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Prognostic Importance of Biopsies and Two-Phase Operations in the Surgery of Breast Carcinoma (Question of Surgical Dissemination of Cancer Cells)

F. PROCHNOW and L. TAPOLCSÁNYI

Department of Surgery, National Cancer Institute, H-1122 Budapest, Ráth Gy. 7–9, Hungary

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The authors performed interval operations in 217 cases of breast carcinoma at the Department of Surgery of the National Cancer Institute, Budapest between 1950 and 1958. The number of 15-year survival followed up was 111 (51%). During the same period, after 667 one-phase operations the number of survivals followed up for 15 years was 184 (27.6%). The significantly better results can be attributed to the fact that tumours (histological cancers) considered to be benign were removed by biopsy. Neither the time of the intervals nor the residual tumours did influence the better results. The prognosis of those operated on for solid carcinoma (c. simplex, and scirrhus) is less favourable. Permanent recovery can mostly be expected by premenopausal female patients with a slow-growing breast tumour of small diameter.

In breast cancer patients operated on without haematogenous metastases the surgical dissemination of cancer cells will not give rise to metastases, since this has been prevented, during the long growth of the tumour, by the defence mechanism of the organism and this is not even reduced by the surgical intervention.

Although the results of interval operations are promising it is still recommended that all nodes should be removed from the breast at an institute where a rapid histological frozen-section examination is available.

Precise preoperative diagnosis is a still unsolved question in the surgery of breast cancer. The biopsy and the subsequent histological frozen-section examination may help in revealing it. Adhering to ethical standard, removal of the breast can only be made on the basis of an accurate diagnosis. The triple requirements of diagnostics, ethics and surgical performance are met at best if, on removing breast tumours, the surgeon is always prepared to perform a radical operation.

It occurred quite frequently that tumours considered to be benign were removed in out-patient services, and a radical operation was only performed in possession of the positive histological results. The radical operation was also delayed if, based on the frozen-section examination, the question of malignity could not be settled. Two-phase operations are generally disapproved since they are supposed to produce enhanced dissemination of cancer cells and they are regarded as one of the causes of the not decreasing mortality rate of breast cancer.

On the basis of our large patient material (1044 patients received combined treatment between 1950 and 1958), considering their 15-year survival rate, it seems to be justified to deal with this question in detail. In 217 cases, i.e. in every fifth case (20.7%), two-phase operation or interval operation was performed.

Historical Survey

Prior to the antiseptic era, Virchow [62] already made microscopic examinations and he was the first to introduce the removal of tumour in intact tissue. With the spread of antiseptic then aseptic surgical procedures, the histological verification was finally eclipsed. Virchow, too, relied in his decision on the macroscopic picture [63]. Heidenhain's histological studies [29] had astonishing results. It turned out that in most of the cases, the cancerous breast had not been excised with a margin of normal tissue. Consequently, the great number of early recurrences as well as the 25–30% 3-year, nontumour-free survivals were understandable. Attempts have been made at increasingly resorting to radical surgery, as a result of which the radical operation of monoblock-dissection was performed [25, 44, 53]. At the turn of the century, breast carcinoma was described by the textbooks as a tumour being connected with the skin. Halsted [26], in case of smaller tumours made an incision through the skin and if the knife caught on the hard edge of the tumour he regarded it as malignant, while if the knife passed through unheeded, he considered it as a benign tumour. The famous "Operative Surgery" edited by Bier et al. [5] was published first in 1912. Breast surgery was discussed by Küttner. No mention at all was made here of the indication and performance of biopsy. Lubarsch called attention in 1912 to the relationship between tumour and trauma. According to him, trauma can give rise not only to its more rapid growth but also to its dissemination [41]. The results of Tyzzer's animal experiments [61] seemed to confirm this, too. After traumatization of the tumour (i.e. repeated excisions, massage, etc.) the number of haematogenous metastases increased.

After World War I, abdominal surgery underwent an amazing development. In Central Europe the care of breast tumours has become the task of the younger generation of surgeons. Parallel to an increase in the average age of population and to the development of the health insurance, the number of patients with mammary tumours also increased. Therefore, biopsies were often performed in out-patients, which not rarely involved complications (bleeding, haematomas, inflammation, suppuration). Owing to inaccurate biopsies explosive cancer-cell dissemination occurred sometimes and the fatal consequences of paraexcision had to be discovered in the neglected tumour of recurring patient [17]. Physicians have learned that even a circumscribed

tumour not attached to its environment can be malignant. However, after a radical operation there still was a great number of early recurrences. Post-operative radiotherapy was introduced on the initiative of German surgeons [4, 34, 47]. The restarting of animal experiments did not produce unanimous results, it was, nevertheless, repeatedly proved that massage of the tumour considerably increased the rate of haematogenous metastases [37, 42, 69, 70].

Evaluation of the results of interval operations first in 1933 aroused a controversy. Based on the patient material of the Memorial Hospital, Adair [2] demonstrated that the 5-year survival rate was 20%, while it was 20% in the case of 7145 one-phase operations. Harrington [28], at the same time, published a report from the Mayo Clinic stating that the survival of patients operated on elsewhere but receiving definite treatment at the clinic was relatively short, similarly to those operated on for mammary carcinoma during pregnancy. Siemens [58], however, reported that, after a total of 59 interval operations, the 10-year survival rate was 35%, while that after 250 one-phase operations only 16.4%. The excellent results are proved by the fact that in out-patients early-stage tumours were removed.

After World War II, the average age has further increased. In Hungary, owing to the general health insurance service, the number of those presenting with benign breast cancers has also enormously increased. It became an almost routine procedure to excise tumour at out-patient clinics where the more experienced clinical and hospital surgeons could make an adequate selection. As a result, the number of histological tumours has increased.

The warning of Lubarsch seemed to have been confirmed in clinical practice by Engell [15]. According to his cytaemic examinations, during breast cancer operation and also subsequently, a large number of tumour cells enter the regional venous circulation (in 57.5% of the cases) but also the peripheral circulation (9.7%). This was followed by a series of reports demonstrating a varying degree of tumour cells in the patients' circulation [11, 45, 51]. Alexander and Spriggs [3] proved earlier that tumour cells cannot be traced in the peripheral circulation during or after operations of operable breast cancers. If such an examination yielded positive results this was in support of the dissemination. Patients with such findings died due to cancerous complications within a couple of months. Invited by surgeons, Fleming [10], studied the dissemination of tumour cells both in the regional and in the peripheral circulation during osteosynthesis of tumorous (metastatic) femur. Their number showed an enormous increase in the regional blood decreasing markedly after a short time, they, however, did not appear in the peripheral circulation. (The fact that the osteosynthesis of a metastatic femur is a much greater trauma than a radical operation performed in normal tissue does not require further explanation.) Foss et al. [20] found tumour cells in the regional blood only in a small percentage of the cases during the biopsies of osteosarcomas.

Engell [16] himself did not attribute prognostic importance to surgical cytaemia, since the 5- to 9-year survival rates of his patients with positive and negative findings were identically 51 %. This opinion has also been emphasized by several other authors [12, 13, 14, 36, 52].

Surgical Trauma of Biopsies

Biopsies were made by the surgeons in regions infiltrated with a 1% Novocain solution, rarely under general anaesthesia. After transecting the skin and the soft parts, the vis a tergo pressure decreases in the tumour since tension is relieved at the surface of the tumour. From the opened lymph vessels and veins the blood is emptied into the wound, so do the tumour cells. The blood coming from the arteries is considered to be an eluent. Excision of tumours 2–3 cm in diameter does not entail greater trauma when performed by experts. Undoubtedly, however, this intervention is not ablative and there are always residual tumour cells. This patient is still in a more favourable position, even if the radical operation is delayed, than the calmed and discharged patient whose tumour keeps on increasing and who is readmitted with metastases.

Result-Statistics of Interval Operations

Roux-Berger and Monod [54] were the first to report in 825 patients with cancer of the tongue, that biopsies did not result in harmful consequences. The innocuity of excising ulcerating tumours is generally accepted. A considerable difference was, however, found by Wilson [68] in cases of breast cancer, since after total excision the 5-year survival rate was 70.9 %, while that after simple excision 47.5 %.

The results of Adair, Harrington and Siemens have already been cited. During the forty years having elapsed since then, 18 such reports appeared in the literature: Lee [40], Haagensen and Stout [23], Rödén [55], Nohrman [46], Dargent et al. [10], Scheel [57], Kaae [35], Wanke [66], Pierce et al. [49], Storres [60], Burkhardt [7], Jackson and Pitts [33], Sayago and Sirebrenik [56], Weber [67], Hultborn and Törnberg [30], Humphrey and Swerdlow [31], Gregl and Thorwirth [22] and Fries [21].

In general, the results after interval operation are better. The exceptions are discussed in detail.

The outstanding result of Siemens were confirmed by Haagensen and Stout [23]. He removed the tumour considered to be benign by radical excision in 42 cases, the radical operation was made later on in view of the histological results. In these cases, the 5-year survival rate was 85 % as opposed to the

average 51.1%. The results of Siemens were confirmed by Wanke from the same clinic. After a total of 149 interval operations the 10-year survival rate increased from 35% to 49.9%, but also in the other cases from 16.4% to 30.9%.

Harrington's discouraging results were improved in each respect by Pierce et al. [49]. They compared the 5-year survival rate after 96 interval operations to that in 675 one-phase operations, with regard to age, size, stage and grading of the tumour as well as to the length of the interval. No difference was found, although they stated that the survival of those operated with a half-year-interval was the best (65% as opposed to the 61.2% of the others).

Of the Scandinavian authors, Kase, Scheel and Fries did not find any difference. According to Rödén, the results are more promising after the interval operations. The substantially better results after the interval operations were attributed, by Nohrman as well as by Hultborn and Törnberg, to the fact one-phase operations were performed in clinically verified malignant cases.

Nohrman proved in a smaller, while Hultborn and Törnberg in a larger patient material, that the survival rate of those operated within three days was better. According to Hultborn and Törnberg, the 10-year survival rate after one-phase operations was 38.5%, that within a 3-day interval 75.3% and that exceeding three days 59%. Probably more patients in grade III belonged to those operated with a longer interval than 3 days.

Gregl and Thorwirth emphasized that the 10-year survival rate of those operated at 7 to 12 day-interval was the smallest, i.e. 28.6% as opposed to that of those operated on the 1st to 6th days or after the 13th day, these being 43.3% and 34.4%, respectively. Scarring procedure terminating during the second week would prevent subsequent "Stossmetastase", as stated by the authors.

Weber, Hultborn and Törnberg as well as Gregl and Thorwirth established that the residual tumour after biopsy demonstrated in the removed breast reduces the chances of survival. In 42 such cases of Hultborn and Törnberg the 10-years survival was 51.7% but this was much better than the 38.5% after the one-phase operations. In cases without residua, the rate was 68.2%. Gregl and Thorwirth ascribed a particularly bad prognosis to the residuum in positive lymph node cases. Of 28 metastatic patients, only 2 survived for 10 years, while in the negative cases 16 out of 30.

Based on 37 interval operations, Humphrey and Swerdlow stated that the 5-year survival rate of those undergoing surgery within 30 days was essentially better than those over 30 days, i.e. 75% as compared to 36.8%.

Sayago and Sirebrenik reported on a 27% 5-year survival rate after 33 interval operations, delayed on an average by 33 days. After their 37 one-phase operations the survival rate was 84.7%.

The results of other authors (Lee, Dargent et al., Burkhardt, Storres, Jackson and Pitts) revealed, however, that the chances for survival after interval operations were similar or better than after one-phase operations.

Present Results

Patient material: In the period from 1950 to 1958, a total of 1044 breast cancer patients received combined treatment (radical operation and radiotherapy). Of these 884 patients belonged to stages I and II according to Steintal. The 160 patients graded as stage III were not considered since in these cases no biopsies were performed.

Based on the histological examination, 884 patients were divided into negative lymph node (in the following negative) cases ($n = 527$; 60%) and positive lymph node (in the following metastatic) cases ($n = 357$; 40%). For 884 operable cases there were 217 biopsies (24.5%).

Interval operations were performed in 136 of 527 negative cases (25%) and in 81 of 357 metastatic cases (22.7%). Out of the 217 biopsies 63% fell into the negative group and 37% into the metastatic group.

The immediate radical operation following the total excision or biopsy and histological frozen-section examination should be called one-phase operation. Here, patients with a follow-up of at least 15 years' survival as well as the follow-up of 5-year losses were included.

General Survey

The number of those with a 15-year survival after 217 interval operations was 111, i.e. 51%; the 5-year losses were 44 (20%).

The number of those with a 15-year survival after 667 one-phase operations was 184, i.e. 27.6%; the 5-year losses were 224 (33%).

The difference is substantial, since after the interval operations every second, while after the one-phase operations every fourth, patient survived for 15 years. In the 5-year losses the difference is also considerable.

Detailed Comparison of Stages

Of 217 interval operations, in 136 negative cases 83 patients (61%) survived for 15 years; 5-year losses: 15 patients (11%).

In 81 metastatic cases 28 patients (34%) survived for 15 years; 5-year losses: 29 patients (35%).

Of 667 one-phase operations in 391 negative cases 138 patients survived for 15 years; 5-year losses: 94 patients (24%).

In 276 metastatic cases 46 patients (17%) survived for 15 years; 5-year losses: 130 patients (47%).

Consequently, after the interval operations, in the negative cases, more than half of the patients, while in the metastatic cases every third survived at least for 15 years. Nevertheless, after the one-phase operations, in the negative cases every third, while in the metastatic cases every sixth, patient survived. In the 5-year survival after the one-phase operations the losses were twofold.

These 15-year survival results wholly confirm the 10-year survival records of Siemens, Hultborn and Törnberg and Wanke. Similarly, we also attributed the better results to the fact that in the out-patient services the surgeons excised breast tumours not arousing the suspicion of cancer. Namely, the surgeons did either not palpate the axillary lymph nodes or having palpated them, they did not regard them as metastatic. The lymph node metastases were proved by histological examination.

The Importance of the Length of Intervals

Based on the length of intervals, the 217 biopsy cases were divided into five groups. To avoid dissipation, the stages are not going to be considered. None of the groups contains 100 patients, therefore percentages will not be calculated (Table I).

TABLE I
Significance of the length of the interval

Length of interval (days)	15 years' survival	5-year losses	Total of cases
A 1—7	33	18	69
B 8—14	21	6	37
C 15—30	23	9	44
D 31—60	16	5	23
E over 60	18	6	44
Total	111	44	217

Based on the above data, no importance can be attached to the intervals. Almost half of the patients survived for 15 years after the shortest (1 day to 7 days) as well as after the longest (over 60 days) intervals; while more than half of them belonging to the other three groups. The smallest losses were recorded in the 5-year survival after the longest interval: only every seventh

patient was lost (6 out of 44). This confirms the data of Pierce et al. In our material the 5-year survival rate of those operated at a half-year interval was greater (65%).

It should be emphasized that the results of all 5 groups are better than after the one-phase operations since after these only every fourth patient survived for 15 years, moreover of the negative cases only every third did so.

Comparison of the Results

Importance of the 3-day interval

As opposed to the results of Nohrman, Hultborn and Törnberg, it can be stated that in our material a total of 29 patients was operated at 3-day intervals. Of these 16 patients survived for 15 years. However, 188 patients were operated over 3 days of whom 95 survived for 15 years. In both groups more than half of the patients survived for 15 years, consequently the importance of the 3-day interval in the survival cannot be proved.

Importance of 7 to 12-day interval

According to Gregl and Thorwirth, the survival of patients operated on at 7- to 12-day intervals was the most unfavourable. In our material the corresponding 8- to 14-day groups were considered. Of the 37 patients 21, i.e. more than half of them, survived for 15 years and this is in keeping with that of those operated at shorter (1 day to 7 days) and at longer (15 to 30 and 31 to 60 days) intervals. The data of the above authors cannot be verified.

Importance of the 30-day interval

Neither can the communication of Humphrey and Swerdlow be confirmed. Within 30 days, however, 150 patients were operated. Of these, 77 survived for 15 years as opposed to the 67 patients over 30 days of whom 34 patients survived for 15 years. More than half of the patients in both groups survived for 15 years.

Importance of the average 33-day delay

The findings of Sayago and Sirebrenik can neither be confirmed although, as opposed to the 33-day average delay, 67 patients operated at intervals over 30 days were considered. Of them 34 patients survived for 15 years (50%), the 5-year losses were 11 patients (83% 5-year survival!).

Importance of residual tumour

In our material histological examinations revealed residua in 44 cases. Of them, 25 patients survived for 15 years, the 5-year losses amounting to 8 patients. Of 20 negative cases 15 (i.e. three-fourth of them) survived for 15 years. Of 24 metastatic cases 10 patients, approximately half of them survived for 15 years. There was a great difference in survival between the negative and metastatic cases, although the harmful consequences of the residuum could be verified not even in the metastatic cases.

Importance of Histological Type

The 217 cases were divided into two groups. The first included 66 patients (53 negative and 13 metastatic). Their tumours proved histologically to be comedo, initial intraductal, papillary and medullary mucinous cancers. The other group contained 151 patients (83 negative and 68 metastatic). The histology of their tumours revealed solid (c. simplex, scirrhus and mixed) cancers. Of the 66 patients belonging to the first group, 44 survived for at least 15 years, i.e. two-third of them. Of the 151 patients of the other group, 67, i.e. almost half of them, did so. Concerning the 5-year losses, in the first group every seventh, in the other one every fourth-fifth, patient did not survive for 5 years. The better results can be partly ascribed to the fact that 80% of those in the first group and 55% of those in the second one, were free of metastases.

Age, Length of History, Size of the Tumour and Survival

Only the survivals for more than 15 years were considered. Their average data are shown in Table II.

TABLE II

Correlation between age, length of history, size of tumour and survival

Data (mean)	Interval operation	One-phase operation
Age	46	51.5
Delay (months)	9	7.5
Diameter of tumour	2.3	3.1
Survival (years)	18.2	17.3

Table II proves that patients having undergone an interval operation due to a tumour regarded as benign can expect a permanent recovery in a larger number and to a greater extent, since at the time of the operation, they were younger ($5\frac{1}{2}$ years) and the growth of their tumour was slower.

The Question of Surgical Dissemination of Tumour Cells

General opinions

Of the pathologists Lubarsch [48], Ewing [18], Ackerman and Wheat Jr. [1] and Kellner [36] attributed haematogenous metastases-inducing effect to trauma. This warning applies to biopsies, and to radical operations of lesser or greater character. Wood, jr. et al. [71] considered the growth and spread of the tumour the most important factors in metastasis formation. Trauma (surgical and also biopsy) are ranked in the eighth place. Büngeler [8] believed that biopsy does not alter the disposition of the organism, even if tumour cells enter the organism metastases cannot occur. Kuzma and Anderson [38] emphasized that the metastasis-forming effect of biopsy is not adequately proved. According to Kellner [36], tumour cells from the local malignant tumours enter the organism only most infrequently. Invasion is associated with cytaemia and, due to the progression of the tumour, a gradually increasing number of tumour cells disseminate in the organism. According to Hamperl [27], the detachment of tumour cells depends primarily on their co- and adhesion as well as on the gradually increasing vis a tergo pressure in the tumour. The existence of tumour cells in the circulating blood is not the same as metastasis [8, 27, 32, 36].

In case of wholly excised tumours within a single block-dissection radical operation, haematogenous metastases are not to be feared.

Results of interval operations

The essentially better results are due to that also well-circumscribed non-carcinomatous tumours have been excised. The circumscribed appearance occurs when tumours of differentiated cells show the compressive invasion described by Hamperl, and tumours with immature cells have delineated edges [30] and a pushing border [39]. Also the lymphocytic border of medullary cancers, the mucous infiltration of mucinous carcinoma and the hyalin envelope of small scirrhous of old women make a cancer well-circumscribed. It is known that the surgical prognosis of these tumours is much better than the average.

The frequently occurring residual tumours do not seem to have an adverse effect not even in cases of axillary metastases. This has also been confirmed by the latest studies. Silverberg and Chitale [59] made biopsy then radical operation in the initial stage of intraductal carcinoma. They found residua in 19 cases with an 80% 5-year survival rate. Wanebo et al. [65] performed ample excision, then radical operation in 167 so-called preclinical mini-carcinomas. Histological examination revealed residua in 52% of the cases. The 10-year survival rate of the patients was 95%. Contesso et al. [9] reported that dissemination did not increase in the excised breast, weeks after the biopsy.

The results of Peters [48] obtained by the so-called salami-procedure are extremely interesting clinically. The smaller tumours situated in the external sectors were removed by lumpectomy (a somewhat greater operation as biopsy), then the patients received intensive radiotherapy. When relapses occurred mastectomy, in case of repeated recurrences, block-dissection were performed. The 3 to 20-year survival rate of his 275 patients was 69%, as compared to the 59% of his radically operated and irradiated 979 patients. Undoubtedly, the one-phase operations were performed in the more frequent cases. The comparison of the two materials is by all means not objective. It is, however, obvious that for a long time the residuum causing recurrences does not have metastatic complications.

Experimental, Clinical, Pathological Observations

By intravenously injecting large amount of tumour cells in 100% successful attempts have been made to produce metastases in rats. Using few hundreds of tumour cells, however, succeeded in causing metastases only in a small fraction of animals [36]. This experiment cannot be an analogy, since the intact, tumour cells are freed from the breast carcinoma by progression [36] or by the vis a tergo pressure [27]. The questions are still unanswered how, as a result of surgical trauma, the detachment of intact tumour cells change, how many of them enter the surrounding tissue, the lymph vessels or, via the regional veins, the organism. Fleming showed that during osteosynthesis of metastatic femurs, a marked dissemination of cells is initiated in the regional venous circulation, however, this is immediately stopped following the surgery. This fairly rough and direct trauma cannot be compared, however, with the operation performed in the intact tissue far removed from the tumour.

It is well known that cancer of the breast is a metastable tumour. It is therefore justified to suppose that in some patients with clinical breast cancer occult, haematogenous metastases have already been formed which cannot be traced by routine examination and which can be recognized only after the operation, often some years later and frequently without local recurrences [50]. According to Marx and Widow [43], the number of these patients at the time of their first visit amounts to 25 to 30%. In their opinion, late metastases may derive from cells the duplication time of which is very slow.

According to Walther [64], the autopsy of patients with cancer of the breast receiving treatment or not actively treated but died of a cancerous complication shows them to be free of haematogenous metastases in 25 to 30%. Their death was due to a cancerous expansion (permeation) and cachexia. Bloom et al. [6] have confirmed this observation in the autopsy material of patients with cancer of the breast.

Patients presenting with operable cancer of the breast can, therefore, be divided—as regards haematogenous metastases—into three classes, namely to (i) those resistant to metastases, (ii) those with preclinical, occult metastases and (iii) those without metastases, however not being resistant.

In case of a more or less definite diagnosis, one-phase operation is performed. The 1 to 5 cm tumour was excised in the apparently normal tissue under general anaesthesia using an electric knife. This was first followed by a histological frozen-section examination, then within half an hour, by a radical operation. The excision of the tumour takes 10 to 15 minutes. This is the time within which the tumour cells becoming detached in larger amounts are a threat to the organism if, entering the circulation, they start to invade it. After removing the tumour, a residuum is bound to be left over. This, however, is of less importance, since this is excised by radical operation in normal tissue. This should be all the more emphasized, since the residuum does not influence the prognosis in radical operations performed at a long interval. After excising the tumour, however, the organism acquires a highly favourable position, since tumour-cell dissemination will abruptly stop. It should namely be borne in mind that cancers of the breast keep on growing throughout long years prior to being diagnosed and operated. If the patient presents without haematogenous metastases, the organism must have effectively combated the tumour cells. It would be an exaggeration to say that the defence mechanism of the organism were to break down just as a result of surgical stress or trauma. This has been disproved by the results of Haagensen [24], the disciple of Halsted. He himself operates on his patients—after small incision (not rarely triple) biopsies—through 4 to 5 hours. Then he performs the classical radical operation, combined with skin grafting. His 10-year survival results are better than average.

Theoretical Remarks

It is known that the individual surgical prognosis of the patients has not been favourable. Even considering the stage, the histological type, the various gradings based on anaplasia and progression as well as the other factors, prognosis can be established only with a statistical probability. One of the causes is that neither the patients resistant to haematogenous metastases nor those with occult metastases can be considered.

The same accounts for that no precise statistics can be compiled. These are suitable only for general assessment of any aspects.

The earlier the stage the patients present with their disease, the less the number of those with occult haematogenous metastases will be. Hence, the predeterminists are wrong, since as a result of the increase of early cases, the number of permanently recovered patients will also increase.

Practical Remarks

A fairly important diagnostic task in operable cases is the recognition of occult, haematogenous metastases by using special procedures. Certainly, the radical and aggressive treatment of these patients will markedly reduce the chances of their survival, while the palliative treatment may even essentially lengthen it.

In cases of well-circumscribed tumours, following biopsy, one should suffice with total mastectomy and with lower block-dissection. If the histological examination of lymph nodes yields negative results, radiotherapy should not be considered.

It is an old rule that every single node should be removed from the breast. Although in such cases, the interval operations have outstanding prognosis, it is still recommended that these should be removed in institutes where the rapid frozen-section examination is available. The interval operation is only indicated if the histologist cannot decide as far as malignity is concerned.

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Über die prognostische Rolle der Biopsie und des zweizeitigen Eingriffes in der Chirurgie des Mammakarzinoms

(Problem der operativen Tumorzellstreuung)

F. PROCHNOW und L. TAPOLCSÁNYI

An der Chirurgischen Abteilung des Landesinstituts für Onkologie wurden in den Jahren von 1950 bis 1958 in 217 Mammakarzinomfällen zweizeitige Operationen vorgenommen; die Zahl der observiert 15 Jahre Überlebenden belief sich auf 111 (51%); im Laufe derselben Periode wurden 667 einzeitige Eingriffe durchgeführt, wonach die Zahl der observiert 15 Jahre Überlebenden 184 (27,6%) ausmachte. Die wesentlich besseren Ergebnisse finden ihre Erklärung darin, daß in den Operationen mittels Probeexzision die als gutartig gehaltenen Tumoren (die histologischen Krebse) entfernt wurden. Die Ergebnisse wurden weder durch die Zeit des Intervalls noch durch das Tumorresiduum negativ beeinflußt. Die Prognose der operierten soliden (simplex, Szirrhus) Krebse ist weniger gut. Mit einer Dauerheilung können am ehesten jene an Mammakarzinom leidenden Frauen rechnen, die sich im Alter vor der Menopause befinden und bei denen es sich um einen langsam anwachsenden Tumor mit kleinem Durchmesser handelt.

Bei den ohne hämatogene Metastasen operierten Mammakarzinomkranken kann durch die Tumorzellstreuung keine Metastase verursacht werden, da dieser Prozeß

während des langsamen Tumorwachstums durch den Abwehrmechanismus des Organismus stets gehemmt wurde, eine Fähigkeit, die durch den chirurgischen Eingriff nicht verringert wird.

Obwohl die Ergebnisse der zweizeitigen Operationen befriedigend sind, wird empfohlen, daß die Entfernung der Mammaknoten stets in Instituten stattfinden soll, wo die rasche Gefriermethode zur Verfügung steht.

Прогностическая роль биопсии и двухэтапной операции в хирургии рака грудной железы (вопрос оперативного рассеивания опухолевых клеток)

Ф. ПРОХНОВ и Л. ТАПОЛЧАНИ

В хирургическом отделении Государственного онкологического института, за период 1950–1958 гг., в 217 случаях выполнили двухэтапную операцию по поводу рака грудной железы; число переживших 15-летний срок после операции составляло III больных (51%). Число оставшихся в живых спустя 15 лет после 667 одноэтапных операций, выполненных в те же годы, составляло 184 (27,6%). Объяснение значительно лучших результатов операций в первом случае заключается в том, что опухоли, которые при пробной биопсии считали доброкачественными (гистологические раки), удаляли в амбулаториях. Ни продолжительность интервала, ни остаток опухоли не оказывали ухудшающего действия на результат. Прогноз менее благоприятный при операциях солидного (простой рак, скирр) рака. Стойкое выздоровление ожидается скорее у больных, находящихся перед менопаузой, с медленно растущей раковой опухолью, имеющей маленький диаметр.

У прооперированных больных с раком грудной железы без гематогенных метастазов, рассеивание опухолевых клеток во время операции не может вызвать образование метастазов, так как этому, за продолжительное время развития опухоли, всегда препятствуют защитные силы организма, хирургическое же вмешательство не снижает эту способность.

Хотя результаты операции с перерывом являются хорошими, тем не менее авторы рекомендуют, чтобы любой узелок из грудной железы удаляли в таком медицинском учреждении, которое располагает возможностью производить быстрое исследование с замораживанием.

Gastric Carcinoma Associated with Other Malignant Tumours

L. MOLNÁR, E. SVASTICS and P. RAHÓTY

National Cancer Institute, H-1122 Budapest, Ráth Gy. u. 7-9, Hungary

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Authors report on 25 patients treated for gastric cancers associated, synchronously or metachronously, with other malignant tumour. Hypotheses for the development of multiple malignant tumours are reviewed. They state that the prognosis of the second tumour is worse for its late detection and stress the importance of follow-up that also considers the possible development of a new tumour.

Occurrence of multiple primary tumours has been observed by early investigators like Procca, Förster, Kaufmann, Virchow, Volkmann [cit. 32]. Nearly 100 years ago (1881) Billroth [5] determined the criteria of multiple primary malignant tumours: (i) the tumours of different histological types, (ii) have different localization, (iii) and possess metastases of their own.

Billroth's definition was soon considered to be exaggerated. Nowadays the classification of Warren and Gates [46] is the generally accepted one.

According to this definition (i) the tumours must show histological signs of malignancy, (ii) they have to be of different histological types, (iii) unequivocal evidence must be provided that the tumours are not one another's metastases.

In agreement with other Hungarian authors [3, 6, 14, 18, 19, 20, 22, 27, 29, 33, 34, 35, 43, 45] we accept the criteria of Warren and Gates [46].

There is a diversity in literature on the occurrence rates of primary, multiple malignant tumours. Double primary tumours usually occur in 3–5%, triple tumours in 0.2–0.5%. The occurrence of even more primary tumours is, however, a rarity [4, 7, 8, 10, 13, 17, 23, 24, 28, 40, 48].

Increasing life expectancy of the population and successful therapy of the first malignant tumours increase the likelihood of secondary tumours [14].

Based on their time of occurrence, multiple primary cancers can be divided into two main groups:

1. Simultaneous or synchronous multiplicity—if tumours appear within one year and the possibility of recurrence can be excluded.
2. Heterochronous or asynchronous tumours—with more than one year interval between their appearance.

The pathogenic factors of multiple primary tumours are not elucidated. None of the several hypotheses available is fully convincing.

Presumable aetiological factors can be grouped as follows:

1. Genetic and familiar factors
2. Long-term effect of some carcinogenic agent(s) (as in skin, breast, lung and gastric cancers)
3. Oncogenic effect of cytostatic or irradiation therapy (chronic immunosuppression)
4. Hormonal factors
5. Immunological factors [1, 12, 13, 20, 21, 26, 30, 31, 36, 37, 38, 39, 41, 47, 49].

Own Material

Retrospective analysis of multiple tumours treated at our department is in progress. To the best of our knowledge no comprehensive study on gastric cancers accompanied by other malignant tumours has been published. Over the period of 1972 to 1981 we treated 215 gastric cancer patients; multiple tumours were found in 25 cases (Tables I–V).

TABLE I
Gastric cancers associated with other tumours

	Synchronous gastric carcinoma	Metachronous gastric carcinoma	
		primary	secondary
Breast tumour	1	9	1
Gynaecological tumour	1	1	2
Tumour of the head and neck	—	3	1
Malignant melanoma	1	1	1
Urological tumour	1	1	—
Colon tumour	—	1	—
Total	4	16	5

TABLE II
Age and sex distribution of patients with multiple primary tumours

Age	Male	Female
31—40	1	2
41—50	—	4
51—60	1	9
61—70	2	2
71—80	2	2
Total	6	19

TABLE III

Time elapsed between the primary and secondary tumours

Case No.	Localization of tumour		Interval between primary and secondary tumour (yr)
	primary	secondary	
1	breast	stomach	13
2	breast	stomach	14
3	breast	stomach	20
4	breast	stomach	3
5	breast	stomach	3/4 (synchronous)
6	breast	stomach	15
7	breast	stomach	2.5
8	breast	stomach	3
9	breast	stomach	3
10	breast	stomach	55
11	stomach	breast	11
12	uterus	stomach	7
13	stomach	uterus	0 (synchronous)
14	stomach	ovaries	1.5
15	stomach	ovaries	4
16	larynx	stomach	2
17	gingiva	stomach	1
18	corpus linguae	stomach	1.5
19	stomach	sinus ethm.	2
20	stomach	melanoblastoma	2
21	stomach	melanoblastoma	0 (synchronous)
22	melanoblastoma	stomach	19
23	penis	stomach	1 month (synchronous)
24	prostate	stomach	4
25	sigma	stomach	6.5

When evaluating our gastric cancer cases none of the aetiological factors enumerated in the introduction could convincingly be proven. Family members' data did not confirm either the genetic or the familial origin. The effect of a carcinogenic agent could not be identified either. The high number of our patients treated with cytostatics or irradiation and the low incidence of double tumours did not make likely the oncogenic effect of chemotherapy or irradiation as immunosuppressed states. The role of some hormonal factors has been propounded as gastric cancers were relatively often associated with breast cancers and gynaecological tumours. We have failed, however, to render convincing evidence for such an aetiology. It is quite probable that these coincidences derive from the special patient material of our Oncological Institute.

As to recent years' studies of the National Institute of Oncology (Budapest) and of other authors, the immunological factors may play the most important role. The immunosurveillance theory of Thomas [44] and Burnet [9] on the defensive reaction to tumour by the T-cells has undergone some revision. Latest investigations in this field suggest that neither the T nor the B cells, but the 'zero' subpopulation of the lymphocytes is responsible for

TABLE IV
*Persistence of symptoms of the primary and secondary tumours
 in months (m) or weeks (w)*

Case No.	Primary tumour	Secondary tumour
1	2 m	1 m
2	12 m	6 m
3	4 m	3 m
4	5 m	1 m
5	1 w	1 m
6	6 m	6 m
7	18 m	48 m
8	2 w	12 m
9	9 m	6 m
10	3 m	5 m
11	12 m	1 m
12	1 w	8 m
13	6 m	0
14	6 m	0
15	24 m	5 m
16	12 m	48
17	2 m	11 m
18	2 m	3 m
19	36 m	11 m
20	12 m	1 m
21	22 m	12 m
22	6 m	0
23	6 m	0
24	17 m	2 m
25	9 m	2 m

the killing of tumour cells. This specific cellular immunoreaction of cancer patients was studied by the natural cell-mediated cytotoxicity (NMC) and by the antibody-mediated cellular cytotoxicity (ADCC) tests in a team work guided by Garam and Bakács [2, 15, 16]. Evaluation of our results is in progress. Better understanding of the immune reaction of the organism is expected to improve prognostics and to promote the introduction of targeted immunotherapeutic interventions (Table VI).

Table VI demonstrates that gastric cancer as a secondary tumour is often inoperable, i.e. no curative operation can be performed. Importance of the careful follow-up of cancer patients cannot be stressed enough. It is a gross error if the physician controls only the previously known and treated tumour, and does not reckon with the possibility of a new tumour. Thorough physical examination should be complemented with laboratory analyses, e.g. identification of tumour markers.

From the point of view of a second tumour, patients having been operated upon for another tumour are considered to be at risk.

Likelihood of developing a second malignancy is increasing with time. In the future the controlling physician is expected to perform examinations

TABLE V
Survival after tumour removal

Case No.	After the removal of the primary tumour alive (months)	After the removal of the secondary tumour	
		alive (months)	dead (months)
1	162		6
2	191		23
3	252		6
4	48		12
5	12	3 (dissemination)	
6	180		10
7	29		9
8	36		6
9	41		5
10	64		4
11	48	36 tumour-free	
12	91	7	
13	1		1
14	48		30
15	57		9
16	28		4
17	60	12 tumour-free	
18	19		1
19	72		48
20	62		38
21	34		35
22	228		2 weeks
23	60		60
24	73	49 tumour-free	
25	80		2

TABLE VI
Curative resection

Primary gastric tumour	1/ 5
Secondary gastric tumour	2/16
Synchronous tumour	0/ 4

not only according to the patient's complaints (e.g. gastroenterological examination) but, on a preventive basis, according to the diagnostic principles of gynaecology and pulmonology (haemocult, Weber reaction, gastric radiology, endoscopy, etc.).

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Magenkarzinom begleitende sonstige maligne Tumoren

L. MOLNÁR, E. SVASTICS und P. RAHÓTY

Berichtet wird über 25 Patienten, bei denen sich zum Magenkarzinom, synchron oder metachron ein anderer maligner Tumor gesellte. Die sich auf die Entwicklung von multiplen malignen Tumoren beziehenden Hypothese wurden überprüft. Es konnte festgestellt werden, daß die Prognose des zweiten Tumors, da dieser meistens nur spät diagnostiziert wird, schlechter ist. Die Möglichkeit der Entwicklung eines neuen Tumors liefert einen neuen Beweis für die Notwendigkeit der laufenden Betreuung der Tumorkranken.

Рак желудка в сочетании с другими злокачественными опухолями

Л. МОЛНАР, Е. СВАСТИЧ и П. РАХОТИ

Авторы лечили в своем отделении 215 больных с раком желудка, среди которых у 25 к раку желудка синхронно или метастатично присоединялась злокачественная опухоль второго органа. Они знакомят с гипотезами возникновения множественных опухолей. В их материале прогноз второй опухоли хуже, поскольку ее обычно диагностируют с запозданием. Подчеркивают значение обслуживания, при котором следует думать также и о возможности наличия второй опухоли.

Joint Occurrence of Aseptic Necrosis of the Head of the third Metacarpal and Freiberg's Disease

J. GURIN

Department of Orthopaedics, Semmelweis University Medical School, H-1502 Budapest, Karolina út 27, Hungary

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Freiberg's disease of the second metatarsal was found together with the aseptic necrosis of the head of the third metacarpal in a 54-year-old female patient. No similar case was found in the available literature. The deformity of the second metatarsophalangeal joint was corrected with an operation, the alteration of the third metacarpal did not need operative correction.

The aseptic necrosis of the head of the third metacarpal is very rare. It was first described by Dietrich [4] or according to Breck [2] by Mauclair [8]. Single observations were reported by Bopp [1], Frank [5], Schinz et al. [9] and Seyss [10]. Aseptic necrosis of the heads of the second and third metacarpals was described by Grosseketler [7], that of the forth metacarpal by Friedl [6] and of the fifth metacarpal by Carstam and Danielsson [3].

The age of the patients ranged from 15 to 51 years. The complaints were generally local tenderness and restriction of the joint motion. If conservative treatment proved to be unsuccessful an arthroplasty of the metacarpophalangeal joint was generally suggested.

In the available literature no description of the joint occurrence of an aseptic necrosis of the head of the third metacarpal and of Freiberg's disease was found.

Case Report

B. A., female, 54 years old. She had pains in the region of the left second metatarsal head, mainly on the plantar surface, and after a longer weight-bearing. In the evening the forefoot became edematous and the pain increased. No trauma was reported. The examination revealed a thickening, a tenderness and dorsal and plantar clavus in the area of the second metatarsal head. Tiptoeing was rather difficult. Only a few degrees and slightly painful motion could be observed in the second metatarsophalangeal joint. The colour, the vascular and nerve supply of the limb seemed to be normal. X-rays showed signs of a former Freiberg's disease (Fig. 1).



FIG. 1. Freiberg's disease of the second metatarsal

A restricted motion (10° – 50°) was similarly observed in the third metacarpophalangeal joint (Fig. 2). No hand injury or pain was mentioned, a restriction of the holding capacity of objects and of clenching the fist was, however, observed since her childhood. X-rays (Fig. 3) revealed a diminution of the third metacarpal head, the unevenness of the articular surface and a palmar enlargement of the distal part of the metacarpus. The alteration described can be considered to be the result of a former aseptic necrosis. Other diseases as arthrosis, arthritis, osteomyelitis, tuberculosis, could be excluded. The arthrosis of this joint is rare and does not show similar X-ray pictures, on the other hand, it causes a painful restriction of the joint motion. Labor-

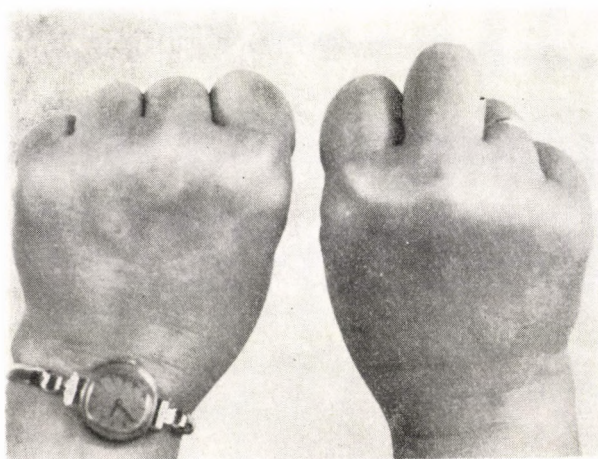


FIG. 2. Restricted motion of the third metacarpophalangeal joint

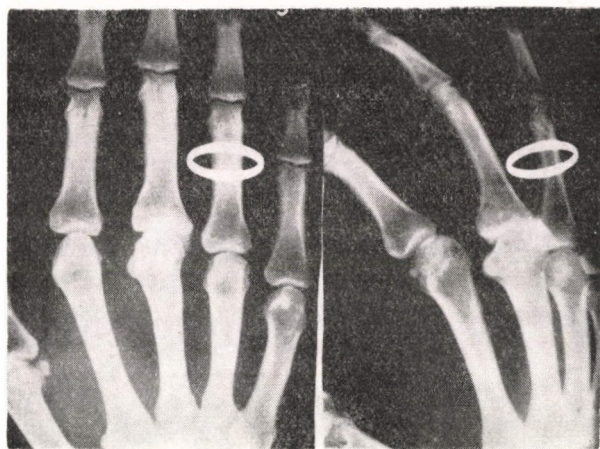


FIG. 3. Diminution of the third metacarpal head

atory findings were normal, and the hand was not edematous, cyanotic or painful. No signs of tumour could be found.

As the alteration found did not cause a disability of the hand, only physiotherapy was suggested. The deformity of the second metatarsophalangeal joint was corrected with an operation. The irregular, circular hyperostosis with an uneven surface was excised together with the basis of the ground phalanx and the head of the second metatarsal was spherically formed (Fig. 4). Six months after the operation the patient was satisfied with the result. The symptoms of her hand were unchanged.

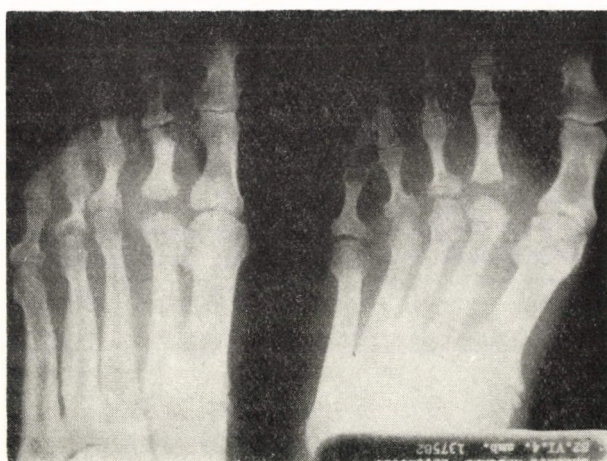


FIG. 4. The head of the second metatarsal after operation

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Gleichzeitiges Vorkommen der aseptischen Nekrose des III. Metakarpalkopfes und der Freibergschen-Krankheit

J. GURIN

Bei einer wegen durch Köhler II-Krankheit verursachten Beschwerden auf die Abteilung aufgenommenen 54 jährigen Patienten war gleichzeitig die aseptische Nekrose des III. Metakarpalkopfes zu beobachten. Das Ziel der Mitteilung war die Aufmerksamkeit auf die Möglichkeit des gemeinsamen Vorkommens der aseptischen Nekrose des Metatarsus und des Metakarpalkopfes zu lenken, zumal in der einschlägigen Literatur die Beschreibung eines ähnlichen Falles nicht vorzufinden war.

Случай одновременного наличия асептического некроза головки третьей пястной кости и болезни фрейберга

Й. ГУРИН

Автор лечил больную 54 лет на основании жалоб, вызванных болезнью Кёлера (II Köhler), и одновременно отмеченного у нее асептического некроза головки III пястной кости. В научной литературе, которой располагал автор, он не встретился с описанием подобного случая. Целью настоящего сообщения является обратить внимание на возможность одновременного наличия асептического некроза головок плюсны и пясти.

Combined Use of Transurethral Resection and Needle Biopsy in the Diagnostics of Carcinoma of the Prostate

J. ZANA, L. POLYÁK and D. FRANG

Department of Urology, Pécs University Medical School, H-7643 Pécs, Munkácsy M. u. 2, Hungary

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On suspicion of prostatic tumour, the authors performed a combination of transurethral resection and needle biopsy to form a safe histological diagnosis as well as to apply an adequate therapy. Transurethral resection combined with needle biopsy is to be performed if patients present with dysuric complaints, and if tumour can be suspected on rectal palpation or based on the clinical picture. This intervention ensures an unequivocal diagnosis and eliminates the urinary obstruction. They also dealt with cases, in which only needle biopsy or transurethral resection could help in forming the correct diagnosis.

Patients with carcinoma of the prostate present at a urologist usually with increased urinary complaints; or in case of metastasis the primary tumour has to be detected [13]. The suspicion of cancer of the prostate arises:

1. On the basis of clinical symptoms, laboratory findings, X-ray examinations and scintigraphy (rapidly increasing dysuric complaints, lumbar pains, loss of weight, microscopic haematuria, increased E. S. R., increased acid phosphatase values, most frequently lung and bone metastases, etc.).

2. On the basis of rectal examination which is unreliable in 10 to 20%.

- a) A false-positive result for tumour in case of chronic prostatitis, prostatic calculus, infarct of the prostate or adenoma. (In two of our patients the nodular prostates of uneven surface proved histologically adenomas [1, 2, 8]).

- b) Prostatic carcinoma cases considered to be falsely negative: carcinomas starting from the frontal surface and from the periurethral region cannot be palpated by rectal examination. Of 9 patients with carcinoma of the prostate one may be liable to this case [11].

Histology is indispensable in the diagnosis of the carcinoma of the prostate [1, 3, 4, 6, 7]. In 80 to 98% of the cases a rapid and safe diagnosis can be achieved by needle biopsy which is decisive also from the point of view of therapy [9, 12]. Our biopsies were most often performed in spinal and less frequently in local anaesthesia by the transperineal or transrectal method. Three samples of tissue cylinders were removed from the region suspect of

tumour. Needle biopsy may lead to unsuccessful results [14]. In case of a small amount of biopsy material, only the suspicion of tumour can be established, and the degree of differentiation of the carcinoma cannot be assessed.

Tumours located periurethrally or on the anterior surface of the prostate cannot be palpated and the needle biopsy will repeatedly yield negative results (in 5 to 15% of the patients with carcinoma of the prostate). In these cases, it is not the rectal palpation but the clinical symptoms which call attention to the possibility of a prostatic tumour.

A combination of transurethral resection and needle biopsy was performed in 50 patients suspect of cancer of the prostate. In this way we wanted to form an exact histological diagnosis as well as to initiate an adequate therapy.

Histological results of the needle biopsies of the 50 patients revealed carcinoma in 37 cases, suspicion of carcinoma in 5 cases and adenoma in 5 patients. In 3 patients the biopsies were unsuccessful. Using transurethral resection, the same 5 patients showed histologically adenoma, while 45 were found to reveal the unequivocal diagnosis of carcinoma (Table I).

TABLE I

Comparison of the histological results of transurethral resection and of needle biopsy

Results of needle biopsies of 50 patients

37 cases of carcinoma
5 cases arousing the suspicion of carcinoma
5 cases of adenoma
3 failures

Results of 50 transurethral resections

5 cases of adenoma (corresponding to the needle biopsy)
45 cases of carcinoma

The detailed histological elaboration of our patient material is still in progress. It can be stated, however, that a considerable part of malignant tumours are early stage cancers.

Transurethral resection in the diagnostics of the cancer of the prostate is applied only sporadically and opinions are conflicting as to the necessity of resections [5, 9a, 10, 11].

In addition to its diagnostic purpose transurethral resection is, at the same time, of therapeutic effect by eliminating the urinary obstruction.

The advantages of the essentially subtotal resections performed at our department are as follows.

1. In all cases, a sufficient amount of material was gained to form a histological diagnosis (there were no false-negative findings on account of the

limited material available. Denton had the same experience with 300 patients [5]).

2. The patients could, at the same time, be freed, for a shorter or longer period, from the indwelling catheter.

3. In case of cancers arising from the frontal surface of the prostate or periurethrally, tissue samples can only be obtained in this manner which ensures the histological diagnosis. Needle biopsy repeatedly yields negative results.

4. In cases, in which, carcinoma underlying the dysuric complaints is not suspected on the basis of rectal palpation and, therefore, no biopsy is performed. Transurethral resection gives a clue for the correct diagnosis (of the 117 patients of Ruszinko belonging to this group 6 had cancer of the prostate [11]).

Discussion

Transurethral resection combined with needle biopsy is suggested, if the patient presents at the urologist with dysuric complaints and, prostatic tumour is suspected on rectal palpation or in view of the clinical symptoms. This ensures an unequivocal diagnosis, helps to adjust an adequate therapy and eliminates urinary obstruction.

If the cancer arises at the anterior surface of the prostate or in the periurethral region (in 5 to 15%) it is mostly by transurethral resection that a tissue sample can be obtained which ensures the histological diagnosis [11]. In case of tumours located at the posterior surface of the prostate subcapsularly, however, primarily needle biopsy will ensure diagnosis. Therefore, the question is not an alternative performance of needle biopsy or resection. Based on our experiences, it is worth performing both with diagnostic and partly therapeutic purposes.

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Kombinierte Anwendung der transurethralen Resektion und der Nadelbiopsie in der Diagnostik des Prostatakrebses

J. ZANA, L. POLYÁK und D. FRANG

Im Interesse der Erstellung einer sicheren histologischen Diagnose und der Einstellung der Therapie kam im Falle eines Prostatatumorverdachts die transurethrale Resektion bei 50 Patienten in Kombination mit der Nadelbiopsie zur Anwendung. Der gleichzeitige Einsatz der beiden Verfahren erwies sich im Falle von dysurischen Beschwerden und eines sich anhand des rektalen Palpationsbefundes oder des klinischen Bildes erhobenen Prostatatumorverdachts im Interesse der Sicherung der eindeutigen Diagnose sowie der Behebung des Miktionshindernisses als lohnhaft. Anschließend finden auch jene Fälle eine Besprechung, in denen beim Verdacht eines Prostatatumors zur richtigen Diagnostizierung eine der beiden Verfahren — Nadelbiopsie oder TUR — genügte.

Одновременное применение трансуретральной резекции и игольчатой биопсии в диагностике рака простаты

Я. ЗАНА, Л. ПОЯК и Д. ФРАНГ

Авторы выполнили одновременно трансуретральную резекцию и игольчатую биопсию у 50 больных с подозрением на опухоль простаты, с целью установления точного гистологического анализа и назначения соответствующей терапии. По их мнению, если больной обратился к урологу с жалобами на дизурию, и если при ректальном обследовании или на основании клинической картины возникло подозрение на рак простаты, то, с целью постановки правильного диагноза и прекращения жалоб, связанных с мочеиспусканием, следует произвести трансуретральную резекцию вместе с игольчатой биопсией. Авторы рассматривают также такие случаи, когда удается достигнуть постановки правильного диагноза при подозрении на рак простаты либо только с помощью игольчатой биопсии, либо только с помощью трансуретральной резекции (TUR).

Haemodynamic Pattern of Formyl-Leurosine Induced Acute Cardiovascular Depression in the Dog

A. JUHÁSZ-NAGY¹, P. SÓTONYI² and L. BERTÓK³

¹ Department of Cardiovascular Surgery, H-1122 Budapest, Városmajor u. 68, Hungary and ² Department of Forensic Medicine, Semmelweis University Medical School, H-1085 Budapest, Üllői út 97, Hungary and ³ 'Joliot-Curie' National Research Institute for Radiobiology and Radiohygiene, H-1125 Budapest, Peutz K. u. 5, Hungary

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High incidence of cardiovascular collapses during clinical treatments with the cytostatic Vinca derivative formyl-leurosine (F-leurosine) prompted efforts to analyse in experimental models the haemodynamic mechanisms underlying the cardiodepression induced by large doses of the drug. A variety of cardiovascular variables was measured in 38 dogs narcotized with sodium pentobarbital. It was found that i. v. administration of F-leurosine (2 mg/kg) elicits, after a very short latency (< 5 min), considerable decreases of arterial and pulmonary blood pressure, ventricular contractile force, cardiac output, ventricular filling pressure, coronary blood flow, and myocardial O₂ consumption. Calculated systemic and pulmonary vascular resistance increased, while coronary resistance did not change. The later phase of F-leurosine action (> 1 hour) was associated with a permanent circulatory depression, a compromised coronary autoregulatory capacity, and serious histological injuries in the heart. Autonomic blocking drugs could not prevent these effects. It is concluded that the F-leurosine-induced rapid primary (pharmacologic) depression is followed by toxic manifestations of a more serious, secondary cardiac damage caused by the direct action of the drug cellular membranes.

Since modern surgical therapy of neoplasmas is regularly supplemented by the administration of antitumour drugs, investigation concerning the various actions of these agents has become an integral part of surgical research. The treatment with antineoplastic drugs is not without its undesirable side-effects: The present experimental study was designed to elucidate the haemodynamic pattern of acute cardiotoxicity induced by the administration of formyl-leurosine (F-leurosine), a semi-synthetic Vinca derivative developed in Hungary [9]. Despite the good antitumour potency of the agent in preliminary clinical trials [5], the accumulation of unexpected adverse side-effects of uncertain haemodynamic background necessitated later an extreme caution with its use.

Materials and Methods

Experimental procedures

A total of 38 mongrel dogs of both sexes, weighing between 10–21 kg, were used. The experiments were carried out under sodium pentobarbital (30 mg · kg⁻¹) anaesthesia. The chest was opened in the fifth intercostal

space and arteficial ventilation was maintained with an RO-5 respirator using room air. Arterial blood pressure was measured with a P 23 Db Statham transducer through a heparin-filled polyethylene cannula inserted into the left femoral artery. In addition, other cardiovascular variables were also determined, alone or in combination with each other to ascertain alterations concerning various aspects of circulatory dynamics:

- Blood flow in the ascending aorta (cardiac output minus coronary blood flow) was measured in ten dogs with a flow probe connected to a Statham SP 2201 electromagnetic flowmeter. Mean flow was obtained with electrical integration.

- Myocardial contractile force (ten dogs) was recorded with a Walton—Brodie strain gauge sewn to the free wall of the left ventricle. Sometimes a second gauge was applied to the right ventricle.

- Pulmonary arterial and left atrial pressures were recorded simultaneously in four dogs. Polyethylene catheters were inserted into the artery through the pulmonary conus and into the atrial cavity through the auricular appendage. Pressures were measured with the aid of a Statham gauge (P 23 Db) and a saline manometer, respectively.

- Left ventricular pressure was measured with a Statham gauge in four experiments through a short stiff polyethylene cannula inserted into the apex: diastolic portion of the pressure tracings was obtained using electronic sensitization. Left ventricular stroke volume was determined in the same experiments with the aid of a thermodilution catheter positioned above the aortic valves. These values were used according to the principle described elsewhere [10,14] to calculate the passive elastic modulus of the relaxed left ventricular wall, i.e. changes of diastolic ventricular stiffness.

- Intrapericardial pressure was measured in two dogs using a saline manometer, through a multiple-hole cannula inserted into the intact pericardiac cavity.

- Coronary blood flow was recorded in five dogs by means of a Statham electromagnetic flow probe (SP 2201) fitted around the left anterior descending (LAD) artery close to its origin. Phasic as well as mean flow values were simultaneously recorded.

- Heart rate was computed either from the arterial pressure curves taken at a paper speed of $25 \text{ mm} \cdot \text{sec}^{-1}$ or from ECG tracings recorded with unipolar electrodes sutured on the left and right ventricles, respectively (six experiments). All the haemodynamic variables were registered on a six-channel direct writing Hellige recorder.

- Blood samples were withdrawn, at regular intervals, from catheters introduced into the coronary sinus and the right femoral artery, respectively (five dogs). The samples were analysed, in duplicate, for pH and pO_2 (Astrup equipment) as well as for haematocrit. Oxygen saturation of the blood was

determined indirectly using the Severinghaus-Astrup nomogram. Taking into account alterations in mean LAD blood flow, relative changes of left ventricular oxygen consumption (per cent $\dot{M}\dot{V}_{O_2}$) was also computed from the values.

Administration of drugs

After the surgery had been completed a 30 min period was allowed for the stabilization of the experimental preparation. F-leurosine was dissolved in 20 ml of saline and administered by slow i.v. injection until a dose of $2 \text{ mg} \cdot \text{kg}^{-1}$ was given. This dose was chosen in preliminary experiments to produce a substantial, but not immediately fatal cardiovascular depression: smaller doses ($0.5\text{--}1.0 \text{ mg} \cdot \text{kg}^{-1}$) elicited effects of variable duration, while larger doses ($\approx 4 \text{ mg} \cdot \text{kg}^{-1}$) often resulted in a rapid total cardiovascular collapse or ventricular fibrillation. Moreover, the time-span of observations was restricted to a period of 120 min duration: in time control experiments (4 dogs) arterial blood pressure of open chest, instrumented animals could be maintained for approximately $2\frac{1}{2}$ –3 hours until a significant ($> 10\%$) diminution was observed in this variable.

In additional experiments a selected number of blocking drugs was given 15 min prior to F-leurosine injection to ascertain the involvement in the toxic response of alpha- and beta adrenergic (2 dogs), cholinergic (2 dogs), histaminergic ($H_1 + H_2$ receptors, 5 dogs), or serotonergic (2 dogs) mechanisms, respectively. The drugs were: pentolamine ($0.5 \text{ mg} \cdot \text{kg}^{-1}$) + propranolol ($0.5 \text{ mg} \cdot \text{kg}^{-1}$); atropine ($0.5 \text{ mg} \cdot \text{kg}^{-1}$) mepyramine ($5.0 \text{ mg} \cdot \text{kg}^{-1}$) + cimetidine ($5.0 \text{ mg} \cdot \text{kg}^{-1}$); methylsergide ($0.2 \text{ mg} \cdot \text{kg}^{-1}$). All these drugs were administered intravenously. Effectiveness of blocking drugs was tested by i.v. injection of appropriate agonists.

Histopathology

The experiments were terminated by arresting the heart with a light DC shock. Subsequently, small subendocardial and subepicardial tissue samples were fixed in a 2.5% glutaraldehyde fixative, whilst the bulk of the heart was fixed with 4% formaldehyde infused into the coronaries. The semithin sections were stained with toluidine blue. Ultrathin sections were made with a Reichert UMO2 apparatus for routine electromicroscopy (JEM 100 B equipment). Light microscopic studies were also performed using standard techniques. Open chest dogs maintained for an appropriate period of time ($2\frac{1}{2}$ –3 hours) served as controls.

Data analysis

Circulatory variables were chosen for data analysis at rigorously selected time-intervals. Most values quoted in the text and figures are mean values $\pm$ S.E.M.;

in a few selected cases, when only two independent observations were made (see Results) the average of the measurements are given. Presentation in absolute terms was preferred to percentage values: however, the latter was used in cases, when the measurement expressed as an absolute value is unrealistic (e.g. segmental myocardial force) or when a comparison between experimental groups seemed preferable to the magnitude of changes. The results were examined statistically using the Student's *t* test for paired and unpaired data.

Results

I. Systemic and pulmonary circulation

Figure 1 illustrates the characteristic pattern of circulatory dynamics that occurred in the anaesthetized dog after F-leurosine administration. The tracings depict dramatic changes in arterial blood pressure, cardiac output, and myocardial force.

Figure 2 summarizes the experimental data related to the general tone of systemic resistance vessels while administering F-leurosine to a total of six dogs. Averaging the measurements smoothed over the undulation in depressive

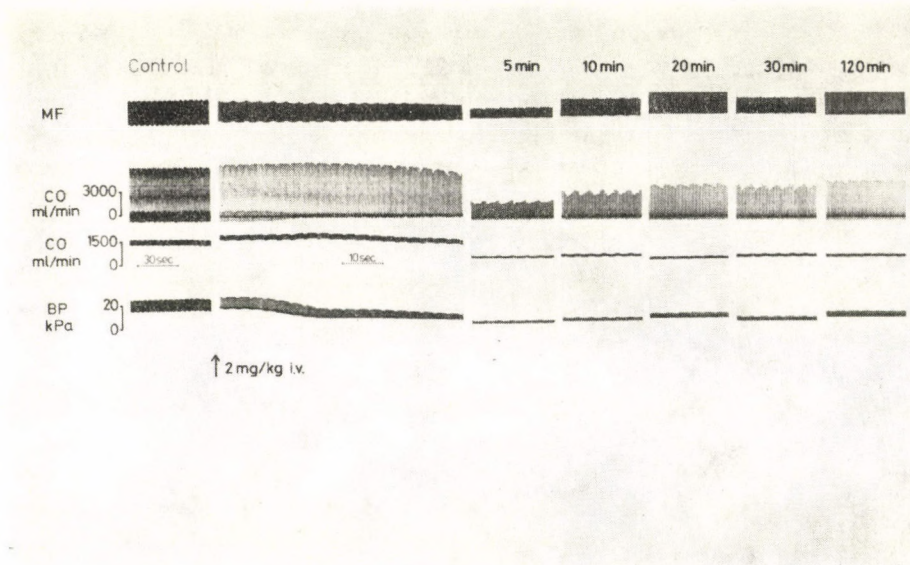


FIG. 1. Cardiovascular depression elicited by F-leurosine (arrow). From above downwards: myocardial contractile force (MF, left ventricle) cardiac output (CO, phasic and mean curves), arterial blood pressure (BP). Note prolonged latency of the cardiac output fall as compared to that of the hypotensive response, and the waxing and waning of cardiac depression during the later periods

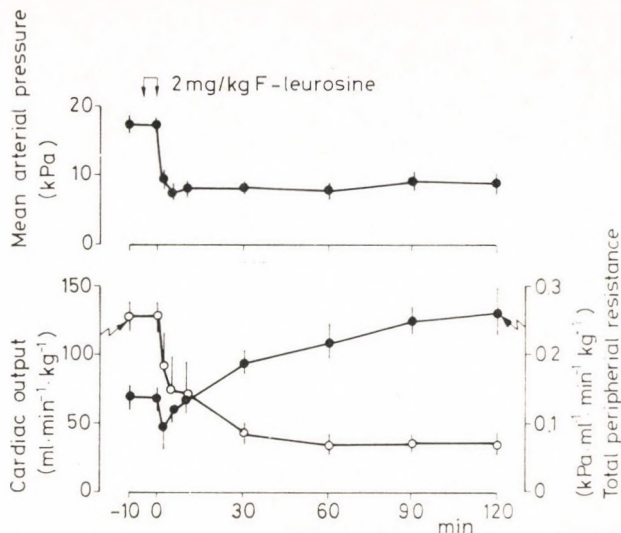


FIG. 2. Effect of F-leurosine on systemic circulation. Mean values $\pm$ S. E. M. of six experiments. All changes are significant statistically ($p < 0.05$) except in the first phase (decline) of calculated vascular resistance

effects which was characteristic in individual experiments (see Fig. 1). Since cardiac output exhibited a more pronounced decrease in response to the drug than arterial pressure, overall circulatory depression was accompanied, except for the first 5 min of the hypotension, by a gradual increase of calculated systemic vascular resistance.

F-leurosine also reduced pulmonary arterial and, to a lesser degree, left atrial pressure as summarized from data obtained in four dogs (Fig. 3). The response resulted in a substantial decrease of the pressure difference (effective driving force) in the pulmonary circulation, although the extent of this reduction lagged behind that of the flow (cardiac output). Thus, a moderate increase of calculated pulmonary vascular resistance ensued after the administration of the drug.

II. Myocardial force and heart rate

Cardiac contractile force was monitored in both types of experiments. It was found that a predominant feature of F-leurosine toxicity is the permanent depression of myocardial contractility (Table I). Cardiac frequency exhibited a modest but statistically significant decrease. Similarly, the changes observed in the ECG pattern were relatively small and variable. During the later period of observation (60–120 min) the appearance of multifocal ventricular ectopic beats was often associated with the deterioration of the experimental preparation. This resulted in ventricular fibrillation in two instances.

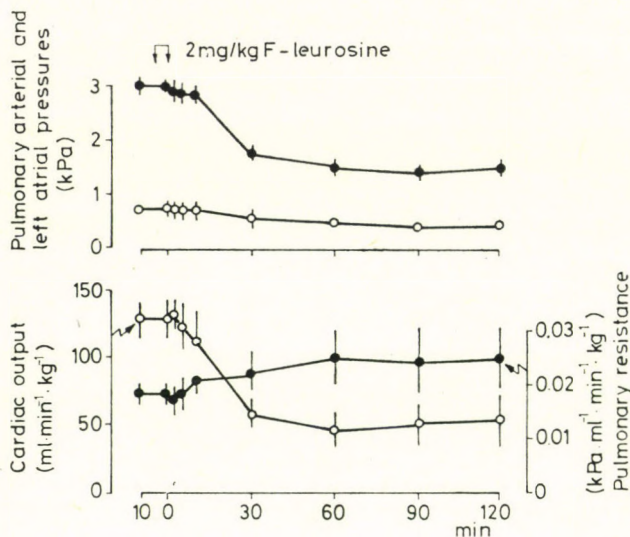


FIG. 3. Effect of F-leurosine on pulmonary circulation. Mean values $\pm$ S. E. M. of four experiments. S. E. M. is not indicated where its bar is smaller than symbol. Changes are significant statistically ($p < 0.05$) after 10 min, except changes in left atrial pressure which are significant only during the latest 30 min

TABLE I
Effect of F-leurosine on cardiac activity

	Time, min				
	0	10	30	60	120
Ventricular contractile force (%)	100 $\pm$ 0	71 $\pm$ 6 ^a	75 $\pm$ 4 ^a	65 $\pm$ 10 ^a	64 $\pm$ 9 ^a
Heart rate (beats $\cdot$ min ⁻¹)	153 $\pm$ 6	144 $\pm$ 7 ^b	137 $\pm$ 6 ^a	139 $\pm$ 6 ^a	139 $\pm$ 5 ^b

Mean values $\pm$ S. E. M., $n = 10$

^a significantly different ($p < 0.01$) from control

^b significantly different ($p < 0.05$) from control

III. Ventricular mechanics

As it is evident from the results summarized in Table II, administration of F-leurosine elicited an equivocal and moderate increase of left diastolic ventricular elasticity (wall stiffness). The time-course of this change approximately coincides with that of the diametrically opposed alteration of the end-diastolic ventricular pressure, suggesting the non-involvement of wall stiffening in the lasting decrease of cardiac output (Figs 1 and 2).

TABLE II
Effect of F-leuosine on left ventricular mechanics

	Time, min				
	0	10	30	60	120
Passive elastic modulus (ml ⁻¹)	0.029 ± 0.009	0.031 ± 0.008	0.032 ± 0.010	0.035 ± 0.013	0.039 ^a ± 0.010
Left ventricular end-diastolic pressure (kPa) ^b	0.66 ± 0.18	0.68 ± 0.19	0.54 ± 0.22	0.41 ^a ± 0.12	0.42 ^a ± 0.15

Mean values ± S. E. M., $n = 4$

^a significantly different ($p < 0.05$) from control

^b 1 kPa $\approx$ 7.52 mm Hg

IV. Intrapericardial pressure

F-leuosine brought about little change in this variable, the average pressure being 0.19 and 0.16 kPa at the beginning and termination of the 120 min observation period, respectively.

V. Coronary circulation

Blood supply to the heart muscle significantly decreased after F-leuosine administration (Table III). An unequivocal parallelism between decreases of coronary blood flow and arterial pressure on the one hand, and $\dot{M}\dot{V}\text{O}_2$ on the other, could be inferred from these results, whereas the interdependence of coronary blood flow, coronary vascular resistance and coronary venous $p\text{O}_2$ was found to be more uncertain. Thus the decrease in flow could probably be attributed to the diminution of the myocardial oxygen demand. At the same time, a proportionate decline of oxygen saturation in the coronary sinus accompanied the continuous decrease of oxygen saturation of the arterial blood. In this series three dogs were subjected to asphyxia of 1 min duration at regular intervals in order to gauge the effect of F-leuosine on the hypoxic dilator capacity of coronary vessels. Figure 4 depicts a typical experiment.

As can be seen, the first phase of the F-leuosine-induced hypotensive response was found to be associated with an increased sensitivity of metabolic coronary autoregulation (an augmented and prolonged vasodilatation), while the terminal phase was not. Instead, a very short-lived hypoxic coronary vasodilatation was followed by the sudden decrease of flow and a consecutive, catastrophic fall of blood pressure due to the reduced hypoxic tolerance of the heart muscle. Patterns of similar quality were observed in each animal, the adaptive capacity (vascular conductance increase) of the coronary vessels being augmented by $77 \pm 33\%$ of its original value, and diminished by $54 \pm 19\%$ in the terminal 30 min of the observation period.

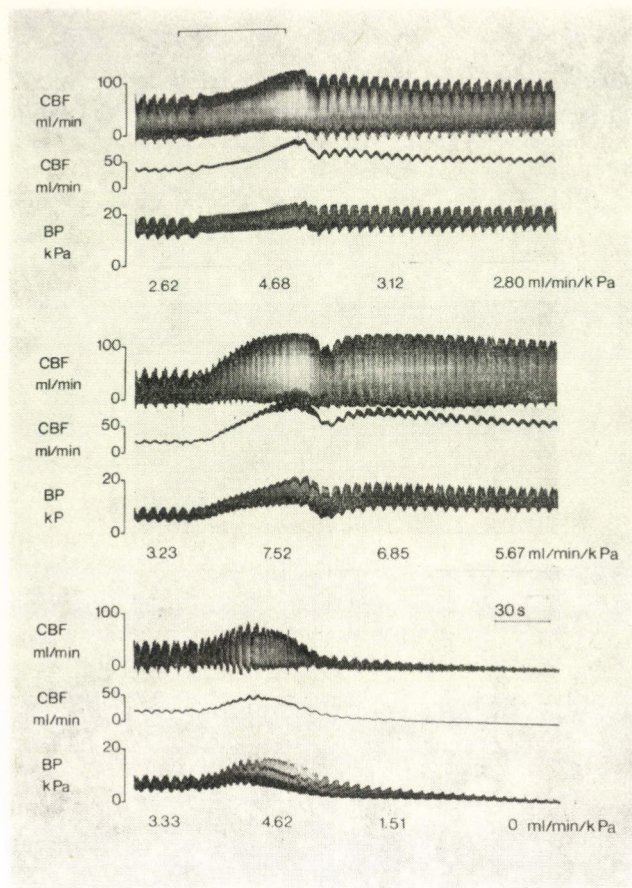


FIG. 4. Effect of asphyxia (—) of 60 sec duration on the coronary circulation in the control period (top tracings) at 30 min (middle tracings) and 90 min (bottom tracings) after F-leurosine administration. From above downwards in each block: Coronary blood flow (CBF, phasic and mean curves), arterial blood pressure (BP). Figures below the blocks denote calculated vascular conductance (reciprocal value of resistance, $1/R$)

VI. Effect of autonomic blocking drugs

To examine the possibility that acute cardiovascular distress induced by F-leurosine administration could, in part, be mediated through the enhanced release of well-defined vasoactive substances, a limited number of dogs was pretreated with blocking agents of adrenergic, cholinergic, histaminergic and serotonergic mechanisms. The results as presented in Table IV showed that these drugs were remarkably unsuccessful in preventing the shock-like syndrome caused by the standard dose of F-leurosine. To facilitate comparison, hypotensive changes are given in per cent values; in each group the initial absolute level of blood pressure is also indicated in parentheses. Blood pressure

TABLE III

Effect of F-leuosine on myocardial blood supply and O₂ consumption

	Time, min				
	0	10	30	60	120
Mean arterial blood pressure (kPa) ^b	17.1 ± 1.5	8.4 ± 1.8 ^a	12.0 ± 1.5 ^a	10.8 ± 2.1 ^a	11.6 ± 3.5 ^a
Coronary blood flow ^c (ml · min ⁻¹)	27.8 ± 2.1	11.6 ± 1.8 ^a	17.2 ± 1.1 ^a	17.1 ± 1.0 ^a	17.3 ± 2.7 ^a
Coronary vascular resistance (%)	100 ± 0	115 ± 5 ^a	113 ± 12	102 ± 15	106 ± 8
Arterial pO ₂ (kPa) ^b	11.3 ± 1.2	—	10.2 ± 1.3	9.1 ± 1.0 ^a	8.3 ± 0.8 ^a
Coronary sinus pO ₂ (kPa) ^b	2.9 ± 0.2	—	2.9 ± 0.2	2.8 ± 0.2	2.3 ± 0.2
Myocardial O ₂ (consumption, %)	100 ± 0	—	63 ± 13 ^a	64 ± 11 ^a	73 ± 10 ^a
Arterial pH	7.41 ± 0.02	—	7.38 ± 0.02	7.30 ± 0.03 ^a	7.27 ± 0.05 ^a

Mean values ± S. E. M., *n* = 5^a significantly different (*p* < 0.05) from control^b 1 kPa ≈ 7.52 mm Hg^c left anterior descending (LAD) artery

responses observed in Section I of Results served as controls. After establishing a combined blockade of H₁ and H₂ histaminergic receptors, a slight tendency for recovery could be observed during the latest phase (120 min) of the experimental observation. However, the deviation from the control group was not significantly different. The other blockers were even more ineffective in this respect.

TABLE IV

Effect of autonomic blockers on F-leuosine induced hypotension (percent change of arterial blood pressure)

Initial value (kPa) ^b	Time, min				Blockade ^a
	10	30	60	120	
16.2 ± 0.9 (<i>n</i> = 10)	-55 ± 5	-42 ± 6	-44 ± 8	-42 ± 10	none (control)
16.1 ± 1.9 (<i>n</i> = 5)	-47 ± 13	-35 ± 11	-36 ± 9	-29 ± 10	H ₁ + H ₂ histaminergic
11.3 (<i>n</i> = 2)	-47	-39	-37	-31	α + β adrenergic
14.8 (<i>n</i> = 2)	-57	-38	-35	-31	serotonergic
17.0 (<i>n</i> = 2)	-51	-34	-40	-45	cholinergic

^a For the drugs used see Methods^b 1 kPa ≈ 7.52 mm Hg

VII. Histopathological studies

F-leucosine administration produced myocardial lesions in every case. The lesions consisted of interstitial edema and severe injuries of the muscle cells themselves. In the light microscopy, the most severe forms of these damages were characterized by homogenization of the muscle fibres, with pronounced alterations in their stain-binding capacity. The electron microscopic findings (Fig. 5) also showed serious edematous changes, the appearance of hypercontractile bands, serrated Z-discs, and disrupted I-membranes. In addition, the findings revealed mitochondrial deformation and swelling, primarily close to the sarcolemma. Pronounced vacuolizations of the capillary membranes were also observed. The autonomic blocking drugs (see above) did not provide protection against myocardial lesions.

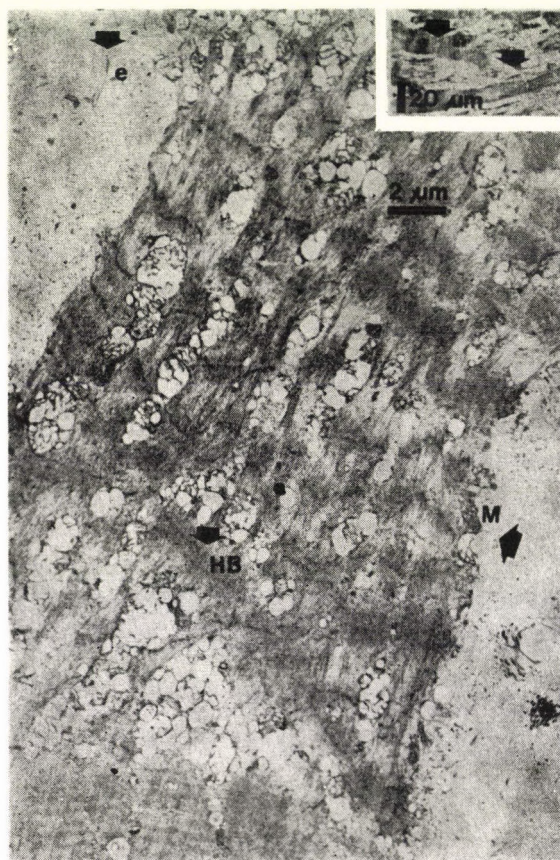


FIG. 5. Ultrastructural changes in the left ventricle. Arrows indicate interstitial edema (e), hypercontractile band (HB) and damaged mitochondrion (M). Also the insert (semi-thin section) top right shows hypercontraction (left) and edematous changes (right). $\times 5600$ and $\times 300$

Discussion

Cardiotoxicity of antitumour drugs remains a major therapeutic problem during the treatment with these agents. Although the most unfavourable cardiovascular side effects were encountered with anthracycline antibiotics such as adriamycin [16], other types of cytostatic drugs also may induce serious myocardial lesions. Claims were implicated on behalf of the newly prepared Vinca derivative Formyl-leurosine that it is not associated with significant cardiotoxic actions [5] but these claims did not stand the test of time: clinical trials with this otherwise promising agent had to be abandoned because of the frequent occurrence of an acute circulatory collapse which, in this particular case, seemed to be the principal dose-limiting factor. The present work was done to give a general phenomenological description of haemodynamic events involved in F-leurosine-induced acute circulatory depression. It was not the purpose of the experiments to perform an overall cardiotoxicologic examination in the traditional sense.

The results indicated that F-leurosine administration may elicit a significant, long-lasting decline in at least three basic interrelated cardiovascular variables, and each of these effects should be considered responsible, although in different manner, for the disturbance of circulatory equilibrium. First, there was a permanent fall in ventricular activity determined with the aid of a strain gauge arch. Since this device estimates the force developed by a myocardial segment which is isolated from the influences of preload and afterload, the results directly indicate changes in myocardial contractility. Further, F-leurosine administration resulted in a dramatic decrease of systemic arterial pressure. Finally, the third important haemodynamic variable displaying a lasting fall was cardiac output. The four fundamental factors that are known to determine the level of cardiac output (heart rate, myocardial inotropism, preload and afterload) apparently contributed in a different sense to the decline of this variable. The heart rate factor did not seem to be a very important one: the cardiac frequency, despite its decrease, remained well within the physiological range throughout the experiment. In contrast, the depression of myocardial contractility was clearly a decisive factor. Similarly, the contribution of diminished preload was indicated by the fall of cardiac filling pressures (Fig. 3. Table II), which occurred despite the significant decline of inotropism and the modest increase of passive ventricular elasticity (wall stiffness). This unusual pattern is highly suggestive of a drug-induced dilatation in the capacitance section of the circulatory system (venous pooling). It is interesting to note that an analogous haemodynamic pattern (impaired contractility + venous pooling) characterizes the circulatory shock underlying acute iron toxicity [2, 20]. It is difficult to estimate the contribution of afterload (i. e. active force per unit cross-sectional ventricular area) to the fall of cardiac output since one of its

chief determinants: the instantaneous change of ventricular size was not measured in these experiments. However, it seems unlikely that the alterations of afterload pointed to the direction of cardiac output decline, because of the enormous fall in an equally important determinant: the systolic arterial pressure.

The general behaviour of the smooth muscle tone of the arterial tree can be characterized by calculating the systemic peripheral resistance. The latter variable displayed a nearly two-fold increase at the end of the 120 min observation period, indicating an overall vasoconstrictor tendency after F-leurosine administration. The constrictor response was preceded by a short-lived phase of vasodilation seen immediately after the injection of the drug. Taken together, these phenomena suggest that systemic vasoconstriction is a compensatory feature of toxicity, evolving in particular cardiovascular sections (small arteries) which are probably less affected by the direct toxic actions of F-leurosine than more vulnerable parts, especially the heart muscle and the capillary-venous side of the circulatory system. A similar increase of calculated vascular resistance was quite evident in the pulmonary circulation.

To the authors' best knowledge, regarding meticulous details, a fully documented haemodynamic analysis of any antitumour drug effect, that is comparable to the present study, has not yet been published previously. At the same time, despite the complexity of haemodynamic events underlying the F-leurosine action, at least two directly measured cardiovascular variables: arterial blood pressure and myocardial contractile force are fairly quantitative and sensitive indicators which reliably describe the state of the circulation after administration of F-leurosine.

It is concluded that the most probable sequence of the F-leurosine induced cardiovascular toxicity is an abrupt general circulatory depression followed by more specific injuries focused on the cardiac muscle and small veins, i.e. the primary 'pharmacological' effects of the drug may be intensified by secondary toxic manifestations of cellular damage. The decisive role of myocardial deterioration is substantiated by histological findings that show serious, often irreversible alterations such as filamentolysis and disseminated necrotic foci.

Whether an impaired capacity of the coronary vessels for adequate myocardial blood supply under the aforementioned stressful conditions contributed to this enhanced cardiac vulnerability remains to be determined. The unequivocal decrease of coronary blood flow seen after F-leurosine injection tallies with the well known fact that the level of coronary blood flow is set by the rate of myocardial oxygen requirement which, in turn, is considerably influenced by the actual cardiac load. Indeed, there was a significantly diminished ventricular performance after F-leurosine administration that may easily be accounted for the reduced oxygen consumption and flow. However, one is no longer concerned with the level of resting blood flow *per se* in determining

appropriate coronary function: it is more important to ascertain whether the vascular potency for adaptive vasodilation (metabolic autoregulatory capacity) could or could not be influenced by a given experimental intervention [1]. This problem was addressed by subjecting the heart to brief periods of hypoxia and it was found that, after a phase of hyperactivity, coronary adaptive capacity became seriously restricted in the later phase of F-leurosine toxicity. In terminal phases of the experiments a short period of asphyxia may lead to total circulatory collapse and virtual cardiac arrest (Fig. 4). The same asphyxiating procedure as it was demonstrated in former studies [11], is usually well tolerated even by the partially ischaemic canine heart: the depression of the cardiac activity was found to be moderate and fully reversible. In contrast, F-leurosine treated animals displayed a reduced autoregulatory flow reserve associated with a poor cardiac tolerance to hypoxia. Accordingly, these observations raise the possibility that the exhaustion of the coronary adaptive capacity could trigger myocardial insufficiency in F-leurosine-treated hearts.

Edematous inhibition within the ventricular wall may be one of the factors involved in genesis of the impaired coronary autoregulation. Accumulation of myocardial edema occurs during treatments with antitumor drugs [16] F-leurosine has been shown to elicit serious edema and a profuse transepicardial fluid flux in the feline heart leading to cardiac tamponade and low voltage in the ECG [18]. Such an enormous transudation was not seen in the dog, suggesting a qualitative species difference in this respect. However, extracellular fluid accumulation was a consistent histological manifestation of cardiac damage (Fig. 5). These changes would be expected to effect the elastic properties of the relaxed ventricular wall, since a close correlation was demonstrated between the extracellular fluid content (thiocyanate space) and elastic modulus of the myocardium [14]. The results substantiated this surmise, albeit the changes were comparatively slight. Alternately, edematously compromised myocardial zones may have liberated some unidentified toxic substances [17] which could further aggravate cardiac function.

There are a number of superficial similarities between the ultrastructural pattern of catecholamine-induced cardiac injury [15] and the morphological manifestation of F-leurosine toxicity, suggesting the possible involvement of an enhanced noradrenaline release from internal stores. However, microtubule disrupters such as colchicine and vinblastine have been reported to block rather than increase noradrenaline release to external stimuli [3, 19]. In agreement with these findings, combined alpha- and beta adrenergic blockade performed in the present study was ineffective in preventing myocardial damage induced by F-leurosine. Thus the excessive release of catecholamines does not seem to play a role in the toxic symptoms. Histaminergic blockade also failed to protect effectively the cardiovascular system against F-leurosine, although Herman and his coworkers reported an augmented release of histamine during

treatment with antitumour agents in the dog [7, 8] and the rhesus monkey [6]. Apparently, histamine liberation, if present, was not a key factor of toxic alterations while administering F-leurosine to the dog. Finally, pretreatment with cholinergic and serotonergic antagonists were also unable to afford protection. The present findings are in general agreement with the results of Hungarian authors that toxic effects of Vinca alkaloids are caused by their direct interactions with the cell membranes [4, 12, 13]. The observations, moreover, also imply that the adverse actions are probably not mediated by either well-known autocoids or transmitters, rendering effective therapeutic prevention against these undesirable side effects a difficult task. Recent studies of our group indicate that this difficulty can efficiently be overcome by enhancing the non-specific resistance of the body (Bertók et al. to be published).

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Hämodynamisches Bild der durch Formyl-Leurosin induzierten akuten kardiovaskulären Depression beim Hund

A. JUHÁSZ-NAGY, P. SÓTONYI und L. BERTÓK

Angesichts des im Laufe der klinischen Anwendung des über eine zytostatische Wirkung verfügenden Vincaderivats, Formyl-Leurosin (F-Leurosin) häufig auftretenden Kreislaufkollapses, wurden die mit großen Dosen des Drogas auslösbaren, die Grundlage der Kardiodepression bildenden Kreislaufmechanismen mit Hilfe eines Versuchsmodells untersucht. Bei 38, mit Pentobarbital narkotisierten Hunden wurde eine Vielzahl kardiovaskulärer Parameter bestimmt. Kurz (< 5 min) nach der i. v. Verabreichung von F-Leurosin (2 mg/kg) waren einerseits die bedeutende Verringerung des arteriellen und pulmonalen Blutdrucks, der Kontraktionskraft der Kammer, des Minutenvolumens, des Kammer-Füllungsdrucks, der Koronardurchblutung und des O_2 -Verbrauchs des Herzens, andererseits der Anstieg der gerechneten vaskulären Resistenz im großen und kleinen Kreislauf zu verzeichnen, während die Koronarresistenz unverändert blieb. In der späteren Phase der F-Leurosinwirkung (> 1 Stunde) traten dauerhafte Kreislaufdepression, die Einengung der Autoregulationskapazität der Koronarien auf und es ließen sich auch schwere histologische Schädigungen des Myokards verzeichnen. Die angeführten Effekte konnten durch die Zufuhr von Blockern des autonomen Nervensystems nicht abgewehrt werden. Aus den Untersuchungsergebnissen ergab sich die Folgerung, daß auf die durch F-Leurosin ausgelöste, sich rasch entwickelnde, primäre (pharmakologische) Depression, toxische Manifestationen einer, mit der die Zellmembranen betreffenden direkten Wirkung der Droge verbundenen, im Vergleich zur ersten viel schwereren sekundären Herzschädigung folgen.

Гемодинамический образчик вызванной формил-лейрозином острой сердечно сосудистой депрессии у собаки

А. ЮХАС-НАДЬ, П. ШОТНИ и Л. БЕРТОК

Коллапс кровообращения, наступающий в ходе клинического применения формил-лейрозина (F-leurosin) — производного винка (Vinka), обладающего цитостатическим действием, — побудил авторов исследовать в экспериментальных условиях механизмы кровообращения, создающие основу кардио-депрессии, вызываемой большой дозой этого препарата. У 38 собак, находящихся под пентобарбиталовым наркозом, они определили большое число кардиоваскулярных параметров. Показали, что, в ответ на внутривенное введение F-лейрозина (2 мг/кг), после довольно короткого (5 мин) латентного времени, значительно уменьшаются артериальное и пульмональное давление, кровоток в коронарных сосудах, минутный объем сердца, давление при наполнении желудочка, сила сокращения желудочка и потребление кислорода в сердечной мышце. Вычисленное сопротивление сосудов большого и мелкого кругов кровообращения возросло, в то же время сопротивление венечных сосудов не изменилось. К поздней (1 час) фазе действия F-лейрозина присоединились стойкая депрессия кровообращения, сужение емкости ауторегуляции коронарных сосудов и тяжелое гистологическое поражение миокарда. Блокаторы вегетативной нервной системы на предотвратили наступление этих изменений. На основании результатов своих исследований авторы делают вывод, согласно которому быстро развивающаяся первичная (фармакологическая) депрессия, вызванная F-лейрозином, связана с непосредственным действием препарата на клеточные мембраны; вслед за первичным эффектом следуют гораздо более тяжелые, вторичные признаки токсического поражения сердца.

Role of the NK Reaction in the Diagnostics of Liver and Pancreas Tumours

S. KARÁCSONYI,¹ YVETTE MÁNDI, GY. FARKAS,¹ M. TÓTH¹ and ILONA BÉLÁDI²

¹1st Department of Surgery and ²Institute of Microbiology, Szeged University Medical School, H-6701, Szeged, P. O. Box 464, Hungary

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The NK (natural killer) and K (killer) activities of peripheral lymphocytes were determined. The peripheral blood was obtained from healthy individuals and from patients with liver and pancreas diseases. Examinations were performed preoperatively. The natural cell-dependent cytotoxicity (NK) was examined against the K-562 cell line, while the antibody-dependent cellular cytotoxicity (ADCC) was examined against human red blood cells. The NK and K cell activities of the 19 patients with malignant tumours were substantially lower than those of the 40 healthy subjects. In the 12 cases of benign diseases of the liver and pancreas, however, the mean percentage cytotoxicity expressing the NK and K activities ($40 \pm 10\%$) agreed with, or was higher than, the value for the controls ($32 \pm 12\%$). Low cytotoxicity levels ($12.6 \pm 5\%$) were characteristic in the malignant processes; in the majority of these, exploration showed local metastases or metastases besides the primary lesion. Since the NK and K cells play an essential role in the defence of the organism against tumours, the decrease in activity of this cell population may be of diagnostic value. *In vitro* interferon treatment in the control and benign cases considerably stimulated the NK reaction, and in some of the malignant diseases it raised the cytotoxicity values close to the control level.

Tumour-immunological investigations during the past decade have indicated that the non-specific immune defence of the organism plays a considerable role in preventing tumour formation and the development of metastases. Primarily the natural killer (NK) cells and the macrophages participate as effector cells in this defence mechanism [21].

NK lymphocytes can be isolated both from healthy humans and from experimental animals [10, 16, 19, 28]. Morphologically, they correspond to large granular lymphocytes, and in humans they comprise 1–6% of the peripheral lymphocytes [25, 26]. Without preliminary sensitization, the NK cells are able to kill certain tumour cells *in vitro*; their role in the defence against tumours *in vivo* is mainly supported by the results of animal experiments [5, 14, 20].

It has been observed that the NK activity is at a reduced level in certain malignant diseases in humans, e. g. mammary carcinoma, malignant melanoma and colonic carcinoma [7, 12, 13, 17, 22]. This is of importance from a theoretical aspect, but it also suggests the possibility of application of this method of examination in the diagnostics of malignant lesions. The present studies have been carried out with these two aims in mind. Since the effector cells of the NK reaction in all probability represent the same population as the killer (K)

cells taking part in the antibody-dependent cellular cytotoxicity (ADCC) reaction [1, 11], it appeared reasonable to measure these two reactions in parallel. (In the ADCC reaction, the similarly non-sensitized effector cells are bound via their Fc receptors to the antibody-covered target cells.)

We have compared the NK and ADCC activities in 31 patients with diseases of the liver and pancreas with the lymphocyte data on 40 healthy control subjects. The examination was performed preoperatively in every case. A study was further made of the extent to which the cytotoxicity was influenced by crude human leukocyte interferon prepared in our laboratories. Interferon stimulates both the NK and the ADCC reaction [11], and this mechanism presumably plays an essential role in the therapeutic action of interferon against tumours [18].

Patients and Methods

The NK and ADCC activities were studied in patients operated on due to focal lesions of the liver or to chronic disease of the pancreas. Table I shows the distribution of the patients with respect to age, sex and disease. The study was performed preoperatively; prior to the examination, the patients did not participate in cytostatic treatment.

TABLE I
Distribution of examined cases according to sex, age and disease

Diagnosis	No. of cases	Male	Female	Average age
Healthy controls	40	25	15	53.2
Echinococcus	2	0	2	45.5
Hepatoma	1	0	1	38
Cirrhosis	3	3	0	42
Chronic pancreatitis	4	3	1	52
Pancreatic pseudocyst	2	2	0	47
Total	12	8	4	46.4
Hepatic carcinoma	7	4	3	48.3
Solid hepatic metastasis	2	1	1	46
Pancreatic carcinoma	10	8	2	59
Total	19	13	6	53.1

The control group consisted of healthy men and women; these were selected on the day of the examination so as to be of the same sex and in the same age group as the patients.

Separation of Effector Cells

The mononuclear cells were separated from 25 ml heparinized (Chemical Works of Richter Gedeon Ltd, Budapest) blood by Ficoll-Uromiro gradient centrifugation [3]. The resulting lymphocyte suspension was adjusted to 5×10^6 /ml in culture medium (RPMI 1640) containing 10% FCS.

NK Reaction

The K-562 erythroleukaemic cell line was used as target cell; it was maintained in a suspension culture in 10% FCS-RPMI 1640 culture medium. The target cells were labelled with ^{51}Cr (Amersham), and the effector:target cell ratio was adjusted to 50:1, 25:1, 12:1 or 6:1. The cells were incubated for 4 hours at 37 °C in a 5% CO_2 thermostat. The percentage cytotoxicity was calculated from the activity of the supernatant via the following formula:

$$\text{cytotoxicity \%} = \frac{\text{supernatant cpm} - \text{spontaneous cpm}}{\text{incorporated activity cpm}} \times 100$$

ADCC reaction

Fresh, human Rh(D)-positive red blood cells were used as target cells. Human anti-D serum was adsorbed onto the cells [8]. The isotopically labelled cells were incubated with the effector cells in a similar way as described in the NK test. The duration of the incubation was 18 hours. The cytotoxicity was calculated as in the NK test.

Pretreatment of Effector Cells with Interferon

The lymphocytes of the patients, and also those of the controls, were incubated for 1 hour with 1000 U/ml crude interferon. The leukocyte interferon was prepared in our laboratories by a modification of the method of Cantell [4, 2]. Only the NK test was set up with interferon-treated lymphocytes.

Results

Figure 1 shows the results of examinations on the healthy controls and on the patients with benign and malignant lesions. The mean value of the cytotoxicity ($12.6 \pm 5\%$) can be seen to be low in the cases with malignant diseases

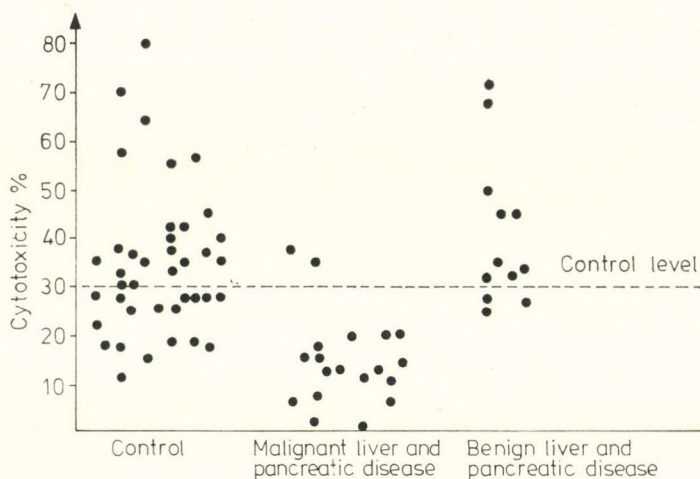


FIG. 1. Natural cytotoxicity of patients with liver and pancreatic disease

independently of the site of the primary tumour. The results reveal that the disease of the liver or pancreas itself is not accompanied by a decrease in the NK activity in the benign cases. (Higher values than the control were found in the patients with echinococcosis.) The cytotoxicity values reflecting the ADCC activities in every case varied in parallel with the values for the NK reaction, a difference of $\pm 2.5\%$ being observed for the individual blood samples.

Figure 2 depicts separately the NK activities for the patients with benign or with malignant liver diseases, and for those with benign or with malignant pancreas diseases. The malignant lesions are associated with significantly lower cytotoxicities. In the event of a malignant transformation, exploration demonstrated local metastasis or distant metastases in nearly 100% of the cases.

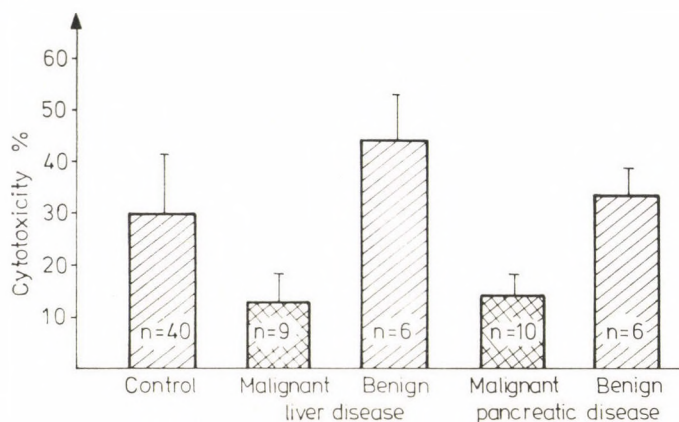


FIG. 2. Natural cytotoxicity of patients with benign and malignant disease of liver and pancreas

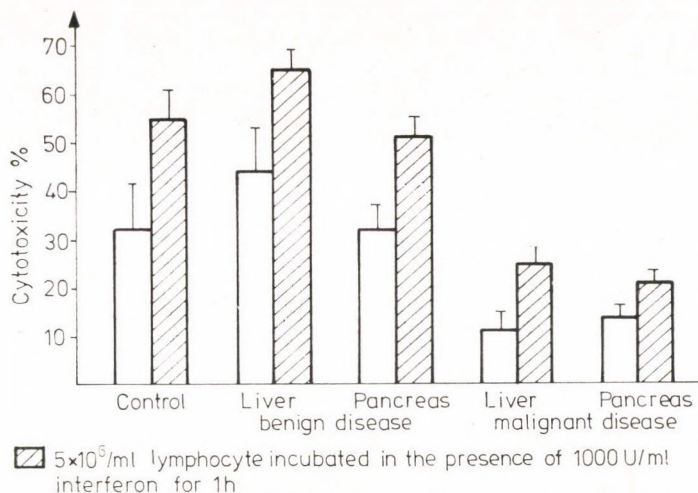


FIG. 3. Effect of *in vitro* interferon treatment on the NK activity. Hatched bars: 5×10^6 lymphocyte incubated in the presence of 1000 U/ml interferon for 1 hour. Open bars represent cytotoxicity without interferon

Although to extents differing from individual to individual, the interferon enhanced the NK activities of the control lymphocytes. It similarly exerted a stimulatory effect on the lymphocytes of patients with benign diseases. In some of the malignant cases, the activity of the lymphocytes initially exerting low cytotoxicity attained or approximated to the control level following interferon treatment. However, in those cases where evaluable cytotoxicity percentages were not obtained (1.7–3.8%), interferon treatment did not lead to stimulation. The mean results are presented in Fig. 3.

Discussion

The investigations by Pross and Baines [23], repeated several times in a large number of cases, confirmed that the degree of NK activity varies with the individual; our own experience agreed with this. Pross and Baines also demonstrated that the activity for a given individual is constant over a long period of time, and accordingly we considered it sufficient to take blood from each donor on only one occasion.

Our data indicated that values below the control level can be observed much more frequently in the cases of malignant lesions. In conformity with the literary data [13], our results showed that the NK and ADCC activities can be correlated not with the size of the primary tumour, but with the presence and extent of the metastases.

It has been proved experimentally that the NK cells play a role particularly in the destruction of the circulating tumour cells; their low activity is

accompanied by an increased incidence of metastases [21, 29]. The decreased activity of the NK cells may be determined by numerous factors (some already known, but others not) in patients with tumours. Parts are clearly played by the suppressor cells [30] and by serum factors [6], which inhibit the activity of the NK cells, and the role of the granulocytes in reducing the NK activity is also considered probable, because of the disturbance of the granulocyte-lymphocyte ratio [15].

In the evaluation of the NK and ADCC activities of patients undergoing surgery due to diseases of the liver and the pancreas, no classification was made on the basis of sex, because of the small number of cases examined so far; hence, the control group chosen for examination was similar in composition from the aspect of sex distribution.

Son et al. [27] reported a depressed NK activity in black African men suffering from hepatocellular carcinoma; this activity could be stimulated with *in vitro* interferon treatment. The selection of the patients we examined was justified on the grounds that even today the diagnostics of surgical diseases of the liver, and especially of the pancreas, gives rise to numerous problems. This is mainly the case when the question of malignancy must be decided. An exact answer is frequently not obtained even on exploration. Accordingly, it appears that the result of the preoperatively performed NK test may be of assistance to the surgeon in this respect.

Clinical trials to date suggest that the application of interferon in the therapy of certain tumorous diseases is encouraging [9, 24]. The results of our *in vitro* investigations indicate that the stimulatory action of interferon on the activity of the NK cells is likewise manifested in certain individuals with malignant diseases of the liver and the pancreas. Thus, its use may lead to a favourable effect in these diseases too.

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Über die Rolle der NK-Reaktion in der Diagnostik der Leber- und Pankreastumoren

S. KARÁCSONYI, Y. MÁNDI, GY. FARKAS, M. TÓTH und I. BÉLÁDI

Bestimmt wurden die NK- und K-Aktivität der peripheren Lymphozyten der an Leber- und Pankreaskrankheit leidenden Patienten. Die Untersuchungen fanden präoperativ statt. Die natürliche zellvermittelte Zytotoxizität (NK) wurde gegenüber der Zelllinie und die durch die beiden Antikörper vermittelte zelluläre Zytotoxizität (ADCC) gegenüber menschliche Erythrozyten mit der Mikrototoxizitätsmethode, durch Messung des Freiwerdens des Isotops Cr^{51} bestimmt.

Die Kontrollgruppe bildeten 40 gesunde Männer und Frauen. Die NK- und K-Zellaktivität der 19 Patienten mit einem malignen Tumor fiel niedriger (12.6 ± 5) als die der Kontrollpersonen ($32\% \pm 12$). Bei den gutartigen Leber- und Pankreaskrankheiten (12 Patienten) hat aber das Zytotoxizitätsprozent das Kontrollniveau erreicht bzw. übertroffen ($40\% \pm 10$).

Durch die *in vitro* angewandte Interferonbehandlung wurde die NK-Reaktion in gutartigen Fällen in bedeutendem Maße stimuliert, während bei einem Teil der an bösartigen Krankheiten leidenden Patienten die Zytotoxizitätswerte durch die Medikation in die Nähe des Kontrollniveaus erhöht wurden.

Роль реакции — в диагностике опухолей печени и поджелудочной железы

Ш. КАРАЧОНИ, И. МАНДИ, ДБ. ФАРКАШ, М. ТОТ и И. БЕЛАДИ

У больных, страдающих заболеваниями печени и поджелудочной железы, мы определяли NK и K активность периферических лимфоцитов. Исследования производились перед операцией. Естественную клеточноопосредствованную цитотоксичность (NK) против клеточной линии K-562 и опосредствованную двумя антителами клеточную цитотоксичность (ADCC) против человеческих эритроцитов исследовали с помощью микроцитотоксического метода, измеряя освобождение изотопа хрома (Cr^{51}).

Контрольная группа состояла из 40 здоровых мужчин и женщин. У больных с злокачественными опухолями (19) активность NK к K клеток ($12,6\% \pm 5$) была ниже, чем в контроле ($32\% \pm 12$). В случаях же злокачественных заболеваний печени и поджелудочной железы процент цитотоксичности достиг или превысил контрольный уровень ($40\% \pm 10$).

Применение *in vitro* интерферона в контрольных исследованиях и при доброкачественных опухолях сильно стимулировало NK реакцию, в части же злокачественных случаев интерферон повышал цитотоксическую активность почти до контрольного уровня.

Roentgenographic Examination of the Subtalar Joint

GY. ZADRAVECZ

Department of Traumatology, 1st Department of Surgery, Pécs University Medical School, H-7643 Pécs, Ifjúság út 13, Hungary

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In fractures of the calcaneus, the traditional roentgenographic technique cannot provide the necessary information for surgically restoring the subtalar joint and correctly judging the prognosis.

The author recommends the oblique view roentgenographic technique which provides essentially more information than Boehler's axial roentgenogram, and can technically be taken more easily.

Data obtained by using the oblique view roentgenographic technique facilitate the diagnosis of fractures of the calcaneus and allow the assessment of the degree of dislocation, and of the displacement of the articular surface, i. e. the correct judgement of the surgical intervention.

The subtalar joint (posterior talocalcaneal articulation) is the most essential part of the lower ankle-joint which is difficult to examine by the traditional roentgenographic technique. In fractures of the calcaneus both reposition and the chances of recovery are considerably affected by the impaired joint.

The lateral view roentgenogram of the heel can provide some information particularly if it is compared to that at the healthy contralateral side. However, to judge the three-dimensional structure of the joint, at least two roentgenograms at right angle are needed. The retrotibial-plantodorsal, the so-called axial aspect recommended by Bühler [1] is meant to provide the other view. According to our experiences, it is technically fairly difficult to take these roentgenograms. In general, an evaluable roentgenogram can be obtained only of a healthy foot or with the willing and active cooperation of a young patient. In case of a fractured calcaneus the injured patient cannot even passively produce the dorsiflexion absolutely required for the roentgenographic representation of the subtalar joint.

At our clinic, the so-called oblique view pictures are routinely taken instead of the axial ones of the calcaneus [2.] The special roentgenograms provide essentially more information than the axial ones, but it is also an important point that these roentgenograms do not require too much skill of the technicians. Even on the basis of pictures of relatively poor quality, the state of the subtalar joint can be evaluated. A similar roentgenographic technique was described by Brodén [3] in 1949 but his method has sunk into oblivion, since at

that level of development of traumatology there was no demand at all for a more precise radiologic diagnosis of fractures.

Technique of Oblique View Roentgenograms

The patient is lying on the examination table in supine position. With the talocrural articulation being at the right angle, the lower limb is rotated inwardly at 45 degrees (Fig. 1).

With the x-ray tube set at different angles, it is moved in the sagittal plane from the sole towards the head and x-ray pictures are taken in several positions. The tube is centred below and before the external ankle by 2 cm each. The distance between the x-ray tube and the cassette is 70 cm. In these exposures the subtalar joint is recorded orthoradiographically. Depending on the position of the tube, various aspects of joints are distinctly represented (Fig. 2).

In the roentgenogram at 45 degrees, the lower part of the joint, in those of 30 degrees and 0 degree, the middle part, while in that at 10 degrees the upper part of the joint can be seen. There is no projection of a disturbing shadow to the joint since the anterior apophysis of the calcaneus was rotated toward the median plane, together with the cuboid bone and with the base of the 5th metatarsus. Information on the shape of the calcaneus is chiefly provided by roentgenograms at 45 and 30 degrees.

Fortunately, oblique view roentgenograms represent the most important segment from the point of view of the load bearing of the calcaneus. Owing to the fact that the axis of the talus is at an angle of 25 to 30 degrees with that of the calcaneus when falling to the heel, the active forces are manifested in a

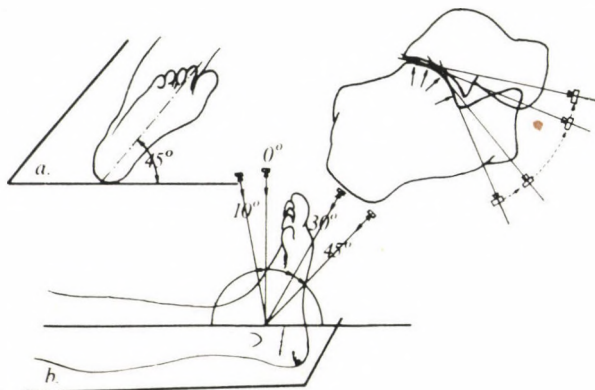


FIG. 1. Exposure of the oblique view roentgenograms. The subtalar joint can be studied as a whole

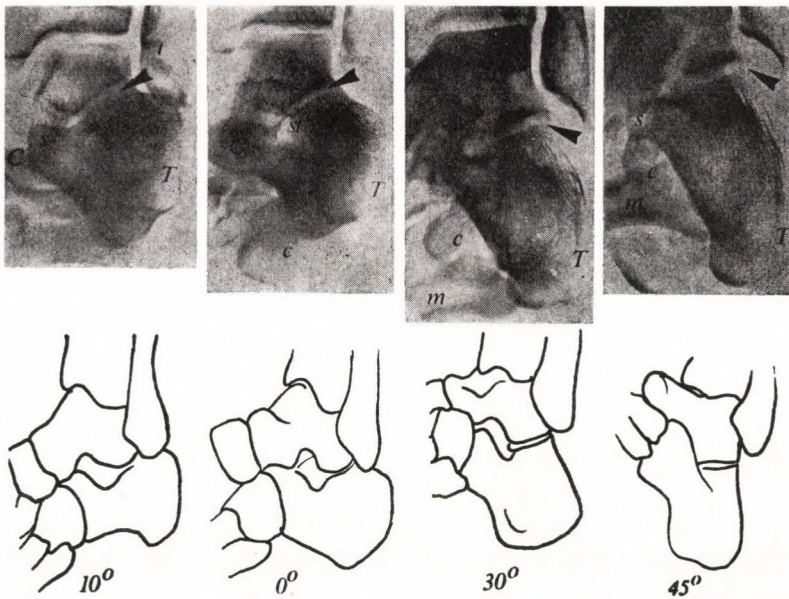


FIG. 2. Oblique view roentgenograms of a healthy foot. C: caput tali, s: sustentaculum tali, m: base of the 5th metatarsus, T: tuber calcanei. The arrows show the subtalar joint. Each picture represents the sustentaculum tali as well as the tuber calcanei, consequently these roentgenograms provide information on their fractures or dislocations

plane traversing the facies articularis posterior calcanei and the tubercles of the tuber calcanei. The trabecular system is arranged at right angle to the articular surface in the direction of the compression forces. This implies that this segment is loaded also under physiological conditions (Fig. 3).

Discussion

The recent years have been witnessing an amazing development in traumatology. According to the new principles, particularly in fractures adjacent to or protruding into, the joint attempts should be made at a possible anatomical reconstruction. Only in these cases combined with adequate after-care can satisfactory functional results, eventually, *restitutio ad integrum* be expected.

The significance of fractures of the calcaneus has been discovered only in the recent years, although this injury occurs primarily in the adult, working age group. Following the fracture, a decreased capacity of work or disablement may remain in 15 to 70% of the patients. The bad results are due to the insufficient x-ray diagnostic background: one has no adequate stereoscopic idea of the fracture. Neither could a generally acceptable therapeutic classification of

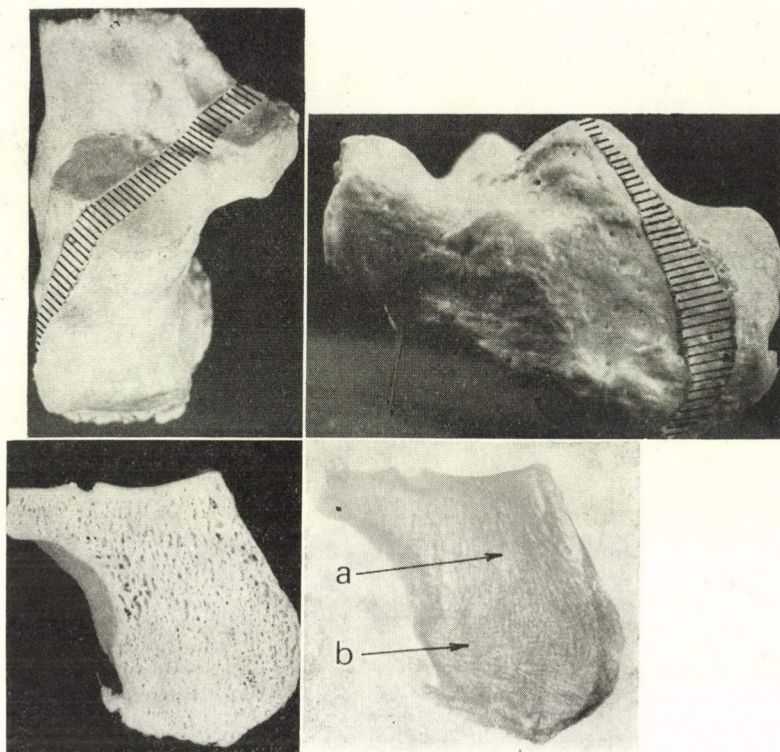


FIG. 3. Concerning loading, the most used segments of the calcaneus are *a* the pulsion trabeculae, *b* the traction trabeculae which are arranged according to the direction of the tractile forces of the plantar muscle

fractures have been developed. Thus, for a traumatologist of average training the therapeutic requirements cannot be unequivocally defined.

According to the new principles, the objective would be to achieve a more precise reposition. However, the traditional radiological technique is not capable of providing information corresponding to the new requirements.

By using the above roentgenographic technique such data can be obtained which may increase the effectiveness of our intervention. It can be stated whether the fracture has protruded into the joint, what the amount and direction of the dislocation is, or whether surgical reconstruction is required. After the operation or reposition, standard roentgenographic technique is available to judge the degree of reconstruction. Consequently, this will be a basis for the prognosis. Considering that with the help of the roentgenogram that segment can be studied where the active forces are manifested, conclusions can be drawn as to the mechanism of the fracture and a classification of fractures can be worked out on the basis of the mechanism and the x-ray morphological signs.

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Röntgenuntersuchung des subtalaren Gelenks

GY. ZADRAVE CZ

Bei den Kalkaneusfrakturen liefert die herkömmliche Röntgentechnik keine entsprechenden Daten zur chirurgischen Wiederherstellung des subtalaren Gelenks bzw. zur Beurteilung der Prognose.

Die in der Arbeit empfohlene schräge Aufnahmetechnik bietet wesentlich mehr Informationen als die Böhlersche axiale Aufnahme und ist auch technisch leicht ausführbar.

Die mit Hilfe der schrägen Aufnahmetechnik ermittelten Daten erleichtern die Diagnostizierung der Kalkaneusfrakturen und ermöglichen die Beurteilung des Maßes der Dislokation sowie der Verschiebung der Gelenkfläche, d. h. die Entscheidung der Frage, ob im gegebenen Fall die Notwendigkeit eines chirurgischen Eingriffs besteht.

Рентгенологическое исследование подтаранного сустава

ДЬ. ЗАДРАВЕЦ

При переломах пяточной кости традиционная рентгенологическая техника не снабжает соответствующими данными для хирургического восстановления подтаранного сустава (*art. subtalaris*), а также для правильного прогноза.

Автор рекомендует применять технику косой съемки, которая дает значительно больше информации, чем съемки в аксиальной проекции по Бёлеру (*Böhler*) и является более простой.

Данные, получаемые с помощью косой съемочной техники, облегчают диагностику переломов пяточной кости, дают возможность определить степень дислокации и смещения суставной поверхности, то есть помогают решить вопрос о необходимости хирургического вмешательства.

Book Reviews

R. BERTOLINI and G. LEUTERT

Atlas der Anatomie des Menschen nach systematischen und topographischen Gesichtspunkten

Vol. III. *Kopf und Hals, Gehirn, Rückenmark und Sinnesorgane*

VEB Georg Thieme, Leipzig 1982. 350 pages with 387 figures, 361 in colour. Drawn by H. Schmidt (Halle-Saale) and R. Welt-Herschel (Leipzig). The preparates were made by G. Pfütze and K. Hartmann. DDR M 65.00

As a result of the cooperation of two outstanding scientists of anatomy in Leipzig also Volume III of their joint atlas has appeared. Experts in the field were looking forward with heightened anticipation to the publication of this book. These positive feelings were provoked by the success of the two previous volumes as well as by the fact that here again anatomists working in a German-speaking country have undertaken the colossal task of compiling an atlas. It is known that German-speaking countries contributed several outstanding atlases presenting always something new to those concerned. These atlases served as basic source for several generations of medical students and for the majority of the practising physicians for brushing up their permanently fading knowledge.

The current educational system has become inadequate for conveying the comprehensive information imparted by the intensive development of medical sciences in a highly differentiated manner. Obviously, the reform of the system, and within that, that of conveying information can be progressive and successful only if it is associated with the bringing up-to-date of the media of communication, i. e. that of textbooks and atlases. This can be experi-

enced, to a still greater extent, in anatomy being one of the basic fields of the general medical sciences.

It would be unfair to criticize the authors – despite the still unsolved problems – for having decided on compiling a systematic atlas of a familiar structure, attempting to be comprehensive. Ignoring the traditions – even if partially – is an extremely risky venture. Its professional and financial implications cannot be judged at present.

The two outstanding experts have adhered to the customary form of making an atlas, however, they give ample evidence of their persistent ambition to present something new by integrating several examples of up-to-date clinical examination procedures into their work. This applies to the five roentgenograms included among the series of cranial bones, the absence of which would have been greatly missed. The same refers to the roentgenographic picture of the masticatory joint. Excellent evidence of their attempt to add something new is offered by their presenting of the angiograms of the internal carotid artery. Also this aids the user of the book in three-dimensional view. The thorough work of editing is shown by the pneumoencephalograms and ventriculograms as well as by pictures of the ventricular casts.

The value of the five myelograms I can only judge as an anatomist, however it would have sufficed to present only myelograms 308 and 311. For those studying anatomy, the presented three computer tomograms provide only minimal infor-

mation. Still there are experts who would miss their absence.

A great value of the book is the presentation of the transparent base of the skull (prepared with Spaltenholz's technique) with the filled up bony inner ear which, in addition to the comprehensive information it imparts it is the only way of demonstrating the three-dimensional structure of the bony inner ear.

Presentation of drawings on the regions of the innervation of the skin together with the cervical and cephalic sections are greatly justified.

The conception of the authors to having made use of the possibility of italicization (using different printing types) should be welcomed.

The words of praise cannot, however, conceal the words of criticism, but by presenting these what the reviewer has had in mind was the idea of improving things.

It is striking that not each drawing has been made of a prepartate, since in this case the unfortunate error, that the Figure on page 265 shows 9 cervical nerves, could not have been produced. The designation of punctum nervosum indicating a small region of efferent nerves is definitely disturbing since the indexline points once to the great auricular nerve, while, in another case, to the trunk of the lateral supraclavicular nerves (Figs 168 and 169). The designation of nucleus tuber is missing despite that it is well visible in Fig. 258.

From the point view of editing, it is regrettable that some Figures contain a fairly great number of the names of structures and this is detrimental to perspicuity and makes things more difficult for the user. Figure 129 shows 86 taxonomical terms. The same applies to Figs 119 and 236 where there are only 71 designations

each. This needless abundance of indexlines is the more confusing as a result of the broken indexlines (Fig. 305). It is disturbing in the drawings of the cranial bones that the otherwise outstanding illustrator could not repeat his achievements of the two previous volumes, and the Figures are darkened. Thus it occurs in more cases that the ends of the indexlines already thickened in Vol. III are very difficult to find set against the almost black background. There are fairly great differences arising from the technical presentation of the drawings, since it is very difficult to believe that Figs 121 and 122 as compared to Figs 123 and 124 on the subsequent pages have been drawn by one and the same person!

Unfortunately, drawings not worthy of the level of Vol. III have also been included in this work as, e. g. Figs 316, 317, 318, 347, 348 and 349.

Although Vol. III is closely connected to the two previous volumes, it still could not achieve their high level concerning the use of space, the technique of drawing, and typography. Even colour distortion (e.g. Fig. 303) has occurred in the present work of the publishing house otherwise of outstanding achievements.

As far as the professional side of Professors Bertolini and Leutert's as well as of their coworkers' book is concerned - as it is otherwise characteristic of them - this volume is a lasting achievement. The volume containing a correct taxonomy provides a useful basis and a reliable guide both for medical students and for physicians. I cannot but join those who congratulate these two authors on their having not only undertaken but also conscientiously and excellently fulfilled this tremendous task.

J. VAJDA

H. GLAUCH and E. HAAF

Chirurgische Instrumente Operationslagerungen Operationsabläufe

Georg Thieme Verlag, Stuttgart-New York 1983. VIII + 285 pages, 139 figures. DM 29.80

In the second revised and enlarged edition of the present handbook, the authors, after presenting information on basic surgical hygiene, give brief and essential

descriptions of the individual surgical interventions completed by drawings of the various lying positions of the patient, photos and detailed listing, functions and directions for use of the instruments required during operation.

In addition to the most frequent surgical operations, the course and the re-

quired instruments of traumatological, vascular, urological, gynaecological-obstetrical, ophthalmological as well as otorhinolaryngological basic operations are discussed in detail.

The didactically successfully elaborated book written primarily for scrub nurses and orderlies provides a reliable basis for

securing teamwork. Being familiar with the essence, course and the instruments used, an adequate cooperation of the operating staff can be ensured. The book is also a useful guide for physicians starting a career in different manual fields.

I. ORBÁN

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Arthroplasty Combined with Cup-Plastics in the Surgical Treatment of Congenital Dislocation of the Hip

I. UDVARHELYI¹, T. RISKÓ¹, K. KREMSIER² and T. BÖRÖCZ²

¹ National Institute for Rheumatology and Physiotherapy, H-1027 Budapest, Frankel Leó u. 17–19 Hungary

² Department of Orthopaedics, Postgraduate Medical Institute, H-1389 Budapest, P.O. Box 12, Hungary

(Received October 31, 1983)

The authors review the arthroplasty combined with cup-plastics in the treatment of congenital dislocation of the hip. The indications and surgical exploration are discussed in detail. Good results are reported. The complications and their solutions are also described. In the recent five years, 100 patients were operated by them. Based on their experiences, they suggest this intervention at an earlier age, too (i.e. 30 to 40 years). Moreover, they believe it to be an important possibility to provide an adequate rehabilitation for patients being still of working age.

Patients with congenital dislocation of the hip are generally operated in adulthood. This state ranging from dysplasia to complete dislocation requires different surgical solutions. The large number of patients operated already in an advanced state proves that the operations in question (osteotomy, pelvic osteotomy, arthrodesis) are often not performed in due time. Our surgical possibilities are partly limited at an earlier age. For the sake of rehabilitation it is often necessary to perform total hip replacement in case of dysplastic acetabulum and of a complete dislocation of the head of the femur. In such cases, the surgical technique is obviously difficult.

Cup-plastics combined with total hip replacement suggested by Harris in 1977 [3] was modified by us insomuch that only an adequately prepared segment of the resected head of the femur is implanted to replace the acetabular roof and neither the middle gluteal muscle nor the iliopsoas muscle are dissected. The operation was performed in 100 patients in the period between December 1978 and July 1983. Sex distribution was 96 females and 8 males aged between 32 and 58 years. Eighty-four patients were over the age of 40.

Surgical Indication

1. Bilateral dislocation of the hip if symptoms of arthrosis, i.e. pain, severe limitation of motion, appear irreversibly (Figs 1 and 2).
2. In a unilateral involvement, if other kinds of surgical intervention, e.g. arthrodesis cannot be made for some reason (Figs 3 and 4).

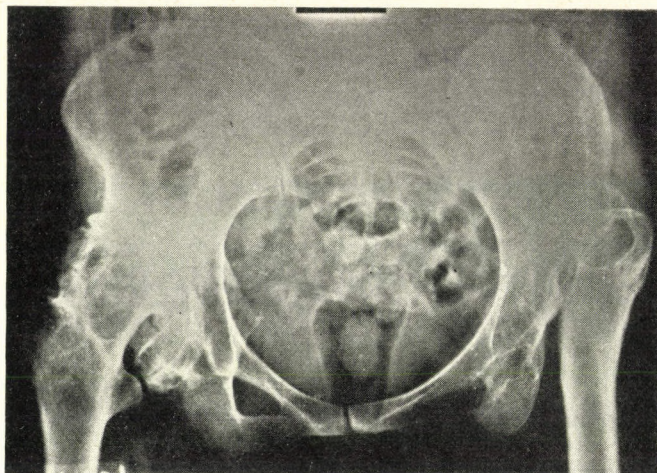


FIG. 1. Bilateral congenital dislocation of the hip. On the right side: severe secondary arthrosis, on the left: a state after subtrochanteric osteotomy and instability

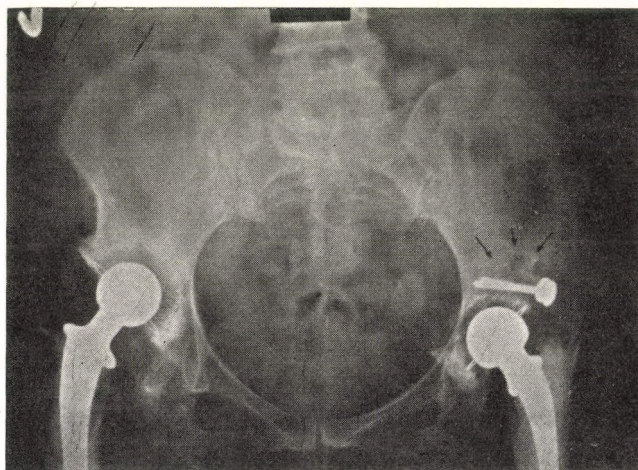


FIG. 2. State after arthroplasty on both sides. The prostheses are implanted in the acetabulum. On the left in the region indicated by arrows, the wedged and fixed bony acetabular roof is seen

3. The operation is performed even at the age of 30 to 40 if there is no other way to ensure adequate rehabilitation. It is not indifferent whether the patient is rehabilitated still at a working age or decades later.

4. The operation is never performed exclusively for cosmetic reasons, e.g. to equalize limb length.

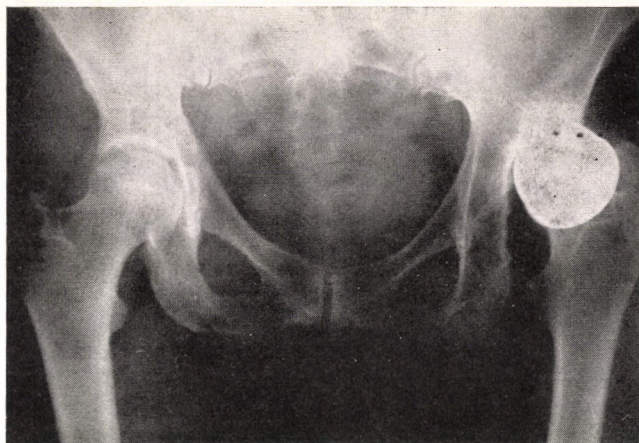


FIG. 3. On the left: eight years after acetabular roof reconstruction. Instability, pain and secondary dysplasia



FIG. 4. Following implantation of prosthesis replaced by a rubbed acetabular roof

Surgical Technique

1. Exposure is made according to Müller but incision is continued distally—only at a distance of a few centimeters from the greater trochanter—because it is sufficient for exposure. Proceeding in front of the middle gluteal muscle, the articular capsule is reached.

2. Following the resection of the head of the femur, the acetabulum is explored and here will the site of the plastic socket be fashioned (Fig. 5). The reasons for this are that (i) the thickness of the pelvic bone over the acet-



FIG. 5. Relation between the acetabulum (indicated by an arrow) and the secondary socket in dislocation of the hip



FIG. 6. The region constructed in the acetabulum is not sufficient for receiving the plastic acetabular cup

abulum increases the possibility of the firm fixation of the acetabular roof. The fixing screws can be longer; (ii) in a prosthesis implanted into the acetabulum the primary aim is not to increase limb length but to change the direction of the middle gluteal muscle and to restore its tension and functions.

3. In advanced secondary arthrosis, an intact segment from the head of the femur can be constructed which supplements the acetabulum. The recipient part of the pelvic bone is fashioned piece by piece thus fixing the segment partly to the spongy bone and partly securing a greater stability in the direction of the loading. The screws fixing the transplant should pierce the inner wall of the pelvic bone to secure better fixation (Figs 6, 7 and 8).

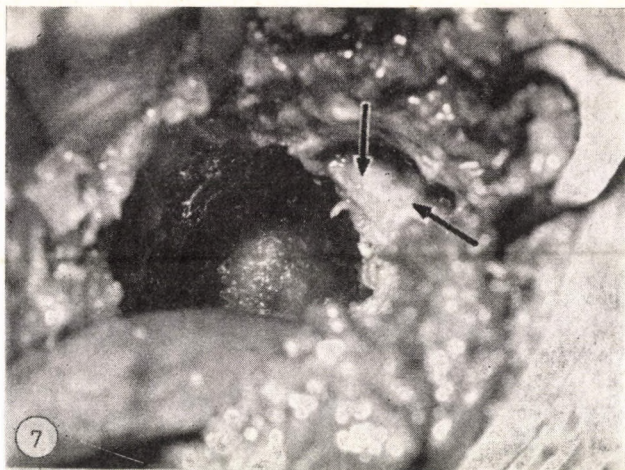


FIG. 7. In the region indicated by arrows a bony base fashioned piece by piece in the secondary socket for receiving the bone to be implanted

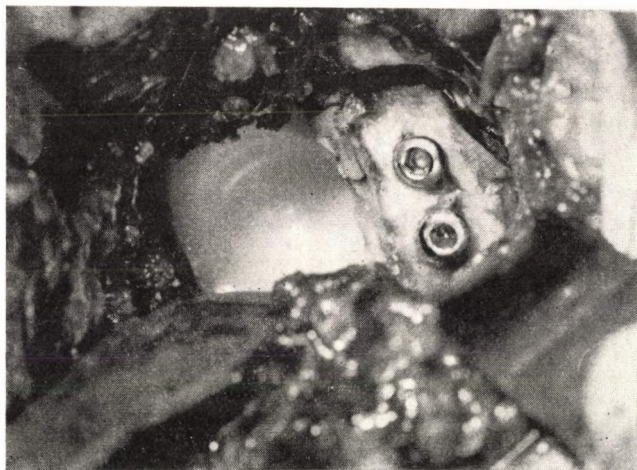


FIG. 8. After replacing the implanted acetabular roof, the plastic socket will have an adequate place

One of the most crucial problems is that after fixation of the transplant, the surface should be further shaped by an acetabular reamer thus the eventual gaps are filled up with chips which prevent the bone cement from getting between the implant and the bony acetabular wall.

The further course of the operation is typical. After reposition, however the ischiadic nerve is explored to control its tension which, due to the increased limb length—even if rarely—may still increase.

5. The most important thing for the patients in postoperative treatment is to use crutches for six weeks. Total loading is allowed only after three months.

Complications

In one case complete lesion of the ischiadic and femoral nerves developed postoperatively. In 24 hours the hip joint was explored. There was no haematoma, the ischiadic nerve stretched in a 'string-like' manner. A 'Z-shape' shortening osteotomy of the femur was performed for reducing the tension of the ischiadic nerve. After half a year of conservative treatment complete recovery followed. In one case, the transitional paresis of the peroneal nerve was successfully treated conservatively. In one case, the implanted bone had to be removed together with the prosthesis due to suppuration. (It was an early suppuration.) One patient was reoperated due to loosening of the prosthesis one year postoperatively. Here, the earlier implanted acetabulum of 44 mm was replaced by one of 54 mm, which indirectly ensured the stability and bony reconstitution of the acetabular roof.

Results

Follow-up time was five years to three months. Apart from the earlier discussed complications, the patients are free of complaints. The Trendelenburg positivity disappeared in each patient. The transplant has undergone radiological reconstitution. There is no loosening of the prosthesis. The functional results correspond to those of typical arthroplasties. The increase in limb length was 1 to 5 cm, stability was adequate in every case.

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In Kombination mit Pfannendachplastik durchgeführte Arthroplastik bei der chirurgischen Behandlung der angeborenen Hüftluxation

I. UDVARHELYI, T. RISKÓ, K. KREMSIER und T. BÖRÖCZ

Zur Behandlung der angeborenen Hüftluxation kam bei Erwachsenen in Kombination mit Pfannendachplastik Arthroplastik zur Anwendung. Die Ergebnisse waren befriedigend. Indikationen, chirurgische Freilegung, Komplikationen und die Lösungsmöglichkeiten finden eine ausführliche Besprechung. Im Verlauf von 5 Jahren wurden 100 Patienten operiert. Im Besitz der Erfahrungen wird die Durchführung des Eingriffs auch bei jüngeren Patienten (im Alter von 30–40 Jahren) empfohlen, es wird sogar als eine wichtige Möglichkeit betrachtet die entsprechende Rehabilitation noch im arbeitsfähigem Alter zu gewährleisten.

Артропластика, выполненная одновременно с пластикой вертлужки вертлужной впадины, в хирургическом лечении врожденного вывиха бедра

И. УДВАРХЕИ, Т. РИШКО, К. КРЕМЗЬЕР и Т. БЁРЕЦ

Авторы знакомят с одновременной пластикой вертлужки вертлужной впадины артродпластикой при лечении врожденного вывиха бедра у взрослых. Подробно обсуждают показания к операции, к хирургическому доступу. Сообщают о хороших результатах. Описывают встречающиеся осложнения и их лечение. За истекшие 5 лет авторы прооперировали 100 больных. Располагая опытом, они рекомендуют проводить это вмешательство также и в более молодом возрасте (30–40 лет), более того — считают важной возможностью обеспечить больным подходящие условия для реабилитации еще в трудоспособном возрасте.

Intravesical Ultrasonography as an Aid to Study the Size of Bladder Cancers

J. RÓZSAHEGYI¹, P. MAGASI¹, F. KISS², ÁGNES SZEBENI²
and L. BOHÁR²

¹ Department of Urology, Department of Pathology and ² Department of Roentgenology, Postgraduate Medical Institute, H-1389 Budapest, Szabolcs u. 33–35, Hungary

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On clinical examination of 50 patients with bladder cancer the authors performed intravesical ultrasonography. By this method they never failed to detect the tumours. The stage of the pathological material obtained by operation or at autopsy was compared with that obtained by the intravesical ultrasonography. In 88% of the cases the two classifications gave identical results. By ultrasonography the pathologic stage was overestimated in 4, and underestimated in 2 cases. Intravesical ultrasonography can be combined with cystoscopy. It is a fast procedure and an ideal supplement to cystoscopy. The combination of the two methods permits the localization of intravesical tumours as well as the estimation of invasion and of the degree of infiltration.

A precondition of treating bladder cancers is the preoperative determination of size and of the depth of invasion [7, 10].

The information obtained by cystoscopy is restricted to the surface of the mucosa. The reliability of the bimanual examination requiring considerable experience is greatly reduced in obese patients. Computer tomography (CT) is suitable rather for demonstrating the perivesical invasion. Pelvic angiography incurs some risk for the patient. All these ambiguities necessitated the introduction of a new diagnostic method [7, 10]. As a sequel to transabdominal [2, 3, 5] and transrectal ultrasonography, intravesical ultrasonography was introduced by Holm [2] and Nijima [8]. This method may be an important aid in diagnosing bladder cancers.

Material and Method

At the Postgraduate Medical Institute intravesical ultrasonography has been performed since January 1982. The examinations were made by 3401 Brüel and Kjaer ultrasonic scanners. The speed of rotation of the 6MHz transducers was 2 to 6 rpm/s. This can be regulated continuously. The axial resolution was 1 mm, the lateral reduction was 2 mm.

After an explorative cystoscopy, the optics in the tube of the 24 Ch-s Storz scanner was replaced by a transurethral ultrasound probe and the bladder was filled with an isotonic solution. The probe was moved backwards and for-

wards in the bladder, the angles changed, and pictures were taken at 5 mm intervals each. During the examination the amount of solution in the bladder could be altered.

In this study, the data of 50 patients with bladder cancer were elaborated. The results of intravesicular ultrasonography could be compared to the pathologic stage of the tumour. The latter was determined by surgery (transurethral resection, suprapubic cystotomy + neoplasm excision, bladder wall-resection, cystectomy) and by studying autopsy materials, respectively. The sex distribution of the patients was 12 females (24%) and 38 males (76%). The mean age was 68.2 years, the youngest patient being 49, while the eldest being 91 years old.

Results

The comparison of the results gained by intravesical ultrasonography with the pathological stage is shown in Table I.

The size of the examined tumours ranged from one of the size of a match-head up to a tumour almost filling the lumen of the bladder. The tumours were always detected by ultrasonography. The result of ultrasonography yielded identical results as the pathological stage in 88%. In 4 cases (8%) the severity of the tumour was overestimated, while in 2 cases underestimated as compared to the pathological stage.

TABLE I

Comparison of intravesical ultrasonogram (U) to pathological stage (P)

Intravesical "ultrasound stage"	Papilloma P_{1s} P_a P_1	Pathological stage			Correlation %	Total %
		P_2	P_3	P_4		
U_1	17				34	17
U_2	1	14	1		28	16
U_3		1	6	1	12	8
U_4	1		1	7	14	9
Correlation n	17	14	6	7	44/88%	
Total n	19	15	8	8		50/100%

Discussion

The bladder cancer is characterized by a tendency to infiltrate. According to Zingg [cit. 10], in 5 to 10% of the more superficial tumours (stages T_{is} , T_a , T_1 and T_2) and in already 30 to 60% of stage T_3 and T_4 tumours, regional lymph node metastases occur. O'Flynn [cit. 10] studied the 5-year survival rate of 465 patients in whom the urinary bladder was resected transurethrally because of bladder cancer. He found 62% survival in stage T_1 , while 59% in stage T_2 . The prognosis is significantly worsened with the involvement of the muscular layer, that is why it is of great importance to learn the invasion within the bladder wall and outside the bladder. Intravesical ultrasonography is the examination of choice. According to the literature [3, 7, 10] and to our own experiences [9], the result of ultrasonography is in good agreement with the invasion of the tumour as shown subsequently by histology.

The basis of the ultrasonography in bladder cancer is the difference between echoes deriving from bladder wall or tumour tissue. Namely, the echo reflecting from the tumour is of a lower amplitude than that returning from the wall. The majority of the ultrasonographic characteristics of bladder cancers are based on the secondary changes due to infiltration, as e.g. the irregularity, deformity and rigidity of the bladder wall, decreased bladder capacity [1, 4, 5, 7, 8].

Nijama [8] reviewed the intravesical ultrasonographic classification of bladder cancers. The various ultrasonographic stages are denoted by U and are compared with the pT stages in a diagram (Fig. 1). The individual U stages are characterized as follows:

U_1 : Intact, entirely conserved bladder wall. The ultrasonogram clearly shows the structure from which the tumours protrude into the bladder lumen with echo-structures of varying intensity. The waving echo-pattern shows the bladder lumen with echo-structures of varying intensity. The waving echo-pattern shows the villous character of the tumours (Fig. 2).

U_2 : Extensive changes in the bladder wall are evident in the whole region of the tumour. Instead of the regular picture of the bladder wall, a sonolucent mass can be visualized with the external bladder contour being preserved (Fig. 3).

U_3 : The bladder wall is totally destroyed, the tumour invades the full thickness of the bladder wall (Fig. 4), and corresponding to the depth of the infiltration, the continuity of the bladder wall has broken.

U_4 : The extravesical invasion is shown by the irregular echo-structure of the ultrasonogram which reaches beyond the contour, too (Fig. 5). Here, in accordance with the absorption caused by the tumour, a looser echo pattern of peripherally weakening intensity can be seen. The extravesical invasion

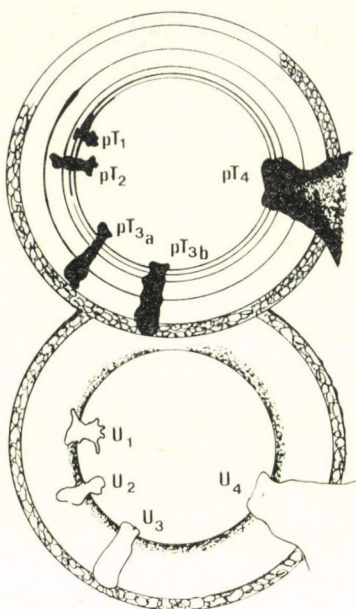


FIG. 1. Comparison of intravesical "ultrasound stages" (4) to the pT stages

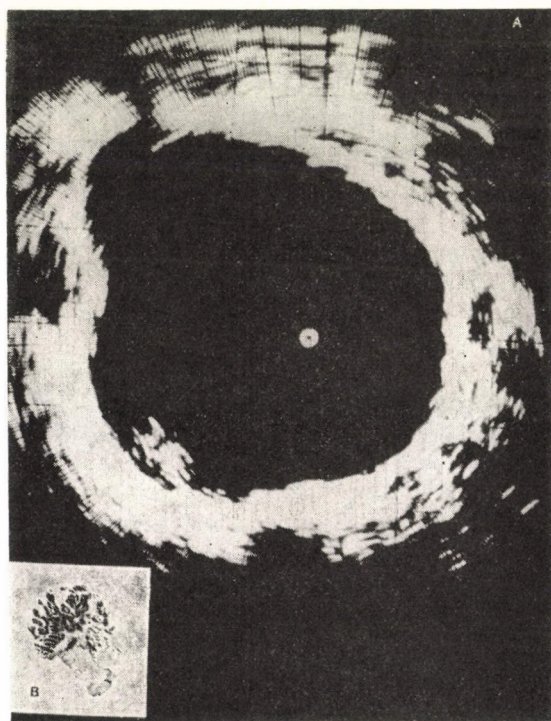


FIG. 2A. U_1 Intravesical ultrasonogram of a tumour of the size of a small bean on the right wall of the bladder. The bladder wall is intact, the tumour protrudes into the lumen. The waving echo-pattern shows the villous character of the tumour. B. pT_1 : Transitional cell carcinoma with papillary structure infiltrating into the submucosa

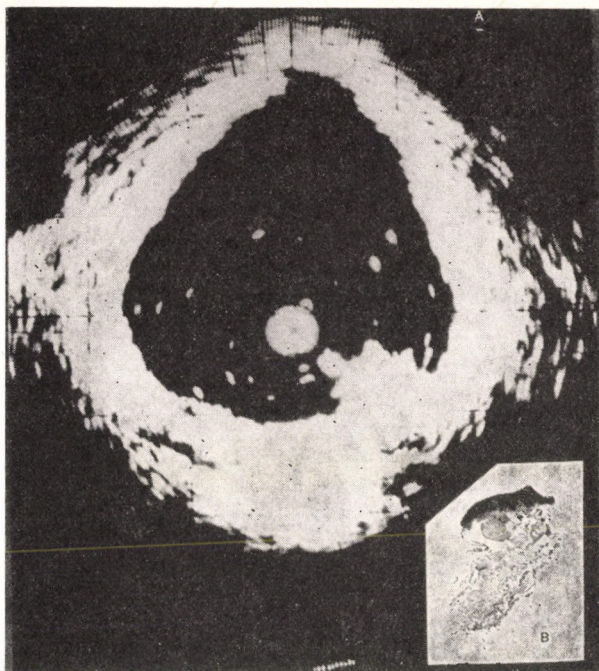


FIG. 3A. U_2 : A cherry-size tumour is situated on the left lateral wall of the bladder. At its base—instead of the regular pattern of the bladder wall—a sonolucent mass can be visualized. The outer bladder contour is conserved. B. pT_2 : Scan of a transitional cell carcinoma superficially infiltrating into the muscle layer

depending on the sound absorption of the tumour appears behind the muscular layer as a structure poor in echoes.

It is difficult to differentiate between the tumours (U_3) deeply infiltrating the muscles and those with initial extravesical invasion (U_4), since both stages yield the same, or fairly similar, ultrasonograms. The penetration of the tumour into the neighbouring organs can be demonstrated only to a certain depth because the penetrating capacity of the high frequency ultrasound beam is limited [10, 11]. In these cases CT would be the method of choice [10].

Among the current diagnostic methods, intravesical ultrasonography for demonstrating infiltration of the bladder wall is the best one. In the filled bladder the ultrasound waves arrive at the bladder wall almost at right angles, the loss in conduction is minimal, the structures, i.e. those of the bladder wall are clearly visualized.

A drawback is that the probe is rigid and cannot be set at the convenient angles which renders visualization of some regions of the neck of the bladder difficult.

An advantage, however, is that, during the examination the volume of the bladder can be altered, and by this dynamic method of examination also



FIG. 4A. U_3 : Intravesical ultrasonograms of a tumour situated on the left lateral wall. The wall is irregular, its part under the tumour cannot be visualized, and depending on the depth of the infiltration, the continuity is broken. B. pT_3 : The transitional cell carcinoma has infiltrated into the deeper muscle layer, too

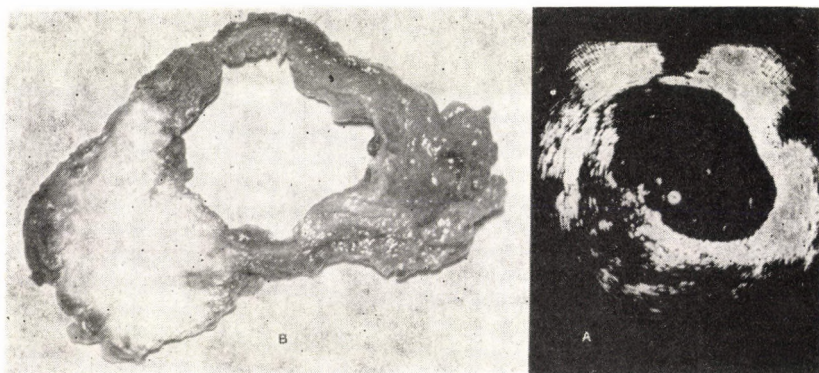


FIG. 5A. U_4 : Intravesical ultrasonogram of an extravesically invading tumour situated on the right lateral wall of the bladder. The irregular echo-structure reaches beyond the bladder contour and a looser echo-pattern of peripherally weakening intensity can be visualized. B. The cancer tissue has penetrated into the bladder wall and is attached to the surrounding tissue

the changes in the elasticity and compliance of the tumorous bladder wall can be judged which cannot be examined with the so-called A-Scanner.

Intravesical ultrasonography combined with cystoscopy is a fast and practical procedure which may ideally supplement cystoscopy. The combined use of the two procedures helps assessing, beside the localization of intravesical tumours, also the degree of infiltration which is important from the point of view of therapy.

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Untersuchung der Ausbreitung von Harnblasentumoren mit intravesikaler Ultrasonographie

J. RÓZSAHEGYI, P. MAGASI, F. KISS, ÁGNES SZEKENI und L. BOHÁR

Im Laufe der Durchuntersuchung von 50 Patienten mit einem Harnblasentumor wurde auch intravesikale Ultrasonographie vorgenommen. Mittels Ultrasonographie konnte der Tumor in sämtlichen Fällen nachgewiesen werden. Das pathologische Stadium des intraoperativ bzw. im Laufe der Sektion gewonnenen Materials wurde mit dem »intravesikalen Ultraschall-Stadium« verglichen; die Befunde stimmten in 88% der Fälle überein. Durch die Ultrasonographie wurde der Tumor, im Vergleich zum pathologischen Stadium, in 4 Fällen überschätzt und in 2 untergeschätzt. Die rasche, praktische, mit der Zystoskopie gleichzeitig durchführbare intravesikale Ultrasonographie

stellt eine ideale Ergänzung der Zystoskopie dar. Durch kombinierte Anwendung der beiden Verfahren können nicht nur die endovesikale Tumorklassifikation, sondern auch die Ausbreitung der Neubildung und das Maß der Infiltration bestimmt werden.

Изучение распространения опухолей мочевого пузыря с помощью интравезикальной ультрасонографии

Й. РОЖАХЕДИ, П. МАГАШИ, Ф. КИШШ, А. СЕБЕНИ и Л. БОХАР

В ходе обследования 50 больных с опухолью мочевого пузыря, авторы применяли также внутривезикальное ультразвуковое исследование. Ультрасонография во всех случаях выявила наличие опухоли. Патологическую стадию материала, полученного на операции или при вскрытии, сравнивали с «интравезикальной ультразвуковой стадией». Совпадение наблюдалось в 88% случаев. Ультрасонография в четырех случаях «переоценила» опухоль в отношении ее патологической стадии, в двух случаях — недооценила. Интравезикальное ультразвуковое исследование можно производить одновременно с цистоскопией, это быстрый, практический способ, идеально дополняющий цистоскопию. При комбинированном применении этих двух методик можно определить — наряду с эндовезикальной локализацией опухоли — ее распространение и степень инфильтрации.

Anorectal Sarcomas

L. MOLNÁR, I. BEZSNYÁK, K. DAUBNER, E. HORÁK, and E. SVASTITS,

National Institute of Oncology, H-1525 Budapest, Ráth György u. 7–9,
Hungary

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The authors report on their observations of nine patients with anorectal sarcoma. They agree with others that best results can be expected from radical surgery. Even in operable patients anorectal sarcomas have a worse prognosis than other malignant lesions in the same region.

Anorectal malignancies of mesenchymal origin are by far less frequent than those of epithelial source. Most authors agree that their incidence, in relation to all malignant tumours, is under 1%. Anderson et al. [1, 2] found 1 or 2 leiomyosarcomas among 8000 rectal tumours. There were only 3 leiomyosarcomas in 1202 malignancies of the rectum in the material of Broders et al. [6]. Ripstein and Flint [30] found 135 leiomyosarcomas in the stomach, 20 in the duodenum, 49 in the small intestine and only 10 in the colon and rectum. In Guret's material [16], related to 840 cases, only 3 anorectal sarcomas could be identified. Dukes and Bussey [11] verified sarcoma in 8 of 2200 patients with malignant anorectal tumours. In Morson's report [23] 17 sarcoma cases were reported of 4435 anorectal diseases. According to Rabinovich et al. [28], the ratio of anorectal sarcomas and carcinomas is 1 : 577. Views differ regarding the age of patients at risk [3, 9, 10, 12, 21, 25, 34].

Patient Material

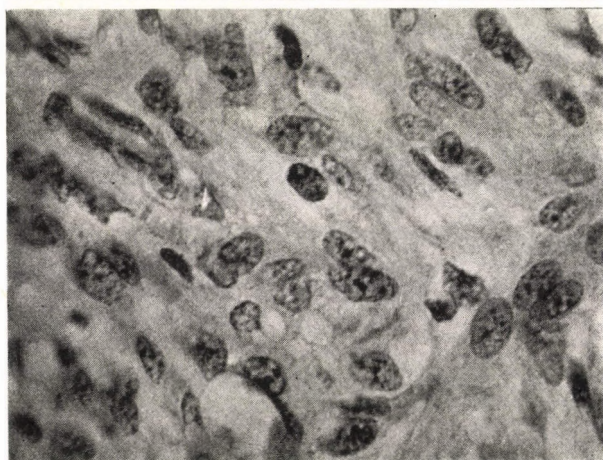
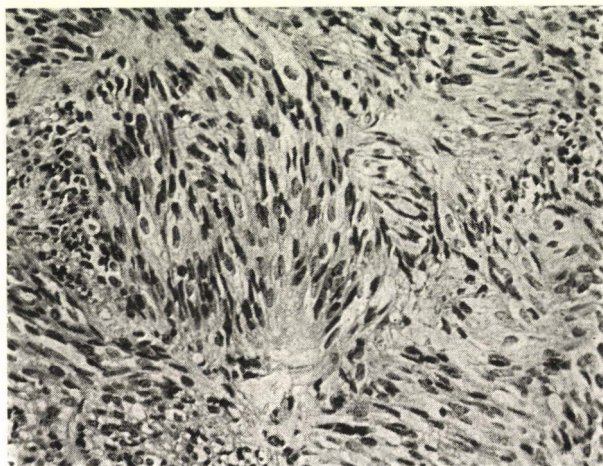
Over a 20-year period (1959–1979) a total of 773 patients with anorectal malignant tumours were operated upon at the Surgical Department of the National Institute of Oncology, Budapest. Sarcoma occurred in 9 patients. Ages ranged from 21 to 78 years with a mean age of 52 years. Symptoms were pain, bleeding, obstipation, etc., all identical with those of carcinomas. Abdominoperineal extirpation was performed in all but 2 patients in whom electrocoagulation and radium needle implantation were tried. In spite of radical surgery all patients died of metastases from 7 to 74 months following operation (Table I).

For histological typing of the tumours sections stained with haematoxylin and eosin were used additionally to Van Gieson, PAS reaction and Gömöri's

TABLE I
Patient material

Case No.	Sex	Age (years)	Histological diagnosis	Therapy	Survival (months)
1	M	21	leiomyosarcoma	APE	24
2	M	62	leiomyosarcoma	APE	36
3	M	44	leiomyosarcoma	APE	72
4	F	74	leiomyosarcoma	E. coag. + R	18
5	M	43	fibrosarcoma	APE	47
6	M	56	fibrosarcoma	APE	60
7	M	78	fibrosarcoma	E. coag. + R	7
8	F	52	fibrosarcoma	APE	23
9	F	41	anaplastic sarcoma	APE	74

APE = abdominoperineal extirpation; E. coag. = electrocoagulation; R = radium therapy; F = female; M = Male



FIGS 1-2. Leiomyosarcoma; female, 57 years. Interwoven bundles compose the characteristic whorl-like pattern of the tumour. The cells have hyperchromic, rounded-off nuclei. H and E; Fig. 1: $\times 350$ Fig. 2: $\times 1000$

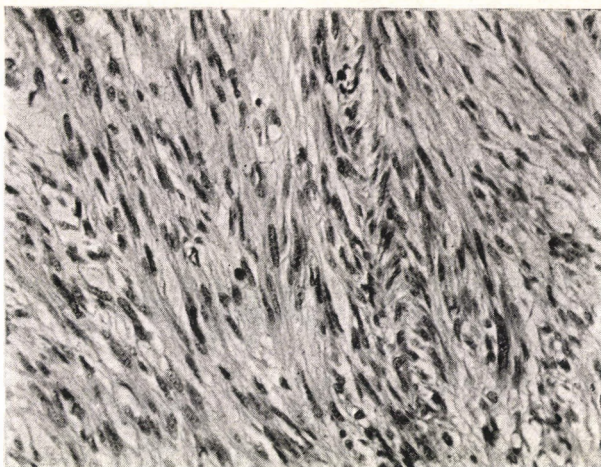


FIG. 3. Moderately differentiated fibrosarcoma; female, 70 years. A tumour of fibrous structure composed of elongated, spindle-shaped cells. Nuclei show various degrees of hyperchromasia. Only a few fibers are present among the cells. H and E; $\times 350$

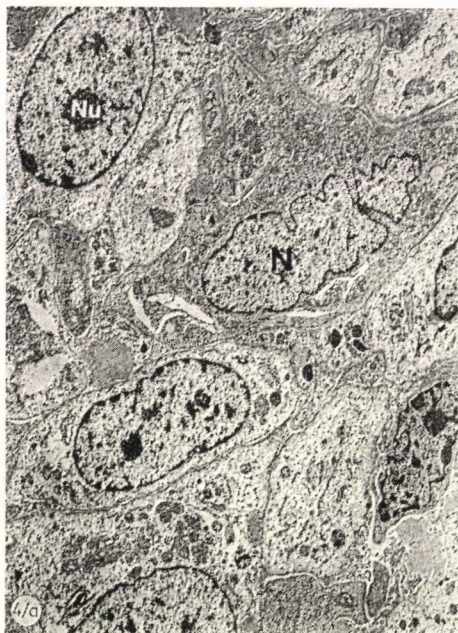


FIG. 4. *a.* Electron micrograph of elongated tumour cell with minimal ground substance. In some parts the nuclei (N) are indented, the nucleolus (Nu) is generally large uranyl-acetate + lead citrate, (1750 $\times$ 2.5). *b.* In the cytoplasm, mitochondria (M) and endoplasmic reticulum (ER) can be identified uranyl-acetate + lead citrate, (5300 $\times$ 2.5)

silver impregnation. Most of our patients had spindle-cell sarcomas which raised the possibility of fibrosarcoma, leiomyosarcoma and neurogenic sarcoma. First the neurogenic origin was excluded, then, having considered the collagen content, palisade arrangement of tumour cells and the presence of 'herring bone patterns', we established the final diagnosis (Figs 1, 2, 3). In one case the fibroblast origin could be verified only by electron-microscopic examination. For this purpose samples were fixed in 2.5% glutaraldehyde and postfixed in osmium-tetroxide. The sections were stained with uranyl acetate and lead-citrate, and examined by the JEM-60 electron microscope. At the electron microscopic level the elongated cell shape, multiple indentation of the nuclear membrane and large nucleoli were characteristic of the tumour (Fig. 4a, b). The absence of myofilaments and basal lamina (at least in fragments around the cells) helped in excluding myogenic origin.

Discussion

Anorectal sarcomas can be divided into different histologic types. The most frequently occurring form is the leiomyosarcoma. Approximately 50% of rectal smooth muscle tumours are diagnosed as malignant, representing 0.1 to 0.5% of all malignant tumours of the rectum [22]. Exner [13] was the first to report on 2 anorectal leiomyosarcomas in 1908.

The publication of four cases was provided by Rankin and Larson [29] in 1932. Papers appearing since then still report very low numbers, for instance, Asuncion [3] found two, Degrell [8] one, Diamante and Bacon [9] one, Mantoudis et al. [21] one, Mindich et al. [22] one, Nemer et al. [25] three and Hishida and Ishida [19], based on a national screening in Japan, accounted for 26 anorectal leiomyosarcomas. These data confirm the rarity of this tumour.

Fibrosarcomas are usually located in trunk and extremities and seldom develop in the alimentary tract. Their occurrence in the anorectal region is, however, an extreme rarity, as conformed by the fact that in over 50 years only 14 cases have been found (Table II).

Other sarcoma types, e.g. the anaplastic ones, are encountered even less frequently.

Symptoms of anorectal sarcomas and cancers are identical. Patients usually consult a doctor because of pain, bleeding and defecation disorders. Their localization and spreading are likewise the same. They may grow as intracolic, dumbbell or extracolic tumours. The close similarities of their clinical appearance explain that correct diagnosis can only be established with the help of a pathologist.

Surgery is the therapy of choice for anorectal sarcomas. They are radio-resistant, consequently no therapeutic effect can be expected from external

TABLE II
Anorectal fibrosarcoma

Author(s)	Case No.	Localization	Therapy	Follow-up period	Present state
Bacon [4]	2 (+ 1)	rectum	APE	30 months	symptom free
Espinoza [12]	1	anus	APE	12 years	abdom. met.
Goldman and Marbury [15]	1	rectum	Lockhart-Mummery res.	11 months	symptom free
Hines and Ridler [18]	1 (+1*)	rectum	APE	13 months	symptom free
Kleitsch and Simon [20]	1	rectum	sacral. exstirp.	11 months	died
Narasimhan [24]	1	rectum	Hartmann resection	11 days	died
Pennington [27]	2	—	—	7 hours	died
Russel and Hughes [31]	1	rectum	APE	—	—
Stoller and Weinstein [32]	2	rectum	APE	20 months	lung met.
Molnár et al. **	4	rectum	—	4 months	symptom free

* No clinical data presented; ** see Table I; APE = abdominal extirpation

radiation. Franklin et al. [14] applied fast neutron irradiation and anticipated good results. In one of our patients with operable leiomyosarcoma and in other with fibrosarcoma, radical surgery could not be performed because of the patients' poor cardiorespiratory condition. Intervention had to be limited to electrocoagulation and implantation of radium needles. They survived only for 18 and 7 months, respectively. In more than 300 patients with anorectal carcinomas we have used electrocoagulation plus radium or gold seed therapy. While some of these patients survived for 10 years, those with sarcoma died within two years. Anorectal sarcomas have a worse prognosis than carcinomas. In our material no 10-year survival was recorded; it is also very rare in the literature.

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Anorektale Sarkome

L. MOLNÁR, I. BESZNYÁK, K. DAUBNER E. HORÁK und E. SVASTITS

Nach Besprechung einiger mit den anorektalen Sarkomen verbundenen Fragen, werden die Erfahrungen mit im 20jährigen Operationsmaterial des Landesinstituts für Onkologie vorgekommenen 9 Rektalsarkomfällen erläutert. Sowohl die Literaturdaten als auch die eigenen Erfahrungen sprechen dafür, daß die erfolgreichste Behandlung die radikale chirurgische Entfernung des Tumors ist. Die Prognose der Neubildung ist — auch dann, wenn der Fall operabel zu sein scheint — schlechter als die des Mastdarmkrebses.

Аноректальные саркомы

Л. МОЛНАР, И. БЕСНЯК, К. ДАУБНЕР, Э. ХОРАК и Э. ШВАСТИЧ

Авторы дают обзор некоторых вопросов, касающихся аноректальных сарком, затем знакомят с опытом лечения саркомы прямой кишки у 9 больных в хирургическом отделении Государственного онкологического института, которые наблюдались в этом отделении за 20-летний период времени. Как показывают данные литературы и собственные наблюдения авторов, наиболее эффективным способом лечения является радикальное хирургическое удаление опухоли. Прогноз при саркоме хуже, чем при раке прямой кишки, даже если больной кажется операбельным.

Lung Cancer: Long-term Survival after Surgical Treatment

F. TENERIELLO, A. DI GIORGIO, P. SAMMARTINO, E. NATICCHIONI and G. DADDI, jr.

1st Surgical Clinic, University Medical School Via Conca d'oro 300, 00141 Roma, Italy

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The authors have carried out an analysis on a series of 1802 patients with lung cancer. 1254 patients were considered operable (69.5%) and 828 were resected. Overall 5-year survival rate was 28.3%. Results of surgical treatment were analysed in relation to the specific features both of primary tumour and the host organism. Although patients affected with epidermoid carcinoma showed a better survival as compared to those affected with tumours of other histotypes. Conversely long-term results were significantly related to post-surgical stage. Patients treated for stage I tumour showed a significantly better long-term survival (5-year survival rate 48.2%) as compared to those undergone resection for stage II and III neoplasms (22.8% and 12%, respectively; $p < 0.001$). From the prognostic standpoint female patients undergone resection showed markedly lower long-term survival (5-year survival rate 12.5%) as compared to male patients (5-year survival rate 29.5%), but the numerical differences between the two groups of patients does not permit to detect statistically significant differences ($p < 0.05$). Type and intensity of the immune response affect significantly long-term survival.

A good knowledge of prognostic criteria of a specific occurrence is significant for its correct setting, for a sensible choice of the therapeutic approach and for an objective evaluation of results.

In oncology, the parameters which are useful in formulating the prognostic statement concern both the features of the tumour and those of the host. In the course of the years, a steady qualitative and quantitative evolution of such criteria have been observed, and in the recent few years, those related to the host immune reactivity have become increasingly important.

The aim of the present study is the evaluation of the most reliable and significant prognostic criteria on the basis of long-term results obtained in a series of patients who underwent surgical treatment for lung cancer.

Material and Methods

The study was carried out on a series of 1802 patients with lung cancer observed at the 1st Surgical Clinic of the University Medical School Rome in the years 1950–1982. Clinical data of these patients were stored in an electronic computer UNIVAC 1100 of the E.D.P. Centre of the University of Rome by means of a computer-oriented medical record fitted for 1600 items [21].

Five hundred forty-eight patients were considered inoperable both on the basis of a functional evaluation (advanced age, renal or cardiovascular failure) or for the local or distant spread of the disease. 1254 cases underwent surgical treatment and 828 were resected; in 218 patients the resection was extended to adjacent organs or structures involved by primary tumor (Tables I, II). In all the cases undergoing curative resection, hilar and mediastinal lymphadenectomy was also performed [16, 17].

TABLE I
Surgical treatment for lung cancer (1254 cases)

Surgical treatment	No. of cases	%
Exploratory thoracotomies	426	34.0
Pneumonectomies	408	32.6
Lobectomies	393	31.2
Minimal (segmental and wedge) resections	28	2.2
Total	1254	100.0

TABLE II
Extended resections for lung cancer (218 cases)

Extent of resection	No. of cases	%
Parietal pleura	104	47.7
Chest wall	57	26.1
Pericardium	19	8.7
Atrium	10	4.6
Diaphragm	10	4.6
Other structures	18	8.3
Total	218	100.0

Before 1977 a limited number of patients received postoperative adjuvant chemo- and/or radiotherapy only for recurrent neoplastic disease and according to uniform treatment protocols. All cases observed after 1977 were entered in a postoperative chemo-radiotherapy trial which is still under evaluation.

Results of surgical treatment were analysed in relation to the specific features both of primary neoplasm and the host organism. For the former the histological type, according to WHO; [78], mitotic index (M. I.), nuclear grading (N. G.), doubling time (D. T.) and postsurgical stage, according to AJC [68] were evaluated. As for the latter sex and immune response both at the level of primary neoplasm (lymphocyte infiltration, L. I.) and regional

lymph nodes free from metastases (sinus histiocytosis S. H., paracortical area P. C. A. and cortical area C. A. development), were considered.

M. I. (number of mitoses $\times 1000$ cells) was evaluated by means of an original method [22] in 105 patients surgically treated. Such method implies the evaluation of mitotic activity through the study of 1000 cells for sample examined by an immersion objective ($\times 970$) on routine histologic specimens. N. G. has been evaluated on the basis of Black's protocol [11], which by means of easily objectified criteria scores N. G. progressively from 0 to 4: first scores indicate a more marked level of anaplasia.

D. T. was evaluated according to an original protocol worked out in our Institute in a joint-study with the Department of Mathematics of the University of Rome [3] which utilizes not only round shaped but also polymorphous radiologic images. By this method it was possible to study the D. T. of 104 lung cancer cases.

Post-surgical stage is based upon findings described at operation, gross pathology report and review of histological material according AJC criteria. The extent of intrathoracic nodal involvement (N) was determined observing a mean of 9.2 lymph nodes for lobectomy (range 4-27) and 14 for pneumonectomy (range 6-30).

As for the host immune response, this was evaluated both at the level of the primary tumour and of the regional lymph nodes. The degree of primary tumour L. I. has been assessed according to Black's method [10, 12, 13, 14]. Regional lymph node reactivity was studied on a standard histological material of 140 patients submitted to surgical resection; S. H. and P. C. A. were used as parameters for cellular immune response and C. A. for humoral immunity. Estimates were based upon a specially designed protocol which combined the criteria proposed respectively by Black for S. H. and by Cottier for P. C. A. and C. A. evaluation [10, 12, 13, 14, 18]. The magnitude of the immune response, both at the site of the primary tumour and in the regional lymph nodes was graded from 0 to 4.

Five-year survival rates were used to evaluate the prognostic value of all previously mentioned parameters (except doubling time evaluation). With the exception of the evaluation of mitotic index, doubling time and immune response at the level of regional lymph nodes, which were carried out only for part of the series, for the other parameters under study only 469 patients submitted to radical resection over a minimal period of five years and with known survival were considered, excluding cases treated by palliation, patients who died in the postoperative course or from causes other than the neoplastic disease, and patients lost during the follow-up.

Statistical analysis of survival data was carried out by the chi-square test (χ^2) modified according to Yates in those cases with only one level of freedom.

Results

Overall operative mortality after resection was 13.5%. It is to be underlined that this parameter showed a progressive decrease in the course of time and in the recent ten years it has shown a mean value of 2%.

Long-term survival evaluated in 469 patients respected from a minimum of five years and followed up was shown to be 28.3%. Patients treated with standard resections had a better long-term prognosis (33.3%) as compared to those undergone extensive resections (14%).

Prognostic value of some features of neoplasm: histological features

From the results of our analysis the histotype of the primary tumour was not shown to be a significant parameter from the prognostic standpoint.

Although patients affected with epidermoid carcinoma showed a better survival at five years as compared to patients affected with neoplasms of other histotypes, the statistical analysis was not able to detect significant differences (p : not significant) (Fig. 1).

On the contrary, data from the analysis of M.I. and N.G. appear to be more significant. Particularly, as for the former parameter, it was evaluated in 105 patients having undergone resection from a minimum of five years and with known survival and showed a mean value of 14.6

Small cell carcinoma and adenocarcinoma were shown to be the more actively growing histotypes (Table III). The analysis of prognosis has shown that cases with a higher mitotic activity ($M.I. \geq 15$) had survival rates markedly lower than those with a lower mitotic activity ($M.I. < 15$; $p < 0.0001$; Fig. 2).

Similarly, N.G. was shown to be a significant parameter from the prognostic standpoint. Patients who, apart from the histotype, showed N.G. equal to or higher than 2 ($N.G. \geq 2$) had a markedly better survival as compared to those with tumours with a high degree of anaplasia ($N.G. < 2$; $p: < 0.001$; Fig. 3).

TABLE III

Lung cancer, mitotic index (M.I.) and histological type (105 cases)

Histological type	No. of cases	Range	M. I. (mean)
Squamous cell carcinoma	35	(1-26)	11.74
Adenocarcinoma	34	(3-30)	14.9
Small cell carcinoma	25	(4-30)	18.4
Large cell carcinoma	11	(7-24)	13.8
Total	105	(1-30)	14.6

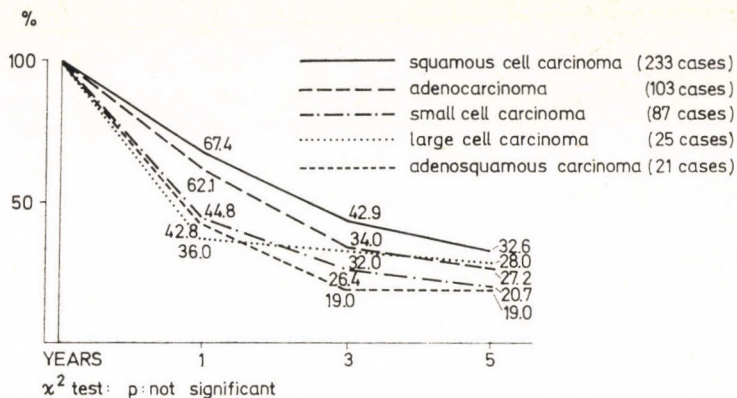


FIG. 1. Surgical treatment for lung cancer; histological type and long-term survival (469 cases)

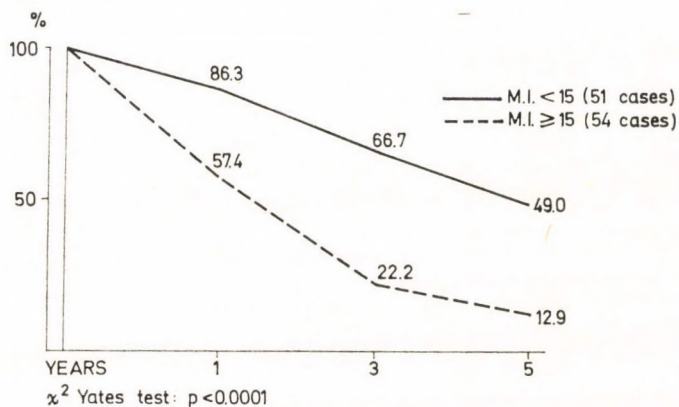


FIG. 2. Surgical treatment for lung cancer; mitotic index (M.I.) and long-term survival (105 cases)

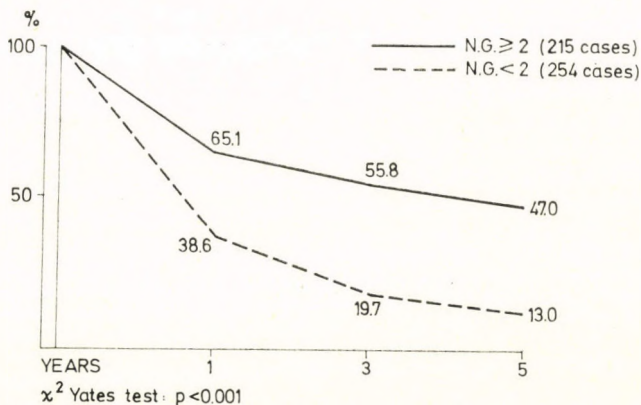


FIG. 3. Surgical treatment for lung cancer; nuclear grade (N.G.) and long-term survival (469 cases)

Doubling time

The analysis of D.T. was carried out in 104 patients affected with lung cancer and undergone resection. D.T. was shown to be 131.88 days on an average and markedly higher in small cell carcinoma as compared to other histotypes (Table IV). Long-term survival was evaluated 24 months following surgery due to the fact that most patients considered in the study were newcomers in our department, for whom a sufficient number of preoperative radiograms were available. Cases with a D.T. higher than the average had a significantly better survival ($p < 0.001$; Fig. 4).

Post-surgical stage

Over 469 patients submitted to radical resection from a minimum of five years and followed up, 133 (28.3%) showed long-term survival. This result, when evaluated with respect to the post-surgical stage of the disease, is highly

TABLE IV
Lung cancer, doubling time (D.T.) and histological type (104 cases)

Histological type	No. of cases	Range	D. T. (mean in days)
Squamous cell carcinoma	30	62-482	176.8
Adenocarcinoma	35	51-441	165.9
Small cell carcinoma	22	24-78	48.02
Large cell carcinoma	12	52-299	140.0
Adenosquamous cell carcinoma	5	47-418	128.7
Total	104	24-482	131.88

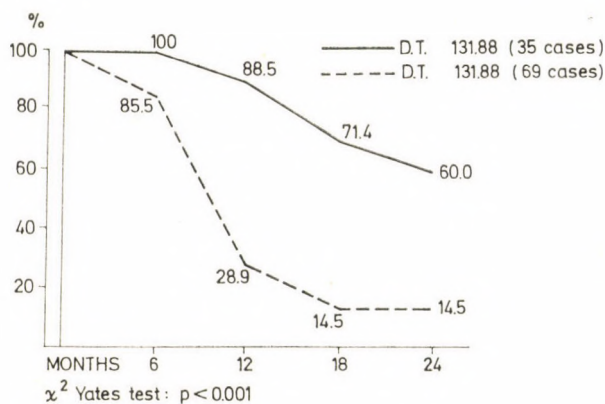


FIG. 4. Surgical treatment for lung cancer; doubling time (D.T.) and long-term survival (104 cases)

significant from the prognostic standpoint. Patients treated for stage I tumour showed a significantly better long-term survival (48.2%) as compared to those undergone resection for stage II and III neoplasms (22.8% and 12%, respectively; $p < 0.001$; Fig. 5).

Prognostic value of some features of the host: sex

In our series, 1671 patients were males and 131 females with a ratio of 12.7 : 1. The behaviour of such ratio has undergone variations in the course of time and in the five years a marked lowering has been observed (5 : 1). From the prognostic standpoint female patients undergone resection showed markedly lower long-term survivals as compared to those of male patients although the numerical difference between the two groups of patients does not permit to detect statistically significant differences ($p < 0.05$; Fig. 6).

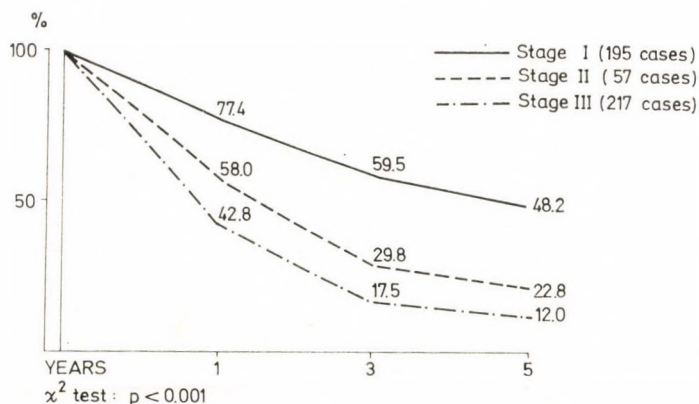


FIG. 5. Surgical treatment for lung cancer; post-surgical stage and long-term survival (469 cases)

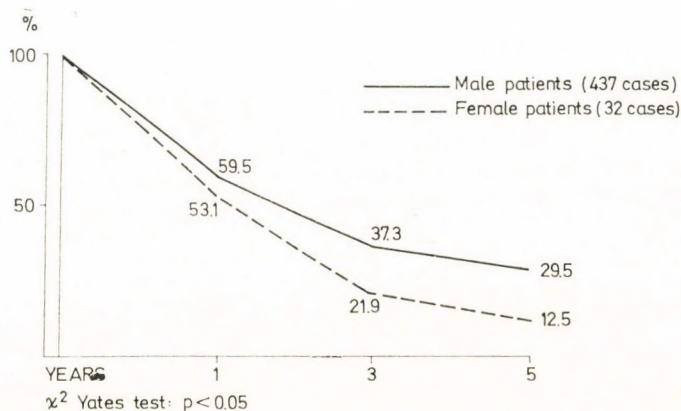


FIG. 6. Surgical treatment for lung cancer; sex and long-term survival (469 cases)

Immune response

The host immune response, concerning type and intensity, is strictly correlated to long-term results. Patients with marked lymphocyte infiltration both inside and around the tumour ($L.I. \geq 2$) showed a significantly better five-year survival than those where this finding was poor or absent ($L.I. < 2$; $p < 0.001$; Fig. 7).

The influence of regional lymph node response has been evaluated considering 4 classes of patients:

1. cases with predominantly cellular response, ($S.H. \geq 2$ and/or $P.C.A. \geq 2$; $C.A. < 2$)
2. cases with combined cellular and humoral response, ($S.H. \geq 2$ and/or $P.C.A. \geq 2$; $C.A. \geq 2$)
3. cases with predominantly humoral response, ($S.H. < 2$ and $P.C.A. < 2$; $C.A. \geq 2$)

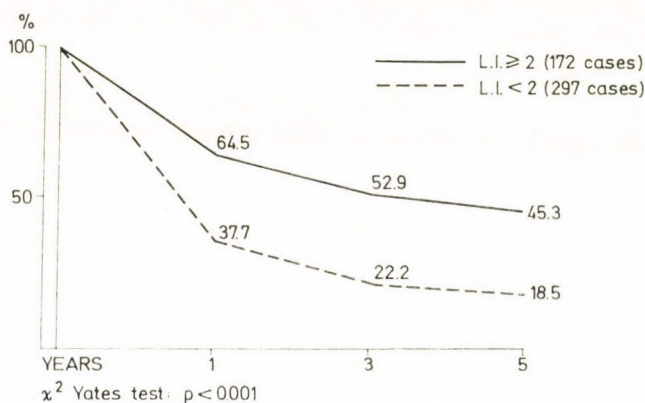


FIG. 7. Surgical treatment for lung cancer; lymphocyte infiltration (L.I.) and long-term survival (469 cases)

TABLE V

Surgical treatment for lung cancer; long term survival according to regional lymphnode immune response (140 cases)

Immune response types	5-year survival	
	No. of cases	%
Predominantly cellular ($S.H. \geq$ and/or $P.C.A. \geq 2$; $C.A. < 2$)	17/24	70.1
Predominantly humoral ($S.H. < 2$; $P.C.A. < 2$; $C.A. \geq 2$)	3/38	7.9
Mixed cellular and humoral ($S.H. \geq 2$ and/or $P.C.A. \geq 2$; $C.A. \geq 2$)	15/33	45.4
No reactivity ($S.H. < 2$; $P.C.A. < 2$; $C.A. < 2$)	1/45	2.2

χ^2 test: $p < 0.001$

4. cases with unresponsive lymph nodes, (S.H. < 2 and P.C.A. < 2 ; C.A. < 2).

Such analysis was carried out in 140 of the 469 patients submitted to surgical resection and followed up; best results were observed with predominantly cellular or mixed cellular and humoral immune response.

Cases with a predominantly humoral response or with unresponsive lymph nodes had lowest five-year survival rates ($p < 0.001$; Table V).

Discussion

In our series 69.5% of cases were considered operable and resectability (as to number of patients resected over the total of those undergoing surgical treatment) represented 66% of the cases. These rates are in agreement with those reported in some series [2, 7, 25, 31, 35, 51, 52, 56, 57, 66, 73, 77]. These data did not show marked variations in the course of time although a trend towards more limited resections, a better selection of patients and the recent progress in anaesthesia and intensive care have allowed a progressive decrease of extended resections and a marked decrease in operative mortality rate. A progressive decrease in indications for pneumonectomy in favour of standard lobectomy has been observed at our Clinic. Furthermore, segmental and wedge resections were only rarely performed and solely for palliation [69]. Values of survival were shown to be related to several parameters partly related to the features of the primary tumour and partly to the host defense mechanisms. As for the former, it is to be stressed that in our study the histological type did not show a particular prognostic value. This fact is explained by results obtained in the treatment of small cell carcinoma.

Because of the poor surgical results obtained, small cell carcinoma was for long considered to be a systemic disease and beyond any possibly radical resection [5, 24, 35, 46, 47, 60]. Subsequently, however, mainly in view of the poor survival obtained by chemo- or radiotherapy alone, some authors [7, 19, 25, 30, 44, 45, 64, 71] have come back to more rational positions stating that, in patients with limited lesions, surgical treatment, combined with an adjuvant therapy, is the only treatment which might yield moderately good results. We share this opinion supported by 20.7% five-year survival rate observed in our patients resected for microcytoma; a rate similar to that reported in the most recent series [42, 62].

Within the histopathological findings, the identification and study of some features of the primary tumour have played an important role. They appear to be more suitable than the histotype in the characterization of its biological behaviour. Among them, N.G. and M.I. have shown a clear prognostic significance in our study as well as in other authors' experience [20, 22, 67, 76].

Although D.T. was also shown to be a reliable prognostic parameter, it is generally seldom used as a systemic aid to the surgeon, both due to its difficult objective evaluation and to the need for starting an immediate treatment. In oncology, a proper therapeutic approach and a homogeneous evaluation of results of treatment cannot leave out of consideration an exact knowledge of the stage of the neoplastic disease.

Since 1973 the American Joint Committee (A.J.C.) for Cancer Staging and End Results Reporting has worked out a system of classifications of lung cancer according to stage, which systematically records the steps of tumour spread [68]. To this purpose, the role played by mediastinal lymphadenectomy is to be underlined as a reliable tool in detecting the intrathoracic spread of the disease.

Long-term survival of patients studied was shown to be significantly related to the post-surgical stage of the primary tumour. Particularly, as reported by others [6, 39, 59, 79] patients resected for stage I tumours showed highly satisfactory survival rates (48.2%). On the contrary, conflicting reports are available in the literature as for results of surgical treatment of patients with advanced neoplastic disease [1, 2, 25, 28, 34, 36, 37, 40, 41, 48, 49, 50, 53, 55, 56, 61, 63, 74].

Based on the long-term results obtained by us, both in the treatment of patients with neoplastic spread by contiguity to parietal or mediastinal structures (5-year survival 14%) and in patients with stage III tumours (5-year survival 12%) as a whole, it is possible to state that these cases, although having a poor prognosis, should not be excluded from whatever surgical treatment.

As for prognostic factors related to the host features, the sex and the immune response were considered in our series.

Up to the present time, it has been implied from the epidemiologic point of view that lung cancer affected mostly, if not exclusively, the male population. More recently, however, and mainly in the highly developed countries, a number of reports [8, 15, 26, 43, 80] have pointed to a marked increase of the disease among females and some have suggested that sex might affect the prognosis. This aspect, nevertheless, is presently not well defined in the literature, since highly contradictory results are often reported [4, 9, 23, 27, 38, 73, 75, 77]. Our study has evidenced a marked increase in lung cancer in female patients but it does not allow any conclusion on the role of sex as a significant prognostic parameter. In fact, in the present analysis, female patients have shown long-term survival rates lower than those of male patients, but the numerical difference between the two groups under examination is not statistically significant.

Yet an important determinant of clinical behaviour is commonly disregarded: the host immune reactivity. The type and intensity of the immune

response significantly affect long-term survival. Our data confirm previous observations on cancer of the lung as well as on other organs, and support the knowledge that a predominantly cellular response as evidenced by regional lymph node morphology (S.H. and P.C.A.) favourably influences long-term results [20, 32, 33, 34, 67, 70, 72]. Conversely, unresponsiveness or predominantly humoral response are associated with an unfavorable prognosis: a possible role of enhancing antibodies might be assumed [29, 58, 65].

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Überlebensrate nach der chirurgischen Behandlung des Lungenkarzinoms

F. TENERIELLO, A. DI GIORGIO, P. SAMMARTINO, E. NATICCHIONI und
G. DADDI jr.

Die Ergebnisse der chirurgischen Behandlung von 1802, an Lungenkarzinom leidenden Patienten — 1254 Fälle waren operabel (79,5%), in 828 Fällen kam es zu einer Resektion — wurden anhand des Primärtumors und einiger Kennwerte der Patienten analysiert. Die Prozentzahl des Fünfjahresüberlebens betrug 28,3%. In den Fällen mit Epidermoidkarzinom gestalteten sich die Überlebensziffern vorteilhafter, als bei den Tumoren von einem anderen histologischen Typ. Das lange Überleben zeigte eine signifikante Korrelation mit der Stadieneinteilung des Tumors. Die Fünfjahresüberlebensrate war bei den Männern besser als bei den Frauen (29,5% : 12,5%). Durch den Typ und die Intensität der Immunantwort wurde das langfristige Überleben signifikant beeinflusst.

Карцинома легких, переживание после операции

Ф. ТЕНЕРИЭЛЛО, А. ДИ ДЖОРДЖО, П. САММАТИНО, Э. НАТИККИОНИ и Г. ДАДДИ мл

Авторы сообщают о результатах анализа материала 1802 больных с карциномой легких. 1254 больных (69,5%) были операбельными, в 828 случаях произвели резекцию легких. Процент больных, проживших после этого 5 лет, составил 28,3%. Результаты хирургического лечения анализировали на основании первичного tumors и специальных некоторых характеристик больных. В случаях с эпидермоидной карциномой результат переживания был лучше, чем при опухолях иного гистологического типа. Продолжительный срок выживания обнаружил достоверную связь с стадией заболевания. Процент выживания был выше у мужчин, чем у женщин (29,5% : 12,5%), при сроке наблюдения пять лет. Тип иммунной реакции и ее сила достоверно влияли на продолжительность выживания.

Diagnostic Value of Bone Scintigraphy in the Complications of Total Replacement of the Hip

Z. MAGYARI, GY. FEKETE and GY. MOLNÁR

National Institute of Traumatology, H-1088 Budapest, Baross u. 23, Hungary

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Scintigraphy with bone-specific ^{99m}m-technetium—Sn—ethylenediphosphonate (phosphon) was performed in 27 patients having undergone total hip replacement before and, in case of complaints, also after operation.

On suspicion of infection a study with ⁶⁷gallium citrate was also made.

Completion of clinical, roentgenological and laboratory findings with an isotope study may help in deciding whether complaints are only due to the loosening of the prosthesis or to infection.

Preliminaries

In the recent two decades a considerable number of total hip replacements have been made. In proportion to the increase in the number of operations, the number of complicated cases has increased, too. The surgeon is, therefore faced with the serious problem of forming a more exact diagnosis for indicating subsequent therapy or reoperation using possibly non-invasive procedures.

The technetium—Sn—phosphate complex isotope studies introduced by Subramanian et al. [10, 11] provide fairly accurate information on the osteoblast-osteoclast activity with a minimal amount of irradiation.* In Hungary experimental and diagnostic isotope techniques in this field have a tradition of their own [1, 7].

In our Institute, we have been dealing with bone scintigraphy for years. We have studied its value, among others, in the diagnostics of vertebral fractures [4] and in judging the loosening of the nails in the medullary cavity [5].

Clinical and roentgenological studies, respectively, fairly often cannot provide the necessary information on the origin of complaints in the site of operation [8]. It is not easy, mainly at an early stage, to differentiate between a hip being painful for any reason and a loosened or infected prosthesis. The technetium phosphate compounds accumulate when integrated into the

* The half-life of technetium is 6 hours.

hydroxyapatite crystal. We are expecting an answer to the differentiation between loosening of the prosthesis or infection of the application of gallium citrate having become recently available in Hungary, too, which is not bone-specific but in an inflammation it is becoming fairly rich in polymorphonuclear MB leukocytes [2, 3].

Method

In bone scintigraphy 370 mBq ^{99m}Tc ethylenediphosphone (phosphon; Isotope Institute, Hungarian Academy of Sciences) was administered i.v. to patients. After four hours, visualization was made by a GAMMA 8100 scanner.

In gallium scintigraphy the 185 mBq ^{67}Ga * citrate made in the U.S.S.R. was given intravenously and registered after 48 hours.

Scintigraphy was performed in 27 patients having undergone total hip replacement. In 11 patients total hip replacement was made because of head necrosis developing after fracture of the neck of the femur. In these cases, the process was unilateral. In the other 16 patients total hip replacement was performed due to coxarthrosis. Of these 7 were bilaterally affected.

In five cases gallium study was also made since in these, suspicion of infection had arisen. The technetium examination is not suitable for differentiating the loosening of an inflammation-free prosthesis from that of an inflamed one.

Material

Follow-up examinations after total hip replacement of 11 patients with fracture of the neck of the femur were performed. According to the data of Manning [6] head necrosis developed in 15 to 20% of patients following nailing, as a result of the cracking of the weight supporting surface or, eventually, of the perforation of the nail. Bone scintigraphy in these cases always showed a considerable accumulation. After total hip replacement—in case of an uncomplicated healing—this important activity gradually disappears. In P.M., a male patient aged 65, head necrosis with pain developed two years after nailing of the neck of the femur. Total hip replacement was made and 22 months later, the pain recurred. The x-ray showed rarefaction, while the ^{99m}Tc -phosphon study an accumulation around the shaft. Beside the possibility of loosening, suspicion of infection due to the somewhat higher sedimentation rate arose. The ^{67}Ga did not reveal accumulation. The time having elapsed since then has proved that it was, actually, no infection.

* The half-life of gallium is 72 hours.

In contrast to our previous patient, in M.Gy., a female patient aged 75, following the osteosynthesis of the head of the femur, as a result of infectious complications, resection of the head was made. Then after healing of the inflammation, total hip replacement followed. Some eight months later she presented with symptoms indicative of recurring inflammation. In Fig. 1a ^{99m}Tc shows obviously diffuse activity in the whole site of operation. Figure 1b

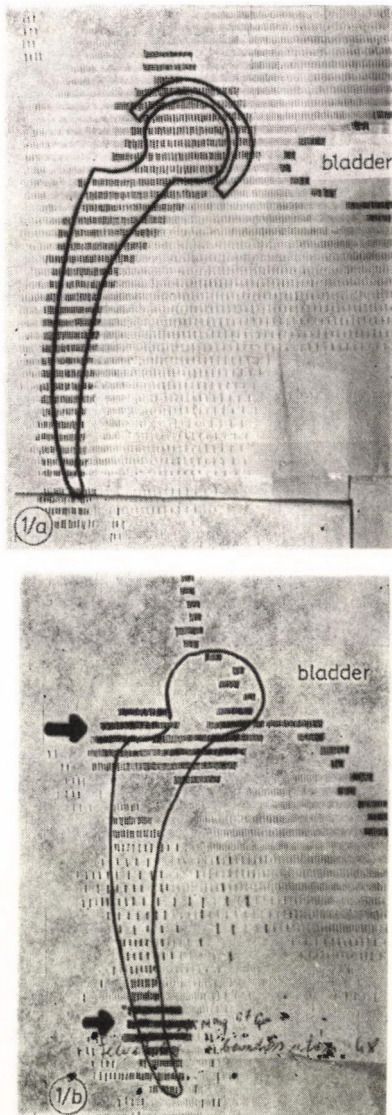


FIG. 1. (a) ^{99m}Tc -phosphon accumulates in the entire region of the operation. It may be indicative of loosening but also of infection. (b) The arrows indicate accumulation of $^{67}\text{gallium}$ citrate over the trochanter and the end of the shaft which is a proof of infection

shows the accumulation of ^{67}Ga . By this the retained focal inflammation over the trochanter but particularly over the end of the shaft being removed during the operation was visualized.

Technetium-phosphate study was made prior to the operation, too, in 5 patients with coxarthrosis. Of them in three, the process was bilateral. The more painful hip replacements with more severe roentgenological changes were made first. The more marked change was always present on the side showing greater activity which can be considered to be a measure of the progression of the disease.

After total hip replacement due to coxarthrosis, 9 patients underwent this examination in the postoperative period ranging from one month to 8 years.

In P.F., aged 72, scintigraphy was performed as a result of increasing pain one-and-a-half years after total hip replacement. A considerable accumulation of technetium was found only around the acetabulum, which as also shown by the x-ray picture indicated loosening. Therefore, operation was performed. On exploration, the shaft was found to be stable and only the loosened acetabulum was replaced.

Figure 2 shows the scintigram of a total hip replacement made five years earlier. It is evident that in the regions of both the shaft as well as the acetabulum there is an increased activity, while the roentgenogram shows a double contour indicative of loosening only between the shaft and the cement. During operation, due to an instability, actually the whole prosthesis had to be replaced.

P.E., aged 68, underwent total hip replacement eight years before the examination. On the present admission, he had intense pain in the operated hip. Clinical, laboratory and x-ray examinations all yielded normal results. Technetium scintigraphy was negative. The gallium study did not show accumulation either. This excluded the possibility of an inflammatory complication. All these considered, exploration was safely contraindicated, which also in itself is not an undangerous intervention with known complications.

The scintigram in Fig. 3 was made eight years after total hip replacement. On the basis of vigorous complaints and of the x-ray study, loosening of the acetabulum was supposed. The labelled phosphon accumulated in the projection of the acetabulum, therefore the loosening assumed on the basis of the x-ray examination was believed to be restricted to the acetabulum. This was also confirmed by the operative finding. The acetabulum together with the broken cement were removed, while the stable shaft was not.

On this basis, bone scintigraphy was found to be a fairly useful supplementary procedure in studying the complications after total hip replacement. The $^{99\text{m}}\text{Tc}$ -phosphate study helps providing information on whether there is

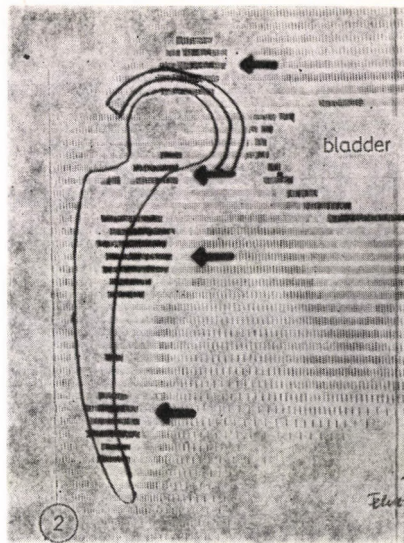


FIG. 2. Intensive accumulation in the whole surrounding region of total hip replacement. The entire prosthesis has loosened ^{99m}Tc -phosphon)

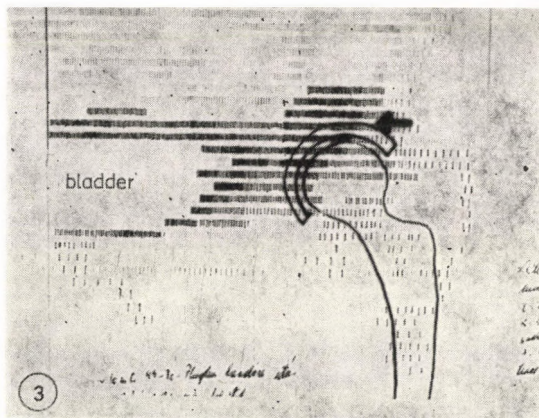


FIG. 3. Considerable accumulation is present only in the acetabulum. The acetabulum has loosened ^{99m}Tc -phosphon)

a pathogenic process in the hip and it can also be an aid in judging the necessity of reoperation.

The labelled phosphate is not suitable in itself for judging the nature of the pathogenic process but, in case of loosening, it may help in its localization.

If there is a suspicion of infection it is recommended to make a gallium citrate study, too. If both labelled materials accumulate at the same place, there is a fairly high probability of bacterial infection.

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Über die diagnostische Bedeutung der Knochenszintigraphie bei den Komplikationen der Hüftenendoprothese

Z. MAGYARI, GY. FEKETE und GY. MOLNÁR

Bei 28 eine totale Hüftenendoprothese-Operation überstandenen Patienten fanden mit knochenspezifischem Technetiumisotop-Untersuchungen statt. Die Methode hat sich — unter gleichzeitiger Berücksichtigung der klinischen, Röntgen- und Laborbefunde — als eine nützliche ergänzende Methode zur Entscheidung der Frage erwiesen, ob die Beschwerden durch die Lockerung der Prothese verursacht wurden. Im Falle eines Infektionsverdachts, wurde bei demselben Patienten, zwecks Klärung der Frage, ob für die Beschwerden nur die Lockerung der Prothese, oder eventuell auch eine Infektion verantwortlich ist, auch die Galliumisotop-Untersuchung vorgenommen.

Диагностическое значение костной скинтиграфии при осложнениях бедренного эндопротеза

Э. МАДЬЯРИ, ДЬ. ФЕКЕТЕ и ДЬ. МОЛНАР

Нами были выполнены исследования с костноспецифическим изотопом технеция на 28 больных, перенесших операцию тотального эндопротеза бедра. Мы считаем, что такое скинтиграфическое исследование, вместе с клиническим обследованием, лабораторными анализами и рентгенографией, является полезным дополнительным методом для решения вопроса: расслаблением ли протеза вызваны жалобы. В случае подозрения на инфекцию, тому же самому больному производилось исследование с изотопом галлия, результат которого решал вопрос о причине жалоб: только ли рыхлость протеза или инфекция их вызывают.

Thermal Injuries of Human Tendons

L. JÓZSA, A. RÉFFY, and L. MÉNESI

National Institute of Traumatology, H-1088 Budapest, P. O. Box 21, Hungary

(Received January 19, 1984)

Forty-two burn injuries and 22 cold injuries were investigated. Both high temperature and cold induced tenocyte necrosis, and denaturated and fragmented the collagen fibres. As a consequence of severe damages of tendon and of long lasting regeneration, it was believed that even in case of incidental healing restoration of the original function could not be expected.

The severity of thermal injury to the tendon is dependent on the parameters of the injurious process itself, i.e. the including amount in a caloric sense, duration, and surface extent, and on the number of host-response factors [3, 6]. A variety of degenerative structural alterations can be seen in the injured skin [2, 4, 7, 8], muscle [1, 5, 9, 10], but little attention has been paid to the pathological changes in the tendon.

The purpose of this study was to examine the pathological alterations to burn and freeze injuries in tendons.

I. Burn Injury of Tendons

Material and methods

Fourteen patients from the National Institute of Traumatology were included in this study. There were 13 males and 1 female. At the time of amputation the youngest patient was 18 and the oldest 67 years old. The interval between burn injury and amputation ranged from 6 hours to 18 days. From 14 patients 42 tendons were examined (Table I).

The tissue samples of tendons were fixed in buffered formaline and embedded in paraffin. Serial sections were stained with HE., van-Gieson, Mallory's trichrome and phosphotungstic acid haematoxylin (PTAH) staining for light microscopy and with Romhányi's anisotropic staining for polarization microscopy.

TABLE I

Examined tendons in cases of burn injury

Tendon	No.
Flexor dig. prof.	20
Flexor dig. subl.	2
Extensor dig. manu	5
Extensor dig. comm. ped.	6
Flexor pollic. long.	2
Extensor pollic. long.	1
Flexor carpi rad.	1
Extensor hall. long.	1
Tibialis ant.	1
Achilles tendon	3
Total	42

Results

Six hours following injury edema was visible in the tendons, it diminished in size toward the end of the observation period (18 days).

In the tendon a zone of acute necrosis was found in which all components (tenocytes, collagen fibres, vascular wall) were altered. Areas more peripheral to the zone of necrosis showed progressively less damage. In the peripheral zone proteinous material was precipitated on the surface of collagen fibres (Fig. 1).

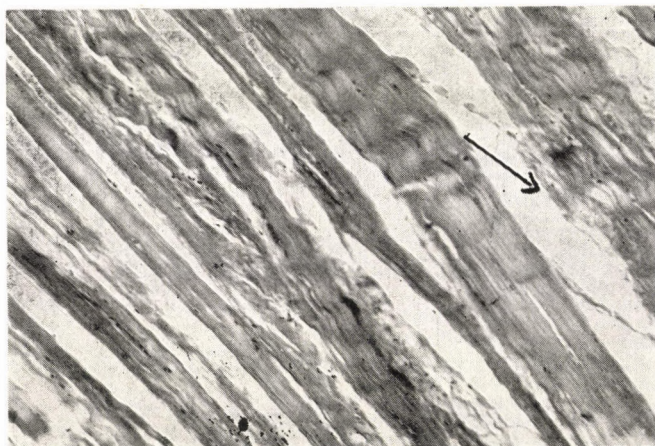


FIG. 1. Proteinaceous material (arrow) was precipitated on the collagen fibres
tendon
Six hours after burn injury, HE, $\times 100$

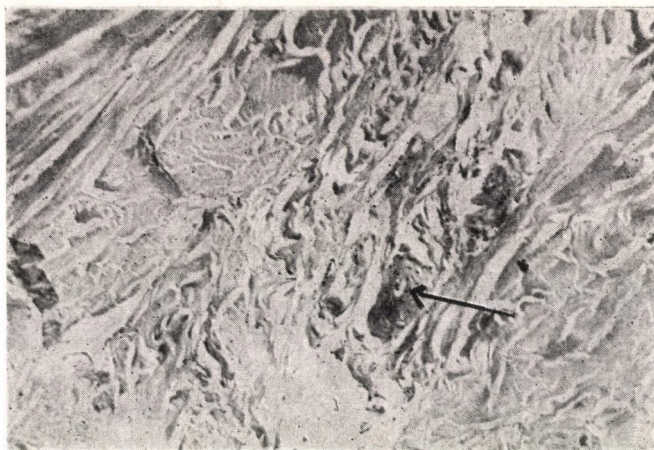


FIG. 2. Patent vessel (arrow) within necrotic area; 2 days after burn injury, He, $\times 100$



FIG. 3 Among the disintegrating fibres leucocytic infiltrations on the day 7 after burn, HE, $\times 100$

One day and two days following burn injury there were patent vessels present in the injured area (Fig. 2), as well as in the areas surrounding the burn site. In the zone of acute necrosis the intraluminal contents of such vessels had red cell aggregates consistent with a low flow or thrombi.

On day 3 the necrotic area extended and contained disrupted collagen fibres. Large amount of erythrocytes, leucocytes and fibrin clots occurred among the disintegrating fibres. On day 7 the degenerative changes in the tendon were less conspicuous than on day 3, but the number of leucocytes and macrophages were more numerous (Fig. 3). On day 18 no regenerative changes were found in the necrotic area and in the transitional zone.

II. Freeze Injury of Tendons

Material and methods

From 3 patients 6 amputated limbs (22 tendons) were examined on days 2, 3, 4, 12, 16, and 20 following cold injury (Table II). The histological methods were given above.

Results

Macroscopically visible edema and swelling were seen in all tendons. On days 2 and 3 a zone of acute necrosis with nucleolysis or nuclear pyknosis of tenocytes was seen. Both in the necrotic area and in the transitional zone



FIG. 4. Edema, acute necrosis, with nucleolysis or nuclear pyknosis of tenocytes. Day 3 after freeze injury, HE, $\times 100$

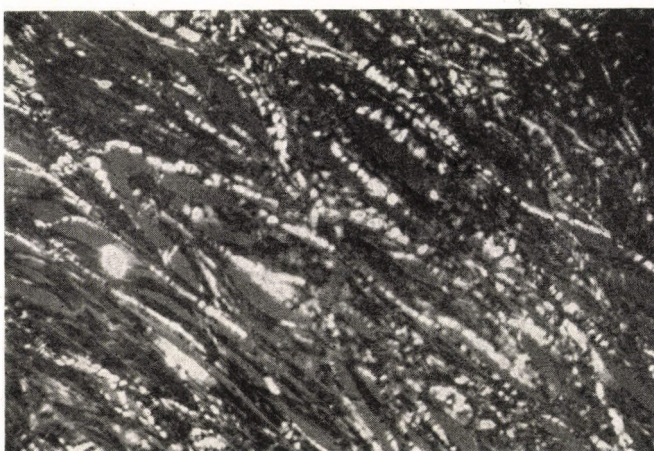


FIG. 5. The collagen fibres are swollen and disintegrated on day 4 after freeze injury. Polarization microscopic picture $\times 100$

TABLE II
Examined tendons in cases of cold injury

Tendon	No.
Flexor dig. prof.	4
Flexor dig. subl.	4
Extensor dig. manu	4
Flexor dig. comm. ped.	4
Extensor dig. ped.	4
Achilles tendon	2
Total	22

the vessels were dilated and numerous thrombi were present. The staining qualities of the vessel walls were typical of necrosis. The collagen fibres were swollen and did not show birefringence. Both in the necrotic and transitional areas the collagen fibres were fragmented and surrounded by proteinous precipitates. Inflammatory cell infiltration was found on day 4 following injury. On day 12 the disintegration of collagen fibres was seen both in the necrotic and transitional zones. No regenerative changes were found in the freeze injured tendons (Figs 4 and 5).

Discussion

The response to tendon injury and subsequent healing involves a number of signaling mechanisms which coordinate the entrance of inflammatory cells, and stimulate the proliferation of tenoblasts.

In burn injury a number of substances are released from the matrix presumably because of direct thermal denaturation of macromolecules. Collagen-derived peptides detected in both serum and urine substantially increased in burns as well as breakdown products from other macromolecular components of the matrix. Such matrix components may act as inhibitors for the promotion of inflammation and for the repair process.

Following injury by cold the cell membranes and collagen structures produced marked degenerative changes within 24 hours. These changes are essentially non-specific and are thought to represent varying degrees of damage. They range from a minimal swelling to complete coagulation necrosis of the cells and fibres. Physical chemistry studies [9] have indicated that lipoprotein complexes, such as cell membranes are prone to damage during freezing and thawing mainly because of a rise in concentration of salts and pH changes during the crystallization of water to ice, and that this can lead to permeability changes that are usually irreversible.

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Thermische Schädigung der menschlichen Sehne

L. JÓZSA, A. RÉFFY und L. MÉNESI

Untersucht wurden 42 eine Verbrennungs- und 22 eine Kälteschädigung erlittene Sehnen. Sowohl durch die hohe Temperatur als auch durch die Kälte wurden Tenozytennekrose, die Denaturation und die Fragmentation der Kollagenfasern verursacht. Angesichts der schweren Sehnenschädigung und der sich verzögernden Regeneration muß damit gerechnet werden, daß die Sehne selbst nach der eventuellen Heilung funktionsunfähig bleibt.

Термальное повреждение сухожилий у человека

Л. ЙОЖА, А. РЕФФИ и Л. МЕНЕШИ

Авторы подвергли исследованию 42 сухожилия с ожоговым и 22 сухожилия с холодовым повреждением. Как под действием высокой температуры, так и при воздействии холода наступали тяжелые изменения: некроз теноцитов, денатурация и расщепление коллагеновых волокон. Из-за тяжелого повреждения сухожилия и затяжного периода регенерации, приходится считать, что сухожилие не сможет выполнять свою первоначальную функцию, даже в случае излечения.

Immunological and Virological Studies of Patients with Tumours of the Urogenital System

S. CSATA¹, GIZELLA KULCSÁR,² P. DÁN,² J. HORVÁTH,² I. NÁSZ,² A. VEREBÉLYI¹
and J. ONGRÁDI²

¹ Department of Urology, Municipal István Hospital, H-1096 Budapest, Nagyvárád tér 1, Hungary and

² Institute for Microbiology, Semmelweis University Medical School, H-1089 Budapest, Nagyvárád tér 4, Hungary

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The possible connections between the oncogenic viruses and the various tumours of the urogenital system were investigated. Examining the patients' cellular immune response by the lymphocyte transformation test, it was found that the non-specific immune response was considerably diminished in almost all cases, while response to adeno- and herpesvirus antigens was enhanced. Structural and functional impairment of T-lymphocytes frequently occurred. Antiviral humoral antibodies were present more rarely in cancer patients than in the controls. However, type 12 markedly oncogenic anti-adenovirus antibody was frequently found. Using the immunofluorescent method, adeno- and herpesviruses were found in more than 50% of the patients' malignant tumour cells. Electron microscopically, in some cases adeno-, herpes- and type C virus particles, too, were isolated in the tumour cells. According to these results besides other factors also adenoviruses may play a role in urogenital tumours.

In the tumours of the urogenital system different viruses or viral antigens have so far been isolated [3, 12, 14, 15]. Data on adenoviruses are hardly available. Since under experimental conditions, several types of this virus group are oncogenic [1, 8, 17] and *in vivo* they show affinity for the cells of the urogenital system [7, 10, 11, 18], the T-lymphocyte reactivity of patients to adenoviruses *in vitro* was studied. Anti-viral antibodies in the patients' serum and virus antigens and particles in the tumour cells were sought.

Material and Method

Various examinations were made on materials from 265 patients. The distribution of patients according to the diagnosis is shown in Table I.

The cellular immune response was studied by the lymphocyte transformation test in 60 tumorous patients and 45 controls according to the earlier described method [6, 9]. Phytohaemagglutinin (RHA), adeno- and herpesviruses were used as antigens. The examination of humoral antibodies was made by complement fixation in the Takátsy microtitrator [4]. Adeno- and herpesviruses were applied as antigens. Cells of tumorous or other tissues of

TABLE I
Distribution of the patients according to diagnosis

Benign tumour	145
Malignant tumour	20
Non-tumorous tissue	15
Prostatic hyperplasia	40
Control patients	45
Total	265

160 patients were studied to demonstrate virus antigens by the immuno-fluorescent method using anti-viral immune serum produced in rabbit against adeno- and herpesviruses [5, 19]. The virus particles were examined electron microscopically in the tumour cells of 30 patients and in other non-tumorous tissues of 20 patients.

Results

By using the lymphocyte transformation test indicating the reactivity of cellular immunity, the lymphocytes of tumorous patients with PHA (non-specific immune response) showed a considerable decrease as compared to the controls. This value usually ran parallel to the severity of the disease. The lymphocytes of the same patients produced a significantly enhanced stimulation with adeno- and herpesviruses (specific reaction). Structural and functional damage of lymphocytes occurred in the case of several cancer patients. The reaction of the lymphocytes of patients with benign tumours of the urogenital system was similar to that of the controls, but during culturing a fairly large number of a typical mononuclear cells characteristic of virus-effect appeared (virocytes, stress lymphocytes, etc.).

Anti-adeno- and herpesvirus antibodies in the patients' serum were found infrequently and in lower titres than in the controls but the anti-12-adenovirus antibodies—mainly those against early non-virion antigens—could be traced often and in higher titres.

Adenovirus antigens were found by the immunofluorescent method in the tumour cells of more than 50% of patients with malignant tumours, first of all oncogenic type 12 antigens. In some patients herpesvirus antigens were also present in the tumour cells. In the cells of prostatic hyperplastic and non-tumours urogenital tissues studied as controls virus antigens were observed only in some cases.

Electron microscopy revealed adenovirus and herpesvirus particles as well as structures showing budding in the cells of malignant tumours. These latter structures were likely to be type C oncornavirus particles. In the control cells virus particles could not be isolated in any case.

Discussion

The relationship between human tumours and viruses have been studied extensively [16, 21, 22]. Among these studies a considerable number of data refer to the tumours of the urogenital organs. So far very probable links have been shown with herpes simplex cytomegaloviruses, papova and type C oncornaviruses [3, 14, 15]. In our earlier investigations antibodies against one of the oncogenic adenoviruses [4] were found in a large proportion of patients with malignant tumours of the urogenital organs. This seems to indicate that, beside other factors these viruses may also have a share in giving rise and maintaining the tumours. In our present investigations the same problem was approached differently. The immunological studies revealed that the patients' non-specific cellular immune response decreased considerably while it showed an increased reaction with the oncogenic adenovirus and herpes virus antigens by the lymphocyte transformation test. The patients' lymphocytes were sensitized with these viruses. Beside the tumour cells, adenovirus was latently carried by a few percentage of circulating lymphocytes of most patients. The association with viruses is also verified by the presence of adeno- and herpes-virus antigens in a high percentage of malignant tumour cells. Virus particles were often seen, too.

As it has been confirmed in the case of some animal viruses, in tumour formation oncogenic viruses activate the oncogens in the cells [22]. Evidence of this has already been offered in case of tumours of the prostate. The patients' immune deficiency may also contribute to the pathomechanism. It is known that adeno- and herpesviruses, too, have a great affinity for the lymphoid system [2, 13, 20]. As a result, mainly by disturbing the cellular immune response, they can also contribute to tumour formation. Namely, cellular immunity plays an important role both in tumour formation as well as in coping with viral infections [1]. Thus, oncogenic viruses and those with an affinity for the lymphoid system may favourably influence oncogenesis also from two directions. Studies are still being made for further verifying the possible correlations.

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Immunologische und virologische Untersuchungen bei an einem Tumor des Urogenitalsystems leidenden Patienten

S. CSATA, G. KULCSÁR, P. DÁN, J. HORVÁTH, I. NÁSZ, A. VEREBÉLYI und
J. ONGRÁDI

Untersucht wurden die möglichen Korrelationen zwischen den Viren onkogenen Typs und den verschiedenen Tumoren des Urogenitalsystems. Die mit dem Lymphozyten Transformationstest durchgeführten Untersuchungen der zellulären Immunantwort wiesen fast in jedem Fall auf die wesentliche Abnahme des Parameters, während die mit den Adeno- und Herpesviren vorgenommenen Bestimmungen die Steigerung der zellulären Immunantwort ergaben. Die strukturelle und funktionelle Schädigung der T-Lymphozyten trat häufig in Erscheinung. Bei den Tumorkranken waren antivirale humorale Antigene seltener vorzufinden als bei den Kontrollen; Antiadenovirus-Antigene mit ausgeprägter onkogener Fähigkeit (Typ 12) ließen sich aber häufiger nachweisen. Mit der Immunfluoreszenz-Methode konnten in den Tumorzellen in mehr als 50% der Fälle Adeno- und Herpesvirus-Antigene ermittelt werden. Mittels Elektronenmikroskopie wurden in den Tumorzellen auch Viruspartikula von Adeno-, Herpes und C-typ nachgewiesen. Die erhaltenen Ergebnisse sprechen dafür, daß in den Urogenitaltumoren nebst anderen Faktoren wahrscheinlich auch die Adenoviren eine Rolle spielen.

Иммунологические и вирусологические исследования у больных, страдающих опухолями уrogenитальной системы

Ш. ЧАТА, Г. КУЛЬЧАР, П. ДАН, Я. ХОРВАТ, И. НАС, А. ВЕРЕБЕИ и Я. ОНГАРДИ

Авторы изучали возможную зависимость между вирусами, обладающими онкогенными свойствами, и различными опухолями уrogenитальной системы. Исследуя клеточную иммунологическую реакцию с помощью теста трансформации лимфоцитов, авторы нашли, что неспецифический иммунный ответ уменьшается почти во всех случаях, будучи в то же время повышенным с антигенами адено- и герпес-вирусов. Часто наблюдались структурные и функциональные повреждения Т-лимфоцитов. Антивирусные гуморальные антитела у опухолевых больных встречались реже, чем в контроле, но у них часто встречалось антитело 12-го тира, обладающее сильной онкогенной способностью и направленное против аденовируса. При исследовании иммунофлуоресцентным методом, больше, чем у 50% больных нашли адено- и герпес-вирусные антигены в клетках злокачественных опухолей. Под электронным микроскопом в некоторых случаях в опухолевых клетках были обнаружены частицы адено-, герпес-вируса и вируса типа С. Согласно полученным результатам, в возникновении уrogenитальных опухолей — наряду с прочими факторами — могут играть роль также и аденовирусы.

Book Review

Actual Problems in Paediatric Surgery

Edited by T. VEREBÉLY

Akadémiai Kiadó, Budapest 1983; \$36

This book contains the papers of the VIIth Congress of the Hungarian Association of Paediatric Surgeons, held in Budapest, between 25–28 August 1982. The Congress was international, many participants came from Europe and from overseas, as from the USA, Japan, etc. The main topics of the Congress were: 1. Special diagnostic examinations in paediatric surgery; 2. Errors and mistakes in childhood traumatology; 3. Surgical conditions of neonates causing respiratory disturbances (except esophageal atresia); 4. Free papers.

This book is the first publication in Hungary which contains the papers of a Paediatric Surgical Congress. The main topics were the so-called 'up-to-date' themes and the lectures discussed the latest results in each of them.

The papers in the first section dealt mostly with ultrasonography, because this method is the best non-invasive examination during pregnancy. The lectures proved that this type of examination can give correct antenatal diagnosis of several congenital malformations, as atresia of the alimentary tract, gastroschisis, omphalocele, spina bifida, hydrocephalus, etc.

All the papers of this section showed the latest results of examination. It was confirmed that this is the best method among the antenatal diagnostic procedures, firstly for its non-invasive type. If a correct diagnosis is formed, either intrauterine, or urgent postnatal intervention can be performed. For this reason the prenatal diagnosis is very important, because it can be possible to perform some urgent prenatal palliative interventions for hydrocephalus, hydronephrosis, giant omphalocele, as well as spina bifida.

Some papers dealt with angiography, with computer tomography, and some others were also presented on scintigraphy and laparoscopy. All these lectures offered the latest results, some the errors and missed possibilities, too.

The second topic, childhood traumatology, was chosen because in the last decades increased mortality could be detected from trauma, firstly from traffic accidents, burns, etc. The papers mostly discussed the cause of the accidents, prevention and therapeutic measures. It is true that in our time the number of traumatic deaths in the child age group is increasing. The lectures clarified the responsibility of parents, for instance, in the cases of the so-called household accidents. Generally the incidence of these is the same all over the world.

The third main topic was related to the surgical conditions of neonates causing respiratory complications in the postoperative period. In this part it was emphasized that the necessity of diagnostic, therapeutic and technical improvement is very important.

The section of free papers was concerned mostly with the problems of cryptorchidism. All the speakers stated the necessity of the early operation, because it is imperative to secure normal fertility in adults.

The book contains the summaries of more than 70 papers. These papers reported on most recent and most up-to-date results in paediatric surgery. The book will be of interest to paediatric surgeons, but it may be very useful for paediatricians, general surgeons and pathologists, as well.

J. LÉB

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Parenchymal Operations of the Lower Pole of the Kidney with a Double Collecting System

F. GÖTZ, J. ZANA, J. HÜBLER and D. FRANG

Department of Urology, Pécs University Medical School, H-7643 Pécs, Munkácsy M. u. 2., Hungary

(Received December 16, 1984)

The authors present four cases of unilateral kidney with a double collecting system where calculus change has occurred in the lower collecting system. In one of them, marginopolar nephrotomy, while in three, heminephrectomies in the destructed lower segment of the kidney were performed. The remaining upper part functioned perfectly later on. The avoidance of unjustified nephrectomy is stressed.

The kidney with a double collecting system as a developmental anomaly does not belong to the rare clinical pictures. The collecting system of the upper segment of the kidney is clearly visible on urograms as a miniature, irregular non-typical structure. The kidney parenchyma belonging to the upper segment is much smaller than that belonging to the lower segment.

The kidney with a double collecting system does not in itself require surgery, but, as a developmental anomaly, it predisposes to various diseases (tuberculosis, calculus, inflammation). These latter diseases may already call for surgical intervention.

The removal of the affected upper pole of the kidney with a double collecting system is a frequent surgical solution. Pathological changes of the lower segment appear less often, thus surgical interventions involving this part are needed more rarely. Balogh et al. [1] reported their three cases of lower heminephrectomy where operation was indicated in one case by calculus, in one by tuberculosis and in one by chronic pyelonephritis. Coleman et al. [2] performed lower heminephrectomy due to calculous pyelonephritis, while Rose and Follows [6] reported on two similar cases. Since the kidneys have a 100% share in function [3], it is important whether in a severe involvement of the lower pole of the kidney, the whole kidney is removed, as it has been often done 10 to 15 years earlier, or only a partial resection is made. Heminephrectomy is worth performing only with an intact contralateral kidney if the remaining renal tissue is expected to be capable of excreting an adequate amount and quality of urine. For judging this, isotope renography, gamma camera examinations and selective renal angiography must be performed preoperatively. Particular

care should be taken in examining the distribution of the main branches, and the arborization, of the vessels. This is stressed by Hamvasi et al., too [5], since the optimal site of resection can be chosen only with the surgeon being fully aware of the distribution of the vessels. When indicating surgery also the patient's age should be considered, in addition to judging the nature of the underlying disease. At a younger age, heminephrectomy ought to be attempted.

Material and Method

In the recent seven years, parenchymal operations have been made in four cases in the lower pole of the kidney with a double collecting system. The underlying disease was calculus of the collecting system in all four cases.

Case 1. Female patient, aged 20, was admitted to the Department due to hypogastric pains having persisted for two months. The urinary sediment contained 8 to 10 leukocytes and 2 to 3 erythrocytes per v.f. Bacterial inoculation: *E. coli*. The laboratory values did not show any change. Selective urography showed that the left kidney had a double collecting system. The plain roentgenogram confirmed the coral calculus of the lower collecting system. After the necessary preparation, the coral calculus was removed from the lower pole of the kidney by marginopolar nephrotomy [4].

Calculus analysis: struvite + apatite carbonate. Uneventful healing.

Case 2. Female patient, aged 67, admitted for right lumbar pain, pyuria and microhaematuria. Bacterial inoculation: *E. coli* + *Proteus*. Selective urography revealed a right kidney with a double collecting system with double ureters. In the ureter belonging to the lower collecting system, a calculus of 1×1.5 cm was found on the x-ray picture. The calculus initiated the prehydronephrosis. After the necessary preparation, lower heminephrectomy and resection of the attached ureter were performed. Calculus analysis: uric acid + struvite. Uneventful healing.

Case 3. A 7-year-old girl was treated for recurring pyuria. Then, as a result of a febrile state after right renal colic, she was admitted to the paediatric department. Bacteriological inoculation: *E. coli*. The plain renogram revealed a coral calculus in the projection of the upper calyceal system of the left kidney and a shadow appearing to be a ureteral stone of 5×0.5 cm. Selective urography showed a kidney with a double collecting system on both sides with double ureters. The calculi were projected on the right into the collecting system of the lower pole of the kidney and into the common ureter, while on the left, into that of the upper pole of the kidney. After preparation right lower heminephrectomy and ureterotomy were performed.

Case 4. A 15-year-old girl was admitted for recurring pyuria and intermittent pyelonephritis. Her urinary sediment contained 30 to 40 leukocytes



FIG. 1. Plain roentgenogram of the left kidney of a 15-year-old girl shows multiple stones of the lower collecting system



FIG. 2. Urography with a dilated lower collecting system



FIG. 3. Preoperative aortorenovasography. Poor vascularity can be seen in the lower pole of the kidney

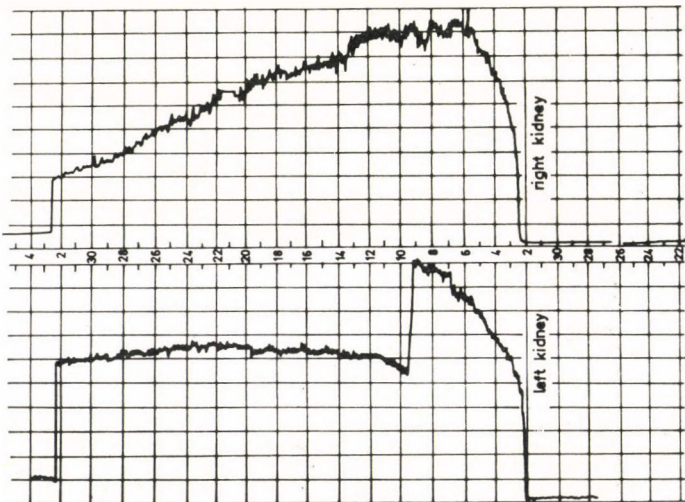


FIG. 4. Preoperative isotope renography. The radiorenogram taken in the recumbent position shows the hippuran intake of both kidneys. On the right (upper curve) cumulation occurs in time, the excretion is prolonged. On the left (lower curve), cumulation occurs in 20 minutes followed by a slow discharge



FIG. 5. Postoperative urography revealing a well-functioning upper pole of the kidney with a slightly winding ureter

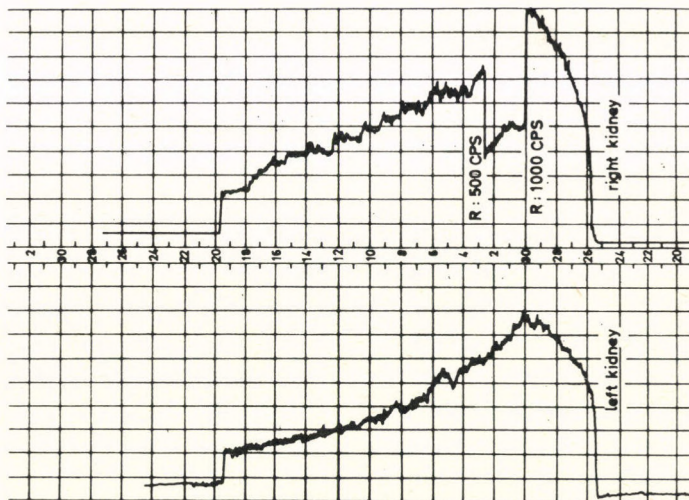


FIG. 6. Postoperative isotope renography. The control renogram performed one year later shows both kidneys with normal functions and discharge (upper trace: right kidney; lower trace: left kidney)

and 5 to 6 erythrocytes. Bacteriological inoculation: *E. coli*. The plain renogram revealed multiple stones in the projection of the left kidney (Fig. 1). Excretory urography showed a marked dilatation of the lower collecting system containing stones (Fig. 2). Selective renal angiography documented a minimally functioning poorly vascularized substance of the affected renal segment (Fig. 3). Performing heminephrectomy, the artery indicated by an arrow was ligated. Isotope renography showed cumulation for 20 minutes then slow excretion (Fig. 4). During renal exploration, the lower pole of the kidney with the thinned parenchyma was resected together with the stone. Calculus analysis: Ca-oxalate-monohydrate. Postoperative phase without complications. Excretory urography performed at a half-year interval shows the adequate excretion of the remaining upper pole with undisturbed urine discharge (Fig. 5). Isotope renography showed perfect hippuran intake and rhythmic discharge (Fig. 6).

Discussion

The surgical interventions in the lower pole of the kidney with a double collecting system are not as frequent as those in the upper one. This is partly due to the fact that involvement of the lower pole of the kidney occurs more rarely, and partly to that, during marked destruction of the parenchyma, the urologist is more liable to prefer the technically easier nephrectomy with less postoperative complications. At the same time, it cannot be guaranteed that vascularization of the remaining upper pole of the kidney should remain intact with an adequate subsequent function.

Assessing renal functions and renal vascularization, the perfection and the exact results of isotope renographic, gamma camera and angiographic examinations in the recent one-and-a-half decades represent a reliable aid in conservative surgery. Consequently, based on the current up-to-date conception, after careful consideration attempts have to be made to conserve the upper segment of the kidney.

The underlying disease in all four of our patients was stone. In this case, the possibility of recurrence should be reckoned with, therefore, beside saving the parenchyma, local lithogenic factors should be eliminated. Simple lithotomy can already at present not be considered to be a metaphylactic intervention. That is why, for example, in case of calyceal stones or stone nests polar resection is the procedure of choice.

In the presented cases, the late morphological and functional results are promising, recurrence of stones or stone formation in the remaining kidney cannot be seen.

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Über die Parenchymoperationen der unteren Nierenhälfte bei Pyelum duplex

F. GÖTZ, J. ZANA, J. HÜBLER und D. FRANG

In den dargestellten 4 Fällen handelte es sich um einseitigen Pyelum duplex mit einer Steinkrankheit im unteren Hohlsystem. In einem der Fälle wurde marginopolare Nephrotomie und in 3 Fällen Heminephrektomie der zerstörten unteren Nierenhälfte vorgenommen. Die zurückgebliebene obere Nierenhälfte zeigte in der späteren Periode in allen drei Fällen eine einwandfreie Funktion. Anhand der ermittelten Ergebnisse wird die Vermeidung der unbegründeten Nephrektomie empfohlen.

Об операции на Паренхиме нижней половины почки с двойной полостной системой

Ф. ГЕТЦ, Я. ЗАНА, Я. ХЮБЛЕР и Д. ФРАНГ

Авторы описывают 4 таких случая, в которых одна почка имела двойную полостную систему, с камнями в нижней системе полостей. В одном случае была произведена маргинально-полярная нефротомия, в трех же случаях произвели геминефрэктомии на погибшей нижней половине почки. Во всех трех случаях оставшаяся верхняя половина почки позже начала безупречно функционировать. Авторы подчеркивают необходимость избегать непоказанную нефрэктомиию.

Auto-alloplastics Closure of Cervical Esophageal Fistulae

G.Y. BORNEMISZA, E. TARSOLY, IRÉN MIKÓ and J. HAJDU

Institute for Experimental Surgery, Debrecen University Medical School, H-4012
Debrecen, P. O. Box 18, Hungary

(Received March 19, 1984)

The authors performed auto-alloplastic replacement with flap through a round incision, 20 to 22 in mm diameter, to elaborate a suitable method for closing the fistulae which may form during cervical esophageal operations. Of the animals three died due to other causes, the others could be evaluated, and, although the operated esophagus had not been relieved from inner pressure, after 24 hours the animals were capable of drinking, later eating. The auto-alloplastic flap was followed up by histological examination for six months.

After resection of the lower segment of the esophagus, reconstruction can be made by using stomach or jejunum. The replacement of cervical esophagus is, however, more problematic. Several attempts have been made at applying free stomach, and jejunal or ileal autografts using microvascular surgical techniques, but finally, colonic interposition proved to be the best solution [3–17]. The isolated right colon with intact vascular-neural connections, is most often pulled through a mediastinal tunnel and an anastomosis is constructed with the esophagus or the pharynx at the upper, and with the stomach at the lower end of the colon. The most frequent complication is cervical fistula formation and possible necrosis of one part of the colon. These complications are fatal in a large per cent of the cases unless an adequate solution is found for replacing the tissue defect. For this purpose, skin grafting was used, sometimes repeatedly, but often without success. To solve this question, auto-alloplastic skin grafting already used by us was applied experimentally. The auto-alloplastic method has already been used by us in other organs, too, as e.g. for replacing the bladder [1], and the ureter [2], that is in places where the new formation is exposed to internal pressure and may contact corrosive fluids. The essence of this procedure is that a thin plastic net inducing cell proliferation (in our case it was a polyamide net) was sewn over a polymethylacrylate cylinder. The cylinder was aseptically implanted into the neck in the vicinity of the esophagus and was left there on an average for three weeks. The cylinder was left in place in the experiments sometimes even for four to five weeks. Three weeks, however, seem to be sufficient and this period can also be endured by the patient in the

hope of success unless it is about an urgent solution. An undeniable drawback of auto-alloplastic grafting technique is the waiting time but this has to be accepted. As a result of the proliferative effect of these plastic materials (the synthetic resin cylinder and the polyamide net), mesenchymal cells invade the holes of the net, aggregate over the surface of the plastic cylinder producing a structure which reinforces the net. This auto-alloplastic structure is well vascularized. After the waiting time the operation proper will take place.

Description of the Operation

Esophageal replacement with flap was made in 28 dogs. The first three operations were considered to be preliminary experiments. A right paramedian incision was made and the esophagus was exposed. It was isolated at a length of 5 to 6 cm and mobilized. Then the easily palpable acrylate cylinder was exposed with the polyamide net and together with the auto-alloplastic structure. The structure was cut longitudinally and the cylinder was eliminated. In our cases, the diameter of the cylinder was 7 mm, the length was 50 mm but in humans it can be larger, corresponding to the fistula formed or to the size of the tissue defect. The plastic net together with the tissues invading it, formed a rectangle. With its inner surface facing the lumen of the esophagus it was stitched by interrupted sutures into the edges of the 20 to 22 mm diameter hole made on the esophagus. The 3/0 black Perlon thread (i. e. non-absorbable suture material) fixed into the end of an atraumatic needle was used for this purpose. After inserting a single row of interrupted sutures, repositioning of the esophagus followed. By uniting the soft parts, the operation terminated.

No tube was inserted into the esophagus, but the dogs were given nothing to drink or eat during the first 24 hours. After 24 hours the animals were fed orally by milk and, after some days, they were given broth to drink, later with bread dipped in it. Thus, they were gradually being fed lumpier food with the exception of bones. The animals tolerated the operations well.

Two to 6 months after the second operation the animals were sacrificed and the macro- and microscopic findings were thoroughly studied. Of the animals three died due to other causes, while 25 animals could be evaluated.

A small piece of the auto-alloplastic formation to be implanted was taken for histology prior to the operation to come. This material is shown in Fig. 1, three weeks after the first operation. The additional figures show the histological findings after the subsequent operation in various periods after surgery. There was no disorder in the peristalsis of the esophagus. Since tissue replacement was limited only to a portion of the esophageal wall, swallowing remained undisturbed.

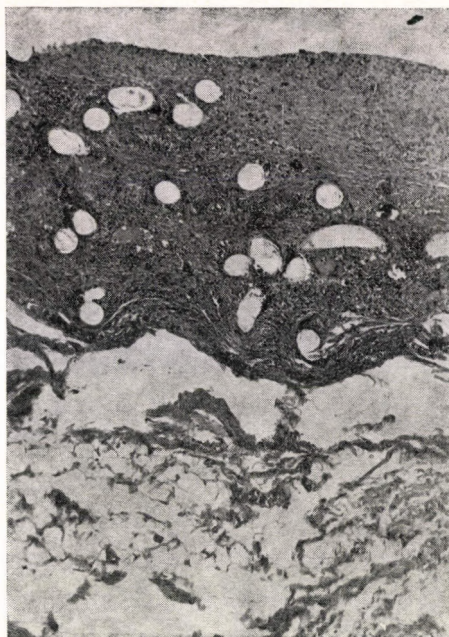


FIG. 1. Picture of the auto-alloplastic structure 3 weeks after the first operation before re-implantation. Among the fibres of the net, a compact tissue layer rich in cells and vessels has developed in which connective tissue fibres predominate. H and E, $\times 20$

Histological Results

Figure 1, as mentioned above, shows the newly formed material taken out but not re-implanted on the third week after the operation. Around the fibres of the net a resistant layer of tissue had developed. On the inner surface of the structure, a cell-rich granulation tissue could be found, the thicker outer layer was mainly composed of collagen bundles and adipose tissue. Here, several cross-sections of vessels could be seen among the fibres (small arteries and small veins, too).

After two weeks following the second operation the inner surface of the round auto-alloplastic flap, 20 to 22 mm in diameter, was intervoven circularly around the edges with epithelial tissue and a stratified non-keratinizing epithelium could be found. The section of the flap also contained cross-sections of polyamide fibres.

Figure 2 shows that after 3 weeks, the middle portion of the auto-alloplastic flap was still not covered by a continuous epithelial tissue and in this region a richly vascularized granulation tissue had grown with a minor leukocytic infiltration. The invading epithelial tissue practically isolated this region of granulation tissue showing inflammation from the subepithelial inflamma-

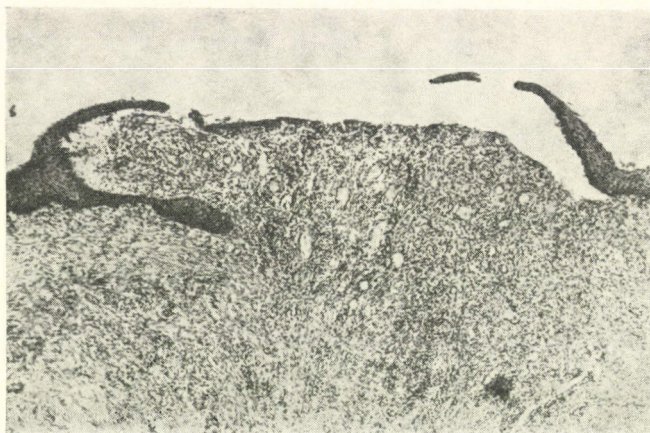


FIG. 2. Three weeks after the additional operation, the middle of the flap, 22 mm in diameter, is still not covered by a continuous epithelial tissue and in this region, a richly vascularized granulation tissue has formed which practically protects the underlying region until epithelialization is completed. Goldner staining, $\times 20$

tion-free portion where marked proliferation of connective tissue could be observed.

One month later, the entire inner surface of the flap was covered by a stratified non-keratinizing epithelium, in some places showing connective tissue papillae. Its substance was a fibrous connective tissue poor in cells. The whole region of the flap was somewhat displaced, since the surrounding intact parts protruded into the lumen as a result of the tone of the muscular layer.

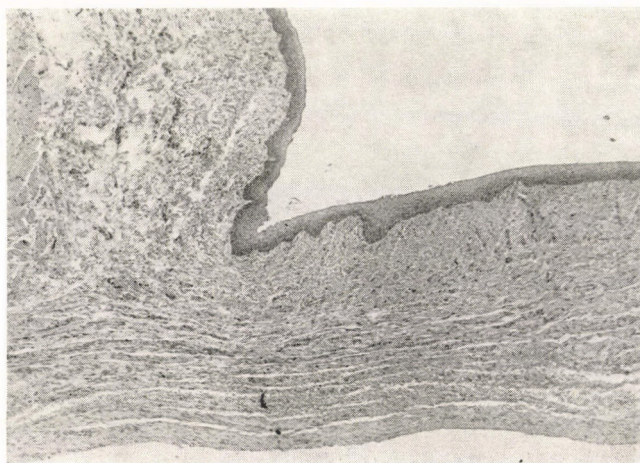


FIG. 3. After 5 months, in the replaced region, the esophageal wall is thinner than in the surrounding areas, but the mucosa consists of a thick regular stratified non-keratinizing epithelium with a loosely structured richly vascularized formation underneath. There is no dilatation. Goldner staining, $\times 20$

Figure 3 shows that after 5 months, in the area of replacement, the esophageal wall was thinner than in the surrounding region, but the mucosa was covered by a regular stratified, non-keratinizing epithelium with a loosely structured richly vascularized lamina propria.

In the 6-month-old auto-alloplastic flap, there was a regular epithelium under the lamina propria. Corresponding to the muscular layer there were several longitudinally transected vessels and along the vessels, the outermost layer was composed of clearly distinguishable outer smooth muscle bundles. These smooth muscle bundles cannot originate from the muscular layer of the surrounding intact region because this layer still consists of striated muscle tissue. On the border between the intact and replaced regions in some places the remnants of the tissue adhesive Histoacryl N-blue could be found with giant cells. The single row of knotted sutures had been fixed from the outside also with tissue adhesive for security reasons because in dogs esophageal sutures cannot be relieved by inner drainage.

This method has proved experimentally suitable for replacing the tissue defect of cervical esophageal fistulae, and no diverticula were formed at the site of intervention in some subsequently dissected animals. In the required region rather some concentric contractions appeared without producing any structure of the esophagus. Since nutrition of the dogs cannot be controlled to the same extent as in human patients, the procedure was subjected to a considerable strain confirming thereby the effectiveness of auto-alloplastic tissue grafting. The strength of the applied polyamide net is bound to decrease after a period of time but in the meantime, as a result of the aggregation of autologous tissues, this has been adequately compensated. Since in the esophagus there is no continuous inner pressure as in the arteries this solution has proved suitable.

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Verschluß von zervikalen Ösophagusfisteln mit autoalloplastischem Verfahren

GY. BORNEMISZA, E. TARSOLY, I. MIKÓ und J. HAJDU

Bei 28 Hunden wurde der fenestrierte Ersatz der experimentellen runden Öffnung ($\varnothing$: 20–22 mm) mit der auto-alloplastischen Methode angebracht, mit dem Ziel ein entsprechendes Verfahren zum Verschluß der im Laufe von zervikalen Ösophagusoperationen eventuell zustandekommenden Fisteln zu entwickeln. 3 der Tiere gingen wegen anderer Ursachen ein, die übrigen Fälle erwiesen sich als bewertbar; obwohl es nicht zur Entlastung der operierten Speiseröhre kam, konnten die Hunde bereits nach 24 Stunden trinken und kurz darauf auch essen. Das Verhalten des autoalloplastischen Flecks wurde mittels histologischer Untersuchungen 6 Monate lang registriert.

Закрытие шейных фистул пищевода методом ауто-аллопластики

ДЬ. БОРНЕМИСА, З. ТАРШОЙ, И. МИКО и Я. ХАЙДУ

В экспериментах на 28 собаках авторы произвели замещение круглого дефекта диаметром 20–22 мм методом ауто-аллопластики, с целью разработки соответствующего способа для закрытия свищей, которые могут образоваться при операциях на шейной части пищевода. Три животных погибли по разным причинам, что касается остальных, то, через 24 часа после вмешательства, они могли пить, а затем и есть, хотя нагрузка с оперированного пищевода не была снята. В течение 8 мес авторы следили за поведением ауто-аллопластической заплаты с помощью гистологических анализов.

Experimental Retroperitoneal Infection

E. KISIDA¹, I. HARKA¹, CH. OKEKE¹ and L. BERTÓK²

¹2nd Department of Surgery, Semmelweis University Medical School, H-1096 Budapest, Nagyvárad tér 1, Hungary and ²National Institute of Radiobiology and Radiohygiene, H-1221 Budapest, Pentz K. u. 5, Hungary

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A bacterial inoculum was positioned intraperitoneally and retroperitoneally in animals who had been treated with various antibiotic programs. The results indicate that the retroperitoneal tissue is more resistant to severe infectious complications than the general peritoneal cavity.

The clinical impression is that bacterial seating of the free peritoneal cavity will less frequently lead to a severe septic process than when a similar inoculum is placed in the retroperitoneum. Meyer [2] in 1934 supported this impression with laboratory studies showing that a bacterial inoculum positioned in the retroperitoneum more frequently led to abscess formation than that injected intraperitoneally [1]. However, similar animal studies have not been performed with the adjunctive use of antibiotics.

The present experiments were designed to evaluate the relative resistance of the retroperitoneum and the general peritoneal cavity to an inoculum of bacteria concomitant with, and without concurrent antibiotic administration.

Materials and Methods

R/Amsterdam $\times$ Long Evans F₁ hybrid female rats weighing approximately 160 g were used for this experiment. An inoculum of 20 g of a dry homogenate of faeces mixture originating from a group of animals of the same cage, was dissolved in 0.9 ml normal saline. In previous experiments this inoculum was equivalent to an LD of 75%. The inoculum was introduced by a small laparotomy into the free peritoneal cavity or into the retroperitoneum just below the lower pole of the left kidney. The animals were anaesthetized with Nembutal. The intraperitoneally and retroperitoneally inoculated rats were divided into three groups. Group 1 received no antibiotics, Group 2 received an i. m. antibiotic consisting of gentamycin (0.25 mg/100 g body weight) and carbinacillin (10 mg/100 g body weight) immediately after the insertion of the

inoculum and repeated twice daily for 7 days. These antibiotics were chosen because the organisms having grown from the faecal homogenate were sensitive to this antibiotic coverage. A third group was treated with wide spectrum antibiotics consisting of chloramphenicol, 5 mg/100 g body weight for 7 days. The animals were kept on rat food and tap water and observed for 7 days, at which time an autopsy was performed. Statistical analysis was performed by the chi-square analysis.

Results

Bacteriologic examination of the homogenate showed an intestinal flora of *E. Coli*, *Proteus vulgaris*, *Serratia marcescens*, *Enterococcus*. Table I summarizes the death rate in these animals. In the group treated by gentamycin and carbinacillin no deaths were experienced in either group. The groups treated with chloramphenicol or with no antibiotic showed a significant improvement in

TABLE I

Antibiotic treatment	Route of infection		Value
	Intraperitoneal death ratio	Retroperitoneal death ratio	
None	8/8	5/8	0.05
Gentamycin and carbinacillin	0/0	0/0	N.S.
Chloramphenicol	7/8	3/8	0.05

survival when their inoculum was positioned in the retroperitoneum as opposed to when it was placed in the peritoneal cavity. Autopsy evaluation of the intraperitoneal group showed that in the animals not treated with antibiotics a diffuse peritonitis was present. In the group treated with gentamycin and carbinacillin there was no evidence of abscess formation or diffuse peritonitis with the exception of one animal where a 0.5×0.5 cm abscess was present in the splenic hylum. In the chloramphenicol-treated group the only survivor had large abscesses throughout the abdomen. The autopsy findings of the retroperitoneally-injected group show that in the non-antibiotic group and in the chloramphenicol-treated group, there was a 1 cm diameter abscess with a thick wall at the site of inoculation. In the animals treated with gentamycin and carbinacillin a smaller, 2–3 mm diameter abscess was found in the same location. (Preliminary experiments in animals treated in the same manner had shown that at 4 weeks there was complete encapsulation of the abscesses).

Discussion

Whether the retroperitoneum or intraperitoneal cavity is more able to handle an inoculum of bacterium is clinically relevant to the general surgeon. The issue presents itself at the time of duodenal mobilization and during colon surgery particularly during a low anterior resection and at the deliberation if one should attempt to retroperitonealize the pelvis. Similarly, during the drainage of abscess, it has to be decided whether drains should transverse the peritoneum or retroperitoneal tissue?

The results of this animal experiment suggest that the retroperitoneum is more effective than the peritoneal cavity in controlling a spillage of bacteria during an operative procedure, particularly if the antibiotics administered are less than ideal for the actual organisms that have been implanted. The results of this experiment may be at variance with some clinical observations, however, patients who die with retroperitoneal abscess, frequently have concomitant intraperitoneal infection and it is suggested that the retroperitoneal phlegmons are terminal complications of suppurative peritonitis. Possibly, as in the animal experiments, the absorption of endotoxins from a large peritoneal surface may occur more rapidly and the development of endotoxic shock may be more profound when the bacteria are inoculated in the peritoneum [2].

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Resistenz gegenüber retroperitoneale Infektionen

E. KISIDA, I. HARKA, CH. OKEKE und L. BERTÓK

In der freien Bauchhöhle und im Retroperitoneum von Ratten wurde mit gemischter Dickdarmflora, klinische Verhältnisse nachahmende experimentelle Infektion herbeigeführt. Laut der Sektions- und Verendungsdaten vermag die Peritonealhöhle die Infektion in geringerem Maße zu lokalisieren als das Retroperitoneum. Den sich auf das unterschiedliche Verhalten der beiden Regionen beziehenden möglichen Erklärungen ist auch eine klinische Bedeutung beizumessen.

Резистентность в отношении ретроперитонеальных инфекций

Э. КИШИДА, И. ХАРКА, Ч. ОКЕКЕ и Л. БЕРТОК

Авторы инфицировали смешанной толстокишечной флорой свободную брюшную полость и перитонеальное пространство у экспериментальных крыс, что имитировало клинические условия. Как показывают данные вскрытий и детальности, перитонеальная полость в меньшей степени, чем ретроперитонеальная, способна к локализации инфекции. Возможные объяснения, касающиеся различного поведения этих двух областей, имеют и клиническое значение.

Percutaneous Aspiration Biopsy in Perineal Recurrences after Abdomino-Perineal Extirpations

A. ERŐS, L. RITTER and A. BAJTAI

2nd Department of Surgery and Institute for Pathology Postgraduate Medical Institute, H-1389 Budapest, Szabolcs u. 33, Hungary

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The authors recommend the introduction of percutaneous aspiration biopsy—a new method used by them for demonstrating perineal recurrences after abdominoperineal extirpations. The method is fast and easy to perform, simple and can be used for screening. It may be an addition to the therapeutic and diagnostic arsenal.

Every surgeon making rectal operations is extraordinarily afraid of perineal recurrence after abdominoperineal extirpations, which develop in a fairly large number—even according to literary data—in about 30 to 50% of the cases [1, 2, 3, 4, 5, 6, 7, 8]. The early stage of relapse is 'silent' producing no specific symptoms. By the time the region has become painful as a result of the compression of the nerves of the pelvis and when palpation yields positive result, it is too late making any intervention. The early diagnosis of the recurrence is very important because the effect of the 2000R irradiation administered at that time is probably better than that of the irradiation of the already palpable alterations. About 80% of perineal recurrences develop in the first two years postoperatively. Therefore routine control of the patients is by all means indicated at checkups made every three months in the form of screening [9]. The percutaneous biopsy developed by us is also adaptable to regular screening and suitable for demonstrating recurrences. This examination procedure is new. One reference was found in the literature where Zelas et al. [10] reported on the percutaneous biopsy with computed tomography. The computer tomography used at our Department is not adaptable to this purpose, therefore we use the so-called blind biopsy.

Material and Method

For the biopsy, the Menghini biopsy set, Truocut needle and the modified Vance prostatic biopsy instrument were used (Figs 1 and 2).

After local anaesthesia (1% Lidocaine), a histological sample is taken from the examined region. Using the needles, a tissue cylinder with a length of about

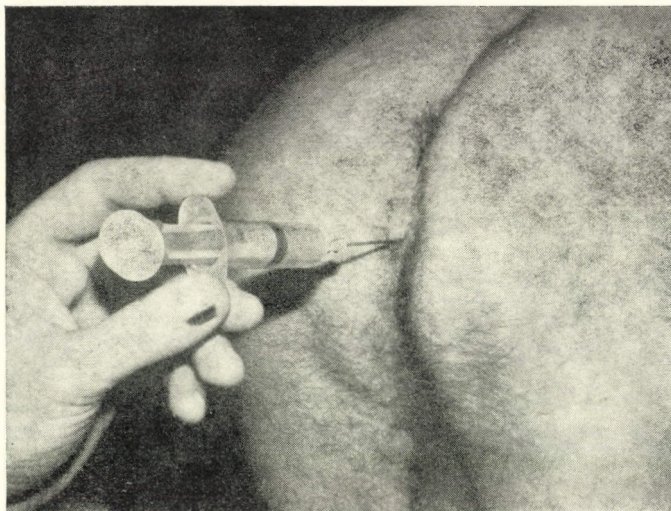


FIG. 1

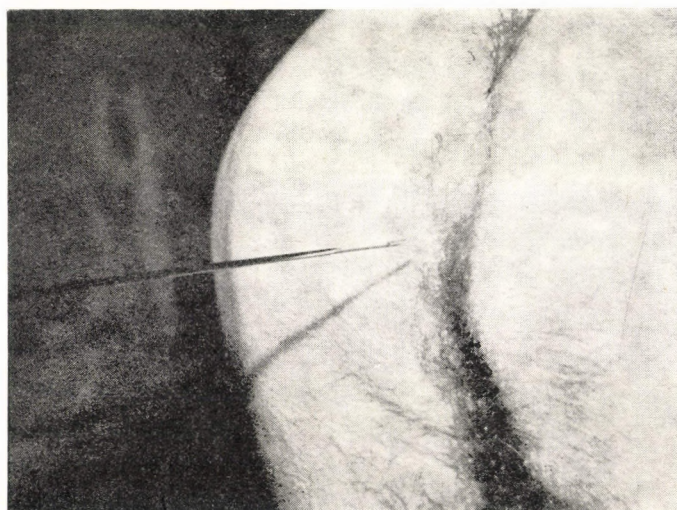


FIG. 2

1 cm and a width of about 2 to 3 mm can be obtained which is evaluated histologically.

The method was first used in 1983 at the 2nd Department of Surgery of the Postgraduate Medical Institute. It has so far been performed on ten patients, the number of samples being 12 (in two patients two biopsies were made). Each patient was male with a mean age of 56 years. One to three years have elapsed since their abdominoperineal extirpation. In one case, however, the biopsy was performed already four months after the operation (the latter was not made for screening). In six out of ten cases histology revealed a recurrence. Four patients presented at our proctological out-patient department with a marked perineal pain. Two patients mentioned the pain radiating into their thighs only when asked by the physician, and finally four patients were completely free of symptoms. The biopsy was performed as an out-patient procedure. Complications (bleeding, fistulization, etc.) did not appear.

Discussion

Following abdominoperineal extirpations, perineal recurrences appear in 30 to 50% of cases, the 80% of which already in the first two years [1, 2, 3, 4, 9].

The first symptom of relapse can be pain appearing in the sacral region and radiating into the thighs and the knees [1, 7, 8]. Perineal pain can therefore raise the suspicion of recurrence. It is usually fairly difficult to form an accurate diagnosis, although it is an imperative because the recurrences diagnosed at an early stage can be effectively treated by a radiation of 2000R.

It is known that the carcinoembryonic antigen (CEA) test, which is very expensive, can indicate only the development of liver metastases. Its diagnostic value has recently, just for this reason, aroused much controversy [7, 8]. The specific liver function tests, too, may help in judging the state of the liver.

The computer tomography used in Hungary (thus also at the Postgraduate Medical Institute) does not yield a safe diagnostic result. This is suitable rather for visualizing the mass filling out the whole perineum, at this time it can already be palpated through the skin. The radiotherapy administered at this stage is already, in most of the cases, ineffective.

By using this method developed by us histological diagnosis can be made by performing percutaneous biopsy of the studied region. The aspiration examinations are currently characterized by a renaissance.

Their introduction dates back to the 30s [11]. They were introduced into the everyday practice in the 60s. In Hungary, too, it is extensively applied for examinations of the breast, the thyroid, the prostate, the liver and the pancreas, etc.

The so-called fine needle aspiration can be used for cytological tests. By the generally applied coarse needles used by us for examination of the perineum, histological results are obtained which in any case may help in reaching a more accurate diagnosis than cytological sampling does where opinion must be based on 20 to 25 cells.

In the first four patients, beside histological study, also cytologic sampling was made by performing biopsy with a fine needle. This was required because the cytological result was obtained immediately after the examination, while histological evaluation takes a longer time.

For percutaneous perineal biopsy, in addition to sampling needles, only lidocaine is needed for local anaesthesia and it can be performed on an out-patient basis. It can be used as a routine follow-up for screening at every three months. During our examinations no complications occurred.

Conclusions

- After abdominoperineal extirpations perineal relapses occur in a fairly great number of cases. For their diagnosis percutaneous sampling by puncture is suitable.
- It helps in obtaining histological result.
- The recurrences recognized at an early stage by the percutaneous biopsy made by puncture can be irradiated more effectively.
- The method is suited for the purposes of screening and can be made as an out-patient procedure.
- It is simple to perform and complications do not occur.

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Perkutane Aspirationsuntersuchung der sich nach abdominoperinealen Exstirpationen entwickelten perinealen Rezidiven

A. ERŐS, L. RITTER und A. BAJTAI

Zum Frühhnachweis der sich nach abdominoperinealen Exstirpationen entwickelten perinealen Rezidiven wird eine neue Methode, die perkutane Aspirationsbiopsie empfohlen. Die Anwendung der schnell und leicht durchführbaren, einfachen, auch zu Reihenuntersuchungen geeigneten Methode, bietet eine nützliche Möglichkeit zur Erweiterung des therapeutischen und diagnostischen Arsenal.

Перкутанное аспираторное исследование перинеальных рецидивов, возникших после абдоминоперианальных экстирпаций

А. ЕРЕШ, Л. РИТТЕР и А. БАЙТАИ

Авторы рекомендуют ввести применяемый новый метод — перкутанную аспираторную биопсию — для раннего выявления перинеальных рецидивов, возникающих после абдоминоперианальных экстирпаций. Метод легко и быстро выполняется, является простым, пригодным для профилактического обследования. С его помощью можно расширить терапевтические и диагностические возможности.

‘Nipple’ Ureterocutaneostomy

A. JILLING and D. FRANG

Department of Urology, Pécs University Medical School, H-7621 Pécs, Munkácsy Mihály u. 2. Hungary

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In 4 years the authors performed 25 cases of ‘nipple’ ureterocutaneostomy elaborated by them. The essence of the operation is that by using skin grafts, the stoma emerges by 1.0 to 1.5 cm above the surface of the skin. Without ureteral drainage, their patients use disposable DANSAC ileostomic urine collecting sacs which can be attached to the skin. This method is presented in detail and the results are evaluated. In case of an adequately long and wide ureter, they consider their surgical procedure to be suitable for permanent supravescical urine excretion.

One of the methods of supravescical urinary excretion is ureterocutaneostomy. The first cutaneous ureterostomy was performed by Simon [10] in 1875. At the beginning, ureters were drained by rubber then plastic tubes which had to be changed from time to time. Even the strictest observance of sterility could not prevent infection arising at drainage which, sooner or later led to chronic pyelonephritis, secondary calculus formation, then to a gradual deterioration of renal function. Without drainage of the ureters, by using urine collecting receptacles, these complications can be avoided.

With technical advancement, a large variety of urine collecting receptacles have become available. Still the spread of this method is limited to some extent mainly by that the lumen of the ureter can be narrowed down in the subcutaneous connective tissue, primarily in the case of ureters of normal lumen [7, 11, 12].

In order to facilitate the use of urine collecting receptacles, it is advisable to bring the ureter above the surface of the skin by applying a skin-tube. Le Dentur [1] was the first to report on the use of a skin flap in 1889, and subsequently a large number of surgical procedures were published [2, 3, 4, 7, 8, 9, 13].

At our Department ‘nipple’ ureterocutaneostomies have been performed in the recent four years, and our patients use ‘DANSAC’ ileostomic urine collecting receptacles.

Method

A 10 to 12 cm long incision is made in medial direction at the level of the anterior iliac spine. After transection of the fascia and muscles, the ureter is

exposed in the retroperitoneal space and dissected as deep as possible towards the bladder. The lower segment of the ureter is mobilized so that it can be brought to the surface of the skin without tension. Then the fascia and the muscles are excised in an area of 1 to 2 cm diam. where the ureter has been pulled out, to prevent the compression of the ureter during wound healing. The muscles and the fascia, with the exception of the excised region, are sutured. Then to create a 'nipple' the skin is resected. A schematic drawing of this is presented in Fig. 1a-f. In the middle of the skin incision two deep perpendicular incisions of 3 to 4 cm are made (Fig. 1a). The cross-hatched areas shown in Fig. 1b are resected from the end of the initial incision at both sides up to the

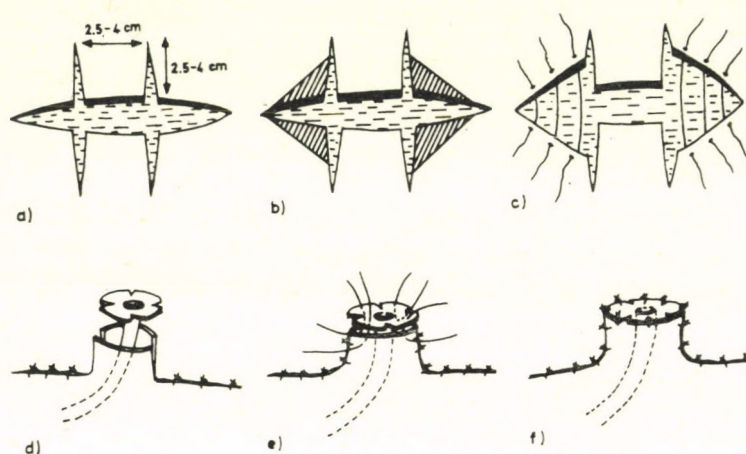


FIG. 1. Method of 'nipple' formation

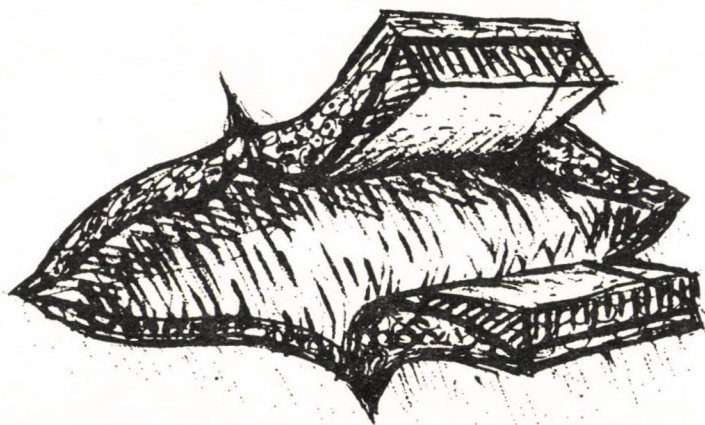


FIG. 2. Method of removing the subcutaneous adipose tissue of skin flaps



FIG. 3. The 'nipple' after removal of the splinted sound



FIG. 4. Urine collecting sac placed on the stoma

middle of the skin flaps. Figures 1c and 2 show the skin surface after resection. Subcutaneous sutures are placed lateral and medial to the skin flaps and the skin is sutured (Fig. 1d). Then the edges of the skin flaps are united (Fig. 1e), and, finally, after incising the ureter, circular subcutaneous sutures are inserted (Fig. 1f). Depending on the lumen of the ureter a silicon-coated 8 to 12Ch plastic tube is used for draining the ureter during wound healing for a period of 8 to 10 days. Figure 3 shows the 'nipple' created after removal of the drain. Figure 4 demonstrates the state after attaching the urine collecting receptacle.

Patient Material

In our clinic 25 cases of 'nipple' ureterocutaneostomies were performed in four years. The distribution of patients according to their underlying disease is presented in Table I. In 3 of the patients with bladder tumour, a combination

TABLE I
Distribution according to the underlying disease

Bladder tumour	14
Gynaecological tumour	8
Vesicovaginal fistula	2
Tuberculous atrophied bladder	1
Total	25

of cystectomy and of contralateral nephrectomy was performed. In the other bladder cancer patients and in those with gynaecological tumours ureterocutaneostomy was made always unilaterally and for palliative reasons. In case of two unreconstructible vesicovaginal fistulae the unilateral outlet was solved by transuretero-ureterocutaneostomy. Our tuberculous patient had already undergone a contralateral nephrectomy.

Table II shows the distribution according to number and years of operations and to complications. Thirteen of the patients died due to their underlying disease within one year, 12 have survived. Necrosis of the 'nipple' occurred only in 3 cases in the initial period. In two patients the terminal portion of the ureter constricted (in these patients ureterocutaneostomy was made with a ureter of normal lumen). In 2 patients with necrosis of the 'nipple' and in one with strictures reconstructive operations were performed, the results of which are going to be reported later on. Finally, 10 of 12 still surviving patients (together with the 3 reconstructive operations) function without drain in the ureter.

TABLE II

Distribution according to the number and years of operations and to complications

Years	No. of operations	Deaths	Survivals	Necrosis	Stricture	Without drainage
1980	8	5	3	1	0	2
1981	9	4	5	2	1	2
1982	5	3	2	0	1	1
1983	3	1	2	0	0	2
June 30						
Total	25	13	12	3	2	7

Discussion

In the present report, the indications of ureterocutaneostomy have not been discussed because these will be dealt with elsewhere [5]. Here only the contraindications are mentioned.

Our method is contraindicated in (i) extremely fat patients, mainly with pendulous abdomen; (ii) in skin diseases where an undisturbed wound healing cannot be expected or a urine collecting receptacle cannot be used; (iii) if the ureter to be used is so short that it cannot be brought to the surface of the skin without tension even in case of a 'high' ureterocutaneostomy [4].

Our 'nipple' creating method is similar to that of Lurz differing, however, in the resection of subcutaneous tissue and skin as well as in the surgical technique of the performance of ureterocutaneostomy. If in the thick subcutaneous adipose tissue the subcutaneous layer is removed obliquely from the edge of the skin flap to the bottom as seen in Fig. 2, skin necrosis ('nipple' necrosis) can be safely avoided. The created 'nipple' should not be longer than 1 to 1.5 cm. 'Nipple' formation is, however, very important because in the recumbent position the urine does not soak the surface of the skin, the wall of the thin polyethylene sac sticking to it can drain the urine. Using our own skin resection and subcutaneous tissue resection techniques combined with the excision of the fascia and the muscles can help in avoiding the stricture of the terminal ureteral portion. Based on our experiences made so far, the present method, in case of a wide ureter, can be used for permanent supravescical urinary excretion. In case of a ureter of normal lumen, development of a stricture over the surface of the skin can unfortunately not be prevented therefore it is not advisable to perform ureterocutaneostomy in this form. In a ureter of normal lumen, development of a stricture on the surface of the skin can be avoided by using a portion of the trigone. Experiments are being made too, with new methods using a Gore-tex vascular prosthesis and a reversed skin graft. These results will be reported later on.

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Ureterokutaneostomie mit „Mamilla-Bildung“

Á. JILLING und D. FRANG

Im Verlauf von 4 Jahren wurden mit der im Institut entwickelten „Mamilla-Bildung-Methode“ 25 Ureterokutaneostomien durchgeführt. Das wesentliche des Eingriffs ist die Anforderung, daß sich das Stoma 1.0 bis 1.5 cm über die Hautoberfläche vorwölbt. Die Patienten bedienen sich ohne Ureterdrainage, eines auf die Haut geklebten DANSAC ileostomischen, zur Harnsammlung dienenden Einmal-Beutels. Nach ausführlicher Beschreibung der Methode und der Auswertung der Ergebnisse wird betont, daß sich das Verfahren — im Falle eines entsprechend langen und weiten Ureters — zur definitiven supravescikalen Harndeviation eignet.

Уретерокутанеостомия с созданием «соска»

А. ЙИЛЛИНГ и Д. ФРАНК

За 4-летний период авторы в 25 случаях произвели уретерокутанеостомию разработанным ими способом создания «соска». Суть операции в том, чтобы, с помощью кожных лоскутов, приподнять поверхность стомы над поверхностью кожи на 1,0–1,5 см. Больные применяли без дренирования мочеточника илеостомический мешочек-мочеприемник однократного пользования DANSAC, который можно приклеить к коже. Авторы подробно описывают свой метод и анализируют полученные результаты. Настоящий метод они считают подходящим — в случае достаточно длинного и широкого мочеточника — для окончательного суправезикального отвода мочи.

Correlation between the Incrustation of Intrauterine Devices and the Duration of their Use

K. PATAI, M. BERÉNYI and M. ASZTALOS

Departments of Gynaecology and Obstetrics, Korvin Ottó Hospital of the Ministry of the Interior, H-1071 Budapest Gorkij fasor 9–11, Hungary and Department of Urology, Semmelweis University Medical School, H-1085 Budapest, Mária u. 39, Hungary

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The usefulness and side-effects of intrauterine contraceptive devices (IUDs) are evaluated on the basis of various aspects (e. g. effect of postabortal and postpartal insertion, expulsion of device, frequency of pregnancies, bleeding and inflammation, etc.) [1, 2, 3, 4]. However, the incrustation of the device has been ignored although the coating on the major part of the surface is easy to study. The rough surface coating is very likely to be associated with some side-effects [5].

In our report we have tried to find some links between the degree of incrustation and the duration of using the device.

Method

Devices were observed mostly during control examinations and, to a lesser extent, because of complications. A total of 56 devices were analysed. Of them 47 were Szontágh's, 5 Copper T, the others Gravigard, Multiload Cu 250, Lippes loop and T. coil types. After extraction the device was carefully rinsed with distilled water and left to dry at room temperature.

The amount of calcium carbonate in the incrustate was determined as follows. The dry device was weighed by an analytical balance and placed in 2 M hydrochloric acid. Then the inorganic part of the incrustate dissolved with bubbling. When development of carbon dioxide had stopped (in 1 to 5 minutes) the IUD was removed from the acid and washed in distilled water, dried and repeatedly weighed. The difference in the two measurements, although the coating contains some calcium phosphate, too, responds to the mass of calcium carbonate. During dissolution in hydrochloric acid, some of the organic substance (matrix) on the device dissolves, the majority remaining, however, on the device.

The calcium carbonate-free matrix adhering to the device was removed mechanically by a wet nail-brush. The difference between the mass measurement before and after the cleaning gave the amount of matrix in the incrustate of the Szontágh device. During extraction of the devices — mainly if it was not

done by the string, some of the incrustate might be lost and therefore the actual amount of incrustate on the devices could only be more than found.

Results

Although several elements have been shown in the incrustate by x-ray microanalysator (Ca, Mg, Cu, Na, K, P, S, Cl) [5], based on the infra-red spectrum, the only compound, we have found was calcium carbonate [5]. Figure 1. shows the amount of calcium carbonate deposit plotted against the duration of use. The linear regression line ($y = 2.4 X + 4$) and the correlation coefficient

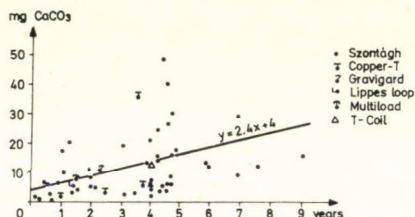


FIG. 1. The amount of calcium carbonate deposited on IUDs as plotted against the duration of use

were calculated for the Szontagh devices but the Figure shows data of other IUDs, too. The correlation between the degree of incrustation and the duration of use ($r = +0.42$) and the fact that, e.g. the amount of incrustate having formed in four years falls between wide limits (2–40 mg), reveal that the individual differences are significant. The scatter among our data will be illustrated with four extreme cases. There was 22 mg of incrustate (17.5 mg calcium carbonate and 4.5 mg matrix) on a Szontagh device used for 13 months, but the same amount (16 mg CaCO_3 and 6 mg matrix) was found on another one used for 9 years and 2 months. On a Copper-T device having been used for 3.5 years, 36 mg calcium carbonate had deposited, while only 4 mg on a similar one used for 4 years. After some time of usage incrustate appears on each kind of device.

There is a closer correlation ($r = +0.81$) between the amount of calcium carbonate and the amount of matrix in the incrustate (Fig. 2.). There is hardly any correlation between the duration of use and the amount of matrix.

The degree of incrustation depends not only on the material of the device and on its surface properties. This is proved by finding privileged or predisposing regions on the devices where the coating appears the most often and in the largest amount (Fig. 3). Strikingly, the non-incrustating parts are not coated even after a use for 10 years. The degree of incrustation of the Szontagh devices having deformed on extraction and not in situ and those having preserved

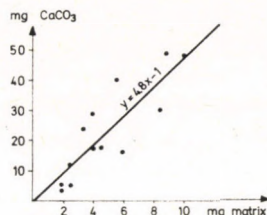


FIG. 2. Correlation between the amount of calcium carbonate in the incrustate and the amount of matrix

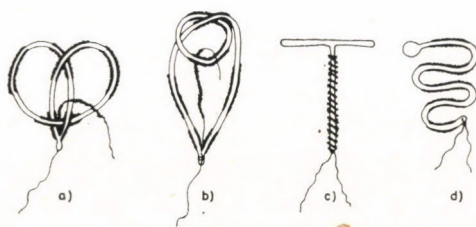


FIG. 3. Frequent sites of incrustation (solid line); a. regular Szontágh-device, b. deformed Szontágh-device, c. Copper-T, d. Lippes loop

their initial form (Fig. 3a, b) did not differ from each other. The string entering the uterine cavity (Fig. 3a) is coated just like, or still more than, the other parts of the device, as a result of which the diameter of the string may even exceed 1 mm.

Discussion

The rough calcium carbonate coating of IUDs as well as the inflammation caused by it are hardly needed for the contraceptive effect since even the non-, or only slightly, incrustated device is effective. The development of an incrustate should be considered an undesirable complication or the cause of additional complications. The hollow, uneven coating is an excellent hiding place for pathogens [7]. According to Spaiks [8], bacteria entering via the string, not the intrauterine portion of the device, give rise to endometritis. If this were true, and the incrustate were produced by bacterial effect, there would be no calcareous coating on the devices without a string. Such investigations are in progress. Otherwise as a result of factory packing, one strand of the string of the Szontágh device often remains in the uterine cavity on insertion. In this case there is only one strand in the cervix instead of two, but this does not produce any changes in the degree of incrustation.

Incrustation occurs at various paces in the different parts of the surface of the device. Calcium carbonate deposits occur in various privileged regions

in different kinds of devices, too. The typical sites of incrustation are arranged symmetrically (Fig. 3). There is yet no explanation for that. It is perhaps the direction of uterine contractions and of intrauterine fluids as well as the deforming capacity of the devices which may play various roles. In the copper-containing devices (Copper-T, Gravigard) mainly the metal-wire part shows incrustation and, therefore, depending on the degree of incrustation the speed of copper deposition is reduced. The Lippes loop was most considerably calcified along the straight segments as opposed to the 'head' and the 'elbow'.

According to Shaw [9], IUDs produce increased vascularization affecting mainly the small calibre surface vessels of the endometrium. On this basis, the irregular bleedings, but even the mycotic infections which get an easier access via the incrustated devices, can be attributed to the rough incrustate.

It is questionable after what time and at which intervals the removal or exchange of IUD is recommended. In view of the large scatter in the degree of incrustation, this study cannot yield any comprehensive answer.

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Das Verhältnis zwischen der Inkrustation der intrauterinen Antikonzipientgeräte und der Tragezeit

K. PATAI, M. BERÉNYI und M. ASZTALOS

Unter Verwendung von 56 intrauterinen Antikonzipientgeräten unterschiedlichen Typs wurde der zwischen der Tragezeit und dem Kalzium-Karbonatgehalt des Inkrustats bestehende Zusammenhang untersucht. Im Hintergrund des niedrigen Korrelationskoeffizienten ($r = +0.42$) steht eine bedeutende Streuung.

Einige Teile der Geräteoberflächen neigen besonders zur Inkrustation, weshalb für einen Teil der durch die Geräte verursachten Komplikationen wahrscheinlich das grobe Inkrustat verantwortlich ist. Beim Vergleich der Effektivität der Geräte sollte somit auch das Maß der Inkrustatbildung in Betracht gezogen werden.

Связь между инкрустированием внутриматочных противозачаточных средств и продолжительностью их применения

К. ПАТАИ, М. БЕРЕНИ и М. АСТАЛОШ

Мы изучали связь между сроком ношения и содержанием Са-карбонатной инкрустации на 56 штуках внутриматочных противозачаточных средств различного типа. Выявленное низкое значение корреляционного коэффициента ($r = +0,42$) указывает на значительное стандартное отклонение.

Отдельные части поверхности противозачаточных средств особенно склонны к инкрустированию. По-видимому, за некоторую долю осложнений, вызываемых противозачаточными средствами, ответственной является грубая инкрустация. При сравнении эффективности разных противозачаточных средств, надо принимать во внимание, среди прочих моментов, также степень образования инкрустации.

Bilateral Urological Tumours

M. FEHÉR, A. VARGA and J. PINTÉR

Department of Urology, Debrecen University Medical School, H-4012 Debrecen,
P. O. Box 29, Hungary

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In the 5-year period between January 1, 1977 and December 31, 1981, 6 patients with bilateral urological tumours localized in various organs were treated at the Department of Urology, Debrecen University Medical School.

As compared to earlier results, the survival of patients with bilateral adrenal renal and testicular tumours may be improved by the early diagnosis, immediate and adequate treatment, by a careful follow-up lasting for years and, when needed, by a delayed intermittent chemotherapy.

In recent years, the number of patients with malignant urological tumours has increased. Bilateral urological tumours, too, are more often encountered [12]. It has still not been proved whether the tumours have become more frequent or this observation is only due to more recent diagnostic possibilities, to a better general patient care or to the lengthening of the patients' life-span. A final statement can only be made on the basis of further statistical evaluations.

Patient Material

Between 1977 and 1981, 6 patients were treated for bilateral urological tumours.

Bilateral phaeochromocytoma

L. T., a nine-year-old boy was admitted to the Department in 1977 because of paroxysmal hypertension and a severe headache. The laboratory findings and the characteristic radiological changes (Fig. 1) raised the suspicion of phaeochromocytoma. After the removal of an about nut-sized resistance, during the exploration of the right adrenal gland the symptoms vanished. Histological diagnosis was phaeochromocytoma. The postoperative phase was uneventful, substitution was not necessary.

In 1981 the child was readmitted to hospital because of a headache and hypertension. The increase of daily vanilin-amygdalic acid discharge (75 $\mu\text{mol/d}$) repeatedly suggested the possibility of phaeochromocytoma. Total abdominal angiography showed enlargement of the left adrenal gland (Fig. 2). After the

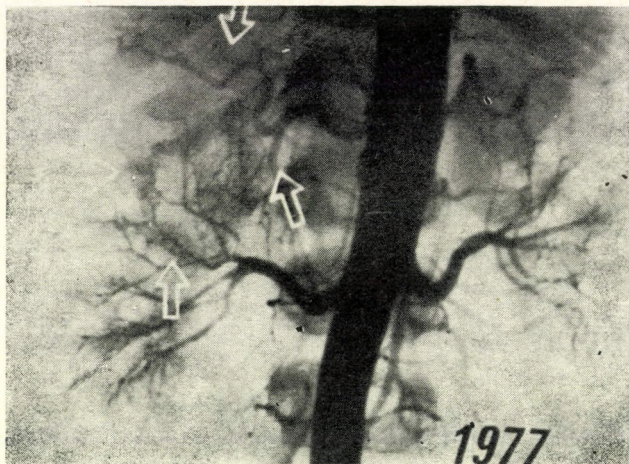


FIG. 1. Aortogram, arterial phase. In a region, the size of a 2 Forints coin, corresponding to the right adrenal gland, a slight hypervascularization is present. The arteries running here are of tumorous character. They are winding and show fluctuations in calibre. The main nutrient artery is the middle suprarenal artery

necessary preparation, left lumbotomy was performed, the twelfth rib was resected. The tumour situated in the adrenal gland was removed together with the gland. Histological diagnosis was phaeochromocytoma. After two years the child is free of complaints.

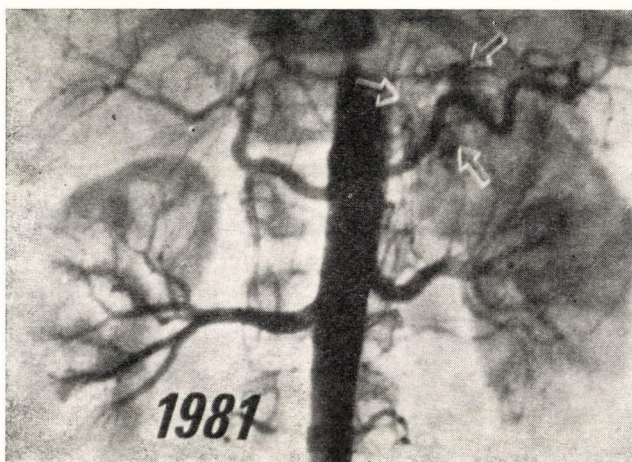


FIG. 2. Aortogram, arterial phase. In the region, the size of a 2 Forint coin, corresponding to the left adrenal gland, hypervascularization, while in the arteries a rough fluctuation in calibre can be seen. The nutrient arteries derive from the inferior phrenic and the inferior suprarenal arteries

Bilateral renal tumours

In the period given above, three patients were monitored. In one patient the intravenous urography indicated characteristic changes in one side, and selective angiography was performed only on this side. In the contralateral kidney, the intravenous urography revealed only slight alterations which was not evaluated as pathological. Half a year after removal of the tumorous kidney, the radiological study due to a newer episode of haematuria disclosed an inoperable renal tumour in the remaining kidney. This case taught us that in case of a renal tumour, even if there is only a slight change in the other kidney, it is advisable to perform total abdominal aortography first to be followed by selective renovasography.

In one patient the renal tumour gave rise to cerebral and bone metastases, the pathologist found a tumour of about the size of a nut in the other kidney.

Sz. L., a male patient aged 50 years, was referred to us due to haematuria. Bilateral renal tumours were diagnosed (Fig. 3). Because of the weak general state of the patient, the operation was performed in two sessions. First the larger left renal tumour was removed through a Nagamatsu thoracolumbotomic incision. After hilar compression the lower pole of the kidney and a part of the middle segment were removed, then lymphadenectomy, too, was made. The pa-



FIG. 3. Intravenous urography. On the left, there is a space reducing process, of the size of a fist. On the right, the lower calyces are moderately deformed

tient's renal function tests were approximately normal one month after the operation. Intravenous urography revealed the adequate function of the right upper calyx (Fig. 4).

Bilateral testicular tumours

Two patients were treated. In one of them seminoma was developing successively. After castrations, irradiation was performed. Presently, there is no evidence of metastasis. The patient has been living for five years after the first tumour.

Cs. L., a patient aged 23 years was found to have a simultaneously occurring embryonal carcinoma. Establishment of diagnosis was rendered difficult by the localization of the tumour, since it appeared that the small resistance on the right side was due to epididymitis. AFP remained elevated after castration of the left side, and lymphography, too, indicated right lymph node metastases. As a result, exploration of the right testicle was indicated. It revealed bilateral testicular tumours. After removal of the tumorous testicle radical lymphadenectomy was performed, then combined cytostatic treatment was administered for two years. The patient has been free of complaints for three years with no evidence of metastasis. The tumour markers were negative.

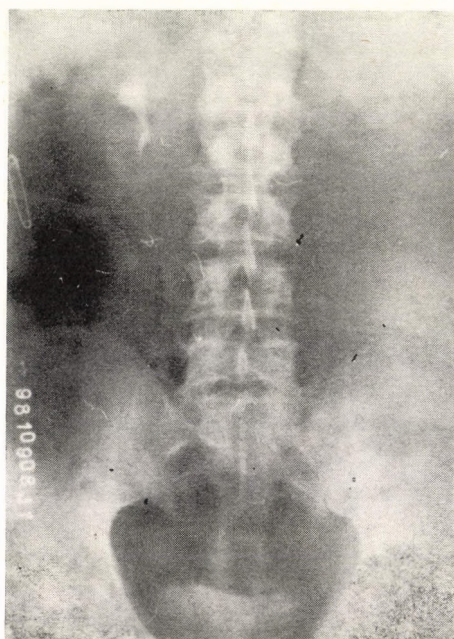


FIG. 4. Intravenous urography (control). Picture taken one month after the renal operations, shows the upper pole of the right kidney with a good function

Discussion

Bilateral urological tumours can occur simultaneously and successively. At present it has not been clarified whether the simultaneously or successively occurring tumours are two primary tumours of the same type or it is about the metastasizing of one of the tumours forming in one of the homotypes. Based on our earlier experiences, both forms may occur.

It is not always easy to diagnose bilateral urological tumours, since the pace of tumorous growth generally varies. Therefore, even x-ray examination cannot provide reliable information in each case. On suspicion of tumour it should be confirmed or excluded by using non-invasive or, in certain cases, also invasive methods [1, 10].

The development of diagnostic procedures has made possible not only the recognition of simultaneous bilateral tumours but also the chances of the operation.

Also in case of bilateral tumours the patients' life should be prolonged by the treatment and complete recovery should be achieved, depending on the histological result and the advanced stage of the tumour.

On treating patients with phaeochromocytoma, radicality was aimed at [4, 10]. The peculiarity of our case was emphasized by the fact that it was believed at first to be a recurrence and only the radiological examination indicated the development of an additional tumour.

Phaeochromocytoma occurs in general in adults. It can be encountered in children only sporadically [13]. Bilateral phaeochromocytoma occurs in children in about one-fourth of the cases [7, 15]. The disease is more frequent in boys than in girls [8].

Bilateral renal tumours can be surgically treated in one or two sessions. If the renal tumour is smaller on one side and can be resected together with the renal parenchyma, an organ preserving operation can be made. In this case resection of the lower or upper pole or enucleation of the tumour can be performed. On removal of the tumour hypothermia should be indicated considering each case individually. An extracorporeal operation should be indicated only if, after removal of the tumours, reconstruction of the calicopelvic system requires a longer time [2, 9, 14].

In bilateral renal tumours, either in case of removal of the kidney or in that of organ preservation, the lymphatic and adipose tissues should be removed involving the region from the hilum of the kidney to the bifurcation of the aorta.

If a conservative operation cannot be made on either side, the patient should be dialysed, following bilateral nephrectomy. If one year after the operation there is no metastasis formation, renal transplantation can be considered [9].

Some of these interventions are still looked upon as great events and the operation can be indicated only by careful individual consideration of each case.

Both simultaneous and successive testicular tumours occur rarely, amounting to hardly 2% of all cases with testicular tumour [11]. The histology in the majority of cases appears to be seminoma or complication of haematological diseases [6]. If it is something different, they are generally reported [3]. According to certain statistics, the successive form is more frequent than the simultaneous one [5, 6]. According to our present knowledge, bilateral chorion-epithelioma has still not been reported, since, owing to the rapid tumour growth the patients die soon. The histological diagnoses of the two testicular tumours are most frequently identical, consequently one can never tell whether it is a metastasis or two primary tumours. In successive tumours the possibility of considering both tumours to be primary ones may arise. Even if several years have elapsed between the onset of them and even in case of identical histological pictures.

The simultaneously occurring bilateral embryonal carcinoma may be of interest because only [9] cases with embryonal carcinoma were presented in the combined statistics made by Javadpour in 1979 [10].

The therapy of bilateral testicular tumours hardly differs from that of unilateral ones. Following castration retroperitoneal lymphadenectomy was performed, then in view of the histological results, irradiation or combined cytostatic therapy was applied.

It should be stressed that the treatment of tumorous patients is an interdisciplinary task. Experiences made so far suggest that in bilateral urological tumours, at an early stage, prognosis of the patient is not worse than in unilateral tumours.

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Zweiseitige urologische Tumoren

M. FEHÉR, A. VARGA und J. PINTÉR

Im 5jährigen Material der Urologischen Klinik der Medizinischen Universität Debrecen (1.1.1977-31.12.1981) kamen 6 Fälle vor, in denen es sich um zweiseitige urologische Tumoren mit unterschiedlicher Organlokalisation handelte.

Durch den Einsatz verschiedener Maßnahmen — Frühdiagnose, unmittelbare adäquate Behandlung, lange Jahre hindurch sorgfältige Kontrolle und nötigenfalls intermittierende Chemotherapie als Spätbehandlung — kann das Überleben der Patienten mit zweiseitigen Nebennieren-, Nieren- bzw. Hodentumoren im Vergleich zu den bisherigen Ergebnissen verlängert werden.

Двусторонние урологические опухоли

М. ФЕХЕР, А. ВАРГА и Й. ПИНТЕР

В период времени между 1 января 1977 г. и 31 декабря 1981 г. (5 лет), в Клинике урологии Дебреценского медицинского университета авторы лечили 6 больных с двусторонними урологическими опухолями различной органной локализации.

По их мнению, шансы на выживание больных с двусторонней опухолью надпочечников, почек и семенников могут быть улучшены по сравнению с результатами, достигнутыми до сих пор, при условии ранней постановки диагноза, немедленного применения адекватного лечения, продолжающегося много лет контроля и — в случае необходимости — применения поздней — интермиттирующей — хемотерапии.

Kidney Scintigraphy in the Diagnostics of Urological Renal Diseases

M. GERVAIN,¹ E. ÁDÁM,² J. LÁNG² and L. CSERNAY²

¹Department of Urology, Orosháza Municipal Hospital, H-5900 Orosháza, Hungary and ²Central Isotope Diagnostic Laboratory, Szeged University Medical School H-6701 Szeged, Vedres u. 6, Hungary

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The authors report on their experiences in the diagnostics of urological renal diseases gained by 256 kidney scintigraphies of a total of 227 patients. The more important trends of progress made in the recent years in nuclear medicine are outlined.

The sensitivity (93%) and specificity (86%) of the examination based on the surgical and histological findings are determined. The technical importance of the study made from several directions using up-to-date radiopharmaca is emphasized in obtaining the results being favourable even in international comparison.

The importance of the coordination between the urologists and experts well-versed in nuclear medicine is pointed out in selecting the examination best suited for the purpose (dynamic, static examination).

Based on the literature and on their own experiences, the diagnostic results of the examination in detecting and controlling renal diseases are summarized.

Although isotope diagnostics as an analytical approach has become widely known in medical practice primarily as a result of the introduction of isotope renography and the examination of thyroid function [1, 4, 10, 11, 15, 19, 22, 25, 27, 29] since 1953, its development in the past ten years can be considered really important. Development was basically characterized by two trends. On the one hand, as a result of technical advancement, the traditional scanners were replaced by the gamma camera and by the attached microcomputer. On the other hand, a number of new diagnostic possibilities were offered by the introduction of ^{99m}Tc having a short half-life and by that of a whole series of new organ-specific radiopharmaca [2a, 15, 26, 30].

Examinations in urological diagnostics made by gamma camera and by the ^{99m}Tc-radiopharmakon have enabled us to use the combination of examination procedures which previously offered only morphological or functional results (e. g. camerarenography) [8].

Our experiences in the diagnostics of urological renal diseases made by ^{99m}Tc and dimercaptosuccinic acid (DMSA) kidney scintigraphic studies are reported to facilitate the selection of a correct examination procedure.

Material and Method

Between June 1979 and June 1981, a total of 256 kidney scintigraphic studies of 227 patients were made. This number includes all patients having undergone a renal operation and also the examined non-operated patients [7]. The patients' age ranged between 2 and 79.

Indication of the examination

The examination was indicated in each case after excretory urography, if pyelography had not accounted for the patients' complaints and for the changes observed, respectively (e.g. macroscopic haematuria in the history) but urography and the other urological examinations on the kidneys, ureters and part of the bladder did not reveal any change responsible for haematuria. Naturally, scintigraphy was also performed if the radiological examination indicated or suspected space reducing process. Examinations were made in the already operated patients to judge the operative results and in the non-operated ones to control the previously documented parenchymal defects (i.e. cyst, renal infarction, unambiguous differences in activity), and to follow up the process.

In evaluating the scintigrams, our attention primarily focussed on the well-circumscribed parenchymal defects of the renal parenchyma (using the internationally accepted term of nuclear medicine 'intrarenal space reducing processes') as e. g. tumours, cysts, fistulae, caverns and large calyceal diverticula. No less attention was paid to any reduction of the renal parenchyma visualized either from the direction of the renal calicopelvic system or from that of the renal contour. Despite that kidney scintigraphy is primarily a morphological procedure, on evaluating the findings, the amount and functioning ability, of the 'tubular mass' are referred to semi-quantitatively by comparing the activity of the two kidneys. Based on our experiences in evaluating a relatively large number of similar scintiscans, we attempted to present to the clinician also a probability diagnosis or diagnoses in addition to an accurate description, on the basis of the characteristic scintigraphic picture of certain changes. In achieving this, we exclusively relied on the scintiscans since the clinician's request for examination revealed only the kidney responsible for the assumed or known changes.

For determining the diagnostic value of kidney scintigraphy, the scintigraphic results were compared with the changes observed during the operation and with the histological findings. The value of a diagnostic procedure in the international literature can be quantitatively characterized by two parameters. One of them is sensitivity the other is specificity.

The patients not operated were continuously monitored and treated due to the progressive nature of a greater part of their pathological processes. Monitoring was completed, beside the laboratory tests, by control pyelography made in some cases and by repeated kidney scintigraphy.

Technical performance of kidney scintigraphy

The study was made three hours following the intravenous injection of 150 MBq ^{99m}Tc -DMSA. The pictures were taken first always from the posterior view, by a Nuclear Chicago Pho/Gamma III camera using parallel collimators. Beside the posterior view, polaroid pictures and/or roentgenograms were taken also from oblique views of 45 degrees. The distribution of activity was judged and the regions with an intrarenally reduced activity were recognized subjectively after carefully studying the scintiscans.

Results

In Table I the patients were grouped on the basis of the scintigraphic findings. The Table also contains the results of control examinations.

Morphological results

The well-circumscribed intrarenal parenchymal defects are summarized in Part A of Table I. The results of the operated patients from this group are shown in Table II. This patient group and their results have already been analysed on the basis of principles described in a previous report [7]. Of 24 non-operated patients in 18 there was no evidence of malignant space reducing process. In 4 cases suspicion of circumscribed space reducing processes could not be eliminated, although in these instances the scintigrams were ambiguous. In 2 cases of hydronephrosis, the dilatation and the bizarre shape of the calico-pelvic system produced a reduced renal parenchyma.

Part B of Table I is a grouping according to the number, size, localization and morphological changes of the studied kidneys. Acquired or congenital changes occurred in 61 patients.

In 45 cases (Part C of Table I) scintigraphy did not help in revealing the pathologic change; this corresponded to 21.7% of all examinations.

Control kidney scintigraphy

Repeated kidney scintigraphic studies were made in 29 cases. Of them in 9 for judging the result of the previous operation, i.e. the state of the renal

TABLE I
Morphological results

		First examination	Repeated examination
A. Circumscribed parenchymal defects	121 patients		
a. operated patients		97	9
b. non-operated patients		24	12
— indication of a space reducing process based on characteristic findings:			
polycystic kidney		6	4
solitary cyst		7	3
renal infarction		4	2
calyceal diverticulum		1	—
— suspicion of a space reducing process		4	3
— hydronephrosis		2	—
B. Changes in number, size, localization and morphology	61 patients		
a. changes in number: without function		3	—
agenesis		2	—
b. changes in size: hypoplasia		2	—
atrophic kidney		17	3
c. changes in localization: renal ptosis		28	—
d. changes in morphology: renal arcuation		4	—
sigmoid kidney		2	—
duplication of renal pelvis and of ureter		3	—
C. Normal kidney scintigram	45 patients	45	5

parenchyma. In one patient Anderson-Hynes plastic operation of the renal pelvis was made due to the stenosis of the pyeloureteral transition zone and the resulting hydronephrosis. In a 7-year-old child ureteroneoimplantation was performed because of the congenital stenosis of the bilateral ureterovesical segment and of the resulting hydronephrosis. In 7 patients marginal nephrotomy performed in hypothermal perfusion was made.

Control examinations were also performed for monitoring the earlier diagnosed changes. Repeated scintigraphy completed by the additional clinical examinations, were performed three months after the initial observation when space reducing process had been suspected. In the other cases, control examinations followed half or one year subsequently. In 17 cases the result of the previous scintigraphy was confirmed, in 3 cases the scintigraphic picture and the diagnosis changed. In one case, the earlier ambiguously evaluated region of decreased activity was suggestive of a solitary cyst. In another case a control study performed 9 months later described the characteristic picture of polycystic kidney and in the third case the unevenness of the previous bilateral

activity disappeared and a normal kidney scintigram was found (perhaps as the result of the one-year treatment). In 6 patients repeated examinations are due in three months' time.

Kidney scintigraphy and clinical diagnosis, control of non-operated patients

As shown earlier, it was interesting to find out to what extent the information obtained by renal scintigraphy was reflected in our diagnostic work in the final diagnosis of the disease. This analysis of the operated patients is shown in Tables II and III.

TABLE II

Distribution of patients according to surgical findings (97 operated patients)

Space reducing process		Non-space-reducing process	
Renal tumour	20	Solitary calculus	10
Renal cyst	24	Irregularly shaped calculus	7
Hydronephrosis	8	Horseshoe kidney	4
Renal tuberculosis	6	Renal ptosis	6
Atrophic kidney	9	Exploration	1
		Nephrosclerosis	2
Total	67	Total	30

TABLE III

Sensitivity (93%) and specificity (86%) of kidney scintigraphy

Scintigram \ Surgical finding		
	+	-
+	63	4
-	5	25

In the group of non-operated patients, information was conditionally accepted in considering the final diagnosis of 20 patients subjected to control kidney scintigraphy. Of them in 8 cases angiographic examination had to be indicated in order to clarify the assumed pathologic process in the renal parenchyma. In this way, renal agenesis could be unambiguously proved in two patients. In one case of intermittent macroscopic haematuria even angiography was of no avail in unanimously explaining haematuria. In 7 additional cases the suspicion of the space reducing processes in the kidney was dispelled. It is to be noted that in these cases obstacles to the urine flow could be demonstrated

and retrograde pyelography and angiography, etc. performed subsequent to scintigraphy, were successful.

Since the final clinical diagnosis can be accepted within limited degree of error—patients whose final diagnosis excluded the renal origin of the disease were most carefully followed up at the regular control examinations. The fate of 6 patients is unknown because they did not present any more for the check-ups after the first observation and did not appear at our special request at the out-patient department. A 80-year-old male patient died. In a 58-year-old female patient the control examination revealed a space reducing process which proved inoperable due to pulmonary metastases already three-and-a-half months after the first negative examination. In the other patients no such symptoms or signs could be observed within more than a year neither in the history nor in any other findings which would have made it necessary to divert from the initial diagnosis.

Discussion

The clinical performance of renal scintigraphy has considerably been improved in the recent ten years by the use of gamma cameras and by the introduction of roentgenological techniques. ^{99m}Tc useful both from measurement-technical as well as from radiochemical points of view, and DMSA electively accumulating in the tubuli are of great importance from the radiopharmacological aspect [4, 5, 11, 26].

Beside technical development, another factor improving performance is if the roentgenologist is familiar with the scintigraphic picture of the intact kidney and of the urinary tract. Considering the large number of potential anatomical variations in the urogenital tract this requires great practice for the roentgenologist. The forming of certain probability diagnoses in addition to describing the scintiscans may already assume the professional cooperation between experts in nuclear medicine and clinicians. This can be extended to the control of the probability diagnosis and to the confirmation of the accuracy of diagnosis made by the roentgenologist.

The diagnostic value of kidney scintigraphy in detecting and controlling urological renal diseases can be summarized on the basis of the literature and of our own experiences as follows.

1. It makes possible the non-invasive examination of the parenchymal pathologic processes and thereby the use of other invasive procedures can, in several cases, be avoided [13]. This procedure is of particular importance in cases of parenchymal tumours or of those still not having invaded the calico-pelvic system. Our experiences on renal tumours have been reported in detail in previous papers [1, 5, 7, 15, 22, 26, 30].

2. Kidney scintigraphy can also be used for detecting congenital developmental anomalies. It provides valuable information particularly in detecting morphological and localizational anomalies. On suspicion of horseshoe kidney, the examination also indicates whether the isthmus is composed of connective tissue or a genuine functioning parenchyma. Being aware of this may be helpful in designing an operative plan. It should, however, be noted that, on suspicion of renal agenesis, for the known reasons, angiography is, generally, indispensable.

3. Renal infarction observed by us in 4 cases is likely to occur more frequently than believed earlier. Parts of the previously silent regions are restored to function as a result of revascularization [10].

4. Since the procedure can easily be repeated it can also be used in the postoperative phase (e.g. after hypothermic perfusion) or to visualize atrophic processes.

5. Renal scintigraphy can be the examination of choice for detecting renal processes in children, since, because of the short half-life of technetium, they are exposed only to an insignificant amount of radiation [14, 26].

6. Differentiation of pyelonephritic atrophic kidney and other morphological disorders may pose great difficulties. In these cases other data or examinations (e.g. ultrasonographic angiography) available for the clinician may contribute to forming the final diagnosis [2, 3, 5, 6, 9, 12, 14, 16, 17, 18, 20, 21, 24, 28].

7. It cannot be ignored that the examination does not require special preparations and is, at the same time, free of complications [13, 14]. Consequently, it perfectly meets the requirements of control examinations which is of particular importance in patient care. It is at present beyond the scope of this paper to evaluate this procedure also from the point of view of nephrological care. It is to be noted, however, that kidney scintigraphy made by the gamma camera has a great share in the diagnostic activity of nephrological centres.

8. It is not indifferent either that, with a meticulously planned laboratory work, the costs involved are lower than those of excretory urography.

9. Finally, it should be mentioned that, in case if excretory urography cannot be performed, kidney scintigraphy is the method of choice without risk.

Our favourable experiences are supported by the sensitivity and specificity results based on our own material which are in concert with data in the international literature.

Non-invasive procedures in the up-to-date diagnostics have undergone a promising development. It should, however, be pointed out that this diagnostic trend also requires further differential diagnostic examinations made by ultrasonography. If even this does not help in clarifying the change, renal angiography may be of possible diagnostic value.

Since in the recent years the number of gamma cameras has considerably increased in Hungary (it should be stressed that up-to-date cameras are manufactured in Hungary), we believe that our favourable experiences may contribute to the more extensive use in urological diagnostics of kidney scintigraphy by the gamma camera.

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Die Nierenzintigraphie in der Diagnostik der urologischen Nierenkrankheiten

M. GERVAIN, E. ÁDÁM, J. LÁNG und L. CSERNAY

Berichtet wird über die Erfahrungen mit bei 227, an urologischen Nierenkrankheiten leidenden, mit diagnostischem Zweck durchgeführten 256 Nierenzintigraphien. Anschließend werden die Hauptrichtungen der im Laufe der letzten Jahre in der Nuklearmedizin erreichten Entwicklung geschildert.

Mit Hilfe der Operationsdaten und der histologischen Befunde wurden die Sensitivität (93%) und die Spezifität (86%) der Untersuchung bestimmt. In der Erreichung der auch in internationalem Vergleich befriedigenden Ergebnisse ist der aus mehreren Richtungen, mit modernen Radiopharmaka durchgeführten Untersuchungstechnik eine besondere Bedeutung beizumessen.

Die Zusammenarbeit der Fachleute der Nuklearmedizin und der Urologen bietet eine Hilfe zur Auswahl der im gegebenen Fall am besten geeigneten Untersuchungsmethode (dynamische, statische Untersuchung).

Schließlich finden die sich auf den diagnostischen Wert des Untersuchungsverfahrens bei urologischen Nierenkrankheiten beziehenden Daten anhand des Schrifttums und der eigenen Erfahrungen eine Besprechung.

Сцинтиграфия почек в диагностике урологических почечных болезней

М. ГЕРВАЙН, Э. АДАМ, Я. ЛАНГ и Л. ЧЕРНАИ

Авторы делятся опытом применения сцинтиграфии почек в диагностике урологических почечных заболеваний. Ими было произведено 256 сцинтиграфических исследований у 227 больных. В статье кратко описываются главные направления прогресса, достигнутого в ядерной медицине за последние годы.

С помощью операционных результатов и данных гистологических анализов они определяли чувствительность (93%) и специфичность (86%) данного метода исследования. Авторы подчеркивают значение техники исследования, проводимого из разных направлений, с современными радиофармаконами, в достижении благоприятных — даже по сравнению с международными данными — результатов.

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In developed countries the number of traffic and road accidents is steadily increasing. As a consequence, in most countries 30–40 inhabitants in every million become paraplegic each year. In some of these cases micturition becomes paralyzed which may lead to the infection and finally to the deterioration of the kidneys. Therefore, the restoration of bladder function proves to be the most important, even by surgical means, if necessary.

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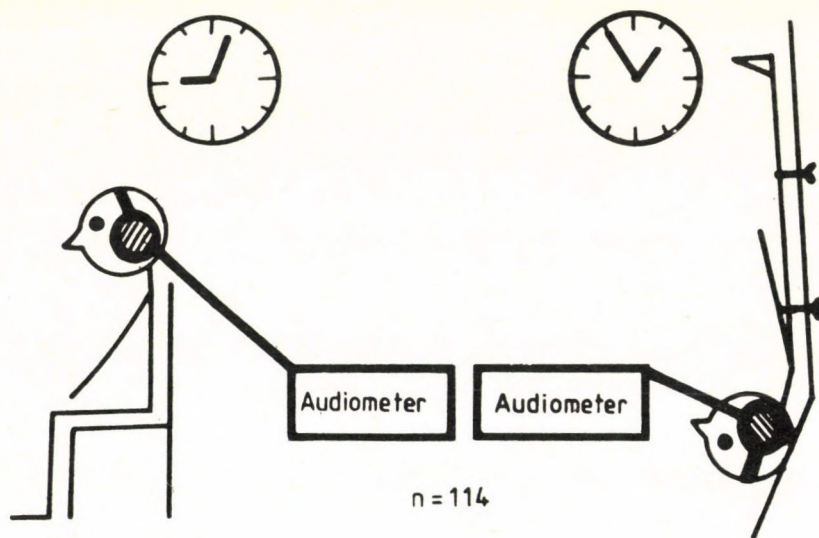
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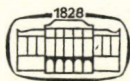
Proceedings of the 7th Congress of the Hungarian Paediatric Surgeons, Budapest, August 25-28, 1982

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In English. 1983. XII + 332 pages. 136 figures. 24 tables. 17×25 cm
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Four main topics were dealt with at the Conference attended by paediatric surgeons from many countries of Europe and from overseas. Papers in the first section deal with special diagnostic examinations in paediatric surgery. The second topic, errors and mistakes in childhood traumatology, was chosen because in the last decades fatalities resulting from trauma have become the most frequent cause of death in the affluent countries. The third domain, relating to the surgical conditions of neonates leading to respiratory syndromes, was necessitated on account of recent improvements in the therapy of these cases. The fourth section includes freely chosen topics in connection with paediatric surgery.



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by

A. CZEIZEL and G. TUSNÁDY

In English. 1984. XV + 358 pages, 31 figures, 123 tables. 17×25 cm.
Hardback. \$ 29.00/DM 69,—/£ 17.40
ISBN 964 05 3223 9

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PATHOMECHANISM AND PREVENTION OF SUDDEN CARDIAC DEATH DUE TO CORONARY INSUFFICIENCY

International Symposium of the Socialist Countries
on the Pathomechanism and Prevention of Sudden
Cardiac Death due to Coronary Insufficiency

18—20 May, 1981, Szeged, Hungary

Edited by L. SZEKERES, GY. I. PAPP, and I. TAKÁCS

In English. 1984. 319 pages, 141 figures, 28 charts, 17 × 25 cm.
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This book is based on 51 reports relating to the fundamental factors of sudden cardiac death investigated in the framework of a complex scientific programme of the CMEA (COMECON) countries. The first part of the book contains experimental studies concerning mainly the pathomechanism and pharmacotherapy of serious heart rhythm disturbances including ventricular fibrillation, the most common arrhythmia leading to sudden death. The relationship between the severity of cardiac dysrhythmias and the risk of sudden death in man and the efficacy of drug treatment in the prevention of lifethreatening ventricular arrhythmias and sudden death in patients are the major problems treated in the second part of the book. Finally, morphological, histochemical and biochemical alterations found in the heart and other organs of man and experimental animals after sudden death are described in the third part of the volume.

The book will be an important aid to all pathophysiologists, pathomorphologists, and pharmacologists engaged in heart research, and also to cardiologists, cardiac surgeons and other specialists wishing to know more about the mechanism, predictability and prophylactic management of sudden cardiac death.



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Primary Ureteral Tumours

MAGDOLNA HEGEDÜS, L. SOMOGYI and L. POLYÁK

Department of Urology, Pécs University Medical School,
H-7621 Pécs, Munkácsy M. u. 2, Hungary

(Received 19 April, 1984)

The authors report on the clinical picture, diagnostics and therapy of ureteral tumours in 4 patients. The most important symptoms are haematuria and pain. Of the diagnostic possibilities retrograde ureterography is the most significant. Their own surgical solution was ureteronephrectomy with excision of the orifice. Also the conservative therapeutic measures were surveyed. The post-operative control for detecting early recurrences is considered important.

Introduction

Despite the advancement of diagnostic methods, primary ureteral tumours belong to those which are difficult to diagnose preoperatively. The number of patients with tumours of the ureter reported so far ranges between 700 and 1000 [1, 2, 10]. In the Hungarian medical literature 55 cases are known.

Clinical Picture, Patient Material

Tumours of the ureter occur twice as frequently in men than in women mostly over 60 years of age [10]. Sixty-three percent is located in the lower third, 22% in the middle and 15% in the upper third of the ureter [9]. Histologically the tumours are most often of epithelial origin, the so-called transient-cell tumours. Less frequently occurring epithelial tumours are adenocarcinoma and planocellular carcinoma. Connective tissue tumours appear less often and they are benign as e.g. fibroma, lipoma, haemangioma or their mixed forms. A fairly rare form of malignant tumours is sarcoma [4, 6, 8, 12].

The main symptom of the disease is haematuria occurring in 70 to 90% of the cases. Haematuria can be of various degrees ranging from microscopic to one with a massively bloody urine. It often occurs that the first episode of haematuria can even be followed by a half-year complaint-free period. Pain appears more rarely and is never of colic nature. The patients present in general with a dull pain in the flank. Of the ureteral tumours only the malignant, infiltrating tumours can be palpated in the advanced stage. Tumours harboured in the region of the pelvis can rarely be recognized either by vaginal or rectal examination [5]. The kidney can be palpated on development of hydronephrosis.

TABLE I
The clinical data

Patient	Haematuria	Pain	Palpability	Cystoscopy	I.v. urography
T. A. male aged 63	macroscopic	—	—	bleeding on left side	silent, atrophic kidney on left side
B. J. male aged 59	—	—	—	negative	nephrosis on left side, ureter dilated to lumbosacral space
I. A. female aged 56	macroscopic	dull perirenal pain	—	negative	on left side, no detectable excretion
T. M. male aged 61	macroscopic	—	—	negative	prehydronephrosis on left side, ureteral filling defect

The first radiological examination is intravenous urography. On the basis of urograms, no unanimous diagnosis can be formed. It reveals most frequently the dilatation of the pelvic cavity and that of the area over the ureteral tumours. In advanced cases the pelvic cavity is hydronephrotically dilated.

Retrograde ureterography is the most important in establishing the diagnosis [7]. On touching the tumour bleeding may occur while introducing the ureteral catheter (Chevassu-Mock sign). Here, the catheter is caught on the tumour elastically but, in general, it can be introduced over the involved region. The ureteral catheter leads off clear urine from above the region of the tumour (Marion sign). Filled from below the affected part, the lower contour of the tumour is delineated which is crescent or goblet shaped [15]. Filled by the catheter introduced over the tumour, its form and size are revealed. A filling defect corresponding to the tumour is seen. The regions of the ureter over and below the tumour are also dilated, the proximal dilatation is called Chaul's bell, the distal dilatation is known as the Bergman sign. Differential diagnostically, the following changes should be considered. Uric acid calculi, air or blood clots are delineated as filling defects [15]. Their contour can, in every case, be differentiated from the ureteral wall. The ureteral wall is never demonstrated at the site of origin of the tumour. Cystic ureteritis involves, in the majority of cases, larger portions of the ureter, it is multiple in occurrence and is often associated with cystic pyelitis. Forming the diagnosis the very rare ureteral endometriosis cannot be disregarded. In infiltrating ureteral tumours, the contour is ragged and uneven corresponding to the size of the involved area. Here, too, the dilatation before and behind the tumour are useful diagnostic signs. If the lumen of the ureter is obstructed by the infiltrating tumour, the cranial margin of the change can be established by percutaneous transrenal ureterography.

of the patients

Chevassu-sign	Retrograde ureterography		Filling defect	Comment
	Chaul-bell	Bergman-sign		
—	—	—	ragged contour on 8 cm	angiography cause, of bleeding not clarified
—	not evaluable	not evaluable	not evaluable	examination due to great weight loss
—	—	—	ragged contour on 2 cm	ultrasound negative
—	—	—	dilatation of 5 cm with inhomogeneous filling defect	febrile occlusion due to stone 2 years earlier

Angiography has not come up to expectations in aiding the diagnosis of ureteral tumours. It provides information of diagnostic value only in case of extensive tumours [13]. Ultrasound and computed tomography do not convey diagnostic information.

Earlier, ureteronephrectomy was the exclusive method of choice in treating primary ureteral tumours. This implied the removal of the intramural ureteral segment together with the orifice by using the so-called sleeve technique [3]. At the end of the sixties, a change of attitudes occurred primarily as to the surgical solution of distal ureteral tumours [11, 13]. The recognition that ureteral tumours, similar to bladder tumours, often appear in the form of diffuse urothelial involvement concomitant with possible malignant transformation in the contralateral ureter and in the renal pelvis, has lead to the extensive use of conservative, organ-preserving operative solutions, which we ourselves do not reject. It can be accepted as a general view that conservative operations should be made in histologically or clinically favourable cases. The absolute indication of organ-preserving operations are ureter tumours associat-

TABLE II
Histopathological results

Name	Operation	Histology
T. A.	ureteronephrectomy of left side	uroepithelial carcinoma (Fig. 3)
B. J.	ureteronephrectomy of left side	uroepithelial carcinoma
I. A.	ureteronephrectomy of left side	uroepithelial carcinoma
T. M.	ureteronephrectomy of left side	ureteral papilloma



FIG. 1. Inhomogeneous, ragged filling defect along an about 8 cm-long segment of the left ureter

ed with functional or morphological solitary kidneys, renal failure, bilateral ureteral or pelvic tumours. Conditions of the operation should be an anatomically and functionally normal kidney, intact ureter (colour, vascularization, blood supply), lack of regional lymph node metastases. Surgical solutions are: ureteral resection (1 cm both distally and proximally from the tumour in the intact tissue) followed by end-to-end anastomosis, oval ureteral resection, ureterocystostomy, with Boari-type reconstructive operation, ureterocystoneostomy with creation of bladder horn, ureterocutaneostomy.

In the period between 1982 and 1983, 4 patients with tumour of the ureter were treated at our clinic. The relevant data of their diseases and operations are summarized in Tables I and II and Figs 1 and 2.

Discussion

Surveying the data of our patients, the most frequent symptom was haematuria. Only one patient complained about pain. In one patient the tumour developed without symptoms.



FIG. 2. Definite dilatation and inhomogeneous filling defect of an about 5 cm-long segment in the left ureter

Of the radiological studies, retrograde ureterography was the most important. It was the shape of the filling defect which led us, in each case, to form the correct diagnosis. The Chevassu-Mock sign was positive in none of the cases. Neither the Chaul bell nor the Bergman sign appeared in any of the patients. The tumours were located in the distal ureteral third.

Organ-preserving operation could not be performed in either of the cases. The contraindications were prehydronephrosis in two patients, atrophic kidney in one case, and a tumour deeply invading the ureteral wall and palpable lymph nodes in another case.

Dissecting the surgical preparate of T. M. (patient No. 4), a black stone, the size of a pepper, was the accessory finding in the tumorous ureter (Fig. 4). Ureteronephrectomy was always made by removing both the intramural ureteral segment and the orifice.

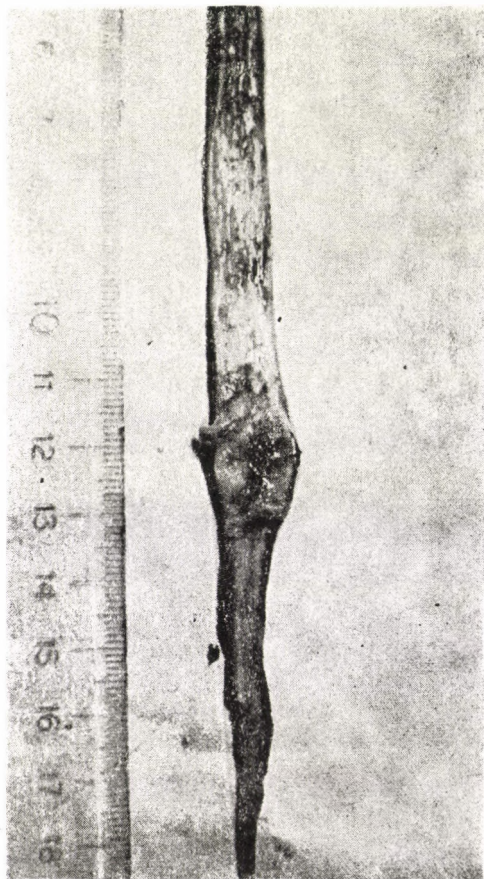


FIG. 3. Dissected surgical preparate of T. A.



FIG. 4. Dissected ureter of T. M. The arrow points to the stone adjacent to the tumour

Monitoring the patients with ureteral tumours is very important for detecting the potential early recurrences in the bladder or on the contralateral side. Our patients underwent half-yearly intravenous urography, cystoscopy and cytological examinations of the urine. All four patients have been free of complaints and recurrences for 0.5 to 2.0 years.

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Primäre Ureterentumoren

M. HEGEDÜS, L. SOMOGYI und L. POLYÁK

Im Zusammenhang mit 4 Ureterentumor-Fällen werden Klinik, Diagnostik und Therapie des pathologischen Prozesses erläutert. Die Leitsymptome sind Hämaturie und Schmerzen. Unter den diagnostischen Möglichkeiten hat sich die retrograde Ureterographie am besten bewährt. In der Folge finden einerseits die eigene Operationslösung — Ureteronephrektomie in Kombination mit der Exzision der Einmündung — anderseits auch die konservativen Möglichkeiten eine Besprechung. Im Interesse der Frühdiagnose eventueller Rezidive ist die regelmäßige postoperative Kontrolle der Patienten von ausschlaggebender Bedeutung.

Первичные опухоли мочеточника

М. ХЕГЕДЮШ, Л. ШОМОДЬИ и Л. ПОЙАК

В связи с наблюдением 4 больных с опухолью мочеточника авторы знакомят с клиникой, диагностикой и терапией этого заболевания. Ведущими симптомами являются гематурия и боль. Среди диагностических возможностей самая существенная — ретроградная уретерография. Разработанное авторами оперативное вмешательство — уретеро-нефрэктомия с иссечением устья. Они знакомят также с возможностями консервативного лечения. С целью раннего обнаружения рецидивов считают важным моментом постоперативный контроль больных.

Cryocaustics in View of the Complications

Zs. SIMON and J. KOVÁCS

Department of Urology, Postgraduate Medical Institute,
H-1389 Budapest, Szabolcs u. 35, P.O.Box 112, Hungary

(Received 8 May, 1984)

The authors compared the complications of cryocaustic operations in hyperplastic patients with those of transvesical prostatectomy, TUR and of cryosurgical procedures. They have found that, considering its complications, cryocaustics is the intervention incurring the smallest risk to patients of bad general condition.

Cryocaustic operations have been performed since 1977 at the Department of Urology of the Postgraduate Medical Institute, Budapest. Transurethral cryocaustics, as an improved method of cryosurgery, was first applied in urological practice in Hungary by Magasi [5]. Reports on the results of the new procedure and on our experiences have appeared earlier [6, 7].

The procedure for the release of urinary retention due to prostatic hyperplasia performed as a palliative operation has so far been made in 400 patients. The intervention succeeded in 81% of them. Cryocaustics was performed in patients with a general condition, i.e. advanced age, previous or associated diseases, contraindicating transvesical prostatectomy or TUR.

As after each surgical intervention, complications may develop also after transurethral cryocaustics which may largely influence the success of operations as well as, the time of recovery and may impose more strain on the patient. Since the cryocaustic operation does not impose a great strain on the patient, it is primarily the complications which involve a risk to an undisturbed recovery.

Surveying the complications of cryocaustic operations in patients with hyperplasia of the prostate, their complications were compared with those of transvesical prostatectomy, TUR and with those of traditional cryosurgical procedures.

The complications of our cryocaustic operations were divided into three groups. Intraoperative, early and late postoperative complications were distinguished. Early complications were found to be those developing within 8 days. In the early phase complications developed in 42 cases (10.5%) later in 26 cases (6.5%; Table I).

TABLE I
Complications of cryocaustics in 400 operations

	Complications	No. of patients	%
Intra-operative	urethral perforation	1	0.25
	urethral-anal perforation	1	0.25
	bladder perforation	2	0.5
Early	bleeding	2	0.5
	acute pyelonephritis	16	4.0
	acute epididymitis	8	2.0
	acute prostatitis	6	1.5
	paraurethral abscess	1	0.25
	urethrocutaneous fistula	1	0.25
	penoscrotal oedema	9	2.25
	urosepsis	1	0.25
Late	acute pyelonephritis	9	2.25
	acute epididymitis	5	1.25
	acute prostatitis	3	0.75
	urethral stricture	2	0.5
	incontinence	0	0.0
	necrotic tissue in bladder	3	0.75
	bladder calculus	4	1.0
	mortality	6	1.5

Intraoperative Complications

a. Urethral perforation (0.2%)

It occurred in one case while the probe being introduced perforated the membranous part of the urethra.

b. Urethral-anal perforation (0.2%)

This complication developed in one case as a result of careless introduction of the probe.

c. Bladder perforation (0.5%)

During two operations, the posterior wall of the bladder was perforated and frozen as a result of incorrect insertion of the probe and inadequate filling of the bladder.

Early Complications

a. *Bleeding* (0.5%)

Copious bleeding from the urethra was observed preoperatively only in two cases. In 21 patients (5.25%), while the bladder was rinsed after removal of the probe and the insertion of the catheter, the eluent contained blood. This mild haematuria did stop, however, in each case on the very day of operation. Due to intensive bleeding, transfusion had to be applied in one case.

b. *Acute pyelonephritis* (4%)

In the early postoperative phase this complication developed in 16 patients. In 11 cases clogging of the catheter preceded the onset of ascending pyelonephritis.

c. *Acute epididymitis* (2%)

This complication occurred in 8 patients in the early phase. In patients having undergone vasectomy preoperatively epididymitis developed in 1.2% (in two out of 164 patients). In patients with no vasectomy (263 patients) it did in 2.5% (6 patients) of the cases.

d. *Acute prostatitis* (1.5%)

Acute inflammation of the prostate developed in 6 cases exclusively in patients who had not previously undergone vasectomy.

e. *Paraurethral abscess* (0.25%)

It occurred in the early postoperative phase in one case. Prior to admission the patient had no indwelling catheter.

f. *Urethrocutaneous fistula* (0.25%)

It developed as a consequence of the freezing of the membranous part of the urethra.

g. *Penoscrotal oedema* (2.25%)

It was observed in 9 patients preoperatively. The oedema due to freezing of the distal portion of the urethra disappeared in some days.

h. Urosepsis (0.25%)

After cryocaustics it developed in one case as a sequel of urethral perforation.

Late Complications*a. Acute pyelonephritis (2.2%)*

Ascending pyelonephritis following the removal of the catheter was found in 9 cases.

b. Acute epididymitis (1.2%)

It developed as a late complication in 5 patients who had previously not undergone vasectomy.

c. Acute prostatitis (0.75%)

It developed in 3 cases after removal of the catheter.

d. Urethral stricture (0.5%)

It was found in 2 cases after an urethral injury suffered during insertion of the probe.

e. Necrosed tissue debris in the bladder (0.75%)

The necrosed detached tissue fragments produced micturition disorder in 3 patients.

f. Bladder calculus (1%)

It occurred in 4 patients preoperatively. According to the calculus analysis, after transurethral removal, the stone developed as a result of incrustation of the necrosed tissue trapped in the bladder.

Mortality (1.5%)

Intraoperatively there were no deaths. In the postoperative phase a total of 6 patients were lost. In two cases intraoperative bladder perforation occurred after detection of which surgical reconstruction was made. Death of a patient was due to circulatory failure, and of another, to general peritonitis.

One patient died of myocardial infarction. In one patient paraurethral abscess, then urethroscrotal fistula developed postoperatively. Death occurred due to circulatory failure. Two patients died of acute cardiac failure.

Discussion

Of the factors influencing the development of postoperative complications, the importance of vasectomy indicates that in the group where preoperatively bilateral vasectomy had not been performed, acute epididymitis was an associated complication three times more frequently (3.7% : 1.2%).

Despite the aimed antibiotic treatment, acute pyelonephritis occurred as an early and late complication in 15 and 13%, respectively, in patients with preoperative chronic pyelonephritis, while it developed in 4 and 2.2%, respectively of all patients. At the same time, in case of postoperative complications, 31% of the patients had a history of chronic pyelonephritis and 44% of cardiac and circulatory failure, respectively.

Because of the age, general state and associated diseases of the patients, their mortality rate, too, was high. Within half a year 16 patients (4%), within one year 20 patients (5%), and within 2 years 52 patients died. Hence, two years postoperatively only 78% of the patients survived.

To what extent does cryocaustics incur a smaller risk to prostatic hyperplasia patients than does transvesical prostatectomy or transurethral resection?

Magasi et al. [8, 9] as well as Végh [20] surveyed and analysed the results and postoperative complications of transvesical prostatectomies based on 750 cases performed at our clinic (Table II).

Comparison of data reveals that the mean age of patients is lower by 10 years than of those who had undergone cryocaustic operation. Only 10% of patients belonged to the age group over 75 years, while in case of cryocaustics 47.4% did. The postoperative care was, on an average, three days longer than after cryocaustics. These data deserve attention because in patients having undergone a cryocaustic operation various previous and associated diseases were also observed, while only 20% of prostatectomized patients were found to have such diseases (in the age group of 70 to 80 years 42%).

During cryocaustic operations intraoperative haemorrhage was not observed. During prostatectomy 8% of the patients received transfusions intraoperatively. After cryocaustics, copious bleeding occurred in 0.5% of the patients, while after prostatectomy in 2%.

Of the postoperative complications pyelonephritis and epididymitis occurred in similar proportion. At the same time, urinary fistula developed 14, bladder calculus 5 and urethral stricture 6 times as frequently as after transvesical prostatectomy.

Incontinence and thromboembolic complications were not found after cryocaustic operations. Despite early mobilization and antibiotic therapy, pneumonia cases were three times more frequent after cryocaustics. The duration of the operation was one-third of that of prostatectomy.

TABLE II
Comparison of cryocaustics and prostatectomy based on complications

	Cryocaustics <i>n</i> = 400	Transvesical prostatectomy <i>n</i> = 750
Average age, years	74.8	64.5
Duration of postoperative care, days	14.5	11.8
Average duration of operation, minutes	10	35
Presence of associated disease, %	100	20
Copious bleeding (intraoperatively), %	0	8
Copius bleeding (postoperatively), %	0.5	2
Reoperation, %	0.9	1
Acute pyelonephritis, %	6.2	7
Acute epididymitis, %	3.2	2
Urinary fistula, %	0.2	2.6
Bladder calculus (incrustate), %	1.7	4.9
Urethral stricture, %	0.5	2.9
Incontinence, %	0	1
Thrombosis, embolism, %	0	0.2
Pneumonia, %	2.5	0.9
Postoperative mortality, %	1.5	0.5

TABLE III
Comparison of the complications of cryocaustics and prostatectomies performed in patients over 75 years

		Cryocaustics <i>n</i> = 400	Transvesical prostatectomy <i>n</i> = 140
Preopera- tive data	average age, years	74.8	79
	complete urinary retention, %	72	55
	pyuria, %	93	65
	presence of associated disease, %	100	100
Complica- tions	bleeding, %	0.5	18.5
	secondary exploration, %	0.9	3.6
	acute pyelonephritis, %	6.2	10.7
	urinary fistula, %	0.2	20.9
	incontinence, %	0	5
	thrombosis, embolism, %	0	2.8
	postoperative mortality, %	1.5	5.7
Postopera- tive data	average time of postoperative use of catheter, days	8	14
	average time of postoperative care, days	14.5	29

The ratio of postoperative mortality after cryocaustics was higher. This was due to that this operative procedure is exclusively performed in the so-called risk patients for whom appearance of even a banal postoperative complication may easily be fatal.

Balogh et al. [1] reported in 1980 on their experiences on the transvesical postatectomies of patients over 75 years. Considering the age and associated diseases of patient groups exposed to the same risks, the results and complications of the two types of procedures can be realistically compared (Table III).

In view of this, it can be stated that postoperative complications occurred eight times as frequently as after cryocaustics with an almost four times higher mortality rate. Postoperative use of a catheter and postoperative hospital care took, on an average, double the time than after cryocaustics.

On the basis of data it can be established that transurethral cryocaustics, an operation associated with less complications and making possible a more rapid recovery, imposes considerably less strain on aged patients of a bad general condition than does transvesical prostatectomy.

Another known and extensively applied method of treating prostatic hyperplasia is transurethral resection (TUR). Its field of indication and the associated complications are well known. By employing the procedure with an adequate practice, the hyperplastic tissue can also be removed transurethrally. It can, however, be performed as a palliative operation for decreasing complaints of micturition and of urinary retention in aged, weakened patients [15]. At the same time, Mauermayer [11] looks upon the individual forms of cardiovascular diseases, bronchial asthma, emphysema, the more severe forms of diabetes mellitus, clotting disturbances and generalized atherosclerosis, as relative contraindications of this operation. According to him, cerebrovascular diseases represent an absolute contraindication of the operation because of the frequency of postoperative problems and of a lack of cooperation.

In addition to the resection syndrome, the most important complications associated with TUR are intra- and postoperative haemorrhage, bladder or capsular perforation, postoperative infections, i.e. pyelonephritis, epididymitis and sepsis, and stricture and incontinence.

Compared with the data of Magasi [10], Kisbenedek [3], Tóth [19], Melchior et al. [12], Steffens [17], a part of the complications occur in an approximately identical proportion with the same mortality rate after cryocaustics and TUR, respectively (Table IV).

The difference lies mainly in the frequency of intra- and postoperative haemorrhage, stricture and of incontinence. According to the data of Nesbit and Conger [14], the average blood loss during TUR is 169 ml, according to Tóth [19], it is 157 ml. Melchior et al. [12] found that 25% of the patients should receive transfusion during, and immediately after, operation. Late

TABLE IV
*Comparison of the complications
 of cryocaustics and TUR*

Complications	Cryocaustics	TUR
	%	
Postoperative bleeding	0.5	2- 5
Bladder perforation	0.5	1- 5
Acute pyelonephritis	6.2	4-10
Acute epididymitis	3.2	2- 3
Sepsis	0.25	1- 2
Urethral stricture	0.5	4- 5
Incontinence	0	1- 5
Mortality	1.5	1- 3

postoperative bleeding after TUR due to a detached thrombus was observed by Melchior et al. [12] in 2.3%, by Steffens [17] in 2.2%, and by Tóth [19] in 6.2% of the cases.

In case of cryocaustics, there was no intraoperative haemorrhage. A more profuse bleeding occurred in two cases (0.5%) after operation. In one case infusion had to be administered. Acute blood loss is badly endured by aged, atherosclerotic patients of a bad general condition even on receiving immediate transfusions. The change of the circulating blood, the transitional relative lack of oxygen imposes a great strain. It may induce mental confusion and collapse postoperatively, therefore in cases like that cryocaustics, as an operation without blood loss and with less strain, is more suitable for securing micturition.

It was studied to what extent cryocaustics means a step forward and what its advantages are as opposed to the traditional cryosurgical operation. Comparison of the two methods was made on the basis of the work of Lutzeyer and Lymbeopulos [4] on their 374 cryosurgical results and complications. They performed the operation only in prostatic hyperplasia patients of a bad general condition as a palliative operation for securing micturition.

The refrigeration time was on an average 3 to 7 minutes at temperatures of -160 to -180°C in both procedures. In case of the traditional method, following refrigeration, the probe was removed, cooled down to body temperature, while in case of the cryocaustic method, it was first warmed for one minute to $+200^{\circ}\text{C}$. The indwelling catheter inserted postoperatively could be removed following the cryosurgical procedure, after 28 to 56, while after cryocaustics after 8 days. According to the data, both operative procedures were successful in equal proportions. On assessment, it should be considered that this result was achieved only 2 to 4 months after the traditional cryosurgical procedure as a result of the slow detachment of necrotic tissues. Postoperative

hospital care took an accordingly longer time—as reported by Lutzeyer and Lymbeopulos [4], it took 23 days.

For a more rapid removal of necrotic tissue after the traditional operations Rouvalis [16] and Jordan and Friedler [2] recommend the performance of transurethral resection. Time of postoperative hospital care can thus be decreased and the risk of haemorrhage is lower. At the same time, a second operation performed within a short time imposes an additional strain and risk on aged patients of a bad general condition.

Complications of traditional cryosurgery and cryocaustics are summarized in Table V.

Comparing them, the first striking difference appeared in the ratio of postoperative haemorrhage. This is due to the fact that, after cryocaustics, as a result of thermocoagulation, there is no secondary bleeding which occurs temporarily in one-third of the patients after the traditional cryosurgical methods. Inflammatory complications occur in a larger proportion after the traditional cryosurgical procedures. In patients with a largely infected urine, the slow detachment and prolonged discharge of necrotic tissues, the prolonged postoperative use of a catheter, and transitional disturbances due to impeded insertion of the catheter promote the development of ascending pyelonephritis. The greater frequency of epididymitis can be ascribed to the fact that vasectomy was not performed before a cryosurgical operation. This complication occurred in almost 1.2% of our vasectomized patients.

TABLE V

Complications of cryocaustics and of traditional cryosurgery

Complications	Cryocaustics	Cryosurgery	
	<i>n</i> = 400	Lutzeyer <i>n</i> = 392	Schmidt Haschek <i>n</i> = 374
Urethral or bladder perforation, %	0.9	0.25	—
Bleeding, %	0.5	29.6	29
Acute pyelonephritis, %	6.2	8.4	15
Acute epididymitis, %	3.2	5.6	9
Acute prostatitis, %	2.2	0.25	—
Paraurethral abscess, %	0.25	0.5	1
Urethrocutaneous fistula, %	0.25	0.75	0.26
Penoscrotal oedema, %	2.2	—	—
Urosepsis, %	0.25	0.5	0.3
Urethral stricture, %	0.5	2.2	0.7
Incontinence, %	—	3.0	3.2
Bladder calculus (incrusted necrotic tissue), %	1.7	3	13
Mortality, %	1.5	1.87	3.58
Postoperative use of catheter, days	8	42–56	28–42
Successful operation, %	81	76	80

The incrustated, necrotic debris having entered the bladder and bladder calculus had to be removed in 3 to 13% after traditional cryosurgical operations. Similar complication developed only in 1.7% of our cases, because by using this method, the necrosed tissues become detached as a result of refrigeration, and are eliminated more easily, through the catheter. Since the time of postoperative use of the catheter is shorter, spontaneous micturition starts earlier, too, than after the traditional cryosurgical methods.

As a result of rapid necrotic detachment and elimination and of the spontaneous micturition starting early, urinary infection, too, decreases more rapidly after cryocaustics. One year postoperatively only 13.3% of our patients were pyuric, while after cryosurgery, the urine of 63 to 73% of the patients was still infected.

Conclusions

Comparing the complications of procedures used in surgically treating prostatic hyperplasia, it can be stated that transvesical prostatectomy—primarily due to the greater proportion of haemorrhages and postoperative complications—imposes a greater strain on aged patients of a bad general condition as a result of the danger of bleeding and of the required general anaesthesia, in transurethral resection made as a palliative operation. The traditional cryosurgery is a procedure with more frequent bleeding, associated, due to the slow detachment of necrotic debris, with more complications, and requiring a longer use of catheter.

Considering the ratio of complications, cryocaustics as a palliative operation, can be performed as a procedure imposing less strain and incurring less risk and it may help in relieving patients of a bad general condition of the use of an indwelling catheter.

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Kryokaustik im Spiegel der Komplikationen

ZS. SIMON und J. KOVÁCS

In der Arbeit werden die Komplikationen der wegen Prostatahyperplasie durchgeführten kryokaustischen Operationen mit den Komplikationen der transvesikalen Prostatektomie, der TUR und der herkömmlichen kryochirurgischen Methoden verglichen. Hieraus ergab sich die Feststellung, daß unter Berücksichtigung der Komplikationen die Kryokaustik für Patienten in schlechtem Allgemeinzustand eine, das geringste Risiko bedeutende chirurgische Methode darstellt.

Криокаустика в зеркале осложнений

Ж. СИМОН и Й. КОВАЧ

Авторы сравнивают осложнения после криокаустических операций, произведенных у больных с гиперплазией простаты, с осложнениями после трансвезикальной простатэктомии, TDR и традиционного криохирургического способа. Показывают, что, принимая во внимание осложнения, криокаустика для больных с плохим общим состоянием является вмешательством с минимальным риском.

Surgical Indication of Dilatations in the Renal Cavity System

A. KARSZA, T. BANYÓ and Z. ENGERT

Department of Urology, Postgraduate Medical Institute,
H-1389 Budapest, Szabolcs u. 33–35, Hungary

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The authors report on the results of examining 20 patients with dilatation of the pelvic cavity associated with developmental anomalies of the kidney. The results are evaluated from the point of view of the indication and the selected type of the operation. The importance of diuretic urography and renography is pointed out in demonstrating the obstruction. Beside isotope gamma camera examinations, the renal function was assessed through determination of the acidifying and concentrating ability of the kidney. The intraoperative pressure measurement in the pelvic cavity is a valuable aid in selecting the adequate type of operation. Finally, the indications of reconstructive operations were outlined.

The majority of chronic dilatations of the pelvic cavity are due to developmental anomalies of the kidney or the ureter. The usual abnormalities of the kidney (i.e. lack of fusion, ectopy, malrotation) are, in each case, associated with dilatation of the renal pelvis, and less frequently, with that of the calyceal system. These dilatations of the pelvic cavity can generally be ascribed to obstructions. This can be an artery or a pair of vessels supplying the lower pole which due to a rotatory abnormality crosses the ureter anteriorly. In case of normal development, this vessel would not have caused an obstruction, so in these cases, the terms 'abnormal', 'accessory' or 'aberrant' vessel are not actually valid [2]. Such misrouted vessels due to a rotatory abnormality are found both in dystopic and horse-shoe kidneys. In the latter cases, the isthmus can also contribute to the development and maintenance of the obstruction. In these instances, the obstruction can be proved unequivocally. Urinary flow obstructions damaging the renal function have been known for decades [1, 9]. Accordingly, depending on the subjective complaints and complications, operation is performed in most of the cases. This operation should not, however, mean a reconstructive operation. There are also developmental anomalies where the dilatation of the pelvic cavity cannot unambiguously be attributed to obstruction. In this group belong the functional disturbances due to the lesions of the wall components in the pelviureteric junction. Abnormal or accessory vessels can often be demonstrated in case of such changes in the pelviureteric junction. According to several authors, the aberrant accessory vessels originating directly from the aorta and vessels aris-

ing irregularly from the renal artery do not in themselves produce dilatation of the pelvic cavity. These may contribute as aggravating factors, but, not as causal ones.

Dilatation of the pelvic cavity is mostly due to the fibrotic changes in the wall of the pelviureteric junction. The injury caused by fibrosis of the wall of the pelviureteric junction and the pelvic cavity implies in some cases only the fact that the peristaltic waves break; not all of them reach the ureters [16].

A definite increase in pressure of the pelvic cavity or disorder of the renal function rarely occur. These cases, as confirmed by Gibson and Hoyt, are rarely progressive [7, 10]. If in case of such dilatations of the pelvic cavity a reconstructive operation is performed for prevention of, or for improving, function it will not be successful.

It may occur that at the pelviureteric junctions a thick fibrotic ring develops which can be an organic flow obstacle. In these patients resection of the pelviureteric junction may yield good results.

In the surgical indication of pyelectases associated with developmental anomalies, partly demonstrable organic causes and partly lesions of the renal function may be of great importance [3, 19]. Whether a plastic operation is performed in case of a dilated pelvic cavity or the patient is monitored depends, first of all, on whether there is such a degree of obstruction which may result in a renal injury. Our decision can also be influenced by the subjective complaints and by the presence of complications. In the past decade, an amazing development of diagnostic procedures has enabled us to get approximately accurate answers to the above questions. Use of diuretic urography and renography help in reliably assessing the degree of obstruction [17, 22]. Computerized isotope examinations using gamma camera and various materials have made it possible to judge the function of the renal substance of a dilated pelvic cavity. Percutaneous nephrostomy used for diagnostic purposes helps in assessing the degree of obstruction not only on the basis of practical experience but on the results of objective measurements [20, 21]. Percutaneous nephrostomy, especially guided by ultrasound is easy and safe to perform [18]. By analysing the urine gained by nephrostomy, the qualitative characteristics, too, of renal function can be established.

Several reports are available on the value, the importance of their combined use and further development of the above-mentioned examination procedures [4, 5, 13, 14]. Based on literary data, it can be stated that by routine application of diuretic renography and urography, cases requiring a plastic operation are likely to be detected. The computerized isotope examinations made by gamma camera may confirm the indication, and are reliable aids in controlling, the renal function of patients monitored postoperatively or of those having not been operated [3].

Since urodynamic examinations at percutaneous nephrotomy represent an invasive method, it is suggested only if other methods do not help in clarifying the presence of obstruction. The intraoperative application may, however, yield in many cases substantial assistance. It should be employed primarily if after an operation (calculus, abnormal vessel, ptosis), persisting obstruction is imminent.

At our clinic diuretic urography using a TV amplifier, renography and isotope gamma camera examination are most frequently made. Intraoperative recording of pressure is made only in some cases. The methodology of the laboratory renal function tests made by us are discussed in previous papers [11, 12].

The examinations were made to fulfil two aims: (i) it was studied how a dilatation without a demonstrable obstruction influences renal function; (ii) in patients with a horse-shoe kidney, which can be considered as a chronic partial obstruction, and in those with abnormal vessels, attention should be paid to the importance of intraoperative assessment in addition to the lesion of all renal functions.

Results

According to the diagnosis, the 20 patients examined by us were divided into two groups. Table I shows the parameters of patients with pyelectasia living with a solitary kidney without a detectable obstruction. Table II contains the results of examinations, the complications and the subsequent fate of the patients. Based on our examinations, all 5 patients had an atonic pelvic cavity due to the developmental anomaly of the pelviureteric junction.

Patients living with a solitary kidney are the most ideal subjects for measuring the damaging effect of a dilated pelvic cavity on the renal function. Beside the information provided by i.v. urography authors who studied also qualitative parameters, made the separation in each case by the indwelling transrenal drain or during follow-up by using urinary catheters. Both procedures can considerably disturb renal function. Data obtained do not adequately reflect the real situation.

In the 5 patients with a solitary kidney, detailed information could be obtained about the damage of the renal function without any invasive procedures.

As shown by Table II, no obstructions, calculous or inflammatory complications were found in the first three patients. There was no sign suggestive of the damage of renal function.

These patients were not operated. It should be pointed out in their history that in the first two patients the contralateral kidney was removed after the reconstructive operations as a results of complications. The third

TABLE I

Renal function parameters of patients with pyelectasia but without detectable obstruction

No.	Creatinine clearance	Na ⁺ -excretion	K ⁺ -excretion	Ca ⁺ -excretion	P ⁺ -excretion	Se-osmol	Urine osmol	Urine pH
		mmol/day				mOsmol/kg H ₂ O		
1	99	179	30.3	4.94	29.67	295	800	4.8
2	90	130	45.0	3.5	25.4	300	850	4.9
3	124	145	35.0	4.5	28.3	290	810	4.9
4	52	182	35.0	7.9	27.0	295	470	5.8
5	45	145	40.0	4.5	29.5	310	650	5.6

TABLE II

Clinical data of patients with pyelectasia but without detectable obstruction

No.	Sex	Age	Diuretic urography + renography	Subjective complaints	Complications	Fate of patients
1	female	32	atonic pelvic cavity	free of complaints	none	observation
2	female	28	atonic pelvic cavity	temporary discomfort under right costal arch	none	observation
3	female	40	atonic pelvic cavity	sometimes imperative urge to urinate	temporary pyuria	observation
4	male	55	atonic pelvic cavity	dull right renal pain	pyuria + impaired function	Anderson-Hynes reconstructive operation
5	male	45	atonic pelvic cavity	right renal colic	pyuria + stone + impaired function	Anderson-Hynes reconstructive operation

female patient had renal agenesis of the right side. The i.v. urogram and arteriogram of patient No. 1 are shown in Figs 1 and 2.

It deserves to be mentioned that, according to the history of cases complicated by calculi and inflammation, both patients were born with a solitary kidney. The solitary kidney had already been operated on. In one case it was lithotomy, in the other one lithotomy and reconstructive operation. Despite that no obstruction could be detected because of the damage of renal function and of inflammation, in both cases reconstructive surgery was made beside lithotomy. Statistical data revealed that in case of a dilated pelvic cavity without an obstruction, stone formation and infection do not occur more often than in the normal population [6]. In our opinion, however, if the

dilated pelvic cavity has already been infected, the elimination of the infection without eliminating the dilatation rarely succeeds conservatively. For this reason a reconstructive operation has been decided upon even in lack of an obstruction in these cases.

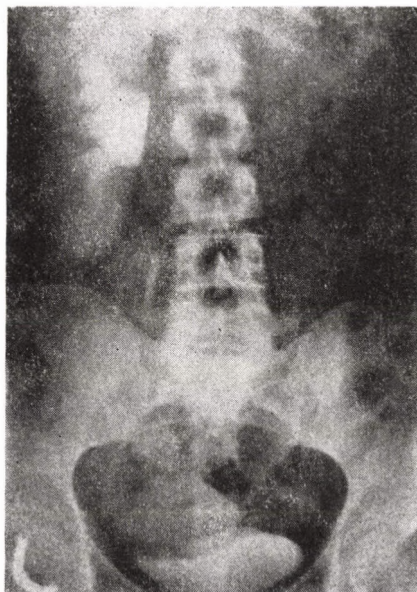


FIG. 1. I.v. urogram of patient with right solitary kidney. The urodynamic examinations showed an atonic pelvic cavity

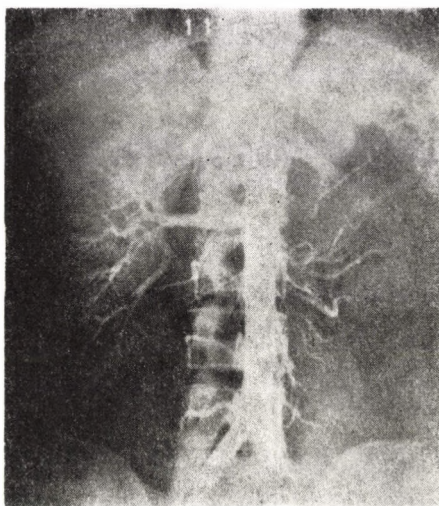


FIG. 2. Angiography of patient No. 1. There was no evidence of abnormal vessels

TABLE III

Clinical data of patients with dilated pelvic

No.	Age	Sex	Diagnosis	Diuretic renography + urography
1	56	male	horse-shoe kidney	partial obstruction on left side
2	54	male	horse-shoe kidney	partial obstruction on left side
3	38	female	horse-shoe kidney	partial obstruction on both sides
4	28	male	horse-shoe kidney	partial obstruction on left side
5	32	male	horse-shoe kidney	partial obstruction on left side
6	34	male	horse-shoe kidney + aberrant vessel	atony on left side
7	29	male	horse-shoe kidney + aberrant vessel	partial obstruction on left side
8	20	female	horse-shoe kidney + aberrant vessel	obstruction on left side
9	22	male	rotatory abnormality	atony on right side
10	26	male	rotatory abnormality	atony on left side
11	30	male	aberrant vessel	obstruction on right, atony on left side
12	38	female	aberrant vessel + ptosis	obstruction on right side
13	24	male	aberrant vessel	atony on left side
14	31	female	aberrant vessel	obstruction on left side
15	28	male	aberrant vessel	obstruction on right, atony on left side

Table III summarizes the data of patients with dilatation of the pelvic cavity due to obstruction caused by various types of developmental anomalies of the kidney.

Table IV shows data of all renal functions. The performed isotope studies revealed tubulosecretory damages in the obstructive cases.

In case of each calculous complication preliminary examination was made for clarifying the endocrine metabolic cause of stone-formation. In cases where the preliminary examinations revealed a partial occlusion, intrapelvic pressure flow studies were made before and after the elimination of the presumed cause (division of isthmus, pexis, resection of abnormal vessel). If the values improved essentially after the relieving operation, a reconstructive surgery was not performed.

Reconstructive operation was indicated (i) by dilatation and infection even if after release of the obstruction free flow and normal pressure were observed; (ii) by a partial obstruction persisting after elimination of the presumed cause; (iii) in case of a demonstrable damage of the entire renal function; (iv) in case of recurrent calculous complications where dilatation of the pelvic cavity could have probably been responsible for stone-formation.

Three of the 8 patients with a horse-shoe kidney shown in Table III, were free of complications. Considering their age no operations were per-

cavity associated with developmental anomalies

Subjective complaints	Complications	Fate of the patient
sacral pain on movement	none	observation
none	none	observation
definite hypogastric pain	none	division of isthmus
colic on left side	haematuria	lithotomy + division of isthmus + endocrine examination
colic on left side	haematuria + stone	lithotomy + division of isthmus + endocrine examination
lumbar pain	stone + infection + deterioration of function	reconstructive operation
colic on left side	stone + infection + deterioration of function	reconstructive operation
hypogastric pain	hypertension	nephrectomy
abdominal discomfort	none	observation
abdominal discomfort	none	observation
none	infection	reconstructive operation on right side
pain on right side	none	torsion pexis
none	none	
pain on left side	infection	reconstructive operation
pain on left side	infection + stone	reconstructive operation

TABLE IV

Results of examinations on total renal functions in cases of dilatations of the pelvic cavity

No.	Diagnosis	C _e ml/min	Urinary Na ⁺ - excretion	Urinary K ⁺ - excretion	Urinary Ca ⁺ - excretion	Urinary P ⁺ - excretion	Urine osmol mOsmol/ kg H ₂ O	Urine pH
			mmol/day					
1	Horse-shoe kidney	122	140	82	4.8	31.2	920	4.5
2	Horse-shoe kidney	130	115	75	3.8	28.2	820	5.0
3	Horse-shoe kidney	115	122	68	3.0	29.0	850	4.9
4	Horse-shoe kidney	100	118	70	8.2	55.0	800	4.95
5	Horse-shoe kidney	110	120	65	7.82	59.1	810	5.0
6	Horse-shoe kidney + aberrant vessel	65	82	32	5.2	40.2	650	5.1
7	Horse-shoe kidney + aberrant vessel	71	65	30	6.0	45.8	700	5.2
8	Horse-shoe kidney + aberrant vessel	75	130	50	2.5	23.4	820	4.9
9	Rotatory abnormality	105	95	45	3.2	19.4	810	5.0
10	Rotatory abnormality	105	100	60	4.1	29.0	790	4.6
11	Aberrant vessel	55	122	30	2.1	15.3	620	5.3
12	Aberrant vessel + ptosis	95	100	60	3.2	28.2	810	5.0
13	Aberrant vessel	110	98	53	2.8	19.5	800	4.9
14	Aberrant vessel	75	80	40	2.1	18.0	620	5.3
15	Aberrant vessel	110	55	30	3.5	13.2	650	5.4

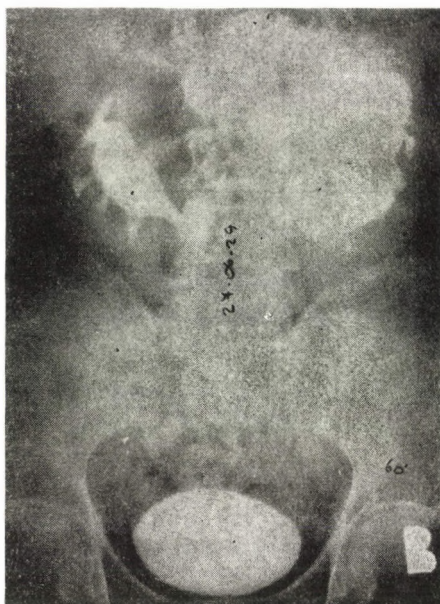


FIG. 3. I.v. urogram of a patient with a horse-shoe kidney (Table II, patient No. 2). Despite the definite dilatation of the pelvic cavity on the left side, no operation was performed. During the 10-year follow-up there was no progression. Patient is free of complications and complaints



FIG. 4. I.v. urogram of patient with a horse-shoe kidney. Formation of the pyelic calculus on the left side was supposed to be due to a metabolic cause. After division of the isthmus and removal of the stone, no reconstructive operation was performed

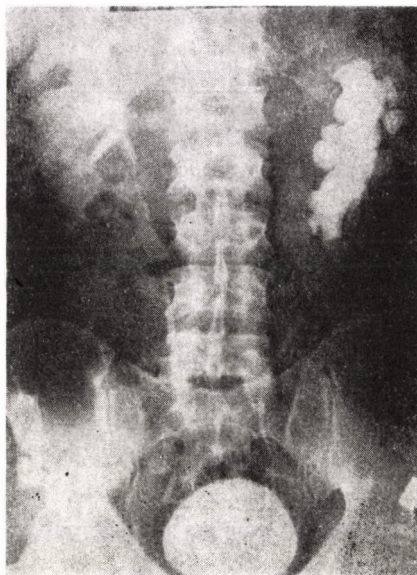


FIG. 5. Left kidney with rotatory abnormality with no detectable obstruction. After a two-year observation period there has been no progression

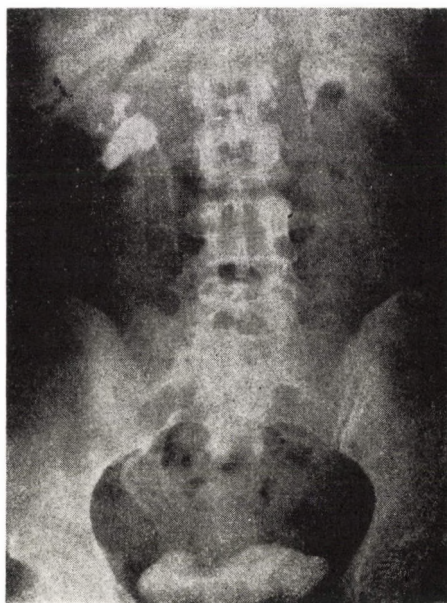


FIG. 6. I.v. urogram of patient No. 12. After performing rotatory pexis, the intra-operative pressure flow study of the pelvic cavity showed normalization of pressure

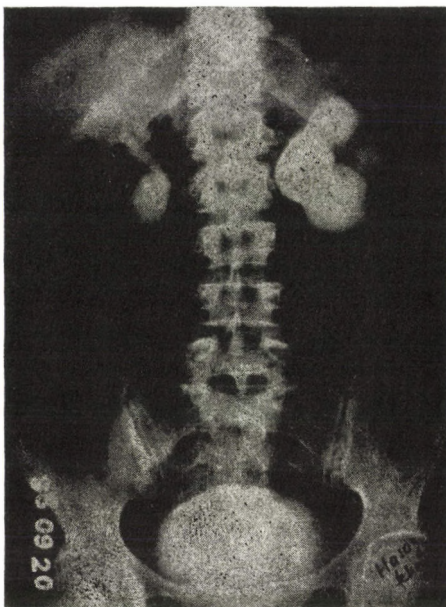


FIG. 7. The definite obstruction on the right side has not been solved even after resection of the abnormal vessel. Reconstructive operation was made

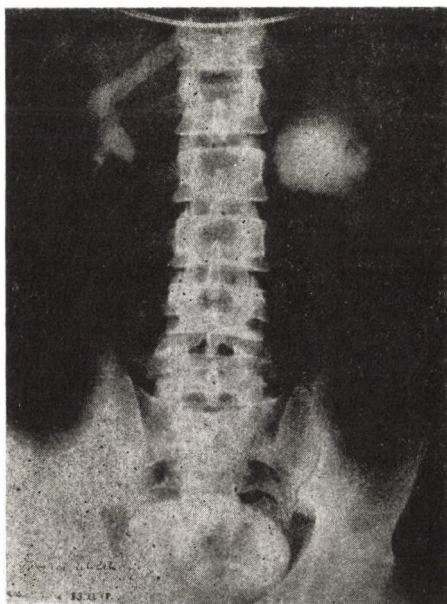


FIG. 8. I.v. urogram of patient No. 15. On the right: atony; on the left: obstruction. Pyeloplasty of the left side was made

formed in patients Nos 1 and 2, despite the considerable dilatation of the left side and the detectable partial obstruction also shown by i.v. urography (Fig. 3). In patient No. 3 division of the isthmus was indicated by subjective complaints. Calculous complications were encountered without inflammation in two cases (patients Nos 4 and 5). According to our results, calcium and phosphate metabolic disorders could have been the cause of stone-formation. After division of the isthmus, the partial obstruction was released. Consequently, no reconstructive operation was made but lithotomy. A characteristic picture of the pelvic cavity is shown by the i.v. urogram of patient No. 4 (Fig. 4). Calculi with infection were found in two patients. In both cases a slight lesion of urinary concentration ability could be observed. Although the intraoperative pressure flow studies of the pelvic cavity made before and after division of the isthmus showed release of the obstruction, in view of the complications no reconstructive operation was performed.

Of the group with pyelectasia due to malrotation or to an abnormal vessel, three patients (Nos 9, 10, 13) no impairment of the renal function or no other complications were found. The urodynamic examination showed atony of the pelvic cavity of the affected side. These patients were not operated. The characteristic i.v. urogram of patient No. 10 is shown in Fig. 5. One patient underwent rotatory pexis (No. 12) because the intraoperative pressure flow study yielded normal results after lifting and rotation of the ptotic kidney. The preoperative i.v. urogram is shown in Fig. 6.

In two additional patients (Nos 14 and 15) considerably impaired renal function was found. This fact, considering the detectable obstruction made indication of the reconstructive operation unequivocal even in lack of complications (Figs 7 and 8).

Conclusions

1. The atonic dilated cavity systems are not associated with impaired renal function in complication-free cases. The so-called preventive reconstructive operations for preserving renal function and for preventing complications are not advisable.

2. Partial obstructions observed in fusional and rotatory abnormalities or in aberrant vessels may be released after eliminating the presumed cause (division of isthmus, elevation of the abnormal vessel). Reconstructive operation is rarely required.

In case exploration was indicated only by the patient's complaints and no complications were detected, a reconstructive operation seems to be indicated only in fairly dilated cavity systems causing compressive pressure symptoms.

3. In case of dilated cavity systems associated with infection and/or deterioration of total renal function, even in absence of a detectable obstruction reconstructive operation is to be made.

4. In calculous complications, the reconstructive operation of the dilated pelvic cavity is indicated if stone-formation could be supposed to be due to an atopic or partially obstructed pelvic cavity. Neither metabolic nor endocrine causes participate in stone-formation.

In partial obstruction, an intraoperative pressure flow study is a valuable aid in selecting the type of operation.

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Operationsindikation der Nierenhohlssystemerweiterung

A. KARSZA, T. BANYÓ und Z. ENGERT

Berichtet wird über die Untersuchungsergebnisse von 20 Patienten, bei denen es sich um eine, sich zur renalen Entwicklungsanomalie gesellende Hohlssystemerweiterung handelte. Die Indizierung der Operation bzw. die Auswahl des Operationstypes erfolgten anhand der Ergebnisse. Zum Nachweis der Obstruktion dienten die diuretische Urographie und die Renographie, während zur Bewertung der Nierenfunktion nebst der Gammakamera-Isotopenuntersuchung auch die auch das Azidifizierungs- und Konzentrierungsvermögen der Nieren bestimmt wurden. Die intraoperative Messung des Hohlsystemdruckes hat sich als eine nützliche Hilfe zur Auswahl des Operationstypes erwiesen. Schließlich finden die Indikationen der Nierenhohlssystemplastik eine Besprechung.

Оперативные показания при расширениях полостной системы почек

A. KAPCA, T. БАНЬО и З. ЭНГЕРТ

Авторы знакомят с результатами обследования 20 больных с расширением полостной системы почек, присоединившимся к врожденному нарушению их развития. Полученные результаты они оценивают с точки зрения показаний к операции и выбора способа вмешательства. Обращают внимание на значение диуретической урографии и ренографии в выявлении обструкции. Для оценки почечной функции, наряду с изотопным исследованием гамма-камерой, были выполнены определения концентрирующей и ацидозной функции почек. Согласно их опыту, интраоперативное измерение давления в системе полостей является ценной информацией и помогает при выборе типа операции. В своих выводах авторы очерчивают показания к пластическим операциям на полостной системе почек.

Significance of Synthetic Sutures in Urological Operations of the Cavity System

A. VÉGH and R. KARDOS

Department of Urology, Postgraduate Medical Institute,
H-1389 Budapest, Szabolcs u. 33–35, Hungary

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The authors report on their experiences on synthetic nonabsorbable and absorbable suture materials in a 12-year material of urological operations of the pelvic cavity.

The synthetic suture materials are compared concerning the basic requirements, the surface properties, knotting safety, tensile strength, manageability, fluid absorption, tissue compatibility, allergizing effect, absorbability and sterilizability.

The experiences of animal experiments are reviewed, primarily on the basis of reaction index studies in noninfected and infected urine.

It is stated that in urological operations of the pelvic cavity, a safe haemostasis and prevention of prolonged complications (e.g. pyuria, scarring, stone-formation) can be ensured mainly by the use of synthetic suture materials.

Research workers dealing with surgical suture materials have long been engaged in creating a kind of suture material which is characterized by a great tensile strength, a tissue compatibility, by a speed of absorption known beforehand, by a great knotting safety, a simple management and by an easy way to knot.

The comparative studies of Large [7] revealed already in 1943 that synthetic suture materials (e.g. polyamide) had better physical characteristics and caused essentially smaller inflammatory tissue reaction than the traditional ones made of natural materials (e.g. flax, silk, catgut).

Subsequently, extensive research was initiated for producing synthetic suture materials of even more favourable characteristics. After having produced several kind of nonabsorbable synthetic suture materials (polyethylene, polypropylene, polyamide, fluorocarbon, etc.), polyglycolic acid (Dexon®), the first absorbable synthetic suture free of toxic, antigenic and teratogenic properties appeared in 1968 which was followed in 1972 by polyglactin 910 (Vicryl®) then in 1980 by polydioxanone (PDS®) [1].

The synthetic suture materials can be classified

1. On the basis of the way they are produced (i) polyamide; (ii) polyester; (iii) polyolefin, etc.
2. On the basis of the biological character of the produced suture materials (i) absorbable; (ii) nonabsorbable.

TABLE I
Requirements of various suture materials

Requirements	Catgut	Silk	Polyamide		Metal (mono)	Absorbable polyester	
			mono	multi		Dexon	Vicryl
Surface properties (saw effect)	—	—	+	—	+	—	—
Knotting safety	—	+	—	—	+	—	—
Tensile strength	—	—	+	+	+	+	+
Manageability	—	—	+	+	+	+	+
Fluid absorption	—	—	+	+	+	+	+
Tissue compatibility	—	—	+	+	+	+	+
allergic effect	?	+	+	+	+	+	+
toxic effect	+	+	+	+	+	+	+
carcinogenic effect	+	+	+	+	+	+	+
specific, irritant effect	—	+	+	+	+	+	+
Absorbability	+	—	—	—	—	+	+
Simple, inexpensive, safe sterilizability	+	+	+	+	+	+	+
Inexpensive, easy availability	+	+	+	+	+	—	—

+: Meets the requirements; —: does not meet the requirements

3. On the basis of the components of the suture materials (i) monofilament; (ii) polyfilament (multifilament); (iii) multifilament with a monofilament coating.

4. On the basis of the diameter of the produced thread: 8–0–11/0.

5. On the basis of the technology of production (i) twisted; (ii) spun; (iii) drawn.

The usability of the various kind of suture materials is determined by the size of reaction between the threads and the tissues. The tissue reaction depends partly on the physical, and partly on the chemical properties of the thread.

The following properties are required which have been best blended in the synthetic absorbable sutures (Table I).

Surface properties: Monofilament threads of a smooth surface produce an even puncture tract, in case of a penetration of identical strength. The consequential inflammatory reaction is less considerable than in the case of multifilament threads of a rougher surface, and of threads of synthetic and natural materials. In addition to nonabsorbable, synthetic monofilament threads, the polyglactin 910 (Vicryl®) with a monofilament coating, and the first monofilament synthetic absorbable thread, the polydioxanone (PDS®), too, are of smooth surface.

Tensile strength, manageability: The tensile strength of the threads are examined in three different states (i) linear; (ii) knotted; (iii) implanted in tissues in the function of time.

Of the synthetic threads of the same diameter, the multifilament sutures

have a greater tensile strength, they are damaged less easily and are more flexible than the monofilament sutures. However, the latter are more elastic. The elasticity of the individual types attains even 23%. Therefore they cut into the tissues less strongly. On the other hand, owing to their smooth surface and elasticity, knotting and the safety of knotting are unfavourable, the knots may slip. For avoiding slipping, it is advisable to place three or four knots, with both the monofilament as well as the synthetic threads.

Of the threads implanted in tissues, those of natural materials lose their tensile strength to various extents, often incalculably, while the absorbable synthetic threads do so gradually. The tensile strength of nonabsorbable synthetic threads remains unchanged practically for months [13].

Time is a factor connected with the time of absorption of the sutures when the tensile strength of the thread decreases in the tissues by 50% as a result of the interactions between the thread and the cells (proteolysis, hydrolysis). The tensile strength of polyglactin 910® (Vicryl) and polyglycolic acid (Dexon®) threads decreases to one-half after 15 days (Fig. 1) [19]. Since, this time amounts to 6 to 8 days in the case of catgut, these synthetic threads can be used in surgical fields where time is not enough for catgut to be used. Applying polydioxanone (PDS®), this occurs still later after the fourth week [15]. In view of this and also the fact that Hastings et al. [6] and Rasmussen [14], studying the healing of a bladder wound, have found that the bladder wall regains its 100% tensile strength from the 14th day on to the 21st day, it seems that synthetic, absorbable sutures are the most suitable for use in bladder operations.

Fluid absorption: the synthetic, multifilament sutures absorb tissue fluids, the humidity spreads along the threads, and they do not absorb bacteria, do not swell and show no capillarity.

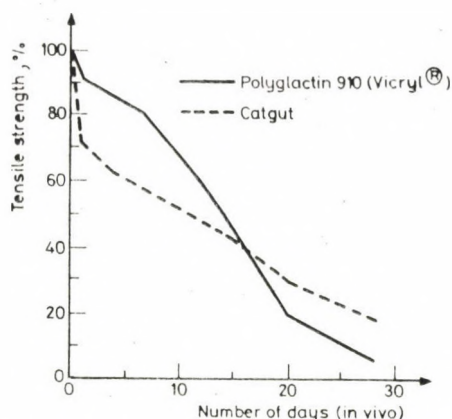


FIG. 1. Decrease of tensile strength of catgut made of natural material and of polyglactin 910, synthetic absorbable sutures implanted into tissue (after Muxfeld [12])

Tissue compatibility (rejection reaction): The thread implanted in tissues, may it be of any origin or composition, should be considered to be a foreign body. The rejection reaction between the thread and the tissue is characteristic of the thread and it changes during the healing process.

For measuring and comparing the reactions of various kinds of threads, the conception of the so-called reaction index has been introduced [2, 5, 9].

$$R_1 = \frac{D \text{ (diameter of thread)}}{X \text{ (sphere of reaction)}}$$

At our Institute, the various threads were compared and analysed by the above formula in 24 operations performed on rabbit bladder. Control examinations and their comparative analysis followed 2, 4, 8 and 12 weeks postoperatively. Table II shows that the lowest reaction index is displayed by the synthetic absorbable sutures and next to them by the nonabsorbable synthetic ones. The reaction index of threads made of natural materials is the highest. In an infected environment the reaction index is higher but after some time it decreases [17].

The histamine-test with absorbable synthetic threads did not show antigenic properties connected with the threads [18].

Absorbability: The absorbable synthetic sutures are composed of aliphatic polyesters. These esters show weak resistance to the hydrolyzing effect.

Polyglycolic acid (Dexon®), polyglactin 910 (Vicryl®), polydioxanone (PDS®) decompose during hydrolysis, the end-products being CO₂ and water (Fig. 2).

Polyglactin 910 (Vicryl®) is eliminated by the organism after the 70th day, polyglycolic acid (Dexon®) after the 120th day and polydioxanone (PDS®) after the 180th day [8, 15].

As a result of the rapid decomposition and absorption stone-formation occurs particularly rarely on the synthetic absorbable sutures. Some cases were reported by Tóth [16], by Francis et al. [4], and we ourselves observed stone-formation in two cases on polyglycolic acid sutures. Stone-formation has still not been reported in the available literature on polyglactin 910 (Vicryl®) and polydioxanone (PDS®) threads.

Sterilizability: Sterilization of nonabsorbable and absorbable synthetic threads with ethylene oxide gas and irradiation can be considered satisfactory.

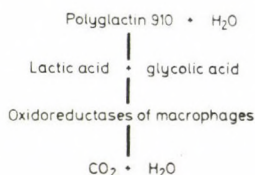


FIG. 2. Decomposition of polyglactin 910 (Vicryl®) in the organism

TABLE II
Reaction indices of various sutures ($\pm s_d$)

Suture	2nd week		4th week		8th week		12th week	
	infected	noninfected	infected	noninfected	infected	noninfected	infected	noninfected
Catgut	22.23 $\pm$ 1.47	12.73 $\pm$ 3.38	19.20 $\pm$ 1.83	11.15 $\pm$ 1.117	9.94 $\pm$ 1.15	9.57 $\pm$ 0.73	non	non
Silk	8.66 $\pm$ 1.02	8.97 $\pm$ 0.64	9.49 $\pm$ 1.16	7.90 $\pm$ 1.14	8.92 $\pm$ 0.91	7.34 $\pm$ 0.71	8.28 $\pm$ 0.77	5.32 $\pm$ 0.54
Polyamide	3.04 $\pm$ 0.58	2.59 $\pm$ 0.30	3.64 $\pm$ 0.72	3.46 $\pm$ 0.36	4.69 $\pm$ 0.68	3.22 $\pm$ 0.52	3.59 $\pm$ 0.70	2.56 $\pm$ 0.35
Dexon®	1.58 $\pm$ 0.67	0.26 $\pm$ 0.24	3.75 $\pm$ 0.98	2.29 $\pm$ 0.37	1.45 $\pm$	1.24 $\pm$	non	non
Vicryl®	1.56 $\pm$ 0.54	1.21 $\pm$ 0.19	1.98 $\pm$ 0.48	1.89 $\pm$ 0.33	non	non	non	non
Metal (steel)	—	4.93 $\pm$ 0.37	—	4.58 $\pm$ 0.23	—	non	—	non

non = cannot be evaluated

TABLE III
Operations performed between 1972 and 1983

Type of operation	1972	1973	1974	1975	1976	1977	1978	1979	1980	1981	1982	1983	Total
Renal operations	190	193	177	207	194	228	146	182	184	179	203	210	2293
Ureteral operations	116	127	116	105	113	89	49	65	107	111	124	119	1241
Bladder operations	93	109	135	116	115	104	39	44	121	118	139	125	1258
Transvesical prostatectomies	93	111	119	125	120	97	106	97	125	131	124	117	1365
Genital operations	285	241	281	287	280	330	255	370	340	321	338	352	3680
Total	777	781	828	840	822	848	595	549	877	860	928	923	9837

Clinical Experiences, Results

The nonabsorbable synthetic threads have been used since 1972, the absorbable synthetic threads since 1975 at our clinic. A total of 9837 operations on the pelvic cavity have been performed so far. The surgical material of our clinic during the 12 year period is shown in Table III. Operations in which no suture materials were used are not included (prostatic biopsy, bladder biopsy, TUR, lithotripsy, lithotomy by the Young instrument, stone extraction by the Dormia basket, etc.).

The youngest patient was 4 years old, the oldest 89.

The ratio between men and women was 60 : 40.

Since 1975 cavity systems have been closed only by absorbable synthetic multifilament threads. In 1984 synthetic monofilament sutures, too, were used in 12 cases for closing the bladder.

Muscles are closed by synthetic absorbable, the fascia by synthetic non-absorbable multifilament, and the skin by synthetic nonabsorbable, suture materials.

Early stitch abscess (within 15 days) was found between 1972 and 1975 in 14% of the patients, between 1975 and 1978 in 3.2% and between 1978 and 1983 in 2.6%.

Late stitch abscess (over 15 days) was found between 1972 and 1975 in 10% of the patients, between 1975 and 1978 in 7% and between 1978 and 1983 in 6% (Fig. 3).

Polar kidney resections, form a special group in our material, because since 1975, the management of renal parenchyma has been made by synthetic absorbable multifilament threads (polyglycolic acid: Dexon®). Since then wound healing time exceeding 15 days has been reduced from 30% to 7% [11].

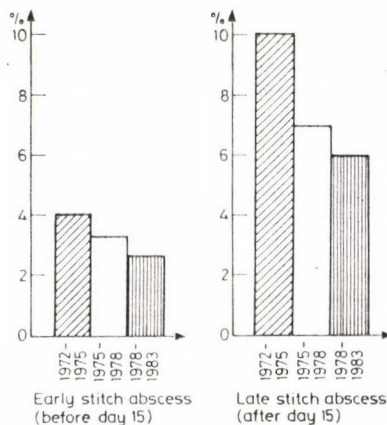


FIG. 3

Between 1972 and 1975, while using synthetic nonabsorbable monofilament sutures [18], in a total of 252 transvesical prostatectomies stones were found in 18 cases on the thread in the edge of the prostate (8.8%) and in 8 cases on thread in the dome. These stones could be removed only by a second intervention.

Since 1975, i.e. since using synthetic absorbable sutures, stone-formation on threads has not been observed in transvesical prostatectomies [17].

Discussion

Survey and comparative evaluation of the various kinds of suture materials show that at present there is no thread which could meet all requirements.

Threads made of natural materials (catgut, flax, silk) get easily torn when being of a small diameter and this endangers safety. They may produce an extensive and prolonged inflammatory reaction and may eventually stimulate stone-formation.

The tissue reaction of synthetic nonabsorbable sutures is smaller and their physical properties are also more favourable. They still cannot be applied within the pelvic cavity because they are not absorbed and cause prolonged inflammation, stone-formation and scar development.

Due to the rapid absorption and also to the outstanding and even tensile strength of synthetic absorbable sutures, they can be best used in places where within the kidney cavity system an accurate and safe haemostasis should be attained. Consequently, in transvesical prostatectomy, arterial haemostasis in the prostatic bed and on its edge can only be solved by these sutures [10, 16].

During polar resections the use of synthetic absorbable multifilament sutures are of a similar importance for closing the pelvic cavity and for arresting parenchymal haemorrhage [11]. In all other operations opening the cavity system, the most frequent prolonged complications as, e.g. inflammation, pyuria, scar development, stone-formation, can be best solved by using synthetic absorbable sutures causing a small tissue reaction and being rapidly eliminated by the organism.

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Bedeutung der synthetischen Fäden bei urologischen Hohlsystemoperationen

A. VÉGH und R. KARDOS

Die mit den synthetischen, sich nicht resorbierenden und resorbierenden Nahtmaterialien ermittelten Erfahrungen werden anhand der im Laufe von 12 Jahren durchgeführten urologischen Hohlsystemoperationen und der Literaturdaten erläutert.

Dem Vergleich und der Auswertung der synthetischen Fäden lagen folgende Gesichtspunkte zugrunde: grundlegende Bedingungen, Oberflächenverhältnisse, Knotensicherheit, Reißfestigkeit, Handlichkeit, Flüssigkeitsaufnahme, Gewebefreundlichkeit, allergisierende Wirkung, Resorptionsfähigkeit und Sterilisierbarkeit.

Die im Laufe der Tierexperimente durchgeführten Reaktionsindexuntersuchungen bei infiziertem und nicht infiziertem Harn finden eine ausführliche Besprechung.

Die praktischen Erfahrungen und theoretischen Daten führten zur Feststellung, daß die zuverlässliche Blutstillung und die Vorbeugung der chronischen Komplikationen (Pyurie, Vernarbung, Steinbildung) durch Verwendung sich resorbierender synthetischer Nahtmaterialien gewährleistet werden kann.

Значение синтетических шовных материалов в урологических полостных операциях

А. ВЕЙГ и Р. КАРДОШ

Авторы сообщают о собственном опыте применения синтетических, не рассасывающихся и рассасывающихся шовных материалов, который они приобрели, производя на протяжении 12 лет операции урологической полостной системы. Они приводят также краткий литературный обзор по данному вопросу.

Сравнивают и оценивают синтетические волокна с точки зрения основных требований к ним, надежности узлов, крепости на разрыв, удобства пользования, гигроскопичности, тканевой совместимости, аллергизирующего воздействия, способности к рассасыванию и возможности стерилизации.

Знакомят с опытом, накопленным в экспериментах на животных, в первую очередь, на основании исследований индекса реакции, в случае инфицированной и неинфицированной мочи.

Указывают, что, при операциях на урологических полостных системах, обеспечить надежный гемостаз, избежать затяжных осложнений (напр. пиурия, рубцевание, камнеобразование) можно, в первую очередь, с помощью применения рассасывающегося синтетического шовного материала.

Study of Renal Acidification in Various Urological Clinical Pictures

T. BANYÓ and A. KARSZA

Department of Urology, Postgraduate Medical Institute,
H-1389 Budapest, Szabolcs u. 35, Hungary

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The authors performed acid loading examinations in 40 patients with obstructive nephropathy and in 47 recurrent Ca-stone-formers. In 16 of their patients (in 13 patients, 14.9%) results characteristic of incomplete RTA were found.

Regression analyses on the pH-TA and pH-AD values of the results of controls were made. Comparison of the data of the healthy and patient groups was made by statistical analysis.

Elimination of acidic materials (H^+ -ions) produced during the metabolic process is the task of the kidney. As a result of an impaired acidifying ability, retention of H^+ -ions occurs with loss of fixed bases essential for the organism. Consequently, metabolic acidosis develops. The kidney is capable of maintaining the acid-base balance of the organism by changing the urinary pH within relatively wide limits. The difference between the pH of the glomerular filtrate identical with the plasma and the pH of the final urine reflects the functioning of the acidifying mechanism along the entire length of the tubuli. However, the role of the individual tubular segments greatly varies. H^+ -ion secretion occurs along the entire length of the tubuli. Bicarbonate reabsorption is largely proximal, while titratable acidity (TA) and ammonium discharge (AD) are functions connected with the distal tubuli [10, 18].

The shift of the acid-base equilibrium of the urine into a too acidic or alkaline direction is prevented by buffer-systems. Urine can be regarded as a complex system of buffers. Its chemical reactions largely depend on the proportion of the components.

In the present paper result of our studies on the acidifying ability of the urine are reported made in patients with obstructive neuropathy and renal calculus, respectively.

Material and Method

Acid loading examinations were made in 40 patients with obstructive nephropathy and in 47 patients with recurrent renal Ca-stone formation. As controls, data of 15 patients with no detectable renal disease were evaluated.

During the study the method of Wrong and Davies was followed, the essence of which is that the serum bicarbonate level is reduced to a level below the renal threshold by producing metabolic acidosis [22]. Thus no bicarbonate is discharged by the urine and the parameters of the distal tubular acidifying capacity (TA, AD) can be clearly studied. The patients were administered ammonium chloride tablets during a period of 20 minutes in 0.1 g/body weight. They collected their urine before starting the examination, then, subsequently at hourly intervals for 5 hours. The pH, TA and AD values of the hourly urine samples were measured and calculated, respectively. Before starting, and during, the examination, blood-gas analyses were made three times. In patients passing urine infected with urease-decomposing bacteria no acid loading was made.

The chemical reaction of the urine was measured by a combined, pH-sensitive glass electrode without a diaphragm. The coulomb-metric procedure was selected for determining TA [16]. Using this method, the known drawbacks of volumetric titration can be eliminated (i. e. difficulties in adjusting the constants in the solutions, inaccuracies accompanying the volume changes). Measurements were made by a Radelkis' Acigraph which is suitable for simultaneous measuring of pH. Our further endeavour is to work out a method for analysing the shape of the curve, too. This requirement can be fulfilled by using the Radelkis Universal Recording Titrating Equipment. The shape of the titration curve can be analysed if the pH of the urine has to be set acidic. TA can be directly calculated based on the known paper speed and the generating current intensity (Fig. 1).

The ammonium-ion concentration of the urine samples was measured by microcapillary ion-selective electrodes. The probe of the microcapillary ammo-

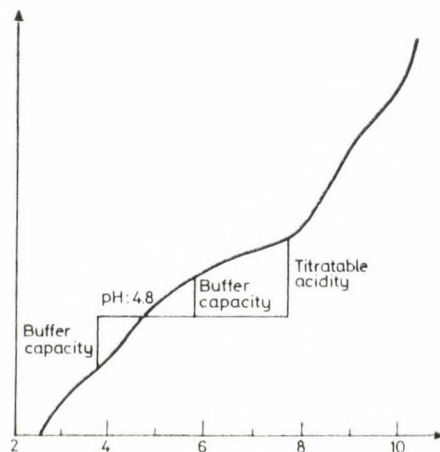


FIG. 1. Complete titration curve of urine of a pH of 4.8. Knowing the paper speed and the generating current intensity, titratable acidity and buffer capacity can be calculated

nium sensitive electrode used by us was a PVC membrane activated by non-actin. For recording, the electrode was integrated in a Radelkis type OP-266 Biological Alkaline Microanalysator and it was connected to the Na-channel of the equipment [3].

Results

As controls, data of 15 healthy individuals were analysed. For the statistical analysis of pH-TA and pH-AD (considering the linear correlation to be supposed on the basis of the Henderson-Hasselbalch equation), regression analysis was made. The equation of the regression line constructed on the basis of the TA values before the acid loading of the controls is

$$y = 3.41 - 0.38x,$$

where $y = \log \text{TA}$ and the value of r is -0.80 . The equation constructed for the line of AD is

$$y = 2.88 - 0.24x,$$

where $y = \log \text{NH}_4^+$ and the value of r is -0.59 . The formulae of the regression lines for the highest TA and AD values after the acid loading are

$$\text{TA}y = 4.11 - 0.49x: r = -0.77$$

$$\text{AD}y = 4.75 - 0.65x: r = -1.91.$$

Based on the r values an adequate correlation can be expected between the variables. Of the regression lines after the loading, the slope representing AD shows a more definite rise than does TA (Figs 2 and 3).

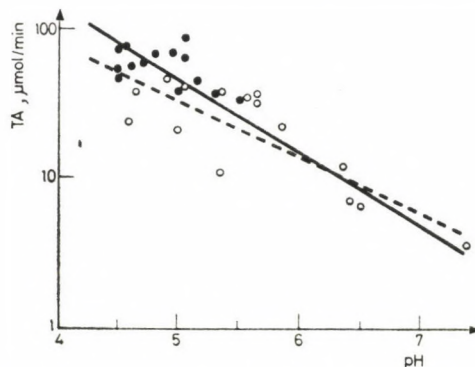


FIG. 2. Regression lines constructed from the values of pH and TA at rest (empty circles), of the lowest pH during loading and of those of the highest TA (solid circles). Broken line: values at rest; continuous line: values on loading

TABLE I

Comparison of the pH, TA and AD values before and during acid loading of 47 recurrent Ca-stone-formers with the controls; Statistical analysis was made by the t-test

	At rest			During loading		
	pH	TA	AD	pH	TA	AD
Control group	5.59±0.74	25.2±14.6	40.0 ±27.65	4.84±0.19	57.8±15.67	107.2±39.63
Stone-formers	5.73±0.77	22.1±18.58	43.7 ±18.67	4.88±0.43	43.3±23.98	93.8±31.6
<i>t</i>	0.36	0.91	0.47	0.37	2.61	1.19
<i>P</i>					0.01	
RTA group	6.42±0.98	17.4±14.8	36.88±15.52	5.73±0.37	29.5 ± 8.22	68.9±39.21
<i>t</i>	2.07	1.25	0.32	5.8	5.53	2.02
<i>P</i>	0.1			0.001	0.001	0.1

TABLE II

Comparison of the pH, TA and AD values of 9 patients with obstructive nephropathy (RTA) with the controls

	At rest			During loading		
	pH	TA	AD	pH	TA	AD
Control group	5.59±0.74	25.2 ±14.6	40.0 ±27.65	4.84±0.19	57.8±15.67	107.2±39.63
Obstructive RTA group	6.52±0.88	15.43±13.7	28.17±15.0	5.87±0.33	30.5±10.3	54.3±29.5
<i>t</i>	2.73	1.65	1.35	5.15	5.15	3.72
<i>P</i>	0.02			0.001	0.001	0.002

Acid loading examinations were performed in 47 patients with recurrent Ca-stone formation. In the calculous group—as compared to the controls—no significant difference was found in either of the parameters measured before loading, while during loading the TA value was significantly lower in the calculous group. In 7 of our patients with stone-formation, data were characteristic of incomplete RTA. (Data of 3 patients are included in both RTA groups. They belong to the obstructive group and were found to have stones.) The measured parameters of the RTA group with stones differed significantly as compared to the control groups (Table I).

Of 40 obstructive nephropathic patients 9 were found to show results characterizing incomplete renal tubular acidosis. Their pH, TA and AD values were compared to the data of the normal control groups. For statistical evaluation, the *t*-test was used. The data on TA and AD before loading showed no significant difference. The pH of the RTA group, however, proved to be significantly higher already before the acid loading. A significant difference was found in the two groups in the lowest pH as well as the highest TA and AD values during loading (Table II).

Discussion

The details of the renal acidifying mechanism under physiological conditions is known. Among others the summarizing studies of Pitts and Alexander [18] and Pitts [19] serve as bases for this knowledge. Several hypotheses are available on the functioning of the acidifying mechanism, as for example,

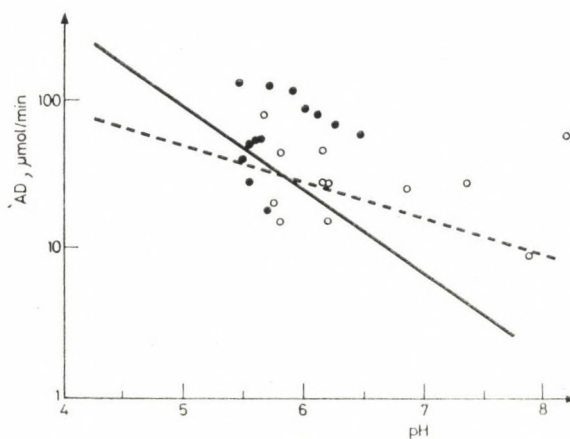


FIG. 3. Regression lines constructed from the values of pH and AD at rest (empty circles), from the lowest pH and highest AD during acid loading (solid circles). Broken line: former, continuous line: the latter

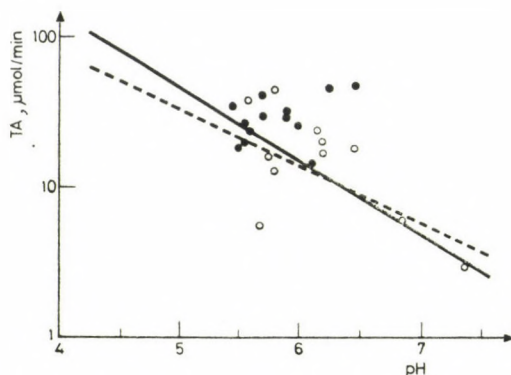


FIG. 4. Relationship between the TA values of RTA patients ($n = 13$) before and during loading and the regression lines for the data of the control group

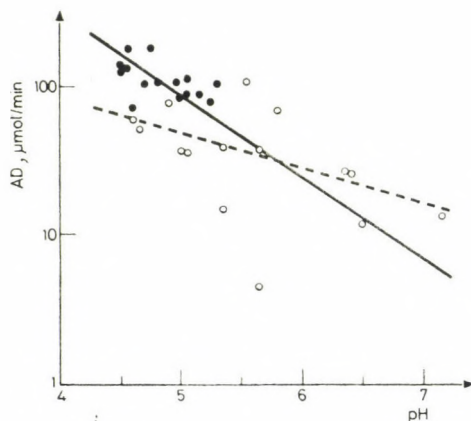


FIG. 5. Relationship between the AD values of RTA patients before and during loading and the regression lines for the data of the control group

the phosphate reabsorption theory, the bicarbonate reabsorption theory, the tubular secretion of molecular acids and the mechanism of ion exchange. A great amount of the titratable acidity is represented by phosphate buffers. The pH value of disodium phosphate-sodiumdihydrogen phosphate is 6.8, therefore it is the most important proton acceptor in the physiological pH range of the urine. Based on the known linear correlation between pH and the logarithm of the ratio of the buffer components, regression analysis was made. The equation describing the regression line was

$$y = a + bx,$$

where $x = \log \frac{C^+A^-}{H^+A^-}$. In terms of the Henderson-Hasselbalch equation, the

value of b should be 1. Evaluating our own data, the value of b happened to be lower than 1 which results in changing of the tangent of the regression line. The above change is attributed to that the quantity of titratable acids can be influenced, beside the phosphate buffers, also by uric acid and creatinine, the amount of these in case of an acidic reaction can be significant [10]. The equation of the regression line of ammonium discharge

$$y = 2.88 - 0.24x$$

is in good agreement with the formula of Wrong and Davies, i.e.

$$y = 2.89 - 0.259x.$$

This agreement is considered important, since the measuring methods were not identical [22].

A potential correlation between the diminishing of the renal acidifying ability and stone formation has attracted the attention of authors a long time ago. Albright et al. [1] were the first to report on the concurrence of nephrocalcinosis and hyperparathyreoidism. Butler et al. [6] observed the association of acidosis with tubular calcification. This was confirmed by Lightwood et al. [11]. According to Marquardt [15], nephrolithiasis and nephrocalcinosis occur associated with renal tubular acidosis in 73%. Cintron-Nadal et al. [7] found incomplete RTA in 6% of those with recurrent stone formation.

The results of the examinations of Marya et al. (1979) indicate the frequent association of decreased renal acidifying ability with stone formation. Diminished acidifying capacity in their stone-formers were observed by Backman et al. [2]. Konnak et al. [14] reported on the simultaneous occurrence of 5 cases of incomplete RTA and stone formation. In the Hungarian literature, Szendrői [17] reported on the effect of urine with constant alkaline pH formation [1, 2, 6, 7, 10, 11, 14, 17].

In our own material there was no significant difference in the preloading pH and the TA and AD values between the control group and the stone-forming group. During loading the TA value was found to be significantly lower than that of the controls. This difference is suggestive of the slight diminishing of the acidifying ability as a result of which, the buffering of acids entering the urine is rendered difficult. In 7 of our stone-formers incomplete RTA was observed. This is 14.8% of our patients which is in good agreement with the incidence rate of 6 to 19%. In the RTA group, the pH increased, while TA and AD decreased significantly as compared to the controls. In these patients, impairment of tubular function produced such a great change in the proportion of the buffer components which caused a significant increase in the urinary pH. The stone-forming effect of urine with constant alkaline pH is well known. This is indicated by literary data according to which in

these patients, nephrolithiasis is more severe, with more recurrences and these patients must be operated several times.

In obstructive nephropathies, among the impaired tubular functions, the diminishing of the renal acidifying capacity is often the first sign of renal injury. The decrease of the renal acidifying capacity after urinary flow obstruction was studied among other by Ericsson et al. [9], Earlay [8], Winberg [21], Berlyne [5] and Walls et al. [20]. The change in the acidifying capacity due to urinary flow obstruction has already been dealt with in our previous studies [4, 12, 13]. In the present report, the results of 9 patients are evaluated who were found to have RTA. They represent 22.5% of our obstructive cases. In 3 out of the 9 RTA patients stone formation occurred. The pH, TA and AD values similar to the stone-former RTA group, showed significant change as compared to the controls.

The measured data of stone formers and obstructive RTA patients are represented together in a coordinate system showing also the regression lines of the control group. The majority of the data measured is situated over the regression lines. This phenomenon can be explained by the fact that the buffer capacity of the urine produced by the impaired kidney increased at the given pH although, as a result of acid loading, TA and AD significantly decreased. The importance of constant pH in stone formation is well known.

During the acid loading of stone formers and obstructive nephropathic patients in both groups diminishing of the acidifying capacity was found. In the loading examinations regression analyses concerning the correlation between the TA and AD help a more subtle analysis of the loading examination. Considering the consequences of the diminishing of renal acidifying capacity (systemic acidosis, urine of constant pH), for an early detection acid loading examination is advisable to perform in diseases causing tubular impairment.

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Untersuchung des renalen Azidifizierungsvermögens bei verschiedenen urologischen Krankheitsbildern

T. BANYÓ und A. KARSZA

Bei 40 Patienten mit obstruktiver Nephropathie und 47 weiteren Patienten, die wiederholt Ca-haltige Steine entleerten, wurden Säurebelastungsuntersuchungen durchgeführt. In 16 Fällen (bei 13 Patienten = 14,9%) wiesen die Ergebnisse auf inkomplette renale tubuläre Azidose hin.

Die pH-titrierbare Aziditäts- und pH-Ammoniakexkretionswerte der Kontrollgruppe wurden mit Hilfe von Regressionsberechnungen aufgearbeitet. Zum Vergleich der Meßdaten der Kontrollgruppen und der Patienten wurden statistische Berechnungen herangezogen.

Исследование Ацидозной функции почек при различных урологических заболеваниях

Т. БАНЬО и А. КАРСА

Авторы выполнили исследование с кислотной нагрузкой у 40 больных с обструктивной нефропатией и у 47 больных с повторным выделением камней, содержащих кальций. Среди обследованных больных в 16 случаях (13 больных, 14,9%) получили результат, характерный для неполноценного RTA.

Был произведен анализ регрессии относительно pH-Ta и pH-AU результатов в контрольной группе. Сравнение результатов измерений в группе здоровых лиц и в группе больных было сделано с помощью статистического анализа.

Ultrasonography in the Diagnosis of Bladder Tumours

J. RÓZSAHEGYI¹, P. GÖBLYÖS², L. BOHÁR² and E. SZÜLE¹

¹ Department of Urology, and ² Institute of Roentgenology, Postgraduate Medical Institute, H-1389 Budapest, Szabolcs u. 33–35, P.O.Box 1112, Hungary

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In the course of the complex examination of 100 patients with bladder tumour also transabdominal, transrectal and intravesical ultrasonograms were taken. The pathological stages (pT) obtained by operation or at autopsy, respectively, were compared with the ultrasonographic stage (U). Transabdominal scanning revealed a concordance rate of 61%, transrectally one of 69% and by intravesical sonography a concordance rate of 92%. Transabdominal ultrasonography is suitable mainly for exploration in assessing the size and localization of the tumour. Transrectal ultrasonography is particularly useful if cystoscopy cannot be performed and it is a valuable aid in examining the size of tumours harboured at the bladder base. Intravesical sonography revealed the tumour in all cases and during scanning, by changing the volume of the bladder, changes in the elasticity and dilatability of the vesical wall could also be judged. Intravesical ultrasonography can be combined with cystoscopy. It is a rapid and straightforward procedure and an ideal supplement to cystoscopy being currently the best possible diagnostic method for revealing infiltration of the vesical wall.

One of the prerequisites of treating bladder tumours is to assess their size and the depth of their infiltration preoperatively [4, 5, 7, 10, 12, 16].

This can be realized as proposed by the UICC (1978) by cystoscopy, bimanual palpation, selective urography, biopsy and by transurethral resection, respectively [14]. If assessment is based on these examinations only, then underestimation of category T is 10 to 20% in superficial tumours and 40 to 50% in invasive tumours [4, 5]. Polycystography, double-contrast cystography and selective angiography do not improve preoperative accuracy of diagnosis [6, 16, 21]. The recently introduced CT is suitable rather for assessing the perivesical infiltration [10, 13]. All these have called for the introduction of new diagnosis methods. One of the latest of them, in addition to transabdominal [8, 17] and transrectal ultrasonography [2, 18, 20], is intravesical ultrasonography [1, 3, 9, 11, 12, 15, 19] (Fig. 1).

Own Material

Instrument and method

At the Postgraduate Medical Institute, transabdominal ultrasonography has been first introduced in diagnosing bladder tumours. It was followed, in early 1982, by the techniques of transrectal and intravesical ultrasonography

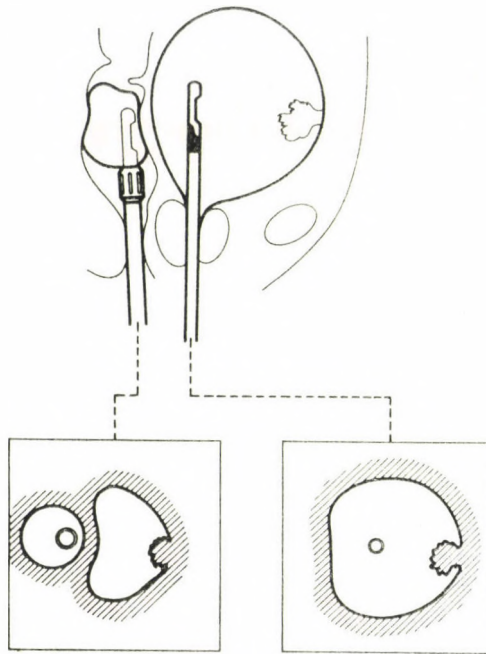


FIG. 1. Schematic drawing of intravesical and transrectal ultrasonography

(Fig. 2a-d). For our examinations a Brüel-Kjaer ultrasonic scanner has been used.

Several consecutive longitudinal and transverse sonograms were made in the course of a transabdominal examination with a filled bladder (Fig. 3a-b).

During transrectal examination the patient was lying on his or her side with knees pulled up. The bladder was filled. The instrument was introduced gradually into the bladder deep enough for the visualization of the apex of the bladder. The rubber balloon forming the contact between the transducer and the rectal wall had been filled with fluid, then by continuously pulling back the instrument, scanning of the bladder was performed (Fig. 4a, b). The examination lasted for a few minutes.

Intravesical ultrasonography was made after explorative cystoscopy. In the tube of a 24 Ch-Storz instrument the optics was replaced by a trans-urethral ultrasound probe and the bladder was filled with an isotonic solution. The tip of the probe, depending on the type of the transducer exceeds the tube by 2 to 4 cm. The transducer rotating around the longitudinal axis of the probe (5.5 and 6 MHz; speed of rotation, which is 2 to 6 rpm/s, can be regulated continuously, the axial resolution was about 1 mm, the lateral resolution about 2 mm) emits sound waves which arrive at the vesical wall through the fluid filling the bladder. A minimal part of sound waves are always

reflected from the acoustic interfaces which are again recorded by the transducer. The transducer alternately serving as a transmitter and receiver records only those sound waves in accordance with the laws of reflection and refraction which arrive at the acoustic interface almost at right angles. As a result, a two-dimensional real-time ('fast' B) scan of the cross-section of the bladder and the surrounding structure is produced composed of numberless fine lines corresponding to a segment of 360 degrees. The density count depends on the speed of rotation of the transducer. At a high speed a rapidly renewing image of lines is produced. At a lower speed an appropriately large number of lines is generated which help in recognizing even the subtler details of the tissue changes.

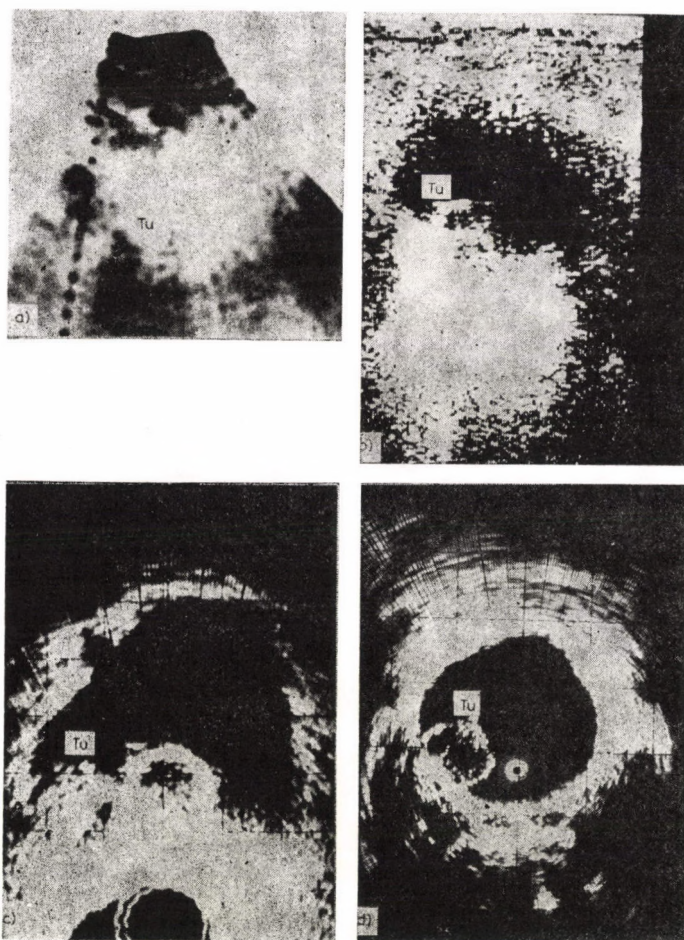


FIG. 2. Ultrasonograms of tumour, the size of a nut, localized on the right side of the bladder. *a.* transabdominal Compound; *b.* transabdominal real-time transverse, section; *c.* transrectal; *d.* intravesical

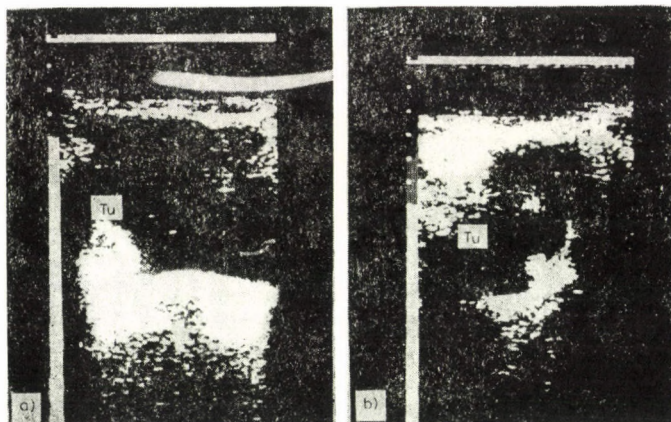


FIG. 3. Ultrasonograms of a small nut-sized tumour on the right side of the bladder. *a.* transabdominal real-time transverse section; *b.* transabdominal real-time longitudinal section

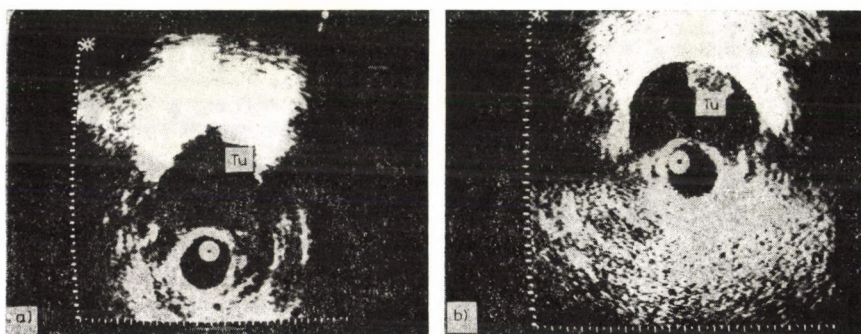


FIG. 4*a.* Scan of extravesically infiltrated bladder tumour (Tu) situated in the dome of the bladder on the left side and on the left lateral wall; *b.* transrectal scan of superficial bladder tumour localized in the dome of the bladder



FIG. 5. Intravesical ultrasonogram of the bladder. In the middle: transducer (T), there is a small tumour (D) behind the two ureteral orifices (USz) and behind the right orifice

The bladder is sonographically visualized like a symmetric and acoustically homogeneous circular structure of a width of 3 to 6 mm. The width of the vesical wall depends on the saturation of the bladder. Its internal surface is well demarcated from its environment, it is strongly delineated with an almost smooth surface. The diameter and shape of the bladder changes at the intersections of various heights. The transducer (TD) can be seen in the middle of a TV monitor with the concentric circles of sound impulses. In the dome of the bladder, the air bubble can be visualized as an image of complete reflection. By alternating the position of the probe or by exerting a counter-pressure on the bladder wall, the portions of the vesical wall concealed by the air bubble will be accessible to scanning. In the region of the base of the bladder, the ureteral orifices (UO) are delineated in the form of bilateral oval echoless zones. In cranial sections the intramural and juxtavesical course of the ureters can often be recognized. The perivesical tissue as a loose tissue structure can be well differentiated from the homogeneous vesical wall (Fig. 5). By changing the volume of the bladder in all transections the considerable elasticity of the vesical wall can be observed. Moving the probe in the bladder

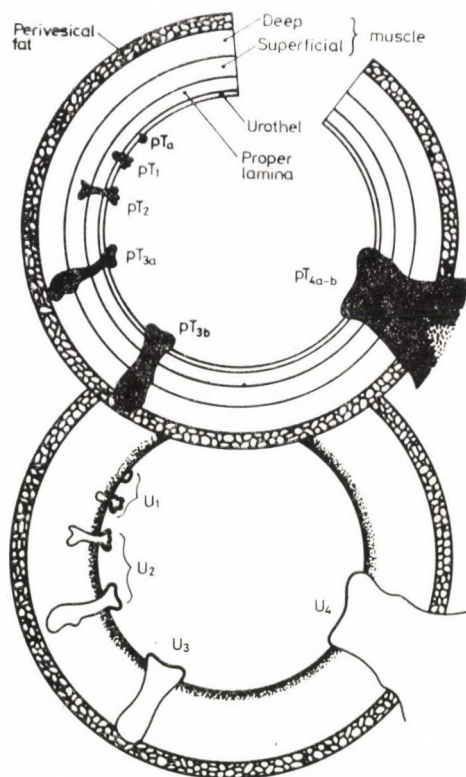


FIG. 6. Comparison of the pT category with the ultrasonogram (U) of a bladder tumour

forward and backward and alternating its angle, section scans are performed by the ultrasound. The dynamic picture displayed by the oscilloscope was photographed at 5 mm intervals.

Results

The data of a total of 100 patients with bladder tumours were elaborated in whom the results of ultrasound could be unanimously compared with the pathologic stage.

TABLE I
Comparison of transabdominal ultrasonogram (U)
and the pathological stages (pT)

Transabdominal "ultrasound stage", U	Pathological stage, pT				Con- cordance	Total n %
	Pap, pT _a , pT _{is} , pT ₁	pT ₂ -pT _{3a}	pT _{3b}	pT _{4a} -pT _{4b}	n %	
U ₀	8	3	1	—	—	12
(Pap, pT _a , pT _{is} , pT ₁)	8	3	1	—	8	12
U ₂	4	31	2	1	31	38
(pT ₂ -pT _{3a})						
U ₃	2	4	11	3	11	19
(pT _{3b})						
U ₄	1	3	3	11	11	18
(pT _{4a} -pT _{4b})						
Concordance	8	31	11	11	61	
Total	23	44	18	15		100

TABLE II
Comparison of transrectal ultrasonogram (U)
with the pathological stage (pT)

Transrectal "ultrasound stage", U	Pathological stage, pT				Con- cordance	Total n %
	Pap, pT _a , pT _{is} , pT ₁	pT ₂ -pT _{3a}	pT _{3b}	pT _{4a} -pT _{4b}	n %	
U ₀	4	2	1	0	0	7
(Pap, pT _a , pT _{is} , pT ₁)	4	2	1	0	4	7
U ₂	14	3	1	0	14	18
(pT ₂ -pT _{3a})						
U ₃	4	32	2	1	32	39
(pT _{3b})						
U ₄	1	5	12	3	12	21
(pT _{4a} -pT _{4b})						
Concordance	14	32	12	11	69	
Total	23	44	18	15		100

The pathologic stages of the tumours were determined from a material obtained by operation (TUR, suprapubic cystotomy + neoplastic excision, bladder wall resection, cystectomy) or at autopsy. The tumours studied ranged from those of the size of a match-head to ones almost completely filling the lumen of the bladder. Of the patients 24 were females and 76 were males. Mean age was 66.4 years. The age of the patients ranged from 49 to 91.

The various depths of infiltrations were determined and a parallel was drawn between their ultrasound stages and the T category of UICC defined in 1978 [15] (Fig. 6).

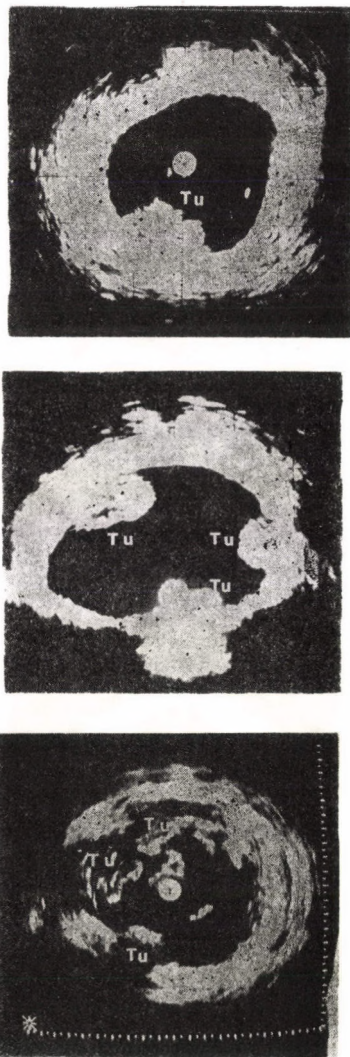


FIG. 7a—c

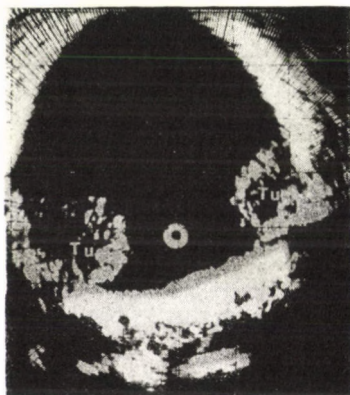
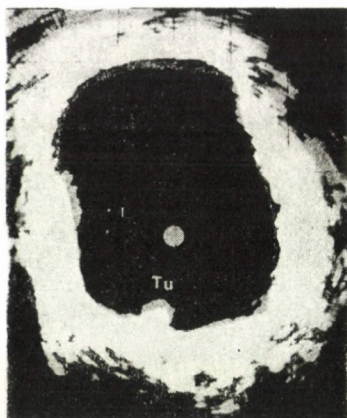


FIG. 7d—f

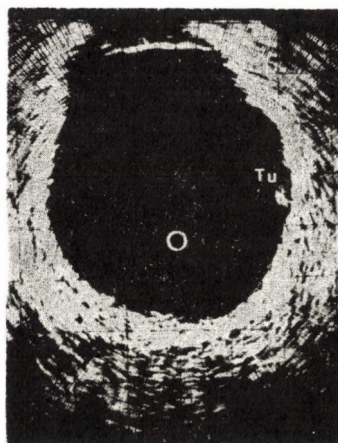
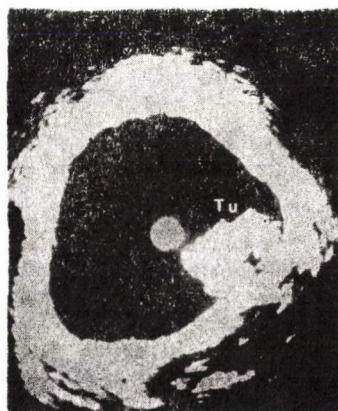
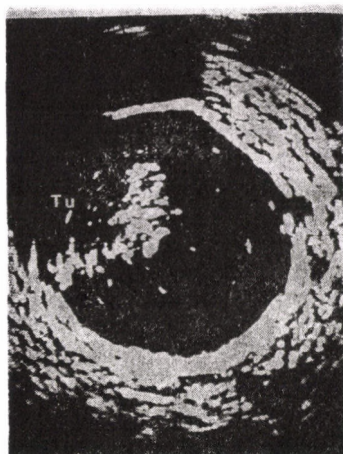


FIG. 7g—i Intravesical ultrasonogram of bladder tumours of various sizes

TABLE III
Comparison of intravesical ultrasonogram (U)
and of the pathological stages (pT)

Intravesical "ultrasound stage", U	Pathological stage, pT				Con- cordance	Total n %
	Pap, pT _a , pT _{is} , pT _i	pT ₁ -pT ₂	pT _{3b}	pT _{4a} -pT _{4b}	n %	
U ₀	0	0	0	0	0	0
U ₁ (Pap, pT _a , pT _{is} , pT _i)	21	0	0	0	21	21
U ₂ (pT ₂ -pT _{3a})	1	43	3	0	43	47
U ₃ (pT _{3b})	0	1	14	1	14	16
U ₄ (pT _{4a} -pT _{4b})	1	0	1	14	14	16
Concordance	21	43	14	14	92	
Total	23	44	18	15		100

Transabdominal ultrasonography did not reveal the tumour in 12% of the cases. The result of ultrasonography corresponded in 61% to the pathologic stage, the tumour was underestimated in 22% and overestimated in 17% (Table I).

Transrectal ultrasonography failed to reveal the tumour in 7%. The pathologic stage corresponded to the ultrasonographic finding in 69%. The tumour was underestimated by ultrasonography in 17% and overestimated in 14% (Table II).

Intravesical ultrasonography revealed the tumour in almost every case (Fig. 7). The result of the ultrasound corresponded to the pathological stage in 92%. The tumour was underestimated in 4% and overestimated also in 4% by intravesical ultrasonography (Table III).

Discussion

The biological behaviour of bladder tumour is characterized by a tendency to infiltrate [4, 12, 15].

Prognosis worsens significantly with the involvement of the muscular layer. That is why assessment of the invasion of the vesical wall and extra-vesically is of great importance [4, 5, 13].

The majority of the ultrasound-diagnostic characteristics of bladder tumours are based on secondary changes due to tumorous infiltration, as e.g. unevenness, deformity, rigidity, diminished bladder capacity of the vesical wall [2, 8, 9]. The essence of the ultrasonographic examination is the dif-



FIG. 8. Transabdominal real-time transverse section scan of extravasically infiltrated tumour filling the left side of the bladder

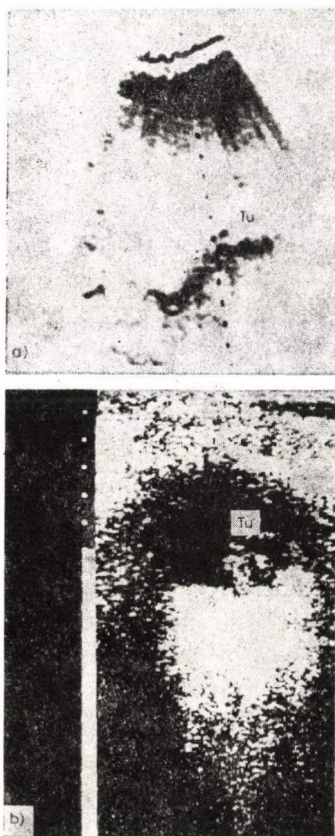


FIG. 9. Nut-sized tumour on the left side of the bladder. *a.* Compound ultrasonogram; *b.* real-time transverse section scan

ference between the echoes of the normal bladder wall and of the tumour. Namely, the echoes reflecting from the tumour are of lower amplitude than those reflecting from the wall.

By transabdominal ultrasonography a noninvasive procedure has been introduced into the diagnostic methods, being more effective and simpler than the traditional radiological methods in revealing bladder tumours and in assessing their localization and size [7, 8, 17, 18]. This simple and easy method allows a rough estimation of the size of the tumour, primarily in patients who have a large tumour occupying an extensive area of the bladder (Fig. 8) or, if prior to intravesical sonography, the contours of the tumour are to be delineated. It helps in assessing the tumours penetrating into the bladder wall. In case of a Compound equipment, the advantage of the small transducer surface is the high spatial resolution (Fig. 9a). The use of new real-time scanners has facilitated and made more rapid the examination of the bladder (Fig. 9b). It is easy to change the position of the transducer. On examination, the patient can even sit up and thus a complete picture of the bladder lumen and its environment can be obtained. The longitudinal scans are preferred in the case of tumours of the anterior bladder wall. On transabdominal examination, the symphysis may pose difficulties in visualizing the tumours of the anterior wall and the bladder base. By using a Compound equipment, the examination takes a longer time because the tumour can be visualized only by making section scans several times.

Other difficulties can arise when performing and assessing the examination from obesity, intravesical blood clot, extensive pelvic scarring, protruding gas-filled intestinal loops. Technical difficulties can be imposed by a tumour of a diameter below 0.5 cm localized in the vicinity of the bladder wall as well as by a reduced bladder capacity which is a sort of prognostic marker, too.

Tumours in the trigone and the bladder base can be accurately delineated by using transrectal ultrasonography developed by Watanabe [18] (Fig. 10). It is particularly suitable for scanning tumours invading the prostate or the seminal vesicle and for exploration if cystoscopy can for some reason, not be performed [7, 18, 20]. In some cases, it is difficult to visualize the most cranial part of the bladder by this short procedure because the depth of introducing the instrument into the rectum is limited. During the examination 4 patients complained of a feeling of discomfort and 2 of pain.

The endovesical ultrasound system presented by Holm in 1974 [3] has afforded the possibility of assessing the intra- and extravesical invasion of bladder tumours more accurately than the earlier methods have done.

Corresponding to the T category of UICC [14], the characteristics of the individual ultrasound stages were defined.

$U_1(T_{is}, T_a, T_1)$: An intact, wholly conserved bladder wall is shown by the ultrasonogram from which the tumours protrude into the vesical lumen with



FIG. 10. Transrectal ultrasonogram of two bean-sized tumours at the base of the bladder

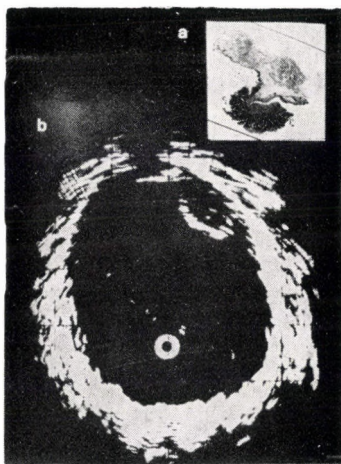


FIG. 11. Superficial bladder tumour in the dome of the bladder. *a.* Overview scan (pT_1); *b.* intravesical scan (U_1)

echo structures of varying intensity. No intramural changes are evident at the base of the tumour it is demarcated from the bladder wall.

The waving echo pattern shows the villous character of the tumours.

By changing the volume of the bladder, the elasticity of the bladder wall is conserved with normal capacity (Fig. 11*a, b*).

$U_2 (T_2, T_{3a})$: The echo structure of the tumour continues to the bladder wall and extensive mural changes are seen on its base. The normal structure of the bladder wall has loosened. Instead of the regular picture of the bladder wall a sonolucent mass can be visualized. The bladder wall can often be ragged at the base of the tumour but the external bladder contour has been preserved. By changing the bladder volume, the elasticity of the bladder wall is diminished, the wall is rigid. The bladder capacity has decreased (Fig. 12*a, b*).

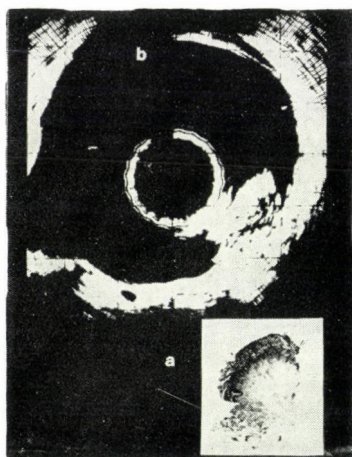


FIG. 12. Infiltrative tumour on the left side of the bladder. *a.* Overview scan (pT_2); *b.* intravesical ultrasonogram (U_2)



FIG. 13. Bladder tumour penetrating into the vesical wall beside the right orifice and infiltrating the perivesical fat. *a.* Overview scan (T_{3b}); *b.* intravesical ultrasonogram (U_3)

U_3 (T_{3b}): The bladder wall is totally destroyed, the tumour invades the full thickness of the bladder wall. At the base of the tumour, the mural structure cannot be recognized, and—corresponding to the depth of the infiltration—the continuity of the bladder wall is broken in the region of the tumour (Fig. 13*a, b*).

U_4 (T_{4a} , T_{4b}): The extravescical invasion is shown by an irregular echo structure of the ultrasonogram which reaches beyond the contour, too. Here, corresponding to the tumour-induced absorption, a looser echo pattern of peripherally weakening intensity is seen. The extravescical invasion—depend-

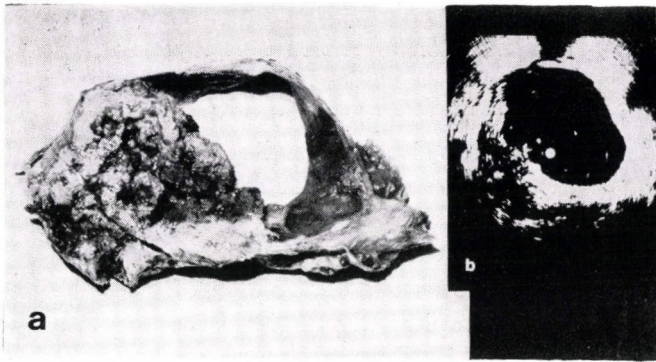


FIG. 14. Extravesically infiltrating tumour invading and penetrating into the right lateral vesical wall. *a.* Overview scan (pT_{4a}); *b.* intravesical ultrasonogram (U_4)

ing on sound-absorption of the tumour—appears behind the muscle layer as an echo-poor structure. The bladder capacity has decreased, by changing the bladder volume, the tumour is fixed. Differentiation of stage T_{4a} from T_{4b} is not possible (Fig. 14*a, b*).

It is difficult, in some cases, to differentiate between tumours deeply infiltrating the muscles (T_{3a}) and initial extravesically infiltrating tumours (T_{3b}), because both stages yield the same, or fairly similar, sonogram. The safer differentiation would require a greater axial resolution. Penetration of the tumour into the adjacent organs can be shown only to a certain depth, since the range of the high-frequency ultrasound beam is about 3 cm. It is difficult to visualize the vicinity of the bladder neck and the anterior wall but this can be helped by the retrograde transducer (of 135 degrees) by changing the bladder volume and the axis of the probe. Tumours situated at the base of the bladder are most difficult to visualize. Longitudinal section scans of the bladder cannot be performed. For this purpose cystoscopy is needed, but if cystoscopy is indicated ultrasonography can provide valuable complementary information.

Superficial lesions of the bladder mucosa were observed in 3 cases, and also in 3 cases a slight haemorrhage requiring no treatment occurred.

The advantage of intravesical ultrasonography in bladder tumours is that, despite the relatively small transducer, most bladder tumours can be fairly well visualized. In the filled bladder, the ultrasound waves arrive almost at right angles at the bladder wall, the loss in conduction is minimal, the structures, thus those of the wall, can be clearly delineated. It is of differential diagnostic importance in differentiating primary bladder tumours and the propagation. During the examination, the bladder volume can also be changed and by this dynamic examination procedure also the elasticity and compliance of the tumorous bladder wall can be assessed.

None of the ultrasonographic methods can safely differentiate between stages T_2 and T_3 , so infiltration of the muscle layer has unanimously been classified into stage U_2 .

Transabdominal ultrasonography is useful first of all for explorative examinations for assessing the size and localization of the tumour. By transrectal ultrasonography tumours can be delineated but those localized in the posterior wall of the bladder are difficult to visualize. It is extremely useful for orientation if cystoscopy cannot be performed for some reason. It is a valuable aid in assessing the extent of invasion of tumours situated at the base of the bladder. It is a rapid and practical procedure which can be combined with cystoscopy. An ideal supplement to cystoscopy is intravesical ultrasonography which is currently the best diagnostic method for visualizing the tumorous infiltration of the vesical wall.

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Über die Ultraschalluntersuchung in der Diagnostik der Harnblasentumoren

J. RÓZSAHEGYI, P. GÖBLYÖS, L. BOHÁR und E. SZÜLE

Im Laufe der komplexen Durchuntersuchung von 100 Patienten mit einem Blasentumor wurden auch transabdominale, transrektale und intravesikale Ultraschalluntersuchungen vorgenommen. Aus dem Vergleich des pathologischen Stadiums des intraoperativ bzw. im Laufe der Sektion gewonnenen Materials mit dem »Ultraschallstadium« ging hervor, daß die Übereinstimmung mit der transabdominalen Untersuchung 61%, mit der transrektalen 69% und mit der intravesikalen 92% ausmachte. Die Erfahrungen ließen erkennen, daß sich die transabdominale Ultraschalluntersuchung zur Orientierung betreffs der Größe und Lokalisation des Tumors eignet, während sich die transrektale Sonographie in Fällen als besonders vorteilhaft erweist, in denen die Durchführung der Zystoskopie auf irgendein Hindernis stößt und es um die Feststellung der Ausbreitung der auf dem Blasenfundus lokalisierten Tumoren geht. Durch die intravesikale Sonographie wurde der Tumor in sämtlichen Fällen nachgewiesen, außerdem konnten während der Untersuchung, durch Änderung des Blasen Volumens auch die Änderungen der Elastizität und des Ausdehnungsvermögens der tumorösen Blasenwand beurteilt werden. Die parallel mit der Zystoskopie rasch und einfach durchführbare, dieselbe ideal ergänzende intravesikale Ultraschalluntersuchung stellt zur Zeit das beste diagnostische Verfahren zum Nachweis der Blasenwandinfiltration dar.

Ультразвуковое исследование в диагностике опухолей мочевого пузыря

Й. РОЖАХЕДИ, П. ГЁБЬЁШ, Л. БОХАР и Э. СЮЛЕ

В ходе обследования 100 больных с опухолью мочевого пузыря авторы выполнили также трансабдоминальное, трансректальное и интравезикальное ультразвуковое исследование. Патологическую стадию (pT), выявленную на операции или вскрытии, они сравнивали с «ультразвуковой» стадией (B). Совпадение с трансабдоминальными исследованиями наблюдалось в 61%, с трансректальными в 69%, с интравезикальной сонографией — в 92%. По мнению авторов, трансабдоминальное ультразвуковое исследование применимо, в первую очередь, в качестве ориентировочного, с помощью которого можно получить представление о размерах и расположении опухоли. Трансректальное ультразвуковое исследование особенно полезно для ориентировочных сведений, если цистоскопию по какой-либо причине произвести не представляется возможным, и ценно для определения распространенности опухоли, расположенной на основании пузыря. Интравезикальная сонография во всех случаях выявила опухоль, с ее помощью — изменения во время исследования объем мочевого пузыря — можно оценить также изменения эластичности и растяжимости стенки мочевого пузыря. Интравезикальное ультразвуковое исследование можно производить одновременно с цистоскопией, это быстро выполняемый, практичный способ, идеально дополняющий зеркальное исследование мочевого пузыря, в настоящее время являющийся наилучшим диагностическим методом для выявления инфильтрации стенки мочевого пузыря.

Experimental *in situ* Renal Hypothermia through the Renal Vein

IRÉN MIKÓ¹, Z. SZABÓ², I. FURKA¹, E. TARSOLY¹ and J. PINTÉR²

¹ Institute of Experimental Surgery, Debrecen University Medical School, H-4012 Debrecen, P.O.Box 18, and

² Department of Urology, Debrecen University Medical School, H-4032 Debrecen, Nagyerdei krt. 98, Hungary

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The authors worked out the technique of *in situ* renal hypothermia in dogs by direct cannulation of the renal vein or through the internal spermatic vein (ovarian vein). The technique is suggested for preventing the ischaemic impairment of the renal parenchyma in operations requiring compression of the renal artery for more than 20 minutes.

In regional organ-hypothermia, the metabolism decreases and surgical interventions lasting for a fairly long time can also be performed which are not possible in normothermia.

In normothermia, compression of the renal artery is possible for approximately 20 minutes without an irreversible damage to the organ. The renal tubuli are damaged the most rapidly after a warm ischaemia lasting for a longer time. This is followed by impairment of the glomeruli and, finally, that of the vascular system.

Some interventions on the renal parenchyma require, even for a longer time, the compression of the renal artery. The associated ischaemic injuries can be decreased or prevented by selectively reducing the temperature of the organ [1, 2, 6, 9, 12, 13, 15, 16, 17, 18, 19]. The oxygen consumption of the renal tissue at 30 °C, is 50% of the normal value, at 23 to 25 °C it is 30% and, at 18 °C, only 20% of the normal value [19].

There are two procedures for *in situ* renal hypothermia: superficial hypothermia [4, 8, 19, 20] and intravasal perfusion. This latter may be performed via the arteries [3, 11], and via the veins [7, 12, 14, 21].

The present paper deals with *in situ* hypothermia via the renal vein.

Experimental Method

The experiments were made in 40 dogs under Na-hexobarbital anaesthesia. The left kidney was explored by upper and median laparotomy. The hilus was infiltrated with a 1% lidocaine solution. Subsequently, both the renal

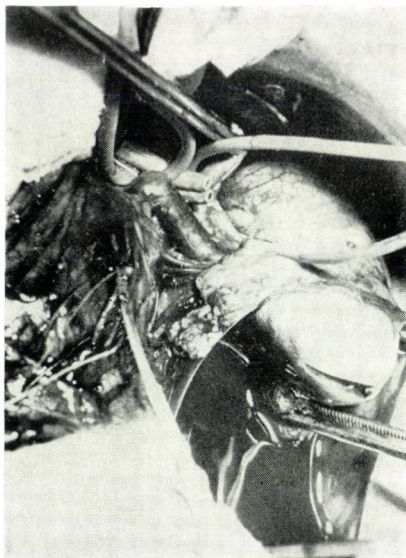


FIG. 1. Hypothermia through the internal spermatic vein with nephrotomy securing the backflow of the fluid

artery and vein were dissected. Following this, the renal artery, then the renal vein was compressed. Venotomy at a length of 1 to 1.5 mm was performed along the vessel. A cannula previously filled with cooling solution was inserted through the opening. Parallel to starting hypothermia nephrotomy was made for preventing the swelling of the kidney and for the back flow of the cooling solution. The solution leaving this way induces some degree of superficial hypothermia.

In other cases the left spermatic or ovarian vein was used for introducing the cannula. This vessel could be ligated after completing hypothermia.

Figure 1 shows the *in situ* hypothermia through the internal spermatic vein. For hypothermia two types of intracellular-type solution were used, i.e. MgSO_4 -free Collins₄ and Sacks II stained with methylene blue, the temperature of which ranged between $+4^\circ\text{C}$ and 10°C . Hypothermia of the kidney was performed from a height of 45 cm instilled in 70 to 75 drops per minute, for a period of 25 to 90 minutes. The temperature of the renal parenchyma was measured through the nephrotomic incision at the corticomedullary border. The nephrotomies were closed traditionally by Dexon, Polyester and Supramide suture material or by the combination of tissue-adhesive and bioplast [10].

In 13 experimental animals also lower pole resection was made using the combination of tissue adhesive and bioplast. The venotomic incision was closed transversely by 6/0 Prolene. Then circulation was restored and the abdominal wall was closed in layers.

Evaluation of Experiments, Discussion

Based on the observations of several authors and of our own experiences, superficial hypothermia yields good results but a 'deeper hypothermia' of the parenchyma is slower and more uneven, i.e. the required temperature is more difficult to achieve. At the same time, the ice bags providing cooling may hinder the interventions increasing thereby the time of operation, moreover, they may even produce cortical necrosis, too [4, 8, 11].

A great risk of *in situ* hypothermia through the renal artery is the relatively frequent consequential stenosis, vascular obstruction and incidental secondary haemorrhage [3, 11]. In addition, the cooling fluid may even enter the systemic circulation.

Due to these complications, we attempted at cooling the renal parenchyma in a third way (i.e. through the renal vein), and at performing various operations in an appropriate degree of hyperthermia.

It is a physiologic contradiction that the cooling solution was circulated opposite to the direction of the circulation.

Marekovic [7] as well as Wilhelm and Sigel [21] showed that, unlike the segmental arterial system, the venous system of the kidney is continuous. Thus venous hypothermia is feasible. Our reasoning was the following: through this system the kidney can be adequately perfused and if it is opened by nephrotomy the cooling fluid will flow out at a certain pressure but, at the same time, the parenchyma can be cooled. An important point is that with hypothermia started, nephrotomy is performed almost simultaneously to prevent swelling of the kidney which would endanger the renal structure. Temperature was recorded at the corticomedullary border in the line of nephrotomy. This happened to be 18 to 26 °C in hyperthermia performed through the renal vein, which was attained by the above-mentioned method within about 10 minutes. This temperature did hardly change during additional perfusion. This value was obtained from the results of the preliminary experiments on 10 animals.

The backflowing cooling fluid produces, at the same time, some sort of superficial hypothermia. This can be regulated by adjusting suction as required. By using this method the kidney can be washed, i.e. cooled. This can be proved also morphologically as shown in Fig. 2 disclosing that the venous system of the kidney has dilated and been washed out with no blood left. Hypothermia can be maintained for the required period, i.e. until the operation is terminated.

The methylene blue stained cooling fluid was advantageous at noticing, 'leakage' at the closure of nephrotomy by adhesion.

The transverse closure of venotomies was made necessary to prevent stenosis.

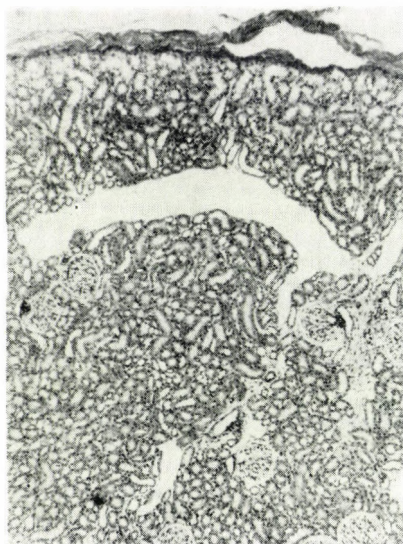


FIG. 2. The stellate veins in the cortical substance and the vessel of the corticomedullary border are dilated, they have been adequately washed; H and E, $\times 20$

Advantages of using the spermatic or ovarian vein were considered to be that the renal vein 'should not be touched' only softly compressed to make the cooling fluid circulate toward the kidney. Thus venotomy and its closure can be avoided and, consequently, the time of operation becomes shorter. In a large percentage of cases, circulation was restored in about 60 minutes, the shortest time being 25, the longest 90 minutes but this can be reduced by about 15 minutes using the above-mentioned lateral branches. The spermatic or ovarian veins can be ligated without injury. There was no difference in the degree and rapidity of cooling, when renal *vs.* the spermatic or ovarian vein was used for perfusion.

The technical complications of hypothermia performed directly through the renal vein were as follows. In two cases, thrombosis was observed on the first postoperative day; in one case the renal vein burst. The venotomies in the renal vein were sutured longitudinally in two cases resulting in stenosis. By introducing transverse closure of the longitudinal venetomic incision such complications could be eliminated. Such technical complications did not occur in cases with hypothermia performed through the spermatic vein.

The following interventions were made on the kidneys of the animals: (i) traditional closure of nephrotomies in 7 cases; (ii) closure of nephrotomies by the combined use of tissue adhesive and bioplastin 10 cases; (iii) lower pole resections by the combined use of tissue adhesive and bioplastin 13 cases.

Already the preliminary experiments have called attention to the glueing performed in hypothermia differs from that made successfully in normo-

thermia because the adhesive material became more rigid on the surface of the kidney and the time of the glueing process lasted longer. These questions must be dealt with further on since this makes newer observations necessary.

In summary, we concluded that local cooling via the renal vein is a suitable method for inducing hypothermia of the renal parenchyma. The use of the spermatic or the ovarian vein, increases safety and reduces the time of operation. In this condition urological interventions requiring the compression of the renal artery for more than 20 minutes can be safely performed.

The method can be used in the clinical practice for its simplicity and easy performance since it does not require any special instrument or equipment.

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Experimentelle in situ Nierenhypothermie durch die V. renalis

IRÉN MIKÓ, Z. SZABÓ, I. FURKA, E. TARSOLY und J. PINTÉR

Im Hundeexperiment wurde die *in situ* venöse Hypothermie der Niere direkt durch die Kanülierung der V. renalis oder durch die V. spermatica interna (V. ovarica) ausgearbeitet. Der Einsatz der Technik wird bei mehr als 20minütige Abklemmung der A. renalis beanspruchenden Eingriffen zur Vorbeugung der ischämischen Schädigung des Nierenparenchyms empfohlen.

Экспериментальная гипотермия почки *in situ* через v. renalis

И МИКО, З. САБО, И. ФУРКА, Э. ТАРШОЙ и ПИНТЕР

В экспериментах на собаках авторы разработали способ охлаждения почки *in situ* прямым канюлированием почечной вены или реоэз v. spermatica interna (v. ovarica). Эту технику они рекомендуют применять пцири операциях, требующих длительного (свыше 20 мин) пережатия почечной артерии, с целью предотвращения ишемического повреждения почечной паренхимы.

Book Review

BEN EISMAN (Herausgeber)

Prognose chirurgischer Erkrankungen. Ferdinand Enke Verlag 1983. DM 168.

This compact book presenting a practical approach and containing detailed comparative statistical and literary data on the individual diseases is the German translation of the 1980 English version.

The 543-page volume containing xiv chapters, provides a comprehensive review of the results of surgery and of those of the adjoining disciplines as well as the statistical and literary data. The data summarized in the tables at the end of each chapter reflect the complications, mortality and lethality based on a number of literary data.

The individual chapters of the book survey the statistical data on neurosurgery, on abdominal, gynaecological, urological and orthopaedic surgery, along with the necessary conclusions.

The reliability of the statistical data presented here has been guaranteed by the fact that the book had been based on the data collected at more than hundred institutes, primarily at the University of Colorado.

This book of high quality, of logical structure containing data in perspicuous tables will prove invaluable for physicians, lecturers and department heads engaged in the cerebromanual profession.

The Ferdinand Enke Verlag (Stuttgart) should be sincerely praised for the excellent editorial control, for the presentation of highly illustrative figures and for the faultless typographic achievement.

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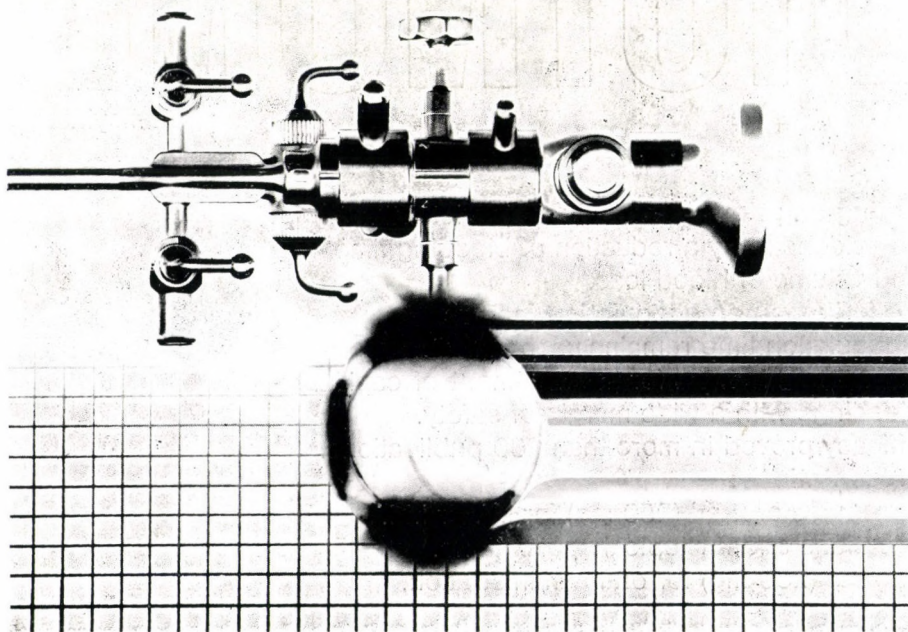
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