации с диссекцией и адьювантной терапией, для повышения радикальности локального хирургического вмешательства.

Study of the Endotoxin Sensitivity of Pregnant Rats and their Fetuses

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The endotoxin sensitivity of pregnant rats and their fetuses was studied and the following conclusions were drawn:

1. In the third trimester the fetus-damaging effect of endotoxin also involves considerable damage to the mother which often ends with the mother's death (in this experiment in 40% of the cases).

2. The endotoxin sensitivity of the fetuses of one mother is relatively the same.

3. Within the race-specific range the endotoxin sensitivity of a given population of pregnant rats largely varies according to the individual sensitivity.

4. There is no "threshold dose" which would kill each fetus and would not kill any of the mothers.

Based also on literary data, it is concluded that the effect of endotoxin causing fetal death is mediated by humoral factors released from the mother's organism, and fetal death is primarily due to anoxia.

Introduction

It is well known that the pregnant individuals of several species are more sensitive to bacterial endotoxin than the non-pregnant ones and that endotoxin has numerous fetus-damaging effects [7, 10, 12, 14, 15]. In the present experiment the maternal and fetal effects of bacterial endotoxaemia in the third trimester of pregnancy were studied.

In the investigation answers were sought to the following questions:

- What is the interaction between the maternal and fetal endotoxin sensitivity?

- Is there an endotoxin "threshold dose" which would kill each fetus but would not kill any of the mothers?

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- Does endotoxin possess any specific fetus-damaging effect or does the damage to the fetus develop secondary to that of the maternal organism?
- How are the endotoxin sensitivities of the pregnant and non-pregnant rats related?

Material and Method

In the experiments female CFY rats (LATI, Gödöllő) of an average weight of 210 g were used. Based on vaginal smear tests, the females in proestrus were kept together with males for 36 hours, then after repeated vaginal smear tests 100 "sperm-positive" females were included in the experiment. The day of seminal examination was considered the first day of pregnancy. Fifty non-pregnant rats were used as controls.

The animals were kept on granulated rat food and tap-water *ad lib*.

Arrangement of the experiments is shown in Tables 1 and 2.

Endotoxin [LPS (*E. coli* 089) P2 87061601 (OSSKI)] was used i.p. diluted in physiological saline in an amount shown in the table.

In the experiment endotoxin was administered on the 18th day, and in the 48 hours following administration the animals were constantly monitored, the dead ones immediately dissected and the visible changes recorded. The surviving animals were exposed under anaesthesia on the 20th day of their pregnancy and the living and dead fetuses were counted.

TABLE 1

The effect of the same dose of endotoxin on pregnant and non-pregnant rats (experiment A)

MOTHERS				
Group (no. of animals)	Endotoxin 1 mg/animal	Physiological saline 1 ml/animal	Deaths	Survival
1. (15) non-pregn.	—	+	—	15
2. (15) pregn.	—	+	—	15
3. (35) non-pregn.	+	—	1	34
4. (35) pregn.	+	—	11	24
FETUSES				
	Live fetuses		Dead fetuses	
in 11 dead mothers	—		127	
in 16 live mothers	—		178	
in 3 live mothers	14		17	
in 5 live mothers	53		—	
Total	67		+	322 = 389

TABLE 2
The effect of increasing doses of endotoxin on pregnant rats
(experiment B)

MOTHERS						
Group (no. of animals)	Endotoxin treatment mg/animal	Maternal		Distribution of surviving mothers according to their fetuses' behaviour		
		death	survival	Fetal death total	partial	Fetal survival
1. (5)	0.1	—	5	1	—	4
2. (5)	0.2	2	3	—	—	3
3. (5)	0.4	4	1	1	—	—
4. (5)	0.6	2	3	—	1	2
5. (5)	0.8	3	2	1	—	1
6. (5)	1.0	4	1	—	—	1
7. (5)	1.2	4	1	1	—	—
8. (5)	1.5	4	1	1	—	—
9. (5)	2.0	5	—	—	—	—
10. (5)	3.0	5	—	—	—	—
Total		33	17	5	1	11

FETUSES		
	Live fetus	Dead fetus
in 33 dead mothers	—	324
in 5 live mothers	—	47
in 1 live mother	3	8
in 11 live mothers	115	—
Total	118	+ 379 = 479

Results

Results of experiment A are summarized in Table 1. In Group 1 (absolute controls) no death occurred. In Group 2 (pregnant controls) no death occurred. In Group 3 one animal died and 34 survived endotoxaemia. In Group 4, 11 mothers with 127 fetuses died within 48 hours after endotoxin exposure. Twenty-four animals survived the endotoxin exposure and the fate of fetuses was as follows in the surviving mothers: in 16 mothers all fetuses (a total of 178) died, in 3 mothers there was partial fetal death (a total of 14 live and 17 dead fetuses), while in 5 mothers all fetuses (altogether 53) fetuses survived endotoxaemia.

Following endotoxin exposure, during the pathological study of the lost animals, organic changes characterizing endotoxic shock were found including pulmonary edema, thymic, bleeding, congestive enlargement of the liver, intestinal edema, segmental intestinal haemorrhage, thin colonic contents, mesenterial lymph node swelling and bleeding, swelling of the Payer's plaques.

Clinical signs of endotoxic shock were also noted in the animals surviving endotoxin exposure.

The results of experiment B were demonstrated in Table 2. Due to different doses of endotoxin exposure, 33 mothers died with 324 fetuses. In 17 surviving mothers the fate of the fetuses was the following: in 5 mothers all fetuses (altogether 47) died, there was partial fetal death in one mother (3 live and 8 dead fetuses), in 11 mothers all fetuses (a total of 115) survived endotoxaemia. The autopsy record of the dead animals corresponded to that of experiment A. The endotoxin effect could be observed in varying degree in the surviving animals, ranging from a mild "indisposition" (e.g. slightly ruffled fur) to endotoxic shock.

Discussion

In experiment A only one animal died in the nonpregnant treated group (Group 3) due to endotoxin exposure. Comparing to the 11 pregnant dead ones, it can be stated that the pregnant organism is essentially more sensitive to endotoxin. This observation is in agreement with our earlier data reported [7, 8, 10, 12]. At the same time, the further results of the endotoxin-treated pregnant group are also striking. One-third of the 35 animals died (11 out of 35), while in 19 of the surviving 35 animals there were also fetal deaths.

It can be established that due to the applied endotoxin dose, 83% of fetuses and one-third of the mothers died. In one part of the surviving mothers the fetuses all died, in the surviving mothers, however, there was only partial fetal death. There were also surviving mothers, where there was no evidence of fetal death at all. This "scatter" can be attributed to the markedly differing individual endotoxin sensitivities within the species.

Due to endotoxin exposure one-third of the fetuses died (127 out of 389) together with the mothers. Endotoxin could kill a part of the fetuses only when killing the mother as well. The mother's organism seems to give a protection for the fetus against the bacterial endotoxin. It should, therefore, be stressed that in the past two decades several research workers [8, 9, 12, 14, 15] have reported primarily the fetus-damaging effect of endotoxin, while devoting less attention to the changes in the mother. Our observation does, however, refer to the fact that the "fetus-damaging" effect of endotoxin is due to the considerable damage to the mother's organism.

It can be concluded from the data of experiment B that on administration of 0.1 mg endotoxin each mother survived, however with some fetal deaths. As a result of an endotoxin dose of 2.0 mg, however, all mothers died. Consequently, it can be stated that the survival of the fetuses is inversely proportional to the endotoxin dose, however with a considerable individual endotoxin sensitivity. It could be noted that the overwhelming majority of the fetuses (90%) within one mother "behaved" the same way—they all died (in 21 mothers) or all survived (in 16 mothers).

Our experiments as well as the literary data suggest that it is probably not the endotoxin itself which kills the fetus but the circulatory failure induced by the bacterial endotoxin in the mother or the resulting fetal hypoxia. This hypothesis seems to be supported by the observations of Bech-Jansen et al. [2, 3] stating that in pregnant sheep during maternal and isolated fetal endotoxin perfusion, the mother is ten times more sensitive to the same concentration of endotoxin infusion than the fetus itself. There is no essential difference in fetal circulation and oxygen metabolism up to the terminal phase of the mother's shock. The fetus is already sensitive to the mediators produced in the mother's organism which are capable of damaging the fetal oxygen metabolism, independent of the presence of endotoxin. As a result, the process of fetal damage can be triggered by maternal endotoxaemia, however, there is no need of endotoxin for the development of damages (better-to-say, for that of anoxic fetal damages). This seems to be supported by the observation of May et al. [13] that in the baboon, due to endotoxin, as a trigger, such mediators are released which are still present in the circulation 24 hours later, when endotoxin cannot any more be detected in the blood even with the limulus test [5], and can be transferred with the serum of the treated animals to other ones, inducing a pathologic process simulating endotoxaemia.

In fetal death a role can also be played, besides the mediators released in the mother's organism, by the circulatory redistribution associated with the mother's shock, since during this placental circulation can be a reliable reservoir and so this may also contribute, together with thrombi appearing in the placenta, to the exacerbation of fetal hypoxia. It seems to be probable, however, that the process aggravating fetal hypoxia is not a primary one in the defence mechanism of the mother. Our experiments (A and B) also reveal that the maternal organism could survive endotoxic shock only in 54%, with total or partial fetal death.

In view of what has been said, perhaps the question is also less important whether the endotoxin penetrates the placenta. This issue has been studied by several authors, including Hungarians as well [8, 9, 10, 15]. Its penetration into the placenta has been assessed contradictorily. The results of the examinations were certainly influenced by a number of experimental circumstances, e.g. the kind of experimental animal used (mouse, rat, rabbit,

sheep, pig), in which period of pregnancy they had been examined, what kind of endotoxin preparation had been used and how endotoxin had been labelled.

Finally, it should be mentioned that recently several therapeutic attempts have been made for treating obstetric septic-endotoxic shock [4, 7, 11, 16, 17]. Of them the work of Lanchman et al. [11] is to be pointed out, who obtained promising results with pooled anti-endotoxin IgM and IgG human antibodies, as well as that of Bende et al. [4] using haemoperfusion.

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Untersuchung der Endotoxinempfindlichkeit von trächtigen Ratten und ihrer Früchte

Gy. SZÓCS, TERÉZ CSORDÁS und L. BERTÓK

Im Laufe der Untersuchung der Endotoxinempfindlichkeit trächtiger Ratten und ihrer Früchte wurde folgendes festgestellt: 1. Das Endotoxin entfaltet eine fruchtschädigende Wirkung im «dritten Trimester» nur durch die wesentliche Schädigung der Mutter, währenddessen meistens auch die Mutter eingeht (im dargestellten Material betrug diese Prozentzahl 40%); die Früchte einer Mutter verfügen über eine relativ identische Endotoxinempfindlichkeit; 3. eine gegebene trächtige Population reagiert unter Wirkung einer gegebenen Endotoxindosis — innerhalb der, die Spezies charakterisierenden Empfindlichkeit — der individuellen Empfindlichkeit entsprechend mit wesentlichen Unterschieden; 4. es existiert keine derartige «Schwellendosis», die sämtliche Früchte, dagegen aber keine einzige Mutter töten würde. Unter Berücksichtigung der erzielten Ergebnisse und der Literaturdaten werden die Konsequenzen gezogen, daß die die neonatale Sterblichkeit der bakteriellen Endotoxine verursachende Wirkung im mütterlichen Organismus durch die unter Endotoxinwirkung freiwerdenden Mediatoren realisiert wird und in erster Linie die Folge der Anoxie ist; der Prozeß, in dem das in den fötalen Kreislauf eventuell übertretende bakterielle Endotoxin keine wesentliche Rolle spielt, setzt sich auch nach der Eliminierung des Endotoxins fort.

Исследование чувствительности к эндотоксину беременных крыс и их плодов

Д. СЕЧ, Т. ЧОРДАШ и Л. БЕРТОК

Исследуя чувствительность беременных крыс и их плодов к эндотоксину, авторы сделали следующие выводы: 1. эндотоксин оказывает повреждающее действие на плод в «третьем триместре» только через значительное повреждение матери, причем по ходу этого часто (в данных экспериментах в 40%) погибает и мать; 2. плоды одной матери имеют почти одинаковую чувствительность к эндотоксину; 3. данная популяция беременных животных реагирует на данную дозу эндотоксина — в рамках характерной для данного вида чувствительности — весьма различно, соответственно индивидуальной чувствительности; 4. не существует такой «пороговой дозы», которая была бы смертельна для всех плодов и не убила бы ни одной матери. Сравнив свои результаты с литературными данными, авторы пришли к выводу, что действие бактериальных эндотоксинов, вызывающее гибель плодов, осуществляется через медиаторы, высвобождающиеся в организме матери под воздействием эндотоксина, и является в первую очередь результатом аноксии; этот процесс продолжается и после элиминации эндотоксина, и бактериальный эндотоксин, если он попал в кровообращение плода, не играет существенной роли.

The Role of Ca^{2+} Level in Liver Transplantation

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During orthotopic liver transplantation Ca^{2+} assessment was made in the recirculation phase and the ultrastructural changes in the liver were studied. It was established that the Ca^{2+} level decreased progressively. The Ca^{2+} level in the hepatic vein was lower than the arterial value. The EM studies performed in the recirculation phase did not reveal any cellular damage, only the swelling of the mitochondria was striking. Based on the results, the question was raised whether Ca^{2+} can have a prognostic role in assessing the viability of the liver.

According to the practice of transplantation, cold ischaemia has implied a reversible state in the human liver for a period of 8 hours. Recently, by using Belzer's solution this time was prolonged to 30–32 hours. It is known from liver surgery that reperfusion contributes to the development of postischaemic liver necrosis [11]. Therefore, most changes can be anticipated in transplantation at the beginning of recirculation.

In our experiment the changes in the arterial and hepatic venous Ca^{2+} levels were examined. In the recirculation phase the ultrastructural changes were studied by electron microscopy. The experiment aimed at assessing the viability of the transplanted liver.

Material and Method

During orthotopic liver transplantation blood samples were collected on 6 occasions from the femoral artery and 4 times from the hepatic vein of 8 female mongrel dogs, weighing 16.9 ± 1.3 kg. Tissue samples were collected for EM study in the recirculation phase, which were fixed in glutaraldehyde.

During transplantation active veno-venous bypass was applied [10/A Ca assessment was made by an AVL (Austria, Graz) equipment].

Three sham-operated animals served as controls.

Results

Arterial Ca^{2+} level decreases progressively during liver transplantation (Table 1). The decrease is significant during the anhepatic phase and at the beginning of the recirculation phase ($p < 0.01$) (Fig. 1). The changes in the blood of the hepatic vein are conspicuous. The 0.0836–0.0951 mmol/l value of

TABLE 1
Change of the Ca^{++} level during experimental liver transplantation

No. = 8	Transplantation					
	Preparation phase		Anhepatic phase		Recirculation phase	
	1	2	3	4	5	6
Blood sample						
Femoral artery	1.0470 ± 0.0841	1.0175 ± 0.0965	0.8411 ± 0.0983	0.8311 ± 0.1239	0.7529 ± 0.0986	0.7784 ± 0.1674
Hepatic vein	1.0250 ± 0.1002	0.9836 ± 0.0951	—	—	0.7259 ± 0.0853	0.7433 ± 0.0834
No. = 3	Sham-operated					
Femoral artery	1.044 ± 0.112	1.041 ± 0.1231	1.042 ± 0.1096	1.047 ± 0.1311	1.043 ± 0.1219	1.039 ± 0.1198
Hepatic vein	1.025 ± 0.1125	1.012 ± 0.1515	1.021 ± 0.1509	1.021 ± 0.1181	1.022 ± 0.0992	1.024 ± 0.0912

All Ca^{++} values were defined in mmol/l.

the preparation phase at the beginning of the recirculation phase is reduced to 0.7259 ± 0.853 mmol/l ($p < 0.01$) (Fig. 1).

The ultrastructural study of the liver, in the preparation phase, shows a normal pattern of the vascular pole of the liver cell. Only the mitochondria are slightly swollen, the cytoplasmic glycogen is of normal amount. In the cytoplasm lipid droplets containing also neutral fats can be noted (Fig. 2). Following a recirculation of 60 minutes, there are enlarged mitochondria in the cytoplasm of the liver cells. The matrix is pale. The amount of glycogen is markedly reduced, without the characteristic rosette-formation. The amount of rough endoplasmic reticulum is similarly reduced (Fig. 3).

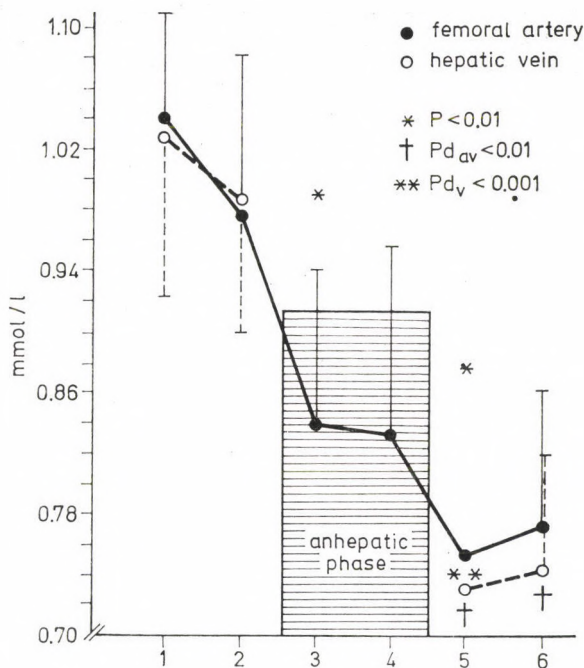


FIG. 1. The change of Ca level during experimental liver transplantation

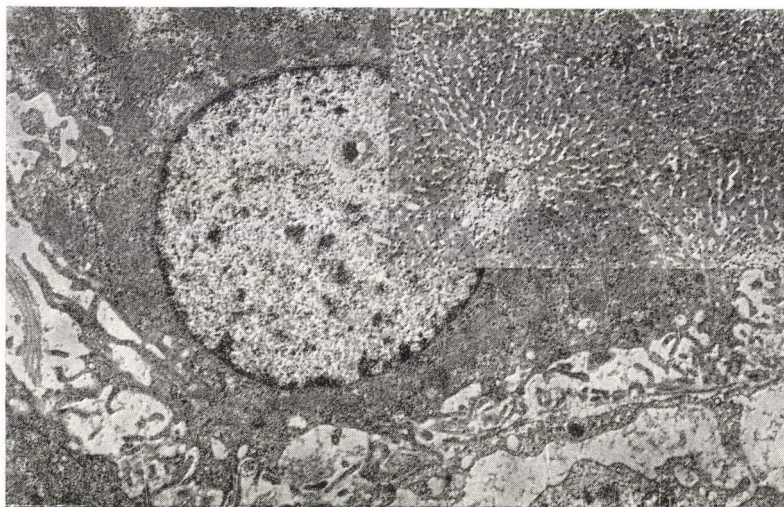


FIG. 2. EM picture of a control dog liver. Basic magnification: $\times 4000$, final magnification: $\times 13,200$

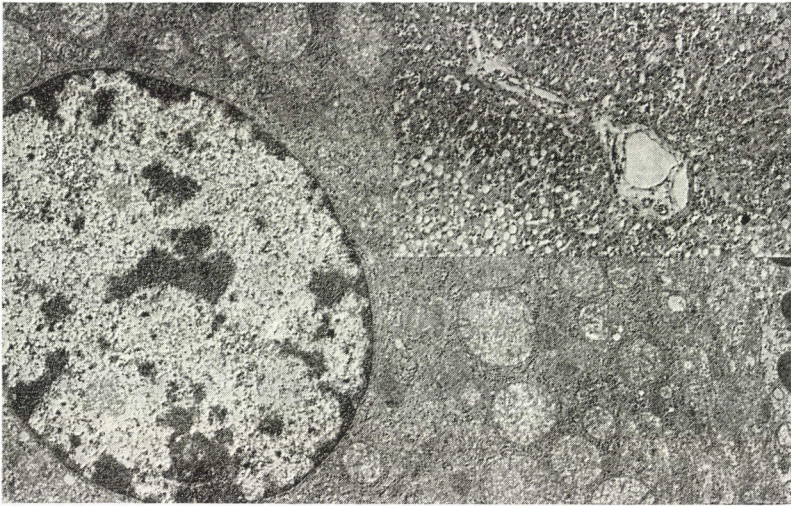


FIG. 3. Sixty-minute recirculation. Transplanted dog's liver. Basic magnification: $\times 4000$, final magnification: $\times 13,200$

Discussion

The 3-hour *in vivo* blockage of the afferent circulation of the liver results in the definitive development of liver necrosis in the rat [3, 4]. Even following reperfusion after one or two hours of ischaemia extensive cellular necrosis was observed [3]. The tolerance to liver ischaemia can be enhanced by several substances and procedures, like e.g. glutathione, allopurinol, methylprednisolone as well as cold and cooling [7, 11, 12].

It was stated that the general characteristics of liver cell death is coagulation necrosis [4]. Seeking the causes of coagulation necrosis of various origin within the liver cell, two hypotheses have been put forward: according to the first one, the effect of Ca^{2+} induces intracellular coagulation [2, 3, 4], while according to the second, the accumulation of the so-called free radicals are assumed to be responsible for the death of liver cells [1, 5].

Concerning the effect of Ca^{2+} , it was proved in intact states and cell cultures that the influx of Ca^{2+} through the impaired plasma membrane produces irreversible damage corresponding to the concentration gradient, and leads to cell necrosis. The structural changes of cellular elements, mainly those of the mitochondria characterizing coagulation necrosis, probably result from the effect of the increased Ca^{2+} level on the macromolecules of the cells [6]. In the extracellular fluid the normal Ca^{2+} concentration is 10^3 M, intracellularly it is 10^{-7} , 10^{-8} M, that is, there is a 10^3 – 10^4 -fold concentration gradient on the plasma membrane. Due to the impairment of the plasma membrane, the entering Ca^{2+} is intracellularly active and damages the mitochondria,

the regulated metabolic functions, the nucleic acids and the cellular proteins [3, 4].

In our studies, during liver transplantation a progressively decreasing Ca^{2+} level and, in recirculation, the swelling of mitochondria were found. The role of the Ca^{2+} level in coagulation during transplantation has already been analysed in an earlier paper [8]. Further investigations are needed for clarifying whether Ca^{2+} concentration increases intracellularly simultaneously with the decrease of Ca^{2+} level. Anyway, the decreased Ca^{2+} level is assumed to be due to their uptake by the liver cells. This assumption is supported by the behaviour of the arterial and hepatic venous Ca^{2+} levels, i.e. the level of the hepatic vein being lower than the arterial one suggests that Ca^{2+} has entered the liver cells.

It is also possible that Ca^{2+} influx is only secondary into the cells of the preserved liver. Due to ischaemia primarily the plasma membrane is damaged and this results in K^{+} outflow, glucose release followed by Ca^{2+} influx into the cell in the recirculation phase [9].

Whatever is the case, what seems to be decisive and of practical importance is that the role of the Ca^{2+} level can be considered prognostic. Undoubtedly, further investigations are required to settle this question satisfactorily. It is also an open question whether this recognition is of therapeutic importance, and whether Ca^{2+} channel blockers (e.g. Verapamil) are of a favourable effect.

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Über die Rolle des Ca^{2+} -Spiegels im Laufe der Lebertransplantation

F. JAKAB, Z. RÁTH, A. ZÁBORSZKY, I. SUGÁR und M. BÖRZSÖNYI

Im Laufe der beim Hund durchgeführten orthotopischen Lebertransplantation wurde Ca^{2+} -Bestimmung durchgeführt und in der Rezirkulationsphase die ultrastrukturellen Änderungen der Leber untersucht. Es ließ sich feststellen, daß der Ca^{2+} -Spiegel progressiv sinkt. Der in der V. hepatica beobachtete Ca^{2+} -Spiegel war niedriger als der arterielle Wert. Die im Laufe der Rezirkulation durchgeführten EM-Untersuchungen vermochten die irreversible Zellschädigung nicht aufzuklären, nur die Quellung der Mitochondrien war augenfällig. Anhand der Ergebnisse wird angenommen, daß das Ca^{2+} bei der Bestimmung der Lebensfähigkeit der Leber eine prognostische Rolle zu spielen vermag.

Роль уровня Ca^{2+} в трансплантации печени

Ф. ЯКАБ, З. РАТ, А. ЗАБОРСКИ, И. ШУГАР и М. БЁРЖЁНИ

В ходе ортотопической трансплантации печени в экспериментах на собаках авторы определяли уровень Ca^{2+} и изучали ультраструктурные изменения печени в стадии рециркуляции. Установили, что уровень Ca^{2+} прогрессивно снижается. Уровень Ca^{2+} , отмеченный в печеночной вене, был ниже артериального уровня. Исследования под электронным микроскопом, произведенные в стадии рециркуляции, не обнаружили необратимых клеточных повреждений, бросалось в глаза только набухание митохондрий. На основании полученных результатов авторы предполагают, что уровень Ca^{2+} может иметь прогностическую роль при определении жизнеспособности печени.

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Prognostic Factors and Treatment Tactics in the Surgery of Liver Abscesses

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(Received: September 13, 1989)

The prognostic factors of 21 patients with pyogenic liver abscess were analyzed. It was stated that survival is unfavourably influenced by hyperbilirubinaemia, the mixed bacterial population, the associated diseases as well as the tumorous process. As a result of portal antibiotic perfusion, there was no difference in the mortality rates of multiple and solitary liver abscesses. Based on the analysis of the prognostic factors, the surgical tactics is developed, i.e. a need for surgical exposure is supported, which imposes three tasks: exposure of the abscess(es), management of the primary process inducing the abscess and introduction of a cannula for portal antibiotic perfusion. Besides some criteria, although the author do not have experience in this field, they suggest the use of percutaneous drainage controlled by echography or CT, basically because of the lower mortality rate.

The mortality of patients operated because of liver abscess has only slightly decreased in the last decades, despite that both diagnostic and therapeutic facilities have considerably improved. The mortality rate still exceeds 25%. It is assumed that a lack of improvement can be ascribed to a shift in occurrence of liver abscesses. Compared with data of the previous decades, patients with liver abscess are nowadays older. The inducing primary disease is more often a tumorous process. Another conspicuous change is that the biliary origin has become the most frequent [1, 2, 4, 13, 17].

An improvement can be expected in each field of surgery from the accurate determination of prognostic factors, risk assessment and of the selection of more careful management tactics. Consequently, the data of our patients with liver abscess, the results of their surgical treatment were analyzed on the basis of the above criteria, then with a view to them, an attitude was adopted for developing more effective management tactics.

Material and Methods

The data of 21 patients with liver abscess were surveyed at the 3rd Department of Surgery, Semmelweis University Medical School, from January 1, 1982 to December 31, 1987 as well as at our Department of Surgery from January 1, 1988 to March 31, 1989.

Liver abscess was diagnosed on the basis of operative finding and autopsy records. The criteria of abscess were represented by the macroscopic picture, the cavity of the liver with purulent contents and a positive bacteriological finding. The clinical history and symptoms, the localization and origin, the microbiological finding, the forms of treatment and the mortality of liver abscess were analyzed. The correlations between clinical data and mortality were examined by the χ^2 test. The p value was considered significant, if $p < 0.05$.

Results

The average age of the 21 patients with liver abscess was 58.5 years, with a sex distribution of 14 males and 7 females. All the abscesses were pyogenic.

In 9 patients the liver abscess was solitary, while in 12 of them multiple abscesses were observed (Table 1). Concerning its origin, it was found that the

TABLE I
The origin of liver abscesses (1982–1989)

Origin	Right lobe	Left lobe	Multiple	Mortality
Gallbladder-bile duct calculus, inflammation, injury, tumour	5	1	5	5
Septic complication of previous operation	—	—	5	2
Previous septic intraabdominal process, operation (appendicitis, perforation of diverticula) via the portal vein	2	—	—	—
Endocarditis, via the hepatic artery	1	—	—	1
Unknown cause	—	—	2	—
Total	8	1	12	8
	21			

abscesses of 11 patients had arisen in the gallbladder. In 7 patients, the primary focus was an intraabdominal septic process. In 5 of the the abscess was due to the septic complication of a previous operation (i.e. suture insufficiency, intraabdominal abscess, etc.), while in 2 patients to a previous septic intraabdominal disease (appendicitis, perforation of a colonic diverticulum). In one patient septic endocarditis had lead to the development of the hepatic, and according to the autopsy record, to a cerebral abscess. In two patients the cause of abscess could not be clarified.

Fever mostly preceded by shivering chills was the most general symptom. Abdominal pain and hepatomegaly were found in about half of the patients. The alkaline phosphatase value was elevated in all cases. The serum bilirubin level exceeded 90 mmol/l in 13 patients.

Two patients were not operated: the patients were referred to us in a dying state in both cases. Diagnosis was similarly made but it was, however, only verified at autopsy.

Nineteen patients were operated. The operation included the transperitoneal exposure, emptying and draining of the abscess/es. In 14 out of the 19 patients, the primary disease inducing the liver abscess was also treated surgically (Table 2). In 7 of the 19 patients, portal antibiotic perfusion was made via the umbilical or a mesenteric vein.

TABLE 2
Surgical interventions for treating the primary disease causing liver abscess

Operation	No.
o Cholecystectomy, T tube	4
o Cholecystectomy, choledochoduodenostomy	1
o Rodney Smith operation	1
o PTD (due to tumorous biliary obstruction)	2
o Liver resection	2
o Emptying and drainage of intraabdominal, interintestinal abscesses	2
o Transformation of Billroth I operation due to insufficiency into Billroth II	1
o Biliary drainage	1
Total	14

In two patients, additional exposure was performed due to residual or recurrent abscess. In one of them permanent thoracic drainage and suction had become necessary as a result of consequential thoracic empyema. In another patient three exposures were made for a similar reason. This latter patient was lost.

Eight of the 21 patients died (Table 3). Death was due to severe, general sepsis in 7 patients. General sepsis was caused by endocarditis in one case, by residual or recurrent liver abscess in 5 patients, and by septic intraabdominal foci in one case. The liver abscess or the septic intraabdominal process could not be cured surgically. It is to be noted that 4 of the 8 patients lost, had an underlying malignant process.

TABLE 3
Cases of death of patients with liver abscess

GENERALIZED SEPSIS	
○ endocarditis	1**
○ residual or recurrent liver abscess	5**
○ intraabdominal abscesses	1
HEPATIC FAILURE	1
Total	8*

* Four of the 8 patients had a malignant underlying process; ** The patient suffering from endocarditis and the one from liver abscess were not operated

Data on the correlation between clinical factors and mortality are shown in Table 4. There was no significant correlation between the serum bilirubin level, the number of microorganisms as well as between the underlying tumorous process, the associated diseases and the mortality. Age, previous operation/s, and to our greatest surprise, the solitary or multiple character of the abscess had not proved to be decisive prognostic factors.

TABLE 4
Prognostic markers in the deaths due to liver abscess

Factors	No. of patients	Deaths	<i>p</i> value
Age over 70	7	3	$p > 0,05$
Age under 70	14	5	
Serum bilirubin level over 90 mmol/l	13	7	$p < 0,001$
Serum bilirubin level under 90 mmol/l	8	1	
Multiple localization	12	5	$p > 0,04$
Solitary localization	9	3	
Combined microorganisms (incl. anaerobic ones, too)	12	7	$p < 0,05$
One kind of microorganism	7	1	
Tumorous underlying process	6	4	$p < 0,01$
Benign underlying process	15	4	
Previous operation/s	14	5	$p > 0,05$
No operation	7	3	
Associated disease (tumour, organic failure, diabetes mellitus)	12	7	$p < 0,05$
No associated disease	9	1	

TABLE 5
Portal antibiotic perfusion in the treatment of liver abscess

Solitary			Multiple			Solitary			Multiple		
No.	Residual or recurrent abscess	Death	No.	Residual or recurrent abscess	Death	No.	Residual or recurrent abscess	Deaths	No.	Residual or recurrent abscess	Deaths
2	—	—	5	1	1	7	2	4	7	2	3
Total 7	Resid. or 1 recurrent abscess	Death	1			Total 14	Resid. or 4 recurrent abscess	Deaths 7			
$p < 0.05$											

In further analyzing the question it is assumed that the favourable change in mortality had been due to portal antibiotic perfusion (Table 5).

The ratio of complications was high in our patient material. The most important complications included pneumonia, concomitant thoracic effusion, empyema, wound suppuration, urinary infection and recurrent sepsis.

Discussion

Based on the advance in the last decades (new antibiotics, the progress in the methods of liver surgery, the improvement of preoperative diagnosis, new methods in anaesthesia and intensive care), a considerable improvement in the results of liver abscess surgery could be expected. However, this has not occurred either in view of the literary data or our own experience [1, 4, 7, 13, 15]. These have led us to analyze the factors influencing mortality data due to liver abscess. The retrospective study revealed that factors unfavourably influencing the outcome were hyperbilirubinaemia, the mixed bacterial population and the associated diseases. Of the associated diseases, the malignant primary process should be pointed out. Age, previous operations and the multiple appearance of abscesses did not prove to be factors influential in mortality.

Bergamini [1], Pitt [17] and Miedema [13] found that on the multiple appearance of abscesses mortality was significantly higher. Based also on earlier experience, now we proved by statistical analysis that portal antibiotic perfusion had favourably affected survival [6]. Supposedly, in the multiple liver abscess the decrease of survival could have been more significant without the portal antibiotic perfusion.

The explicit prognostic value of the elevation of bilirubin level is emphasized by Bergamini [1]. Our observations are in agreement with this statement.

Percutaneous drainage [7] has become accepted in treating liver abscess in recent years. The results are favourable in selected cases. Although in our material no case has been treated with percutaneous drainage, by adopting Gerzof's view and strict criteria [7], we assume that percutaneous drainage is an excellent procedure in treating liver abscess provided the abscess is solitary and there is no urgent need for solving the underlying primary intraabdominal disease (Table 6).

TABLE 6

Indications for the percutaneous drainage of liver abscess

-
1. Besides the liver abscess, there is no other intraabdominal focus requiring surgery
 2. The cavity of the abscess can easily be reached by percutaneous technique
 3. If laparotomy involves a serious risk for the patient
-

Since, in the majority of cases liver abscess is a consequence, the advantage of exposing the liver abscess transperitoneally is that it also offers a possibility for the surgical solution of the primary intraabdominal disease producing the abscess.

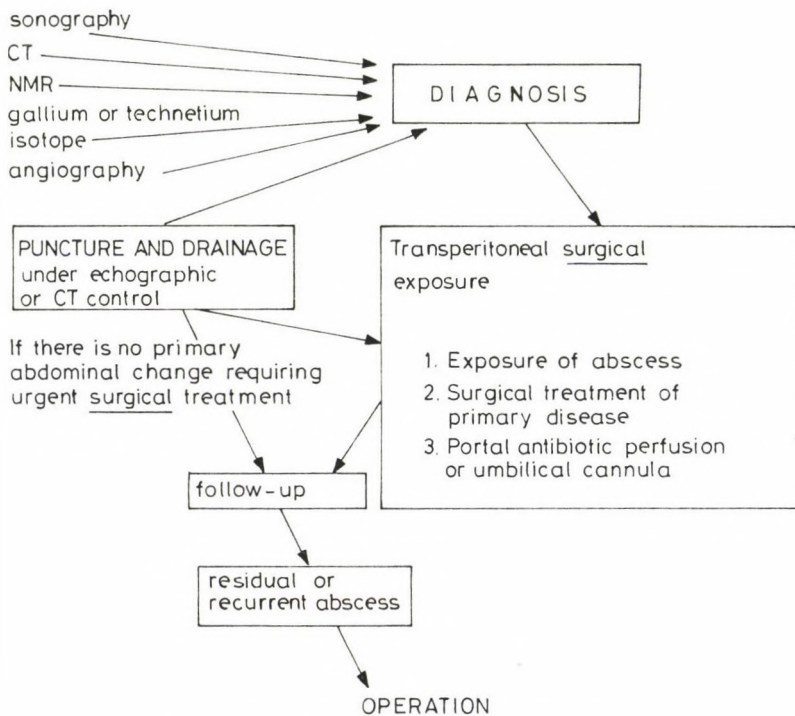


FIG. 1. Treatment tactics in the surgery of liver abscesses

It seems to be an important observation that portal antibiotic perfusion has favourably influenced the development of residual or recurrent abscess and survival. That is why we have adopted the opinion that introduction of a portal cannula should be the third component of surgical exposure (Fig. 1).

Provided that there is no detectable primary abdominal change requiring urgent surgical treatment and the other criteria are also present, sonography or drainage of the abscess under CT control is an effective procedure resulting in lower mortality than surgical exposure.

It is important to discuss the question of residual or recurrent liver abscess because this is the factor which also influences mortality unfavourably

TABLE 7
Mortality of liver abscess

Treatment	Author/year	No. of cases	Mortality, %		
Surgical exposure	Brodine 1973	234	51		
	de la Maza 1974				
	Hill 1982				
	Lazarchick 1973				
	Ranson 1975				
	Rubin 1974				
	Wintch 1982				
	Pitt 1975			29	21
	Cheung 1978			14	29
	Miedema 1984			65	26
	Bergamini 1987			31	32
Jakab 1984	21	38			
		Total	394	32.8%	
Percutaneous	Novy 1974		1		
Percutaneous drainage	Tetz 1973	1	0		
	Novy 1974	2	0		
	Stephenson 1978	1	100%		
	Haaga 1980	7	0		
	Perera 1980	3	0		
	Kraulis 1980	2	0		
	Scheinfeld 1982	2	0		
	Karlson 1982	6	0		
	Brolin 1984	2	0		
	Gerzof 1985	12	0		
Bergamini 1987	4	2	50%		
		Total	42	3	7.1%
Percutaneous or surgical drainage or without treatment	Brodine 1973	62	90		
	Pitt 1975	38	97		
	Cheung 1978	6	95		
	Miedema 1984	41	95		
		Total	147	91.25%	

[7, 21]. Any form of treatment is applied, if fever does not occur, or it recurs with septic symptoms, a residual or recurrent abscess is to be considered which can be detected by sonography or CT. For the time being we believe that in residual or recurrent abscess the surgical solution is justified.

Table 7 demonstrates the overall results on the treatment of liver abscess. The mortality rate of 91.25% of the 147 patients of Brodine [2], Cheung [4], Miedema [13] and Pitt [17], having not been treated either percutaneously or surgically, seems to indicate that much yet remains to be done in detection.

The results of percutaneous drainage are far better than those of surgical exposure. It cannot be ignored, however, that the procedure was applied in a selected group of patients.

The mortality rate after surgical treatment of liver abscess has ranged between 21 and 15% in the past 15 years. It is assumed that in order to improve the results the careful analysis of prognostic factors, portal antibiotic perfusion as well as percutaneous drainage under sonographic or CT control can be recommended.

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Prognostische Faktoren und Behandlungstaktik in der Chirurgie der Leberabzesse

F. JAKAB, Z. RÁTH, F. SCHMAL, I. SUGÁR und J. FALLER

Analysiert werden die prognostischen Faktoren von 21 Patienten mit pyogenem Leberabszeß. Es wird festgestellt, daß durch Hyperbilirubinämie, durch eine gemischte Bakteriumpopulation, interkurrente Krankheiten ferner durch einen tumorösen Prozeß das Überleben ungünstig beeinflusst wird. Dank der portalen Perfusion meldete sich betreffs der Mortalität zwischen multiplen und solitären Leberabszessen kein Unterschied. Die Taktik der chirurgischen Behandlung wird aufgrund der Analyse der prognostischen Faktoren zusammengestellt: namentlich wird für die chirurgische Freilegung eine Stellung eingenommen; diese hat drei Aufgaben: Freilegung des Abszesses bzw. der Abzesse, Versorgung des, den Abszeß auslösenden primären Prozesses und Einführung einer Kanüle zur portalen antibiotischen Perfusion. Nebst gewissen Kriterien wird — obwohl diesbezügliche eigene Erfahrungen fehlen — wegen der grundlegend niedrigeren Mortalität, die ECHO- oder CT-gesteuerte perkutane Drainage als indiziert gehalten.

Прогностические факторы и лечебная тактика в хирургии абсцессов печени

Ф. ЯКАБ, З. РАТ, Ф. ШМАЛ, И. ШУГАР и Й. ФАЛЛЕР

Авторы анализируют прогностические факторы у 21 больного с пиогенным абсцессом печени. Они показывают, что гипербилирубинемия, смешанная бактериальная популяция и сопутствующие заболевания, а также опухолевый процесс неблагоприятно влияют на выживание. При портальной перфузии антибиотиков не отмечали разницы в летальности от множественных и одиночных абсцессов печени. На основе анализа прогностических факторов авторы разрабатывают тактику хирургического лечения, имеющего три задачи: вскрытие абсцесса(-ов), лечение первичного процесса, вызвавшего абсцесс, и введение канюли для портальной перфузии антибиотика. При наличии определенных критериев — хотя в этом отношении авторы не располагают личным опытом — они считают оправданным перкутанный дренаж под контролем ультразвука или КТ из-за существенно меньшей летальности.

Experience Obtained during Liver Resections Made under Experimental Conditions by a Telescopic Compressor (AKE)

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(Received: November 27, 1989)

Liver resection experiments in dogs made by the AKE telescope compressor are reviewed. It is established that the instrument can be applied to the liver parenchyma of varying size and compressibility. The time of resection is short and the intervention entails only minimal loss of blood. Using this solution, it is not necessary to produce the transitory warm ischaemia of the liver.

The first papers on liver resection are known from the last century [3, 4]. In the past twenty years an important role has been attached to the research and morphological study of transhepatic interventions in experimental and clinical work. These included mainly the functional and morphological changes of the organ, as well as the regeneration of the liver parenchyma.

In the practice of liver resections the method controlled according to Adson and Jones [1] and the finger fracture technique used by Lin [5] have become the most widely used. These latter operations were initially performed by the author by the temporary compression of the structures of the hepatoduodenal ligament in warm ischaemia of the organ, inducing a consequential splanchnic stasis. To overcome these disadvantages a "clamp" named after him [6] was applied by him and also by others with success [7, 9, 12]. Based on reports, the resection line can be marked out 2.5–3 cm from the edge of the instrument, blood loss amounted to 500–3500 ml. The finger fracture technique has simplified the surgical management of liver parenchyma and so it has come to be widely used.

The operation is performed by several authors in warm ischaemia of the organ. All the drawbacks are partly known. Currently, research concentrates on the consequences of the lesions due to ischaemic, reperfusion and splanchnic stases.

In addition to the above-mentioned "clamp", to eliminate these drawbacks, as well as to reduce operative risk, an instrument was used for the same purpose created by Nakayama [8] and Storm [11], which have not come to be widely used.

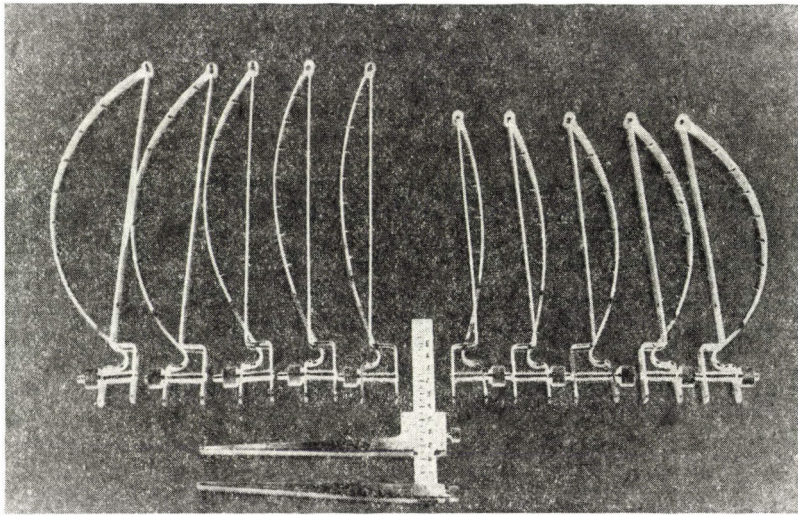


FIG. 1. Some pieces of the instrumental series and the attached height gauge

The telescope compressor set (AKE) was devised on the basis of studies on a large number of cadaver livers (Fig. 1), the technique of which has already been reported elsewhere [2]. Using this instrument, the experience of operations performed under experimental conditions are reported in the present work.

Experimental Methods

The investigations were carried out in mongrel dogs of both sexes, weighing 12–60 kg. Following 16 preliminary experiments, 10 acute and 42 surviving operations were made. The dog's liver is lobulated, consisting most often of six lobes. The biggest is the left middle lobe constituting 40% of the parenchymal substance. Its shape and blood supply render it suitable for resection experiments. The length, width and height of the lobe were measured in each case.

The course of the operation was as follows:

After preparation with atropine morphine, following upper median laparotomy, the middle lobe was isolated under hexobarbital anaesthesia. The width of the hepatic lobe was measured in the required resection line, then the thickness and compressibility of the parenchyma were established by using a height gauge. Based on the data obtained, the instrument suitable for the given region was selected and introduced (Fig. 2). As a result of compression a moderate venous stasis could be noted in the segregated portion of the liver. Two to 10 mm from the edge of the instrument the Glisson capsule was transected,

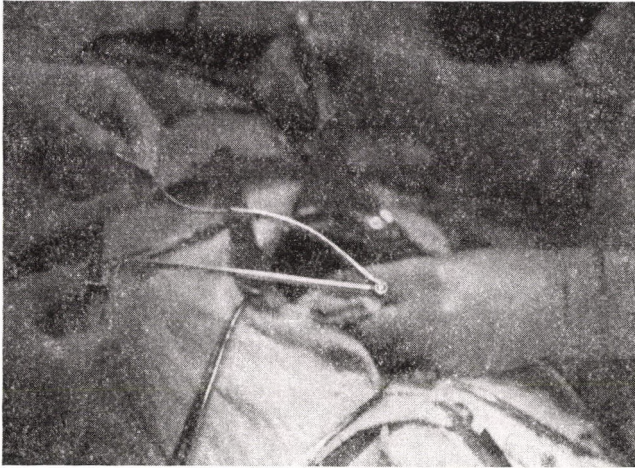


FIG. 2. For explanation see text

then liver parenchyma was crushed by finger fracture technique, the vessels, the bile ducts were clamped, transected, then ligated (Fig. 3). This manoeuvre takes on average 6 to 8 min, the shortest one lasting for 4, the longest for 15 min. Subsequently, compression was gradually stopped by a screw-thread and the resection surface monitored. Haemostasis was made by a pack absorbed in saline solution, by clamping of the vessel and by inserting sutures into the liver parenchyma. The stump was left uncovered. Then the length, width and thickness of the remaining stump were measured. Drainage was not performed. After revision, the wound was closed in two layers.



FIG. 3. For explanation see text

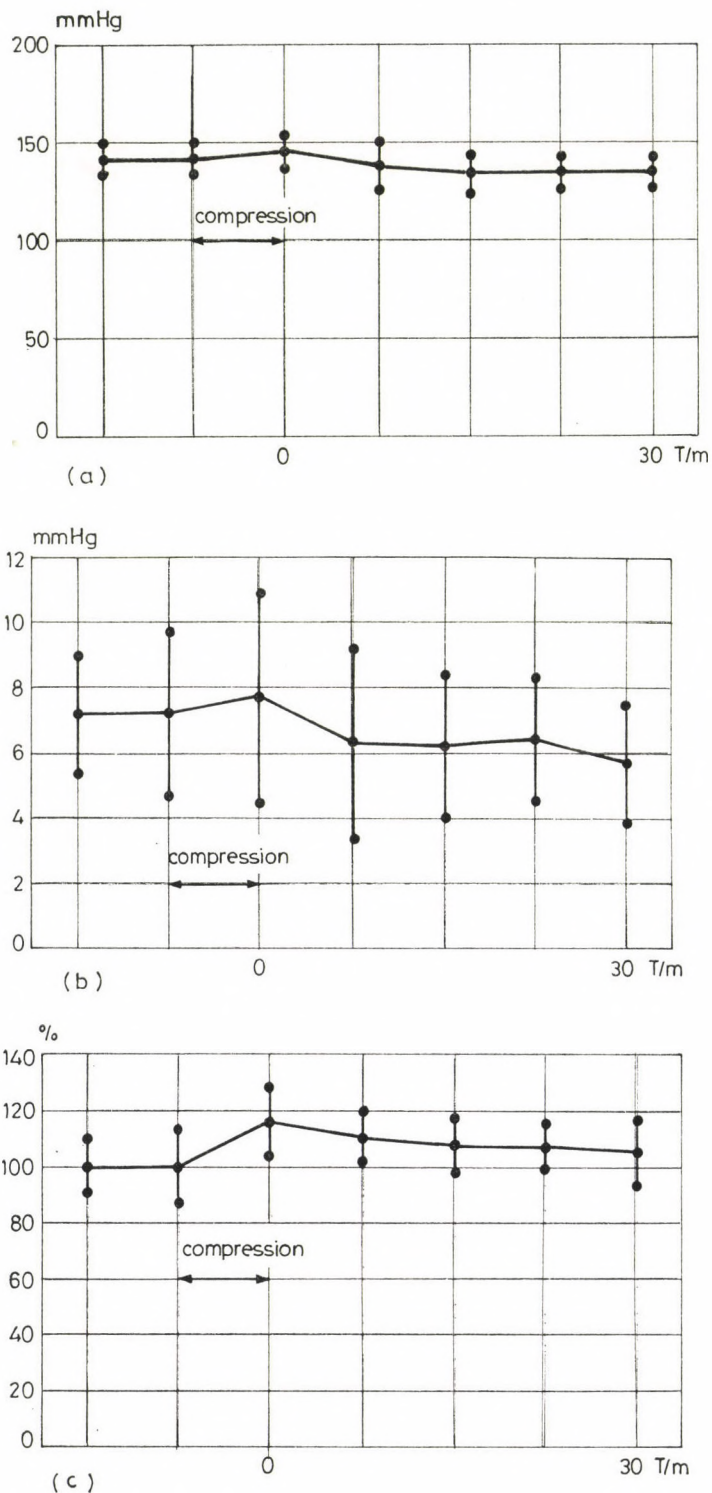


FIG. 4. (a) — mean arterial pressure; (b) — left ventricular end-diastolic pressure; (c) — speed of relaxation change in pressure. $n = 5$. The changes are in the physiological range

In ten animals, blood was collected 3 h prior to and after the operation for laboratory tests on the 1st, 3rd, 7th, 14th, 21st, 28th, 42nd and 180th postoperative days. In five animals also haemodynamic studies were performed completed by Astrup examination. During the preliminary experiments the operated animals had not received infusions, during the test series they were administered a 10% fructose infusion of 300–1000 ml pre- and intraoperatively.

Results

Based on the measurements, the length, width and height of the left middle lobe ranged from 11 by 10 by 2.5 to 15 by 15 by 6 cm.

According to the haemodynamic studies, circulation was balanced during the operation and during the monitoring time of 30 min following haemostasis (Figs 4 a, b, c).

During the Astrup examinations there was no change (Table 1).

Of the laboratory tests, the K^+ level and the Hb values are of importance displaying no change. Intraoperative blood loss, a part of which had derived from the segregated liver portion was estimated at about 15–30 ml.

TABLE I

Astrup examination based on samples taken from the femoral artery (upper values) and the external jugular vein (lower values)

	Before resection	After resection	30 min after resection
PH	7.36–7.39	7.32–7.36	7.34–7.38
PCO ₂	35–40	36–42	34–38
PO ₂	92–99	86–94	90–96
HCO ₃	23–26	21–25	23–27
TCO ₂	23–25	25–28	23–26
ABE	–5.0– –1.0	–5.0– –2.0	–4.0– –2.0
SBE	–2.0– +2.0	–4.0– –1.0	–2.0– 0.0
SAT	88–96	82–90	85–91
SBC	21.8–22.7	21.0–22.2	21.6–22.3
PH	7.30–7.32	7.26–7.31	7.28–7.30
PCO ₂	51.1–53.4	54.4–54.8	51.4–53.0
PO ₂	55.4–56.8	54.3–55.6	55.2–56.1
HCO ₃	22.3–23.8	22.0–23.4	22.1–23.4
TCO ₂	24.2–26.2	24.0–25.8	24.4–26.4
ABE	–3.8– –2.0	–4.4– –2.8	–3.2– 2.6
SBE	–4.8– –3.0	–6.2– –3.8	–5.6– 3.2
SAT	82.8–86.0	80.2–83.3	81.8–84–8
SBC	20.1–21.0	19.2–20.2	20.2–21–1

During a single resection, 6–10 ligations were necessary. Haemostasis decisively by using a pack absorbed with warm saline solution—except in the cases—was sufficient. In three cases, on stopping compression, minor arterial bleeding was noted, solved by ligation. On one occasion, a ligature detached from an about 6–8 mm vein, after the defective cutting of the ligature. After rapidly restoring compression, it was clamped, then ligated. During the preliminary experiments and the experimental series 2 animals were lost in each due to infection or to attacks by the other dogs. These occurred 4 to 20 day-postoperatively. Their operative region was normal. The animals were sacrificed after the operation—in acute cases after 4 h, in the surviving series on the 1st, 3rd, 7th, 14th, 28th, 42nd, 180th and 365th postoperative days. In case of the 4 h survivals 10, while in the others in all cases 5 animals each were evaluated.

The following conclusions were drawn:

- No secondary bleeding and bile flow were noted.
- The resection surface was covered in all cases by the lesser omentum, in 4 cases, however, also the stomach showed adhesion in a small region.

On the first postoperative day the omentum could be pulled down and the resection surface was covered by a thin coagulum. There was no evidence of accumulation of blood or bile on the surface either. There was no trace of the fixing nails of AKE, in two cases, a pale subcapsular suffusion could be noted along the resection line.

On the third day adhesion of the omentum was strong, but detachable. On the seventh postoperative—day it could be removed only by sharp dissection from the resection surface, therefore, this time can be considered as the duration of healing. Although the resected stump and the more distant parts of the liver showed considerable macroscopic and microscopic changes—reported in a separate paper—there was no parenchymal damage in the entire region of the liver. The vessels and bile ducts were patent and of an average lumen. The wall of the gallbladder was normal, and contained the usual liquid bile. The pressure of the bile ducts was measured by a Caroli–Hess manometer. Prior to it, basic examinations were made in 10 cases, during which the pressure was found to be 9–17 water cm in the dog's common bile duct. In view of this, examinations were made in 5 acute operations 4 hours after resection and in the surviving series on the 1st, 42nd and 180th postoperative days. The obtained results ranged between 8 to 15 water cm, i.e. within the physiological range. The pressure of the pancreatic duct was measured in the same animals. This was done on the basis of Sápý's work [10], who found the physiological range to be 15–20 water cm using the same instrument. The value measured by us was 13–17 water cm, which was also physiological. No adhesions occurred

in the abdominal cavity with unheeded passage, and the organs of the abdominal cavity were found to show no pathological sign.

The animals tolerated the intervention well, they woke after some hours and were fed the following day.

Discussion

According to our experience, the instrument can already be introduced at 1–2 cm from the entering of the large vessels. Due to its variable size, it can be applied for any region of the hepatic lobe. During the experiments about 40–80% of the left middle hepatic lobe was removed in planes of varying direction. During this resection was performed at 2 to 10 mm from the edge of the instrument and so the ischaemic zone was very narrow. This small distance was sufficient for keeping the compressor stable. The finger fracture technique is easy to master, the animal experiments providing an adequate training for it. In six cases during the preliminary experiments resection was made with normal circulation by the crushing technique on the left middle lobe, during continuous, leaking bleeding. By using a compressor the interventions can be made without bleeding and under the inspection of structures.

The thin venous and bile structures do not need to be clamped and ligated because they display considerable contractility. Therefore, we exerted considerable traction on them while crushing the liver and they were torn and retracted into the parenchyma.

On haemostasis, a coagulum develops in the recesses of the parenchyma, which according to our observations, provides an adequate barrier for these small structures. That the haemostasis of the resection surface is relatively easy to solve is due to them, as well as to the stasis during the temporary compression of the parenchyma and also to the possibility of recompression.

During these experimental liver resections it was found that the instrument:

- could be applied to a piece of liver parenchyma of varying size and compressibility;
- by using it, an organ-preserving operation is possible;
- the intervention produces only an insignificant blood loss;
- the blood supply of the remaining stump is unheeded;
- postoperative bleeding, and spillage of bile were not observed;
- warm ischaemia involved only a small amount of tissue and only for a short time;
- duration of the operation is short and causes only a small strain;
- it is easy to apply and to master.

Before introducing it into human practice it was found necessary to try the possibilities offered by this instrument under, experimental conditions and to make a detailed evaluation of results.

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Erfahrungen im Laufe der unter experimentellen Verhältnissen mit dem Kompressions-Teleskop-Gerät durchgeführten Leberresektionen

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Erörtert werden die beim Hund mit dem Kompressions-Teleskopischen-Gerät «AKE» durchgeführten Leberresektionsversuche. Es wird festgestellt, daß das Gerät bei Lebersubstanzen mit unterschiedlicher Größe und an jenen die zusammendrückbar sind, eine Verwendung finden kann. Die Resektionszeit ist kurz, der Blutverlust minimal. Im Falle der Anwendung dieser Lösung erübrigt sich das Zustandebringen einer vorübergehenden warmen Ischämie der Leber.

Опыт, полученный в ходе резекций печени, выполненных в экспериментальных условиях компрессионным телескопическим инструментом (AKE)

A. АНТАЛ, Л. ПАПП, И. МИКО и И. ФУРКА

Авторы знакомят с экспериментальными резекциями печени, выполненными на собаках с помощью компрессионного телескопического инструмента (AKE). Было установлено, что данный инструмент применим на веществе печени различного размера и сжимаемости. Время резекции короткое, она сопровождается минимальной потерей крови. В случае выбора этого способа отпадает необходимость в преходящей теплой ишемии печени.

The State of the Testicle and the Epididymis Associated with Exstrophy of the Bladder in Undescended Testes

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In undescended tests, the large number of testicular dysplasias/hypoplasias and of that of the fusion abnormalities of the epididymis, and the joint occurrence of the two, can achieve even 50%. The frequency of the above anomalies were studied in undescended testes associated with exstrophy of the bladder. Bilateral undescended testes were observed in 5 out of 26 boys born with vesical exstrophy. In 3 of them bilateral orchiopexy had already been performed. In 5 of the 6 operations intact testicles and intact epididymis were found. Fusion abnormality was observed only in one case, but the testicle was intact also in that case. This can be attributed to the fact that in exstrophy of the bladder, the testicles have failed to descend not due to the insufficient effect of fetal androgen, but due to anatomical causes. This is also supported by the fact that were the disorder of descension has been caused by mechanical factors, there was a much lower ratio of testicular-epididymal fusion abnormality.

It is well known that some developmental disorders or congenital states are often associated with the absence of descension of the testicles. Retained testicle can be observed in a large number in 100% of the classical form of prune-belly syndrome, in Kallman's syndrome, in Prader—Willi's syndrome, in the more severe forms of hypospadias (scrotal hypospadias, but chiefly in perineal hypospadias). The frequent occurrence of undescended testes is also conspicuous in boys born with the closure abnormalities of the abdominal wall (e.g. omphalocele, exstrophy of the urinary bladder). It can only be guessed in these conditions that which factors have affected unfavourably the descension of testes. In the majority the aetiological factors have still not been clarified nor is it known whether it is uni- or multifactorial whether it has been due to undescended testes in several clinical pictures or due to other factors varying by clinical pictures. As several hypotheses have been put forward for each step of the physiological process of descension, similarly are the pathologic events explained diversely in the above conditions. In these congenital disorders the careful analysis of the state of the patient, and the observation during the surgical management may answer the above questions. In the present paper our examinations on the surgical fixation in the scrotum of the undescended testes of boys born with vesical exstrophy are reported.

Patients and Methods

In the 16 years between October 1, 1973 and October 1, 1989, operations because of vesical exstrophy were carried out on 38 children (26 boys and 12 girls). In the patients with the conditions given, primary closure of the bladder was performed. In those where this was impossible, and in those where primary closure of the bladder had failed, the ureters were opened into the sigmoid. Subsequently, in a second session, reconstruction of the abdominal wall was made. This was followed in boys by urethroplasty to correct epispadias and by orchiopexy in undescended testes, while in girls by the plastic operation of the external genitals. Undescended testes were found in 5 of the 26 boys which were palpable in 4 children inguinally on both sides. In one of them there were abdominal retained testes bilaterally. In three children bilateral orchiopexy was made, in two boys orchiopexy had still not been made in the operative series. During orchiopexy the position of the testicle, its relation to the inguinal canal, as well as its size and turgor, and the state of the epididymis, and the intact or pathological state of the testicular-epididymal fusion were observed.

Results

During orchiopexy the testes were found in all cases in the inguinal region, distal to the outer orifice of the inguinal canal. In 5 of the 6 operations, testicles of an adequate size and of a good turgor were noted and their fusion with the epididymis was also sufficient. In these cases the vaginal process of peritoneum was closed. In one case with testes of normal size the epididymis fused with the testes only at a small region at the head, the other parts were removed from the testicle. Here, the vaginal process remained open towards the abdominal cavity.

Discussion

In undescended testes, it can often be observed that the testes are smaller than usual, of a flaccid consistence, and, at the same time, imperfect testicular-epididymal fusion occurs in a strikingly large proportion [4, 6]. In other cases the testes are of normal size, of good turgor and in such cases also the epididymis is intact, with a full fusion between the testicles and the epididymis. Our observations during 1386 operations made for undescended testes have earlier been reported [6]. Intact testes and intact adnexa were found in 55.9% of the operations, with pathological state of the testes or epididymis in 44.1%. There are several reasons for why undescended testes are in one case adequately developed, while in others flaccid and hypoplastic. Since the normal

development of the testes and the epididymis are testosterone-dependent on the effect of which is needed for the descension of the testes, it is obvious that small testes, or testes, imperfectly or not fused with the epididymis, are due to reduced hormonal effect. The explanation is less obvious in the case of intact testes and epididymis. According to accepted views, anatomical causes or a mechanical obstruction to its passage are assumed to be responsible for the maldescent. In this group the so-called ectopic testicle is well known where the end of the gubernaculum testis is not attached to the bottom of the scrotum, but to somewhere else and so the testes do not descend into the scrotum. The resultant perineal, femoral ectopy is very rare. However it occurs frequently, that the fibres of the gubernaculum testis end around the inguinoscrotal region or in the scrotum, but not at its bottom. In such cases the testes can most often be found inguinally, and regarding their position, no difference can be made between the state of these testes and that of testes retained because of hormonal deficiency. Only careful examination of the bundles of the gubernaculum can reveal the ectopic nature. So the diagnosis of this "superficial inguinal testicular ectopy" as well as its frequency of occurrence are divergently reported by different authors. Moul and Belman [5] observed its occurrence in 66%, while Kleinteich et al. [3] in 11.5% of the cases.

The pathogenesis of retained testes due to exstrophy of the bladder is explained several ways. One of the theories is based on the assumption according to which the intraabdominal pressure present in healthy fetuses is necessary to the passage of the testes through the inguinal canal. According to this theory, this force, similar to carbon dioxide uncorking the champagne bottle, pushes the testes through the inguinal canal, contributing thereby to the other factors producing descent [2]. In the fetuses with a defect in the abdominal wall, intraabdominal pressure decreases. Retained testes is accounted for by intraabdominal pressure in 33–55% in omphalocele and 15–18% in gastroschisis [2].

Another theory, which appears to be more convincing, attributes the absence of descension to the abnormal position of the inguinal canal [1]. Since in exstrophy of the bladder the pubic bones are separated and the symphysis is often widely open. Consequently, the two inguinal canals are localized lateral, their direction deviating from the normal. The course of the gubernaculum testis is also abnormal: distally it is not attached to the bottom of the scrotum so the guiding role of the gubernaculum is not effective. If this were to cause the incomplete descension, then undescended testes is expected to be present in those with a more severe structural abnormality of the pelvis. Therefore, it was studied whether in boys with exstrophy of the bladder, there was a difference concerning the distance between the pubic bones in the groups with descended and undescended testes. It was found that while in children with undescended testes this distance was between 40 and 60 mm at the age of

2 years (average value : 53 mm), in boys with undescended testes this value ranged between 60 and 70 mm (average value: 62 mm).

In our patients it was striking that in 5 out of 6 orchiopexies intact testes and epididymis were found with an adequate fusion of the two organs as well. This is a much favourable ratio than the one in the 1386 operations made because of undescended testes. Our observation supports the fact that, in cases where the cause of retained testes has obviously been anatomical-mechanical, intact testes and epididymis as to their development and structure, should be reckoned with, because testicular development has been undisturbed. In these individuals the effect of factors promoting the development of the testes and the epididymis is undisturbed. This observation may, support our earlier views [6] that in individuals with undescended testes infertility cannot be basically attributed to thermic effects but to such congenital abnormalities which are inherent in the structural retardation of the testes and in the hormonal effects of intrauterine life, one of their manifestations being abnormal testicular-epididymal fusion.

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Zustand des Hodens und des Nebenhodens im Falle eines sich zur Blasenexstrophie gesellten nicht deszendierten Hodens

M. MERKSZ und J. TÓTH

Im Falle nicht deszendierter Hoden melden sich in einer bedeutenden Zahl der Fälle Hodendysplasie/Hypoplasie und eine Fusionsanomalie des Nebenhodens; das gleichzeitige Vorkommen dieser Anomalien kann sogar 50% erreichen. Die Häufigkeit dieser Anomalien im Falle von sich zu einer Blasenexstrophie gesellten, nicht deszendierten Hoden untersucht. Bei 5 von 26 mit Blasenexstrophie geborenen Knaben waren nicht deszendierte Hoden zu beobachten, in 3 dieser Fälle wurde die beidseitige Orchidopexie bereits durchgeführt. In 5 der 6 operierten Fälle waren intakte Hoden und Nebenhoden vorzufinden, eine Fusionsanomalie des Nebenhodens meldete sich nur in einem Fall, der Hoden vor aber auch in diesem Falle intakt. Die Erscheinung wird damit erklärt, daß im Falle einer Blasenexstrophie die Hoden nicht wegen der Insuffizienz der fötalen Androgenhormon Wirkung, sondern anatomischer Ursachen zufolge nicht deszendierten. Dies wird durch den Umstand unterstützt, daß in Fällen, in denen für die Deszensusstörung kein anatomischer Faktor verantwortlich ist, zwischen Hoden und Nebenhoden Fusionsstörungen viel seltener zu beobachten sind.

Состояние яичек и их придатков при задержке опускания яичек, сопряженных с экстрофией мочевого пузыря

М. МЕРКС и Й. ТОТ

При задержке яичек довольно часто наблюдаются дисплазия/гипоплазия и фузионное нарушение придатка яичка, одновременное наличие этих отклонений может достигать 50%. Авторы изучали частоту встречаемости вышеуказанных аномалий в случае задержки опускания яичек, сочетающейся с экстрофией мочевого пузыря. У 26 мальчиков, родившихся с экстрофией мочевого пузыря, у 5 наблюдалась двусторонняя ретенция яичка, у трех из них произвели двустороннюю орхидопексию. При 5 операциях из 6 обнаружили интактные яички и придатки яичек и лишь в одном случае отметили нарушение фузии придатка яичка, но и в данном случае яичко было интактным. Причину этого авторы видят в том, что при экстрофии мочевого пузыря ретенция яичек происходит не из-за влияния недостаточности андрогенного гормона у плода, а вследствие анатомических причин. Подкрепляет это предположение тот факт, что в тех случаях, когда задержка опускания яичка вызвана механическим фактором, гораздо реже наблюдается нарушение фузии между яичком и придатком яичка.

The Possibilities of CO₂ Laser in Anorectal Surgery

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Based on their own experience and on literary data, authors have found the use of CO₂ laser most suitable for performing anorectal operations.

The basic lasers in surgery—CO₂, Nd : YAG—can be used beneficially for the operative treatment of body regions with an abundant blood supply, e.g. the face, the skullcap and the perineal region.

Zhao and Chen [13] reported about 1000 haemorrhoidectomies performed by laser.

Zadech [12] have published the favourable experiences obtained by over 1000 laser haemorrhoidectomies.

Both the CO₂ [2, 3, 4] as well as Nd : YAG lasers [2, 3, 7, 10] are used in haemorrhoidectomies.

The CO₂ laser can be used with benefit for removing perineal and genital condyloma acuminata. The relatively high temperature arising during such operations kills viruses, condyloma being a viral disease [5, 6, 8, 9].

Material and Methods

Our operations were carried out by a TUNGSRAM RT TLS₆₁ CO₂ laser equipment. The equipment was operated continuously, at a performance of 40–50 W.

The minor changes, like fibroma pendulum, small circumscribed condyloma acuminatum, are evaporated by a short continuous radiation. The larger condylomata of a wider base are excised by laser knife.

Haemorrhoidectomies were performed by routine Langenbeck operation with the difference that the tied piles are excised with laser knife. The focussed beam of light sort of seals the incision line and no bleeding occurs. The residual incision line is sutured by running catgut.

Anal polyps are excised by laser knife and the site of excision is sutured by catgut 8/0.

Rectal villous adenoma is similarly excised.

Excision and reduction of tumour by laser knife were performed only in poor risk patients with rectal carcinoma, being unfit for radical operation.

Table 1 shows the operated patients according to diagnosis and surgical solution.

TABLE 1
Perianal laser operations

No.	Diagnosis	Operation	
1.	Piles	Langenbeck operation	21
2.	Perineal condyloma	Excision, evaporation	12
3.	Fibroma pendulum	Evaporation	4
4.	Anal polyp	Excision	2
5.	Rectal carcinoma	Excision	3
6.	Rectal villous adenoma	Excision	2
Total			44

Figure 1 demonstrates that the patient's haemorrhoids were removed by electrocautery: note the enormous perineal oedema.



FIG. 1. Following haemorrhoidectomy by electrocautery a large mucosal oedema developed

In Fig. 2 the perineal region of a patient operated for haemorrhoid by CO₂ laser is presented: there is no evidence of edema.

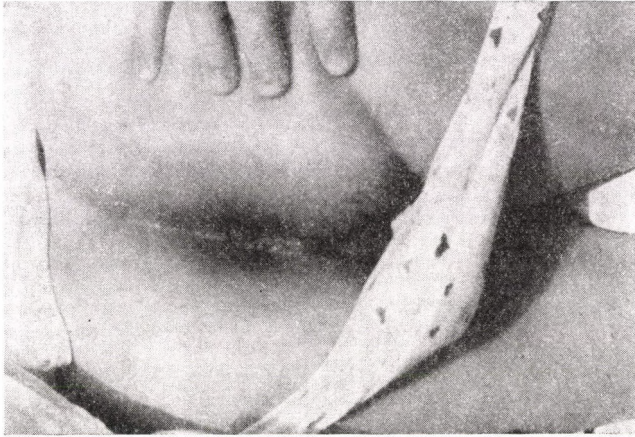


FIG. 2. After Langenbeck operation with CO₂ laser oedema never develops

Discussion

According to the literature, following laser haemorrhoidectomies, there is no postoperative edema, accompanied by less pain, the patients need less pain killers. There are also less dysuric problems. The same was observed in our own patients, although the number of cases is still low. It should be emphasized that postoperative edema does not always occur after haemorrhoidectomy performed by electrocautery either, but it is bound to develop in a small percentage of the cases. This slows down the discharge of the patients, the number of days in the hospital increases. In China — where the number of patients with haemorrhoids is known to be high — Zhao and Chen [13] made over 700 haemorrhoidectomies. In a part of the cases the laser haemorrhoidectomies were performed on an out-patient basis! This possibility affords considerable savings in costs.

The laser knife can also be used with benefit for the evaporation or excision of condyloma acuminatum. These operations are performed with a slightly defocussed beam of light. Since also the CO₂ laser produced heat, this kills viruses reducing thereby the ratio of recurrence. For the further reduction of recurrences, Krebs [9] applied 5-fluorouracil ointment (in condyloma of the female genital organ) once weekly after condyloma operations with laser, and this reduces the ratio of recurrences from one-third to 10%.

Perineal condylomata and fibromas of small size can be evaporated by simple continuous laser radiation within a short time, without bleeding and without insertion of sutures.

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Möglichkeiten des CO₂-Lasers in der anorektalen Chirurgie

T. TÓTH, ZS. BÁNYÁSZ und F. SZALAI

Anhand der eigenen Erfahrungen und der Literaturdaten wird betont, daß bei der Durchführung der anorektalen Operationen der CO₂-Laser eine äußerst vorteilhafte Anwendung finden kann.

Возможности СО₂-лазера в аноректальной хирургии

Т. ТОТ, Ж. БАНЯС и Ф. САЛАИ

На основании собственного опыта и литературных данных авторы считают вполне обоснованным применение СО₂-лазера для выполнения аноректальных операций.

The Use of CO₂ Laser in Plastic Surgery and Dermatology

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The applicability of TLS₆₁ CO₂ developed in Hungary was investigated in dermatological-plastic surgery.

This apparatus can be used with benefit in certain plastic operations, like lipectomy, dermabrasion, removal of keloid-tattoo and skin excisions.

Kaplan and Ger [9] were pioneering in the use of CO₂ laser in plastic surgery, while Apfelberg [1] and Goldman [7] were the first to use argon laser. Since then an increasing importance has been attached to lasers in this field.

Applied Lasers

Argon laser. It emits a bluish-green light at a wave length of 488–514 nm. This light is selectively absorbed by haemoglobin, the pigments of tattoos and melanin. The light of argon laser is capable of penetrating the intact skin over the change by being absorbed by the vessels and pigments of that region.

CO₂ laser. It produces an invisible light at a wave length of 10600 nm, which is absorbed by water. Since biological tissues contain 75–90% of water, these cells explode under CO₂ laser exposure and the tissues evaporate in the focussing point of the beam of light. The advantage of carbon dioxide laser in the surgery of haemangiomas is that it cuts like a knife and seals at the same time the minor vessels. By using carbon dioxide laser the skin can be cut by great precision. Defocussed CO₂ light can be used for precise superficial vaporization or the ablation of superficial changes with great precision. Laser dermabrasion (laser abrasion) is capable of selectively remove superficial skin layers with outstanding consequential healing of the wound.

Nd : YAG laser. Its wave length is near the range of the infra red light, i.e. 1064 nm. This light can be conducted by fibreoptics and penetrates the skin down to a depth of 5–7 mm [6, 11]. This ray penetrating deeper than the light of the argon laser enables its use in the thicker and more bulky changes of a much deeper localization. Installed with a sapphire headpiece of various shapes it can be used for cutting, vaporizing skin and for arresting bleeding.

Material and Methods

Our operations were carried out with a TUNGSRAM RT TLS₆₁ CO₂ laser system of a performance of 60 W. The performance of the device can be continuously altered between 0 and 60 W. The device was operated continuously and in impulse mode (0.1 s; 0.2 s; 0.5 s; 1 s). Aiming with the invisible CO₂ light is made possible by the well visible purplish light of the He-Ne laser built in parallelly. The beam is operated by a pedal. For cutting focussed beam is used, at the end of the handpiece. For evaporation a slightly defocussed light, at 2.5 cm from the end of the handpiece, is suitable. For superficial dermabrasion a strongly defocussed beam of light is applied at 8–10 cm from the focus.

All these manoeuvres and possibilities can be mastered in the process of continuous practice.

Table 1 shows our eyelid operations: some 56 such interventions were made by CO₂ laser. The minor benign changes, like fibroma pendulum, warts,

TABLE 1
Eyelid operations with CO₂ laser

No.	Clinical diagnosis	Operation	No.
1.	Palpebral basalioma	Excision	37
2.	Palpebral fibroma	Evaporation	6
3.	Palpebral wart	Evaporation	3
4.	Palpebral cyst	Excision	2
5.	Palpebral pigmented naevus	Excision	2
6.	Palpebral atheroma	Excision	2
7.	Adenoma sebaceum	Excision	1
8.	Palpebral haemangioma	Excision	1
9.	Palpebral papilloma	Excision	1
Total			55

etc., are simply vaporized with a slightly defocussed beam. The advantage of the method is that there is no intraoperative bleeding, the site of the operation should not be closed by suturing and it heals by a nice scar. Its drawback is, however, that no material is available for histology and so this can be used only for operating some benign changes. Of the operations of eyelid lesions basalioma occurs more frequently. Basaliomas are always excised by focussed laser beam, in accordance with the ablatic principles, in the intact tissue. In such cases the removed material is sent for histology. The eyeball is protected from injury by a metal spatula. Wound healing is excellent, rapid and highly



FIG. 1. Basalioma of the eyelid

aesthetic, and an almost invisible scar remains. In Fig. 1 a patient operated for basalioma is presented before and, one day and 4 months after operation (Figs 1, 2, 3).

Table 2 shows our plastic operations performed by laser in other regions of the body. Removal of tattooing figures in the largest number. The tattoos are evaporated in the adequate regions. The operations are made with a slightly defocussed beam of light. Care should be taken that each part of the skin containing pigment be vaporized. These operations, too, are made on an out-patient basis under local anaesthesia. The patients carry on their everyday activities and work.



FIG. 2. Laser excision of eyelid basalioma one day after surgery



FIG. 3. Wound healing after the laser excision of eyelid basaloma

Also lipectomy can be performed by laser knife. Fig. 4 demonstrates the scar of a subumbilical lipectomy made by laser knife. The patient was susceptible to keloid-formation, that is why she had asked for laser lipectomy.

TABLE 2
Plastic operations by CO₂ laser

No.	Clinical diagnosis	Operation	No.
1.	Tattoo	Evaporation	12
2.	Keloid	Evaporation	8
3.	Lipodystrophy	Lipectomy	1
4.	Naevus flammeus	Laser abrasion	1
5.	Unguis incarnatus	Matrix plasty	1
Total			23

In Fig. 5 a 60-year-old female patient is presented who has had an increasing naevus flammeus on her forehead since birth. Superficial laser evaporation was made under local anaesthesia. The control picture taken half a year later shows a very nice healing almost without scar (Fig 6).

Table 3 summarizes the cases operated for benign, semimalignant as well as malignant skin changes. The definitely benign changes of small size, like warts, fibroma pendulum, are evaporated by defocussed light. The larger benign changes are excised and the remaining wound is sutured with primary suture. It is advisable to remove the sutures 3–4 days after the sharp excisions.

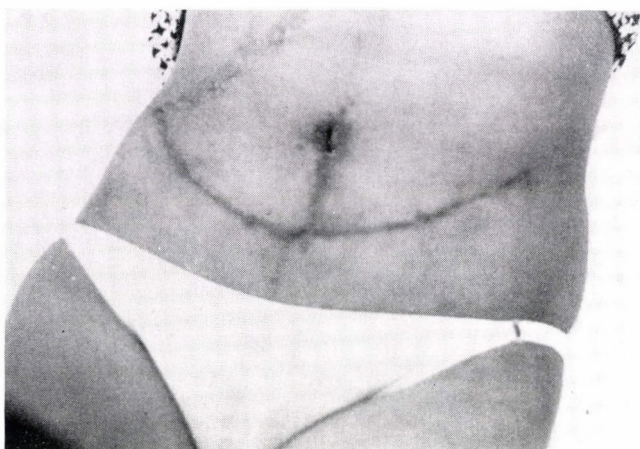


FIG. 4. Wound healing after laser lipectomy

The skin wounds made by laser have a tendency to heal somewhat slower. In Fig. 7 a pigmented naevus excised by laser can be seen ((Fig. 8). Figure 9 shows the healing of the wound.



FIG. 5. Naevus flammeus on the forehead



FIG. 6. Six months after laser abrasion of naevus flammeus

TABLE 3

Removal by CO₂ laser of dermal or subdermal changes

No.	Clinical diagnosis	Operation	No.
MALIGNANT AND SEMIMALIGNANT TUMOURS			
1.	Basalioma	Excision	5
2.	Malignant melanoma	Excision	3
3.	Cylindroma	Excision	2
4.	Subcutaneous sarcoma	Excision	1
BENIGN CHANGES			
1.	Warts	Evaporation	61 (12 patients)
2.	Pigmented naevus	Excision	24
3.	Fibroma	Excision	10
4.	Transitory dermatolysis acantholyticus	Evaporation	10
5.	Atheroma	Excision, enucleation	6
6.	Fibroma pendulum	Evaporation	5
7.	Prurigo nodularis	Evaporation	5
8.	Lipoma	Excision	4
9.	Plasmocytic granuloma		3
10.	Haemangioma	Excision	2
11.	Epidermoid cyst	Excision	1
12.	Cysta colli	Excision	1
Total			143



FIG. 7. Pigmented naevus on the thoracic wall

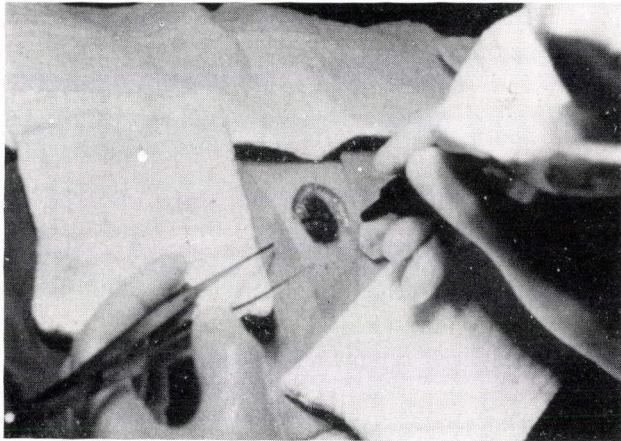


FIG. 8. Laser excision of pigmented naevus, there is no bleeding



FIG. 9. Wound healing after laser skin excision (pigmented naevus)

Discussion

The extensive use of CO₂ laser in surgery has been started in our department three years ago. The device was tried in septic, paediatric, pulmonary and thoracic, gastrointestinal and biliary, pancreatic and liver surgery. A large number of out-patient operations were made, i.e. tattoos, keloid and skin tumours were removed. The laser treatment of prurigo nodularis and transitory acanthosis dermatolyticus was performed with dermatological indication in clinical trials in some cases. The laser treatment of these two diseases is otherwise not mentioned among the indications in the international literature. This indication has therefore been omitted.

CO₂ laser can find outstanding use in out-patient surgery. After a considerable practice, it has been a favourable finding that there is no intraoperative bleeding or nothing or almost nothing should be done about arresting bleeding. The beam of the carbon dioxide laser seals the minor vessels during cutting. So the surgeon's work is becoming more undisturbed: he does not need to wipe, compress or ligate vessels with a better visibility.

For a beginner in laser surgery it is obviously very complicated to work with one arm only, however, after acquiring some practice, this does not impose any problems (for a beginner also a "simple" appendectomy may be difficult to perform). It can be said about minor operations that the operation is more rapid if performed by laser (however, thoracotomy or laparotomy are already slower to perform by laser).

The CO₂ laser can be used also for tasks which could hardly or not at all be solved by the conventional methods. The skin is vaporized in circumscribed regions at the required depth under visual control. So the benign tumours, keloid and tattooed skin are removed [4, 3]. The scars formed are soft and hardly visible. During a laser operation the temperature produced in the tissue is not high, no burns are induced, but rather evaporation. The accessory skin appendages, like hair follicles, sweat glands, are preserved and the skin regenerates outstandingly.

Since tumour cells are destroyed in the incision line, local recurrences are less likely to occur [15, 16]. It is recommended to excise malignant skin changes by all means with CO₂ laser knife.

Our patients operated for malignant melanoma were operated and referred to oncological treatment after dermatological diagnosis.

Based on international experience and our own practice, our view is that laser has significantly broadened the arsenal of the surgeon.

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Einsatz des CO₂-Lasers in der plastischen und dermatologischen Chirurgie

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Untersucht wurde die Anwendbarkeit des CO₂-Lasers heimischer Entwicklung, Typ TLS₆₁ in der heutzutage plastischen Chirurgie. Bei gewissen plastischen Operationen—Lip-ektomie, Dermabrasion—Keloid-Tetovierungsentfernung und Hautexzisionen, kann das Gerät eine erfolgreiche Anwendung finden.

Применение CO₂-лазера в пластической и дерматологической хирургии

T. TOT и T. БАРТА

Авторы исследовали возможность применения разработанного в Венгрии CO₂-лазера типа TLS₆₁ в кожно-пластической хирургии.

Исследования показали, что этот лазер можно эффективно определенных пластических операциях: при липектомии, дермабразии, удалении келоидных рубцов татуировки и при кожных эксцизиях.



Partial Splenectomy Performed by a Special Technique in Dogs

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Closure of the splenic surface is solved at splenectomy by placing a row of sutures using a double thread inserted at the same level by two straight needles. This technique does not require interpositions with a good haemostasis and so favours wound healing. It does not need many instruments and is easy to perform.

About 25% of all lymphatic tissues can be found in the spleen and thus it plays an important role in the defence mechanism of the organism. Its removal may produce disorders both in the early and late postoperative periods [4].

Following splenectomy overwhelming postsplenectomy infection/syndrome (OPSI) may occur [8]. Its course is lethal in about 75% of the cases [9]. This syndrome may develop in 2.1–6.3% of the cases after splenectomy [11]. Bacterial, viral and parasitic infections, may also occur at a high rate following splenectomy [13]. So attempt should be made by all means to preserve the organ.

If the hilar blood supply of the spleen can be preserved in 50% during partial splenectomy, then it protects much better against pneumococci than autotransplantation of splenic pieces [12].

Analyzing the possibilities of preserving the injured spleen it can be stated that if the spleen can be safely sutured, this is superior to partial splenectomy. On the other hand, partial splenectomy should be preferred to autotransplantation [4].

The spleen is difficult to suture, it is prone to bleeding, fragile and thus the technique of partial splenectomy is not an easy task. In a previous study the wound surface of the spleen was covered by bioplast combined with tissue adhesive [2]. In spite of the fact that good results were obtained foreign substances had to be introduced into the organism, where it had to disintegrate, be absorbed, which drains energy from the organism. Therefore a still better technique of splenectomy was sought for [6].

Material and Methods

The experiments were carried out in 30 mongrel dogs, disregarding their age, weight and sex. The abdominal cavity was opened by upper median laparotomy under i.m. hexobarbital-sodium anaesthesia. Then, after elevating the spleen starting from its lower pole, the organ was exposed up to the devised resection line. The two intertwined layers of suture were placed about 2–3 mm below this line: the two ends of the 70 cm long 1/0 or 2.0 Tewdek suture (of polyester material and polyfilic thread) was threaded through one straight needle each encompassing the thickness of the spleen and were sutured opposing each other at the same level in a way that the threads should cross each other in the splenic substance (Fig. 1). Pulling both ends a corner suture was created (Fig. 2). Suturing is continued, being placed at a distance of 5 mm from each other, until the opposite side was reached. Then both ends of the thread were pulled and the substance of the spleen becoming draped (Fig. 3). After adequately pulling the threads they could be knotted. Then the exposed spleen was transected in the planned resection line above the intertwined layers of suture. The thread-ends were cut only if the apposed wound surface was not bleeding. Otherwise, any of the strands could be threaded back if an oozing bleeding was about to occur, and so the required haemostasis can be achieved and a splenectomic surface of reduced size was produced (Fig. 4). The remaining spleen was restored in its original place, and the abdominal wall was closed in the usual way.

After the extirpations, following the examination of the abdominal cavity, the splenic surface and its environment, microscopic work-up of the resection stump followed. The histological sections were stained by haematoxylin-eosin and Masson—Goldner techniques.

Results

Our observations covered the period from the minute of starting of the resection up to 10 months. Insertion of the intertwined sutures was not problematic, but the adequate pulling of the strands of the thread required great care. Since there are “many layers of suture” the substance does not get torn. In dogs, the spleen has a great storing capacity—the so-called predatory type—however the layers of suture tolerated the great changes in volume quite well. Tearing, rejection, bone necrosis were not observed. If a minor vessel had escaped suturing, this did not present any problem, since it could be threaded back by any, or both, strands of the suture, thus providing appropriate haemostasis. Bleeding to death did not occur in either of the cases. The layer of suture proceeding about 2–3 mm from the planned resection line,

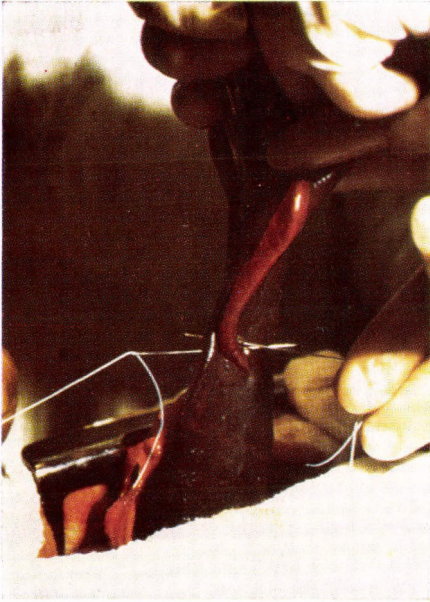


FIG. 1. The splenic substance is sutured by two straight needles 2-3 mm above the planned resection line



FIG. 2. Insertion of the corner suture

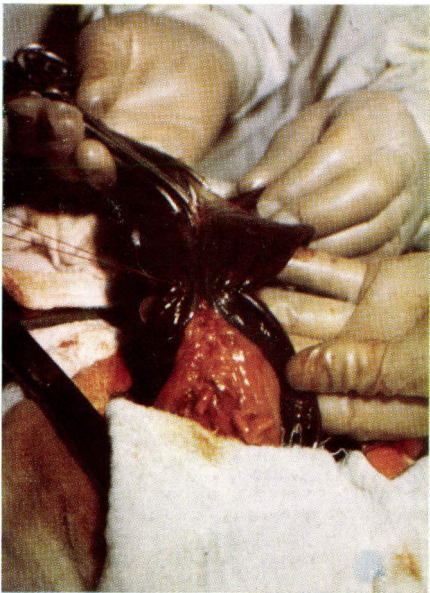


FIG. 3. By pulling the two threads, the substance of the spleen is draped



FIG. 4. The stump of the spleen (reduced wound surface of the spleen)

carried possibly at the same level was not damaged by transection of the spleen to be resected. The smallest possible splenic surface hardly means a greater adhesive surface than other splenorrhaphies do, which was also documented by the autopsies. Some minor adhesions were observed only in 3 cases.

The histological study of the splenic stump revealed the following:

The suturing material in the surface substance of the spleen in the resection line could be clearly detected in the study period for 10 months. Initially, round-cell infiltration could be noted around the suture material, then, from the 6th month on, hyaline degeneration of the connective tissue poor in cells was present in its environment.

In the splenectomic surface, an extremely cell-rich, inflammatory granulation tissue was present even 2 months postoperatively. After 6 months the resected region was covered by a scarry layer of thick connective tissue still containing cell-rich areas.

After 10 months, hyaline degeneration of the thick surface developed in the superficial splenic substance where even the remnants of sutures could be traced (Fig. 5).

In the splenic substance somewhat removed from the resected surface, the usual structure was characteristic, with no evidence of change following resection (Fig. 6).

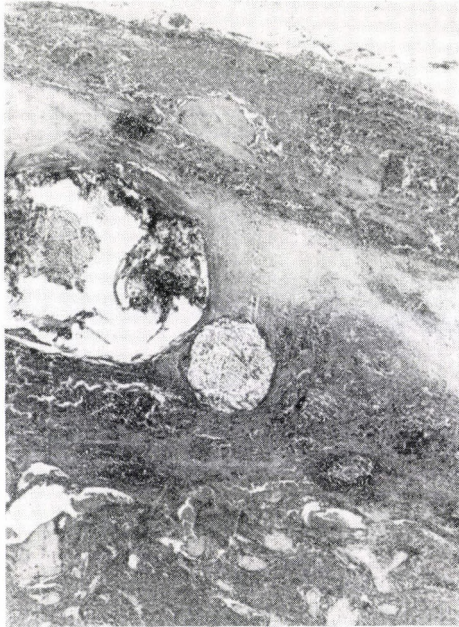


FIG. 5. Ten months after the operation the remnants of the suturing material can be clearly seen on the resected surface (H.E. $\times 60$)



FIG. 6. There is no change in the structure of the splenic substance removed from the resected surface (HE, $\times 60$)

Discussion

The spleen is difficult to suture, it is fragile, prone to tearing and not even the technique of partial splenectomy is easy to learn. The diversity of methods also shows that an optimal solution is still sought for.

Goldenberg et al. [7] have found using a CO₂ laser, that although haemostasis was good, no microscopically extensive necrosis could be noted, as on using sutures where, bleeding was more massive.

Using CO₂ laser in dogs, better results were obtained by Reynolds et al. [11] than with suture introduced through Teflon plates, because in the latter case after 3 weeks the remaining spleen adhered to the greater omentum, the mesentrium, the small intestine and the colon. By using CO₂ laser only minimal adhesions occurred and also haemostasis was sufficient due to the coagulant effect.

Lately, partial splenectomy has been performed not only in injuries. Morgenstern et al. [10] made neartotal splenectomy also in Gaucher's disease.

Partial splenectomy [7] can also be reckoned with in cases of splenic cysts and abscesses [1].

As compared to the reviewed method, our one is easy to perform and does not require many instruments. Only two straight needles are needed.

Haemostasis was adequately ensured by the two intertwined layers of suture. A large necrotic zone did not occur, like in electro- or laser coagulations. There is no need of accessory materials (such as Teflon plates, bioplasts, adhesives, etc.) avoiding the troubles with either acquiring the material or eliminating it from the organism. This latter is considered important from the point of view of wound healing, because the organism should not spend some excess energy on complete healing.

In humans the ramification of splenic vessels enables to perform segmental resection.

We consider our method simple, ensuring good haemostasis, providing the smallest possible splenic surface, which is not indifferent concerning adhesions. It does not require special devices, and instruments, etc. and besides, there is no need to fix the sutures by interpositions, which is advantageous concerning wound healing.

Splenectomy or partial splenectomy is considered a method of preserving the spleen, and in spite of the fact that the method has been developed in dog, based on our results, it is found to be introducible with proper consideration also into clinical practice.

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Mit spezieller Technik durchgeführte partielle Splenektomie beim Hund

I. FURKA, IRÉN MIKÓ, T. MIKÓ und L. PAPP

Der Verschluss der Milzfläche bei der Milzresektion wird mit eigenartiger Technik, mit sich ineinander verschlingenden, in einer Ebene angebrachten, doppelten Fäden, mit einer mit zwei geraden Nadeln gefertigten Nahtreihe gelöst. Diese Technik beansprucht nebst guter Hämostase keine Interposite und begünstigt auf diese Weise die Wundheilung. Die Methode beansprucht keine besonderen Instrumente, ihre Durchführung ist einfach.

Парциальная спленэктомия у собак, выполненная с помощью специальной техники

И. ФУРКА, И. МИКО, Т. МИКО и Л. ПАПП

Авторы производят закрытие поверхности селезенки после ее парциальной резекции с помощью своеобразной двойной лигатуры, состоящей из двух сцепленных шовных ниток, расположенных в одной плоскости. Шивание производилось двумя прямыми иглами. Эта техника при хорошем гемостазе не требует интерпозитов, поэтому имеет преимущества с точки зрения заживления раны. Не требуется сложного инструментария, шивание выполняется просто.

New Surgical Procedures for the Management of Carotid Kinking

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Three new operative techniques for the management of the kinking of the internal carotid artery are reviewed. Method 1: Resection of the internal carotid artery, end-to-end anastomosis with patch-graft angioplasty. Method 2: *In situ* reimplantation of the internal carotid artery by grafting. Method 3: Shortening of the internal carotid artery by suturing and its dilatation by patch-grafting. The advantages and the conditions of application of these methods are reported. Their application is also recommended to others.

According to autopsy records and angiographic studies, carotid kinking occurs in 10–20% of people [24]. It becomes evident during life, mostly if it induces cerebral ischaemia. The term kinking implies the distorting and coiling associated with the pathological elongation of the artery. The ischaemic symptoms, including an excruciating, almost irreducible headache, frequent vertigo, dead limbs, clumsiness, loss of consciousness, psychic and visual disturbances, a stricture disturbing the blood supply [22]. Carotid kinking is responsible for 15–20% of overall cerebral ischaemia cases.

The change was described already in 1898 by Edington [5]. Raiser [20] was the first to recognize its clinical significance in 1959 and for its management he applied arterioplexis to the sternocleidomastoid muscle. The first surgical resection was reported by Hsu and Kistin [11] in 1956. A larger number of cases was reported in 1959 [6, 18]. The first common carotid resection was performed by Quattlebaum et al. [18]. Resection and end-to-end anastomosis of the internal carotid are linked with the name of Hurwitt et al. [12].

The three major causes of kinking are atherosclerosis, hypertension and congenital abnormality. The internal carotid artery runs between two fixed points, i.e. the base of the skull and the common carotid artery, in a less compact tissue. On elongation it diverts laterally, becomes kinked and coils.

Morphologically, three types can be distinguished [2, 10]:

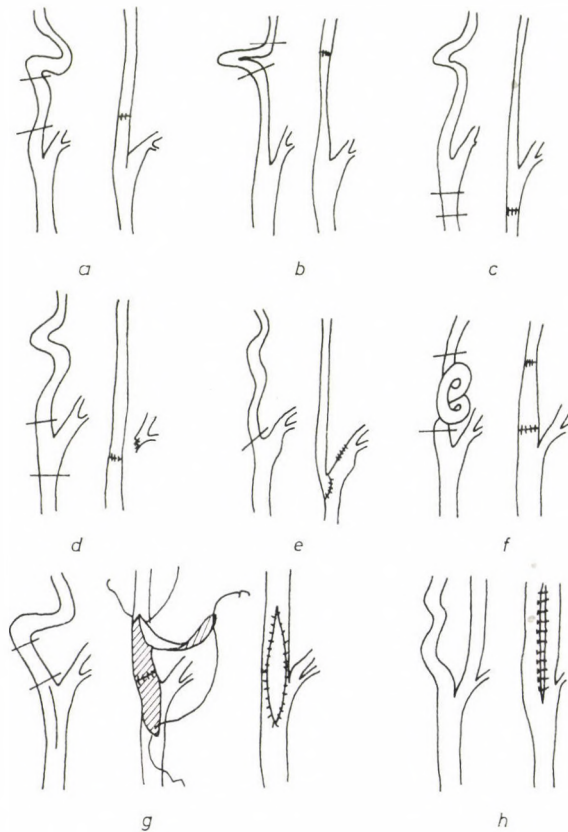
Type I: form C or S (tortuosity) when elongation is also associated with dilatation. It is due to atherosclerosis. Haemodynamically it is only important if there is also a stricture at the initial segment of the internal carotid artery.

Type II: Sigmoid-shaped coiling. Probably, it is congenital in origin and in more advanced age, intermittent kinking, occasionally complete thrombotic occlusion can occur.

Type III. Kinking. There is usually double kinking in the first third of the internal carotid artery. It is due to atherosclerosis or fibromuscular dysplasia.

The above-mentioned forms can be combined and may assume different configurations in the various positions of the head or at varying times (Figs 1a-h).

Surgical treatment is recommended if the association between the change and the cerebrovascular insufficiency has been verified. The operative treatment consists in the complete mobilization of the affected segment, the straightening of the kinking and coiling, the shortening of the elongation, and solution of the atheromatous or other stricture. The surgical procedures are as



FIGS 1a-h Sketches from the literature of the surgical solution of internal carotid arterial kinking

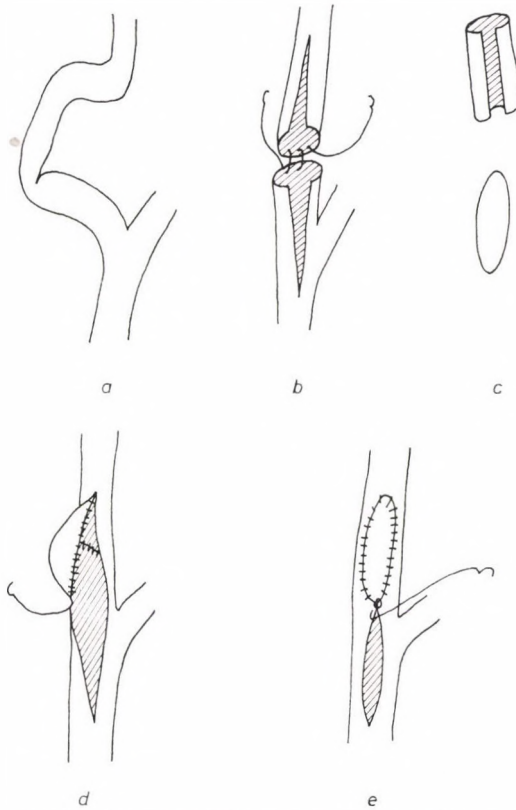


FIG. 2a Resection of the internal carotid artery
 FIG. 2b The longitudinally incised vascular ends are united by oblique sutures
 FIG. 2c The excised arterial portion is cut and fashioned into a patch
 FIG. 2d Patch-grafting of the internal carotid artery is performed
 FIG. 2e The common carotid artery is closed by running sutures

follows: (Figs 1a-h) fixation to the sternocleidomastoid muscle [4] or the, external carotid artery [14]; segmental resection of the common carotid artery, union by end-to-end anastomosis of the common carotid and internal arteries [13]. End-to-end anastomosis after internal carotid resection [1, 7, 16, 25] or with patch-grafting [23]. Lower reimplantation of the internal carotid artery into the common carotid artery [3, 17, 19]. Reimplantation of the internal carotid artery by patch-grafting [26]. Resection of the internal carotid artery, replacement with individual patch-graft [2]. Not all of the above methods can be adapted for each situation, but the solution of choice should be the one most suitable one for the change.

In this report our surgical alternatives for the reconstruction of carotid kinking are reviewed (Figs 2a-e).

Method 1. The narrowed and kinked segment of the internal carotid artery is resected (Fig. 2a). After straightening the tortuosity of the distal seg-

ment, arteriotomy is performed on the central stump of the internal carotid involving the common carotid artery as well, as also on the peripheral stump along a shorter segment on the anterior wall. The stumps of the internal carotid artery are united by running sutures (Fig. 2b). The excised piece of the internal carotid artery is incised longitudinally, it is fashioned to an adequate size and laurel-leaf shape and the arteriotomy of the internal carotid is terminated with patch-grafting (Figs 2c, d). The arteriotomy is united by running sutures at the portion involving the common carotid artery (Fig. 2e).

This method can be used when the longitudinal elongation is considerable, and the excision of a segment of at least 2 cm is needed. Its advantage is that the narrow internal carotid segment can be dilated as required and an ideal anatomical and haemodynamic situation can be produced. The optimal substance of the patch is the arterial wall of the patient [9]. This method was first applied by us in 1978 and it was reported in a lecture already at that time [8]. Recently, its successful application has also been described by others [21] (Figs 3a-d).

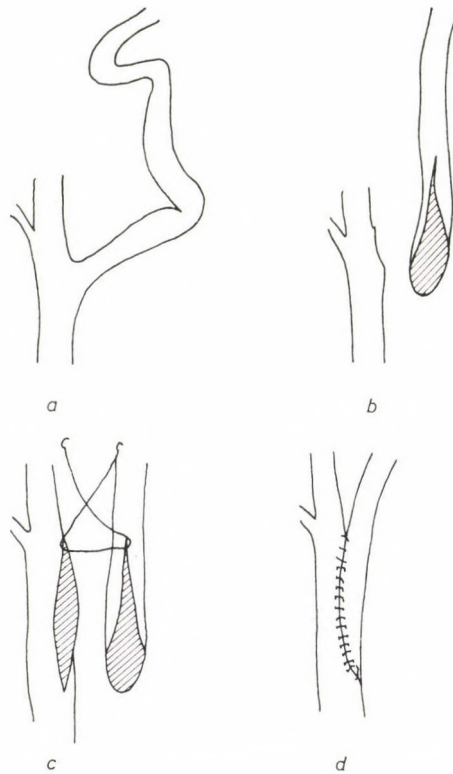


FIG. 3a Incision of the internal carotid artery at its origin
 FIG. 3b Cutting of the internal carotid artery at its length to be shortened
 FIG. 3c Cutting of the common carotid artery
 FIG. 3d Reimplantation by grafting

Method 2. The internal carotid artery is obliquely cut at its origin (Figs 3a, b). The coiling is undone, then the facing walls of the common carotid artery and of the straightened and lowered internal carotid artery are incised (Fig. 3c). Subsequently, a long tongue-shaped anastomosis is created (Fig. 3d).

This method can be employed in any case of kinking where there is no stricture or plaque distal to the union. It affords a good anatomical reconstruction, without any blind stump. In site of the arteriotomy endarterectomy can also be performed. The operation was performed by us successfully in 1982 (Figs 4a-c).

Method 3. An arteriotomy is performed from the common carotid to the internal carotid arteries (Fig. 4a). No resection is made of the internal carotid artery, only the width of the longitudinal portion is plicated and excluded by an U-shaped suture from the lumen (Fig. 4b). The lumen is closed by patch grafting from the vein thus dilating it as well (Fig. 4c).

The method can be used when the excess in length is less than 1 cm and the initial segment of the internal carotid artery is narrow, requiring dilatation. The operation was successfully performed by us in 1981. Reviewing the literature, one report has been found on a similar method [15].

In the operations Brenner a shunt was applied. This is a T-shaped tube conic-shaped on its horizontal shaft introduced into the lumen. Its advantages are that, thanks to its optimal measurements, it affords a better circulation; it enables the control of flow; it is suitable for measuring pressure, for rinsing with heparin and for collection of blood samples. It can be de-aerated well.

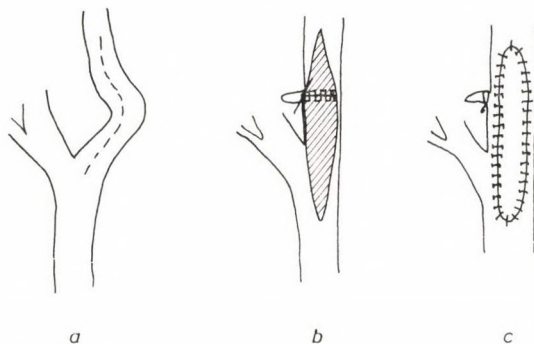


FIG. 4a Arteriotomy of the communication between the common carotid and internal carotid arteries

FIG. 4b Plication of the internal carotid artery by U-shaped sutures

FIG. 4c Closure of the arteriotomy with a venous patch graft

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Neuere Operationsverfahren zur Lösung des Karotis-Kinking

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Zur Lösung des A. carotis interna-Kinkings werden drei neuere Operationsmethoden beschrieben: 1. Methode: A. carotis interna-Resektion, End-zu-End-Anastomose mit eigenem Arterien-Patch; 2. Methode: In situ Reimplantation der A. carotis interna mit Lappen-Verfahren; 3. Methode: Verkürzung der A. carotis interna mit Vernähung und ihre Erweiterung mit eigenem Vena-Patch. Anschließend werden die Vorteile der Methoden und die Bedingungen ihrer Anwendung erläutert. Der Einsatz der Methoden wird empfohlen.

Новые способы оперативного разрешения перекручивания сонной артерии

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Авторы описывают три новых оперативных метода для разрешения перекручивания (*kinking*) внутренней сонной артерии. 1-й способ: резекция внутренней сонной артерии, анастомоз «конец-в-конец» и ангиопластики лоскутом из самой артерии. 2-й: реимплантация внутренней сонной артерии *in situ* с лоскутной ангиопластикой. 3-й способ: укорочение внутренней сонной артерии ушиванием и расширение с пластикой лоскутом из собственной вены. Авторы знакомят с достоинствами методов и условиями их применения и рекомендуют пользоваться ими.

The Evaluation of Safety Drain after Cholecystectomy

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In the literature there views are controversial concerning the use of safety drain after the so-called ideal cholecystectomy. Some authors consider it necessary, while others superfluous. Authors wish to voice their opinion based on the analysis of their own material. In the last 5 years a total of 771 gallbladder operations were performed at their clinic. Of them 472 were judged retrospectively to be ideal cholecystectomies. The safety drain applied in these cases was brought out in a separate opening in 72.7% and in the line of the wound in 27.3%. In the former case healing was accompanied by wound infection in 3.2%, while in that of the drains introduced in the line of the wound in 8.5%. The quality and quantity of discharge through the drains were studied. In the majority of cases a small amount of bloody serum was conveyed by the drain tubes, this amounting on average to 45 ml. A larger amount was only noted in a few cases: 300–450 and 800 ml of bloody serum, in 3 patients. In one case there was a more serious bile leakage associated with fever, while in another patient arterial bleeding through the drain tube was observed. In diagnosing these and judging our tasks, drainage was of great help. Based on this experience, authors consider the use of safety drain justified.

The first cholecystectomy was made by Langenbuch on August 15, 1885 [20]. Since that time operative technique has been marked by great progress, still there remained open questions in the literature. There is no uniform view concerning e.g. surgical exposure; there is a similar situation as to drainage after cholecystectomy.

There has been a long-lasting controversy among surgeons about the drainage of abdominal operations [2, 10, 11, 13, 27, 32, 35]. This particularly refers to gallbladder operations [1, 2, 3, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 21, 22, 23, 24, 25, 26, 28, 29, 30, 31, 33, 34, 35]. Some authors oppose them, moreover they consider them harmful, while others consistently apply them.

Our clinic has for long advocated safety drainage, even in the cases of the so-called ideal cystetcomy. Since many surgeons regard this procedure as superfluous, in the are of up-to-date surgical technique it was found expedient to decide on the correctness of this method based on the retrospective analysis of the case-histories of our patients.

Selection of Patients, Examination Method

Patients with acute inflammation, or those operated for phlegmonous, gangrenous and perforated gallbladder, were not included in the study, because in these cases drainage is generally always applied. Only the course of disease of those patients was controlled whose cholecystectomy had appeared to be "uneventful", there was no bleeding, the cystic duct and the "site of the gallbladder" seemed to be normal, there was only a slight or no possibility of complication. In such instances a closed drainage system was applied; the best system appears to be the Redon, Robinson [28] or similar systems, with an attached polyethylene bag. (If these are not available, they can be home-made.) The material of the drain tube is a non-occluding silicon, about 20 Chan. in diameter. The end of the drain tube is fashioned to be atraumatic, with several side holes. The drain should be brought out of the abdominal cavity through the shortest possible way. In the recent 5 years a total of 771 gallbladder operations were made, of them 472 were judged to be so-called "ideal" cholecystectomies. It was studied in how many cases the drain had been introduced subhepatically in the region of the foramen of Winslow brought out in the line of the wound or through a separate opening. The time, and complications with their removal were also examined. The percentage of cases associated with suppuration of the wound of the drains brought out in various places was analyzed as well as the amount of serum or bile drained by the tubes.

Results

According to our analysis, at cholecystectomy 72.2% of drains had an outlet through a separate opening and 27.3% were brought out in the incision line. The drains passed through a separate opening were associated with wound infection in 3.2%, those with an outlet in the incision line in 8.5%. The drains, when drawing off no more fluid, were generally removed on the 4th-5th day. In one case on pulling out the drain tube it broke off in the abdominal wall and could only be surgically removed by exposure. The patients were routinely waken early the day after the operation. The amount and quality of discharge drawn by the drain was examined. The amount generally ranged between 0 and 150 ml, corresponding on average to 45 ml; it was most often serous-bloody in character, rarely bilious. In a patient 800 ml, in another case 450 ml, while in a third 300 ml bloody serum were drained. The use of a drain tube was particularly useful in two cases. In a patient first 200 ml, on the subsequent day 300 ml bile were discharged with a fever of about 38 °C and a tenderness in the lumbar region on pressure. Bile flow gradually stopped and the patient was discharged from hospital free of complaints on the 13th postoperative

day. In one patient within some hours after cholecystectomy a large amount of fresh blood appearing to be arterial blood was drained. The arterial bleeding originating in the liver bed could be arrested at immediate reoperation. This patient was discharged from hospital complaint-free on the 9th postoperative day. No patient was lost during drainage.

Discussion

One should be unbiased in stating that using a drain has its advantages but also its drawbacks [1, 3, 4, 5, 7, 11, 13, 17, 19, 26, 28, 33, 35]. The advocates of closure without drainage argue that in such cases respiration after the operation is easier and the patient can be up and about earlier; postoperative development of adhesion can be prevented, there is a reduced risk of ileus and abdominal hernia is less likely to occur.

—Routine drainage can be associated with complications. The tip of the drain may injure abdominal organs (liver, vessels, intestines), as a result of prolonged pressure, erosive bleeding and intestinal fistula may arise. Due to its fluid content, ascending infection may occur in the lumen of the drain, and intraabdominal infection may develop in spite of the aseptic operation. As a result, there is a risk of healing by second intention, of disruption of the wound and of development of abdominal hernia, in particular if the drain has been passed through the surgical wound; the time of hospitalization is also prolonged. In case of deficient fixing, the drain may fall from the abdominal cavity or may even slip into it. On pulling out the drain tube it may break off in it calling for surgical revision. The aim of drainage is to draw off the discharge from the abdominal cavity. The lumen of the drain may be clogged due to fibrin formation or to any other causes. In such cases blood, bile, and pus may accumulate in the abdominal cavity. A drain not drawing off discharge may mislead the external observer. And, finally, another kind of risk of drainage should be noted, although we doubt its occurrence: drainage gets the surgeon out of the habit to proceed with caution and to work precisely. In the belief that drain is a guarantee for everything, he may fail to precisely manage the operative region.

The most serious risk of the closure of the abdominal wall without drainage is the possibility of biliary effusion which may derive from the stump of the cystic duct, from the pancreatic accessory ducts left open. The bile is susceptible to infection, biliary peritonitis, subhepatic and subphrenic abscesses can develop. Another great risk is the massive secondary bleeding which, in lack of drainage, may escape detection or is detected only late.

In practice it appears that while performing a large number of cystectomies, all bleeding can be arrested and all the bile ducts can be adequately

managed. Therefore, in such cases some surgeons consider it completely unnecessary to apply drainage. According to this group after cholecystectomy the use of drain is assumed to conform to tradition, and bleeding and bile effusion can be due to a major technical error. According to the other view, routine use of drainage, because of bleeding and the possibility of bile effusion, seems to be indispensable for safety reasons. For characterizing the stormy debates between advocates and opponents of drainage, it is worth mentioning, e.g. the dramatic aphorism describing the ultimate danger of an operation without drainage cited by Deaver [4], according to which "The cemeteries are filled with patients whose gallbladders were removed without drainage".

Experience obtained by analyzing our case-histories have convinced us that drain tubes conduct a small amount of bloody serum from the abdominal cavity in the majority of cases, this may probably help in reducing the amount of postoperative adhesions. A larger amount of bloody serum was only found in a few cases while more serious bile flow accompanied by fever in one case and arterial bleeding in another. Drainage was of great use in diagnosing these and in judging our tasks; in lack of drainage the course of the disease could have entailed more serious complications.

It follows from what has been said that the use of safety drainage after cholecystectomy is still not a closed chapter of biliary surgery. We feel that Schreiber [32] is right in saying that it is good to trust the spontaneous absorbing capacity of the peritoneum, but in the case of need, drainage is still better. We found that drainage after cholecystectomy, if performed by observing the procedures of operative technique, has no disadvantage. We agree with Béla Molnár [26], according to whom closure without drainage after cholecystectomy "would be justified only if also drainage had its lethal complication". He states that "the facultative standpoint of authoritative quarters is not correct, according to which in an uncomplicated case complete closure can be performed; it is just for defending these uncomplicated cases that one had better to take a definite stand, because these are actually exposed to the risk of closure without drainage". It is important to note that the surgeon should be aware, at every operation, of the potential risks and this is valid also in the cases of the so-called ideal cholecystectomy.

Therefore, we accept the view of Hess [13], according to whom the use of drainage is similar to life insurance: "It is better to have it without needing it than need it without having it".

We do not wish to decide the drainage debate by our study, but we continue to be advocates of the routine use of safety drainage.

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Bewertung des Sicherheitsdrains nach Cholezystektomie

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Untersucht wurde der Wert des nach Cholezystektomie angewandten Sicherheitsdrain. Die Beurteilung der Bedeutung des Drains ist nicht einmal in der Weltliteratur einheitlich. Anhand der Analyse des eigenen Materials wird die Meinung geäußert, daß sich selbst im Falle einer idealen Cholezystektomie — obzwar sehr selten — Komplikationen melden können (kleinere der größere Blutungen, Gallenfluß) und zur Beurteilung der erforderlichen Maßnahmen der Sicherheitsdrain eine Hilfe zu bieten vermag; demzufolge wird der Einsatz des Sicherheitsdrains nicht einmal im Zeitalter der modernen chirurgischen Technik als überflüssig gehalten.

Оценка страховочного дренажа после холецистэктомии

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Авторы изучали ценность страховочного дренажа, применяемого после холецистэктомии. Они установили, что оценка значения такого дренажа и в мировой литературе не однозначна. На основании анализа собственного материала они считают, что даже в случаях идеально проведенной холецистэктомии могут — правда, очень редко — возникнуть осложнения (слабое или сильное кровотечение, истечение желчи), когда страховочный дренаж может оказать помощь; поэтому авторы не считают излишним его применение даже при современной хирургической технике.

The Extent of Bile Reflux and Development of Gastric Cancer after Resections in Rat

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Authors performed gastric resections (Billroth II, Billroth I, Billroth II⁺, Braun anastomosis and Roux Y reconstruction) and laparotomies in five groups, of 110 Wistar male rats. Thirty-eight weeks postoperatively the surviving 91 animals were sacrificed, and histological study was made of the frequency of gastric stump cancer in the individual groups and the extent of bile reflux characteristic of the individual GEA types was measured.

Based on their results, the risk of stump cancer was higher in operation types associated with considerable bile reflux (a cancer incidence rate of 50% after Billroth II, 28.5% after Billroth I). Following gastric resections accompanied by insignificant bile reflux (Billroth II + Braun, Roux Y) the risk of gastric stump cancer was significantly lower.

It is clinical experience that several years after gastric resections because of peptic ulcer, malignant tumour and stump carcinoma may arise in the operated stomach. The detection of the late complications of gastric resections and their radical therapy are difficult, the 5-year-survival statistics of the patients are disappointing. The factors playing a role in gastric stump cancer are still obscure [11].

Based on clinical data, it can be assumed that after the various types of operation, there are different risks of stump carcinoma development. The operations for the surgical management of benign peptic ulcers are associated with different degrees of change in the physiology of the stomach. Pathological studies in humans have verified that, particularly after Billroth II resections, reflux gastritis is likely to occur more frequently, the severity of which may increase parallel with the time elapsing after the operation [1].

Following gastric resection enterogastric reflux may also have an important role in the pathogenesis of tumours developing in the anastomosis [2].

Data were obtained for assessing the risk of cancer in the operated stomach after gastric resections in rat. It was investigated whether there is a relationship between the individual types of operation and the frequency of cancer. The rate of enterogastric reflux and its correlation with cancer frequency were measured.

Material and Methods

Experiments were carried out in Wistar male rats, weighing 200–220 g (LATI, Gödöllő). The animals, four at a time, were placed in type II plastic boxes and kept on standard LATI food. The gastric operations were made from upper median laparotomy under intraperitoneal Nembutal anaesthesia (40g/kg body weight) after fasting for 24 h.

1. Billroth II resection (n = 20). After elevation of the stomach the lesser and greater curvature of the stomach were denuded. After ligation of the left gastric artery the two-thirds of the glandular stomach was resected in the height of the mid-third of the lesser curvature, and the duodenum was transected under the pylorus. The resection line and the duodenal stump were closed by one row of running sutures (Mersilen 6/0). Between the first jejunal loop after the duodenojejunal flexure and the gastric stump, an antecolic gastroenteral anastomosis of the thickness of a small intestine was created with one row of running sutures.

2. Billroth I resection (n = 20). Following denuding and distal resection of the two-thirds of the stomach (see point 1) one layer of gastroduodenostomy was constructed between the gastric stump and the duodenum (Mersilen 6/0).

3. Billroth II + Braun anastomosis (n = 20). A 5–6 mm Braun anastomosis was created between the afferent and efferent jejunal loops 5–6 cm from the antecolic gastroenteral anastomosis created after resection of the two-thirds of the glandular stomach and mobilization of the duodenal stump (see point 1).

4. Ventricular resection, reconstruction according to Roux X) (n = 20). After resection of the stomach and mobilization of the duodenal stump the continuity of the alimentary canal was restored by a Roux loop. Between the aboral end of the small intestine transected after the duodenojejunal flexure an end-to-end gastrointestinal anastomosis was created. Ten to 12 cm below the GEA an end-to-side entero-enteroanastomosis was placed (Mersilen 6/0).

5. Laparotomy (n = 30). After upper median laparotomy the stomach was elevated from the abdominal cavity, then after some minutes' waiting, it was placed back into it. The abdominal wall was then closed layer by layer (Mersilen 4/0).

After waking up the operated animals were given only tap water for 48 h, then also normal rat food. On the 38th week, after a fasting period of 48 h the surviving animals were dissected under i.p. Nembutal anaesthesia, and the intra-abdominal organs were examined. Following the compression of the esophagus above the cardia and of the efferent ileal loop below the stomach/gastric stump, the stomach and the duodenum were removed together with the afferent and efferent ileal loop. Prior to incision the gastric content was washed with 10 ml distilled water and filtered. The stomach, duodenum

and jejunum cut along the greater curvature were fixed in 4% formalin and histological sections were prepared from the regions of the stomach, duodenum and the gastroenteroanastomosis (haematoxylin-eosin). Histological analysis was made by considering the criteria of Saito et al. [8].

Total bile acid and pH determination of the gastric contents. The total bile acid of the gastric content was made by the MERK α 3 hydroxy-steroid dehydrogenase enzyme test, pH measurement was performed by pH meter.

For the statistical analysis the 2-sampled *t*-test and the Fisher test were used.

Results

Of the 110 operated rats 15 were lost due to pulmonary infection and 4 due to ileus in the first two months of the experiment. After 9 months 91 animals were evaluated. The incidence rate of tumours is shown in Table 1. In the

TABLE 1
Incidence of gastric tumours after resections

Operations	No. of animals (n)	No. of carcinomas	%
Billroth II	16	8	50
Billroth I	14	4	28.5
Billroth II+			
Braun anastomosis	15	1	6.7
Roux Y reconstruction	16	2	12.5
Laparotomy (control)	30	0	2

Significant differences in the following groups B II-control ($p = 0.0001$), B I-control ($p = 0.0074$), B II+ Br-B II ($p = 0.01$), R Y-B II ($p = 0.02$)

laparotomized control group no histological change was observed. The highest number tumours was noted after the Billroth II operations (50%), with two cases of severe dysplasia. Following Billroth I operations tumour occurred at a rate of 28.5%. After Billroth II + Braun anastomosis and Roux Y reconstruction, besides two cases each of severe dysplasia, tumours occurred at an essentially lower rate, i.e. 6,7% and 12.5%. During resections no tumour was found in the craw (epithelial part) (Fig. 1). In general, it can be stated that in the epithelial part proximal to the GEA the presumably reactive hyperplasia and moderate polymorphism of the stratified epithelium could be noted. The majority of tumours developed in the line of the GEA in the glandular residual stomach. Here, adenocarcinoma could be observed in all cases. The tumours proved to be well-differentiated with a characteristically marked leukocytic inflammation (Fig. 2).

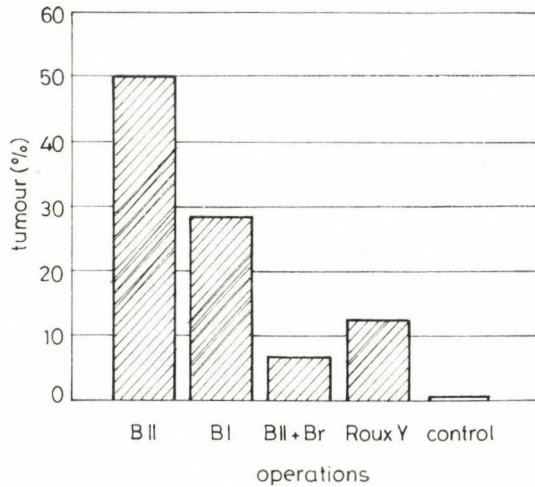


FIG. 1. The incidence rate of gastric tumours after resections. Rate of tumorous animals in the groups of various types of operation

For characterizing the ratio of enterogastric reflux, the total bile acid concentration ($\mu\text{mol/l}$) and pH of the gastric content were measured in the individual experimental groups (Table 2). Comparing to the value measured in the control group (31.4 ± 14.8) there was no significant difference in the total bile acid concentration of the gastric content after Billroth II, Billroth I and Roux Y reconstructions ($p = 0.0001$).

The Braun anastomosis reduced the extent of bile reflux to a value approximating the controls (27.35 ± 13.8). After Billroth II resection the measured total bile acid concentration as compared to any of the operated

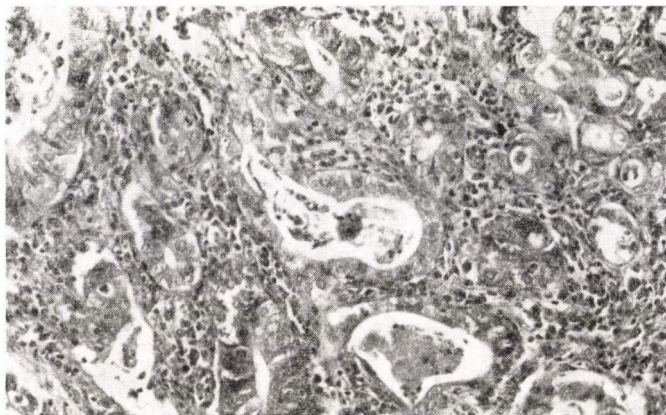


FIG. 2. Histological picture of a well-differentiated gastric stump carcinoma, adenocarcinoma (haematoxylin-eosin, $\times 300$)

TABLE 2

Average total bile acid concentration and pH values of gastric content

Operation	No. of animals (n)	Total bile acid* ($\mu\text{mol/l}$)	pH**
Billroth II	16	133.84 ± 43.9	5.71 ± 1.03
Billroth I	14	69.06 ± 25.5	4.50 ± 0.51
Billroth II+			
Braun anastomosis	15	27.35 ± 13.8	4.70 ± 0.49
Roux Y reconstruction	15	11.34 ± 8.7	4.61 ± 0.49
Laparotomy (control)	20	31.40 ± 14.8	3.26 ± 0.38

The above values (*,**) are averages \pm S. D. * Significant differences in the following groups: B II-control ($p = 0.0001$), B I-control ($p = 0.0001$), R Y-control ($p = 0.0001$), B II+Br-B II ($p = 0.0001$), B I-B II ($p = .0001$), R Y-B II ($p = 0.0001$)

groups was significantly higher ($p = 0.0001$) (Fig. 3). The alkaline change of the pH of the gastric contents was observed in comparison to the controls in all the resected groups (Table 2).

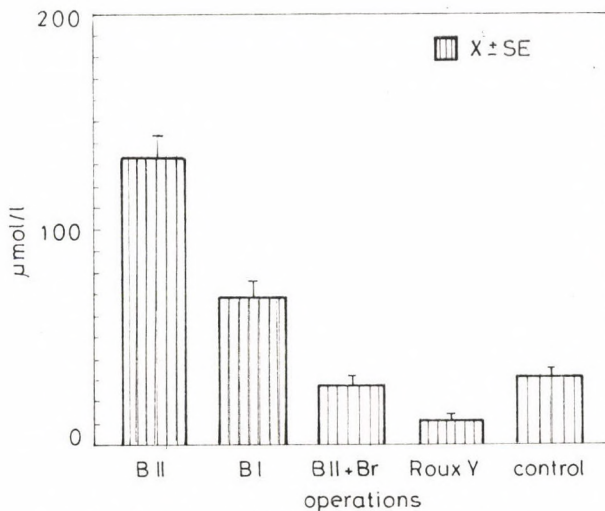


FIG. 3. Extent of bile reflux after resections

Discussion

The predisposing factors and external carcinogenic agents playing a role in the development of gastric stump cancer have not been fully clarified. In the relevant experimental studies the general effect of some carcinogenic substance was examined after various operations. The strategy of experiments,

the results and the conclusions to be drawn are divergent. The most well-known exogenous carcinogenic agent is MNNG (N-methyl-N-nitro-N-nitrosoquandine), which, given in drinking water, induces gastric cancer in the rat. The operated rat stomach is more sensitive to a small dose of MNNG than is the non-operated one, resection implies a cocarcinogenic effect [12]. There is only a limited number of experiments where the incidence rate of experimental gastric cancer has been studied without an exogenous carcinogenic agent (3.7). Langhans observed a tumour incidence rate of 30% after Billroth II operations, 23.1% after Billroth II + Braun and one of 10% after Billroth I resections at the end of the 56-week experiment. Following Roux Y reconstruction no tumour occurred. Dittrich [3] found an adenocarcinoma incidence rate of 58.8% in the group resected according to Billroth II, 40% after Billroth II + Braun and 33.3% after Billroth I operations 40 weeks postoperatively. He observed no tumour in the Roux Y group. The frequency of tumours has been correlated in the individual operated groups with bile reflux to be assumed theoretically.

In the present experiment the gastric resections applied in clinical practice were modelled but no carcinogenic compounds were used. Due to the comparability of data in the literature and the differing susceptibilities of sexes attributed to hormonal causes, the observations were made on Wistar male rats. In this species no spontaneous gastric tumour occurrence has been noted [10].

The individual resections differing in the modes of reconstructing the alimentary canal were associated with different physiological changes. Among them enterogastric reflux is of prime importance. The determination of the concentration of the trypsin [5], bile acid [4], lysolecithin [9], bilirubin or choleic acid labelled with ^{14}C isotope of the gastric content is used for characterizing the extent of reflux [13]. After gastric resections in rat the bile acid concentration labelled with isotope remains the same in the liver parenchyma, the operation does not alter the secretion of bile acid. The total bile acid concentration of the gastric content shows namely well the ratio of reflux characterizing the given type of operation [13].

Based on our investigations, reflux after Billroth II resections is almost five times greater than the control. This corresponds to the results measured in this group of animals by a similar method of Hellerer [4]. Compared also to then other resections, bile reflux was significantly of the greatest extent at the Billroth II operation ($p = 0.0001$). Braun anastomosis is of great importance in reducing reflux. The advantage of Billroth I resection can be essential in maintaining duodenal passage, the loss of the antropyloric region concerning reflux seems, however, not to be advantageous. In Roux Y reconstructions the distance between the entero-entero anastomosis from the GEA is fairly important. As also revealed by our measurements, the 10–12 cm loop of Roux does

not fully eliminate the passage of the duodenal content into the gastric stump. Despite the relatively high reflux in the laparotomized control group, the intact rat stomach is protected, no carcinoma occurs. After gastric resection, besides the increased pH value also observed by us, the change in the bacterial flora, the mucosal impairment due to reflux, the exogenous and endogenous tumour promoters (e. g. nitrosamines) may be the factors playing a role in the aetiology of stump carcinoma [3].

Comparing the incidence rate of the tumour, with the ratio of bile reflux after resections, a parallel change can be demonstrated.

There is a correlation between the mode of operation, the extent of reflux and the risk of cancer. The intensive reflux largely contributes to the development of stump carcinoma.

Based on our results, the type of Billroth II operation is the most disadvantageous, since cancer incidence is the highest in this group (50%). After Billroth I operations a relatively high tumour frequency was noted (28.5%). The difference compared to the previous group is not significant. Tumour occurrence after resections associated with low or minimal reflux (Billroth II + Braun, Roux Y) was significantly smaller in comparison to Billroth II resection ($p = 0.01$, $p = 0.02$). Considering all the reservations by extrapolating from the results of animal experiments to human situations, the experimental results suggest that in gastric resection an attempt to create an anastomosis without reflux (Braun anastomosis, Roux Y) may reduce the risk of development of stump carcinoma.

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Größe des Gallenrefluxes und Entwicklung des Magenkarzinoms nach Resektionsoperationen bei der Ratte

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Bei in fünf Gruppen eingeteilten 110 Wistar-Rattenmännchen wurden Resektions-Magenoperationen (Billroth II., Billroth I, Billroth II. + Braun-Anastomose, Roux Y-Rekonstruktion) und Laparotomie durchgeführt. 38 Wochen nach den Operationen wurden die noch am Leben gebliebenen 91 Tiere abgetötet und in den einzelnen Gruppen die Häufigkeit des Magensrumpfkrebsses histologisch untersucht; außerdem wurde auch die Größe des, die einzelnen GEA-Typen charakterisierenden Gallenreflexes gemessen.

Die Ergebnisse sprachen dafür, daß bei den mit großen Gallenreflux einhergehenden Operationstypen die Gefahr der Entwicklung eines Stumpfkrebsses größer ist (nach Billroth II. 50%, nach Billroth I. 28.5%). Nach den mit niedrigem Gallenreflux einhergehenden Magenresektionen (Billroth II. + Braun., Roux Y) ist die Magenkrebs-Gefährdung wesentlich geringer.

Величина желчного рефлюкса и возникновение рака желудка после у резекций у крыс

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У 110 крыс линии Вистар, разделенных на пять групп, авторы произвели операции резекции желудка (Бильрот II, Бильрот I, Бильрот II + анастомоз Брауна, У-реконструкция Ру Б) и лапаротомии. Через 38 недель после операций оставшихся в живых (91) животных умертвили, гистологически определили частоту встречаемости рака желудка в отдельных группах и измерили величину желчного рефлюкса, характерную для отдельных типов ЕА.

На основании полученных результатов установили, что при операциях, сопровождающихся большим желчным рефлюксом, опасность возникновения рака культуры выше (после резекций по методу Бильрота II встречаемость рака достигает 50%, Бильрота I — 28,5%). После резекций желудка, сопровождающихся низким желчным рефлюксом (Бильрот II + анастомоз Брауна, У-реконструкция по Ру Б), риск возникновения рака культуры желудка значительно ниже.

Nephrolithotomy in Childhood by Extracorporeal Shock-wave Lithotripsy

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Extracorporeal shock-wave lithotripsy (ESWL) performed on 19 occasions in 6–15-year-old nephrolithic children is reported. The stones were present in the calyceal ends in the renal pelvis. The possibilities of treatment and its effects were examined by urography, ultrasound, camerarenography and magnetic resonance imaging procedures. After three months 13 children are free of stones.

Introduction

In recent years, as a result of the progress in technical facilities, our approach to the management of nephrolithic patients has undergone a great change. It is known that nephrolithiasis has a high incidence rate in Hungary [2]. Extracorporeal shock-wave lithotripsy has become available in Hungary since June 1988 [1]. It can be used also in children.

Patients and Methods

In the period between January to December 1989 a total of 58 nephrolithic patients have been treated in our department, of these 16 were considered fit for ESWL therapy (11 girls, 5 boys). The youngest patient was 6 years old (mean age was 11.2 years). The stones were located in the calyceal apices in 7 cases, in the renal pelvis in 9, and pyeloureterally in 2 cases. In 5 instances there were multiple stones, with bilateral occurrence in 3 children.

The patients presented at our department partly with typical symptoms and partly their nephrolithiasis had been diagnosed in other institutions. Nine children had had a known history of nephrolithiasis and they were admitted because of stone recurrence. Seven had already had a history of lithotomy.

Basic principles. Attempts were made to possibly avoid surgical intervention. If also ureteral obstruction was present and this is not rare in children due to congenital disorders (in 4 out of 16), the stone was also removed simultaneously with the required plastic operation. If the fragments of the stone subjected to lithotripsy could empty without obstruction, or the good ureteral

function had been restored with the previous operation, calculus removal by crushing was suggested (in our material the number of those having undergone the previous operation was 8).

In all cases the following procedure was adopted: physical examination, including measurement of blood pressure several times, blood count and urinalysis, serum ionogram, carbamide nitrogen, creatinine, alkaline phosphatase and uric acid as well as blood group determination. ECG was made. The size of the kidney and the calculus and the lumen of the cavities were measured by sonography. Urography was made and the functional state of the kidneys (Ij1)¹ was examined by camerarenography. In one case also nuclear magnetic resonance study was made on intact kidney and in one operated for calculus (Ij2)². After assessing the accomplished examinations the possibility of ESWL was judged.

Crushing of the calculi of the examined and prepared children was performed in the lithotripsy centre of János Hospital by a Siemens Lithostar equipment. Within an hour after lithotripsy the child was transferred back to our department for observation and further management [4].

Results

The ESWL was made in 16 children on 19 occasions (in 3 children in two sessions). Emptying of the fragments of the calculi was observed within 1 to 7 days after treatments. A mild pain-killer had to be administered only rarely and not to all the children for stopping the lesser or greater colic due to calculus fragments. Nursing lasted for 5–14 days. Eleven children were discharged after treatment free of stones and only in one single patient did one from the three larger stones, the size of a pepper remain. Two children left the hospital after six days with disintegrated stone fragments, which, at later controls, could not be observed any more. There was no need of general anaesthesia, except in a child with Little disease, where lithotripsy had to be performed under anaesthesia. In a girl patient our attempt failed, in whom previously a struvite calculus had been removed by pyelotomy. In another child the closing calculi in the branches of the calix had earlier been removed via the renal pelvis. In this caliceal apex the stone recurred and so ESWL was performed. The fragment of the stone did not empty from the apex of the calix even after one month.

For assessing the result of ESWL, the following examinations were made. Immediately after lithotripsy: plain abdominal X-ray and ultrasound for the detection of the subcapsular or perirenal haematoma and the obstruc-

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tion due to calculus fragments. Prior to discharge from the hospital camera-nenographic control, and if needed, nuclear magnetic resonance controls were made [3].

No complications were observed. Macroscopic haematuria lasting for some days was not regarded as complication. Haemoptoe, elevation of tension and fever did not occur.

The chemical analysis of the removed sand was performed in all cases (Harzalit). Twelve children emptied calcium oxalate dihydrate and 2 calcium oxalate monohydrate fragments.

Further lithotriptic management of the children is being made.

Discussion

Childhood does not contraindicate ESWL treatment. After intervention most children do not even take notice of their treatment.

During emptying of the calculus fragments, the sand, only moderate symptoms, occasionally haematuria or mild nausea were noted.

Children having calculi should be prepared for ESWL like those before surgical exposure. The control after the intervention is indispensable, because complication is likely to occur [5, 6].

With due indication, shock-wave lithotripsy is regarded as a highly valuable and beneficial procedure both for the child as well as the attending physician. Considering but the facts that no abdominal exposure is necessary and so the numerous associated complications and the surgical scar retained to the end of life can be eliminated, then only the most evident ones are mentioned. The risk of iatrogenic harm is low, such damage was not observed in our patients. ESWL implies only a minor strain for the children and it means only a few days absence from school. In case of calculus recurrence, the procedure can be repeated.

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Nierensteinentfernung im Kindesalter mit extrakorporaler Wellenstoßbehandlung

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Berichtet wird über die bei 16, an Nierenstein leidenden 6-15jährigen Kindern 19mal durchgeführten ESWL-Behandlung. Die Steine lagen in den Kelchenden und im Pyelum. Möglichkeiten und Wirkungen der Behandlung wurden mittels Urographie, Ultraschall, Kamerarenographie und magnetischer Kernresonanz untersucht. Drei Monate später waren 13 Kinder steinfrei.

Удаление почечных камней у детей с помощью экстракорпоральной ударной волны

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Авторы сообщают о литотрипсии, выполненной в 19 случаях у 6–15-летних детей с помощью экстракорпоральной ударной волны (ESWL). Камни располагались на концах почечных чашечек, в почечной лоханке. Возможности и эффекты лечения изучали с помощью урографии, ультразвука, камерной ренографии и магнитного ядерного резонансного исследовательского метода. Спустя три месяца у 13 из 16 детей камней не было.

Successful Culturing of Infections, Oncogenic Adenovirus from the Stimulated Lymphocytes of a Patient with Bladder Tumour

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During their attempts at culturing viruses from tumour cells and circulating lymphocytes, authors obtained oncogenic type 18 infectious adenovirus from the phytohaemagglutinin-stimulated, peripheral T lymphocytes of a patient with bladder tumour. They found that the lymphocytes of other patients with urogenital tumour often show sensibility to the viral antigens. The successful culturing of the virus proves that patients with urogenital tumour carry the functioning genomes of the ontogenic virus, not only in their tumour cells but also in their circulating lymphocytes. It is assumed that these genomes jointly with the immune system impaired by other DNS viruses might have a role in tumour development.

It is known that the tumour cells and circulating lymphocytes of patients with malignant urogenital tumour may carry viral components, latent viruses. However, infectious virus—in the mentioned cases—could not be isolated. In the present study attempt was made to culture infectious virus from the tumour cells and the *in vitro* stimulated circulating T lymphocytes of patients with urogenital tumour.

Patient Material and Methods

Attempts were made to culture virus from the surgically removed tumour of 25 patients with malignant urogenital tumours of various types. The separated tumour cells as well as tumour-cell extracts were placed in primary and permanent cell cultures susceptible to viruses. The separated T lymphocytes and the extracts of the same cells of the patients were similarly placed on sensitive cultures.

Since virus culturing (see above) remained unsuccessful, the following method was tried. The separated T lymphocytes of a total of 30 urogenian tumour patients were activated by a mitogen of strong effect, phytohaemagglutinin, and were cultured in Parker 199 solution in a thermostat for three days, i.e. the cells were stimulated. After culturing the stimulated T lymphocytes and their extracts were introduced onto *in vitro* human primary amniotic cell culture, human primary embryonic cell culture and HEP-2 permanent cultures. The cultures were studied light-microscopically for observing viral

effect every other day. The identification of the cultured virus was made with the complement-binding reaction, agar-gel precipitation, virus neutralization and restriction enzyme test.

Results

Infectious virus could be isolated in one out of the 30 patients, namely from the stimulated lymphocytes of a patient with bladder tumour.

Case-report. B. Zs. a 68-year-old female patient was admitted to our department for frequent urge to micturate as well as haematuria on March 14, 1988.

Findings. Moderately developed, well-fed female patient, mucosae moderately filled with blood. Chest, abdomen: without pathological change.

Laboratory findings: sedimentation rate 35 mm/h. Urinary sediment: 40-50 WBC, RBC covering the visual field. Others: without pathological change.

Findings. Plain film + i.v. urography: on plain film there is no density suggestive of calculus corresponding to the region of the kidneys. The gall-bladder is the size of a plum, filled with stones. There is no excretion on the right side on the 10-min and subsequent pictures. On the left side intact cavital system and free ureteral passage are seen. Cystogram reveals the missing right half of the bladder (Fig. 1).



FIG. 1. Cystogram reveals the missing right half of the bladder

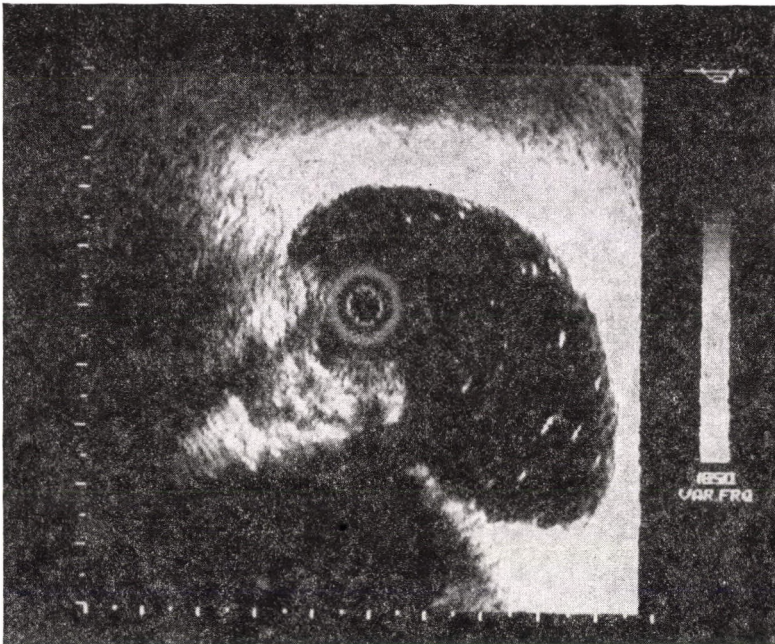


FIG. 2. Intravesical US: Tumour of a solid echostructure involving on the right side of the bladder, the region from the bladder to the base of the bladder, penetrating also into the wall and invading the environment (stage T₃b)

Intravesical US: Tumour of a solid echostructure involving on the right side of the bladder, the region from the pneumatic space to the base of the bladder, penetrating also into the wall and invading the environment (stage T₃b) (Fig. 2).

Cystoscopy: capacity: 150 ml. The tumour filling the right side of the bladder, but also invading the posterior wall and infiltrating the right orifice, with bullously edematous surface, covered occasionally with necrotic fibrin. The left half of the bladder and the left orifice are intact.

Because of the advanced stage of the tumour, electrocoagulation and electroresection were performed from suprapubic cystotomy.

Histology: Microscopically, a tumour of a nest-like structure can be seen in the wall of the tumour composed of urothelium. The tumour cells are atypical. Diagnosis: invasive urothelial carcinoma (Stage T₃b).

The separated and PHA-stimulated lymphocytes of the former patient were placed onto cell cultures. The cell displayed no change for weeks. In the meantime, for keeping the culture alive, the maintenance solution was changed every week. After 7–8 weeks, such swollen cells with uneven margins, possibly cell focus, etc., started to appear on the cell cultures, which indicated the presence of cytopathogenic agents. Then the cells were scraped off from the wall

of the dish and were placed onto fresh cultures. Here, the number of cells indicating the presence of virus had accumulated and the cytopathic effect had become increasingly conspicuous. The material was repeatedly placed on a fresh HEp-2 and amniotic cell culture, and the time of development of the cytopathic effect was reduced to a week. From that time on, the unknown agent (virus) could be propagated. A larger amount of it was produced, and the identification of the virus was started.

Performing the test with immune sera produced against various viruses, complement-binding and agar-gel precipitation, the new agent proved to belong to the adenovirus group. A more precise determination, i.e. typing, was made by using immune sera against 10 kinds of adenoviruses. By applying the 10 kinds of sera virus neutralization test was made in tissue culture. The DNS virus cultures from the stimulated, circulating lymphocytes of the bladder cancer patient did not respond to 9 sera against 9 types, it was, however, completely neutralized by one serum. The virus proved, finally, to be an oncogenic type 18 adenovirus. The DNA test performed by the Hind-III restriction enzyme confirmed its belonging to the adenoviruses.

Discussion

It is known that latent adenovirus carrier state is not indifferent for the organism. These viruses do not produce striking symptoms or changes. Being infected by them and being carriers of them is difficult to recognize. However, alertness to them is also indicated, besides a proneness to latency, by that the whole virus group has a great affinity to the lymphoid organs, and in addition, they are oncogenic.

That is why the possible correlation between the virus, the lymphoid system and tumour development was studied in the tumorous diseases of the urogenital system. Our earlier investigations had revealed that oncogenic adeno- and herpes viruses may be present in the tumour cells of tumorous patients, in the form of their components or that of their functioning genomes. It was proved that specific antibodies against protein-containing virus components can be detected [10, 11]. The virus components were found to be present also in a small percentage of the circulating lymphocytes of tumour-patients [3]. No infectious viruses have so far been isolated either from the tumour cells or from lymphocytes. That is why we consider it important that we succeeded in isolating an infectious oncogenic adenovirus from the circulating PHA-stimulated lymphocytes of a patient with advanced bladder tumour (stage T₃b).

The infectious virus isolated from T lymphocytes is a direct evidence for the presence and functioning of oncogenic adenoviral genomes in the peripheral lymphocytes of patients with urogenital tumours. The result of this function

is the formation of certain viral components, i.e. latent viral infection. If the lymphocytes are possibly stimulated or suppressed, the genomes are capable of producing a genuine infectious virus.

The importance of the new virus is, in our opinion, enhanced by the fact that, in lymphocyte transformation tests made so far, using this type of virus, besides the other adenovirus types, the lymphocytes of patients with urological tumours react primarily with it. Thus it can be assumed that, together with immune cells, viral genomes, can also play a role in the formation and maintenance of tumours.

Currently, the more precise mapping and study of the function of adenoviral genomes is being carried out [1, 7, 8, 9, 12]. It has been documented how and by which mechanism the individual gene segments affect, e.g. the functioning of the immune system [2, 6, 14]. The results obtained so far also suggest that the oncogenic trait of adenoviruses verified also under experimental conditions may manifest also in humans, primarily jointly with other DNS viruses or on alteration of the immune function [5, 13] In our case examined the patient's immune functions are assumed to have been weak due to his advanced tumour, but as a result of the strong mitogenic effect of the latent virus genomes, they were capable of forming a genuine virus.

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Erfolgreiche Züchtung des ansteckenden, über onkogene Eigenschaften verfügenden Adenovirus aus den stimulierten Lymphozyten von, an Harnblasentumor leidenden Patienten

S. CSATA, G. KULCSÁR und I. NÁSZ

Im Laufe der Virenzüchtungsversuche aus Tumorzellen und zirkulierenden Lymphozyten waren aus den mit Phytohaemagglutinin stimulierten T-Lymphozyten eines an Blasentumor leidenden Patienten über onkogene Eigenschaften verfügende, ansteckende Adenoviren (Typ 18) zu gewinnen. Es ließ sich feststellen, daß gegenüber die Antigene des Virus die Lymphozyten der übrigen, an Urogenitaltumor leidenden Patienten häufig eine Sensibilisiertheit zeigen. Die erfolgreiche Züchtung des Virus liefert einen Beweis dafür, daß die an einem Urogenitaltumor leidenden Patienten Träger der funktionierenden Genome des onkogenen Virus sind und dies bezieht sich nicht nur auf ihre Tumorzellen, sondern auch auf ihre zirkulierenden Lymphozyten. Es wird angenommen, daß in der Entwicklung des Tumors die Genome in Wechselwirkung mit sonstigen DNS-Viren geschädigten Immunsystemen wahrscheinlich eine Rolle spielen.

Успешное культивирование инфекционного, онкогенного аденовируса из стимулированных лимфоцитов больного с опухолью мочевого пузыря

Ш. ЧАТА, Г. КУЛЬЧАР и И. НАС

В ходе попыток культивирования вируса из опухолевых клеток и циркулирующих лимфоцитов авторы получили из стимулированных фетогемагглютинином периферических Т-лимфоцитов одного больного с опухолью мочевого пузыря обладающий онкогенными свойствами инфекционный аденовирус 18 типа. Они нашли, что лимфоциты остальных больных с урогенитальной опухолью часто обнаруживают sensibilizirovanность по отношению к антигенам вируса. Удачное разведение вируса доказывает, что больные с урогенитальными опухолями являются носителями действующих геномов онкогенного вируса, причем не только в клетках опухоли, но также и в циркулирующих в крови лимфоцитах. Авторы предполагают, что геномы должны играть роль в возникновении опухоли во взаимодействии с поврежденной другими ДНК вирусами иммунной системой.

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