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Investigations on the Diagnostic Value of Enzymuria, Proteinuria and Cell Excretion in Experimental Renal Diseases.

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Enzymuria, urinary cell excretion, and proteinuria were simultaneously determined in renal diseases of female wistar rats to point out the diagnostic value of urinary enzymes.

Methods
1. E. coli-pyelonephritis, facilitated by estradiolundezylate (1 mg/kg/week), induced by endovesical application of the 025:19:12 strain.
2. Nephrosis by aminonucleoside (15 mg/kg/day).
3. Tubular necrosis by tobramycin (100 mg/kg/day).
4. Pyelonephritis treated with therapeutic (2,5 mg/kg/day) or toxic (100 mg/kg/day) doses of tobramycin.

Enzymes (AP, GOT, LDH, MDH), protein and cells daily were measured in the 12^{h}-urine volume. Kidneys were investigated histologically.

Results
1. Parallel increase of leucocyturia and enzymuria (LDH-activity prevailed) related to the infectious activity.
2. Parallel increase of enzymuria, cell excretion and proteinuria 1 week after starting the treatment.
3. Parallel increase of cell excretion and urinary enzymes (MDH-activity prevailed) followed by proteinuria.
4. Decrease of elevated enzymuria and cell excretion under therapeutic dosage. Increase of urinary enzymes under toxic dosage, while the pathologically elevated cell excretion remained almost unchanged.

Conclusion
Hence the main diagnostic value of urinary enzymes is detecting drug induced tubular lesions in individuals with preexisting renal diseases.

Experimental Studies on the Reactivity of Renal Leucinaminopeptidase.

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Elevations of specific urinary leucinaminopeptidases (LAP) were described in several renal and extrarenal diseases (3, 4). The experiments presented in this paper were carried out to clarify whether insults to the energy supply system of the cells may lead to renal loss of enzyme. This may explain some of the non-specific elevation of enzyme activity in urine.

A decrease of serum free fatty acids (FFA) and serum glucose was achieved by intraperitoneal infections of methyl-pyrazol-carbonic acid (MPCA) (2) in 280 Wistar rats. Similar infections of phenyl-isopropyl-adenosine (PIA) (5) lowered only FFA levels. The determinations of LAP were done in 6 hour urine specimens. PIA initiated a significant rise of LAP. Of other enzymes also measured only the acid phosphatase activity (AP) showed a similar reaction. MPCA also induced significant elevations of LAP and AP. In the serum, however, the activities of these enzymes were lowered. This means that some of the urinary activities were excreted from the serum. This points toward a comprehensive damage of the kidneys.

As the experiments have shown tubular epithelial cells loose enzyme activity as a reaction on energy reduction. This may also occur as a non-specific response to similar damage to the whole organism. The similar response of AP can be explained by the adjacent position of this enzyme in the tubular epithelial cells. It is not possible to judge upon the amount of renal damage by the determination of LAP excretion rates alone.

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Haemodynamics in Nephroptosis. An Experimental Investigation in 30 Dogs.

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In patients with evidence of nephroptosis we found a "swinging" urinary LDH-excretion: a normal activity in supine position and significantly increased values in prone position.

Our experiments should answer the question whether a decreasing arterial inflow, an increasing venous pressure or a ureteral occlusion produce an increase in urinary LDH-excretion. Under controlled conditions we measured LDH-activities in the urine of both the manipulated and the controlled kidney.

A reduction of only 30% of the arterial flow (measured electromagnetically) significantly increases urinary LDH-excretion, consisting to a great amount of LDH-I. This isoenzyme is localized mainly in the medullary region. The measurement of the regional flow by the 133-Xenon-wash-out method shows a percentually equal reduction in all compartments. By this we conclude that there must be a "swinging hypoxic damage" in the outer medullary region of the ptotic kidney which could be neutralized by nephropexy.

Renogram and Split J^{131} - Hippuran Clearance in the State of Experimentally Decreased Renal Perfusion.

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Nuclear medical techniques are increasingly used in the diagnostic work-up of nephrogenic hypertension. The relevance of the renogram and the split J^{131}-hippuran clearance in unilaterally decreased renal perfusion was studied in animal experiments.

In 17 dogs renal arterial pressure and blood flow was varied unilaterally by the use of a pump mechanism. At the same time 2 - 4 sequential J^{131}-scintigram series were recorded. In 20 other dogs one renal arterial branch was ligated and subsequently the catheter-free split J^{131}-hippuran clearance with EPA compensation was studied. The results of a subsequent split clearance study in "steady state" were used for comparison.

In the first series of experiments a close correlation between renal blood flow and the integral of the impulses in phase II of the renogram (R) as determined by sequential scintigrams was found. The time necessary to reach the maximum activity (T_{max}) and the half-time of the evaluation ($T_{1/2}$) also depended on renal blood flow. The latter was, however, strongly influenced by the conditions of urinary flow.

In the second series of experiments a close correlation was found between the catheter-free split J^{131}-hippuran clearance and the split clearance under "steady state" conditions. These results also correlated with renal blood flow. This was only evident when the "extraparenchymal activity" (EPA) was correctly subtraced.

Two valuable techniques with minimal trauma to the patient are therefore available to evaluate decreased renal blood flow:

1. The renogram and its technically improved variant, the renal sequential scintigram may indicate the side of decreased renal perfusion. The result may be misleading if other pathologic conditions of the kidneys are present. Sequential scintigrams may also indicate morphological changes in the kidneys.
2. The catheter-free split J^{131}-hippuran clearance with EPA compensation allows the exact quantitative determination of the effective renal plasma flow.

Comparative Studies of Renal Perfusion after Normothermic and Hypothermic Ischemia.

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Considerable improvement of functional parameters was shown for the ischemic kidney under hypothermic perfusion. The experiments presented were carried out to produce further information on renal blood flow and the renal vascular condition after hypothermic perfusion.

Method
Renal blood flow and blood distribution in the kidney was determined with ^{133}Xe prior to and after selective renal perfusion. Serial renal arteriograms were carried out for visualization of the intrarenal vascular system.

Results
1. Normothermic ischemia (2 hours): Immediately after surgery total renal blood flow was increased as shown by ^{133}Xe determinations and serial angiography. 24 hours after the operation renal blood flow was decreased.
2. Hypothermic ischemia (2 hours): Due to the vasoconstriction caused by low temperature, the first compartment was low immediately after surgery in this group. However, 24 hours later normal values were found.

Conclusion
Renal flood flow is decreased 24 hours after normothermic ischemia. To the contrary, 24 hours after hypothermic ischemia renal perfusion is normal. This confirms previous nuclear medical functional studies from this laboratory.

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Local Oxygen Uptake and Cellular Energetics after Renal Ischemia.

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In the kidney in situ of rat, rabbit, and dog the influence of different periods of warm ischemia on local oxygen uptake and cellular energetics was studied.

Method
For the experiments PO_2 and pH electrodes for tissue measurements (1) as well as electromagnetic flowmeters were used.

Results
The local oxygen uptake increases proportionally with the duration of ischemia. A significant change is found after 30 min of ischemia. 10 min after recovery the oxygen uptake reaches normal values. The PO_2-distribution of the tissue shows a small right shift with increasing ischemia. The initial blood flow of the kidney is usually unchanged after releasing the arterial occluder. During ischemia we observed an increasing interstitial acidosis of the tissue.

Discussion
The postischemic increase of the oxygen uptake is caused presumably by an increasing cellular lactacidosis. Investigations on ischemia in the isolated perfused rat liver showed that an intracellular acidosis causes distinct changes of the interstitial activity of potassium, sodium, and calcium ions (2). It is likely that during ischemia of the kidney similar ionic changes may induce the disturbances of cellular energetics.

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The Value of the Quantitative Urine Culture in the Progress of the Acute Pseudomonas Aeruginosa Pyelonephritis in Rabbits.

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Introduction
In the present study a correlation between the bacterial count of the bladder urine and of the tissue with the histopathological findings in the acute pseudomonas aeruginosa pyelonephritis

of untreated and chemotherapeutically treated rabbits is demonstrated.

Material and Methods
In 22 rabbits after ligature of the left ureter intravenous injection of 1 ml of physiological saline solution with 10^{11} living pseudomonas aeruginosa bacteria per ml. After slipping the ureteral ligature, bacteriological and histopathological control of the bladder urine, of the renal pelvis urine and of the renal tissue. After the infection was initiated treatment began (Carbenicillin - 200 mg per kg per body weight per day and Gentamycin - 7 mg per kg per body weight per day). As a follow up study suprapubic aspiration and bacteriological control of the bladder urine at intervals of 2 days. On the twelfth day nephrectomy with bacteriological and histopathological examination last bacteriological control of the bladder urine.

Results
1. 17 of 22 animals: After slipping the ureteral ligature in the urine of the renal pelvis 10^9 - 10^{11} pseudomonas aeruginosa bacteria per ml, histopathologically an acute pyelonephritis. After 10 - 12 days of chemotherapy, in the bladder urine 10^0 - 10^2 bacteria per ml, in the renal tissue 10^3 - 10^4 bacteria per ml, histopathologically sporadic leucocytic infiltrations.
2. 5 of 22 animals: Without manifestation of a pyelonephritis due to reduced virulence of the bacterium or defectiveness of the ureteral ligature.

Conclusion
The level of the urinary bacterial count being taken as the parameter for the severe histopathologicals changes. Bacterial counts of renal tissue of up to 10^4 bacteria per ml in histopathological and urobacteriological residual findings after a 12 day periods of treatment indicate the importance of a long-term antibiotic treatment of the pseudomonas aeruginosa pyelonephritis.

Experimental Lipid A Nephritis in the Dog.

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The effect of radioactive lipid A (1), obtained from E. coli, on the kidney of adult dogs and puppies was investigated.

Injection of lipid A into the temporarily occluded renal pelvis of adult dogs, caused abacterial interstitial nephritis in all animals tested.

The intensity and duration of the kidney response correlated will with the lipid A dose administered. Lipid A was demonstrated autoradiographically in the renal cortex.

Radioactivity was still present after 10 weeks in 16 out of 20 examined dogs. In the remaining 4 dogs the interstitial nephritis had subsided.

Fourteen puppies showed no histological reaction in the kidney following the same procedure.

Lipid A antibody titers could only be detected in adult dogs, never in puppies. Lipid A apparently provoked an immunological process in the kidney damaged by the operative manipulations, resulting in nephritis.

It is concluded that chronic abacterial pyelonephritis may be induced clinically through lipid A and thus may have a pathogenesis similar to abacterial interstitial nephritis.

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Susceptibility of the Single Kidney to Infection: An Experimental Histological, Fluorescence-microscopical and Immunological Study.

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Question
Is a healthy, hypertrophic single kidney after unilateral nephrectomy of a pyelonephritic kidney more susceptible to infection? Is the "hypertrophing" kidney more endangered by infections than a grown up kidney?

Methods
Group I: Guinea pigs were infected in a retrograde manner after ligation of one ureter with E. coli 02:K1. After nephrectomy of the infected kidney, the other single kidney was infected in the phase of compensatory hypertrophy as well as 12 weeks later.
Group II: In a control group the single kidney was infected as before after nephrectomy of the healthy contralateral kidney.
In both groups the homologous 0-antibodytiters were determined. The infected kidneys were examined bacteriologically, histologically and partly by immunofluorescence.

Results
1) The homologous antibodytiters reached after the first infection in both groups 1:64 to 1:128. After reinfection there was seen a booster effect in group I with titers of about 1:1024.
2) In the first 2 weeks after nephrectomy there were no significant differences between the

single kidneys of both groups in the susceptibility to infection.
3) 12 weeks after nephrectomy it was nearly impossible to infect the single kidneys of group I without ureteral obstruction. These kidneys showed less histological lesions than those of the control group. After 24 h the kidneys were sterile on culture. The bacterial antigenic material in the renal parenchyma of group II could be demonstrated over a longer period than in group I.

Conclusions
A "growing kidney" in the compensatory phase shows a lower resistence to infection. The homologous antibodies show to have only partly protective functions, because the highest titers were seen in the phase of compensatory hypertrophy.

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Functional Changes in the Residual Kidney: An Experimental Study.

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Literature data on functional changes in the kidney after nephrectomy of the contralateral organ are often contradictory. We did follow-up investigations on 10 dogs using Oberhausen's method of the split hippuran clearance; in some cases we determined GFR by means of chrom-EDTA-clearance additionally. There was a sudden rise of both ERPF and GFR two hours after nephrectomy. A maximum of an average 100 per cent functional increase was reached after 7 to 14 days and leveled off to a value of 75 per cent of the preoperative total renal function 4 to 8 weeks after nephrectomy. The causes of this "reaktive hyperemia" are not known. A sudden drop of renin - angiotensin may be a possible factor.

The Continuity of Renal Cysts and Renal Pelvis in Polycystic Disease of the Kidney during Hypothermic Perfusion.

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The question of the special relationship between the cysts in polycystic kidneys and the renal pelvis is not clearly solved as yet. Although Osathanondh and Potter, using microdissection techniques, have shown the existence of a connection between these two cavities (1), there are contradictory reports in the literature (see Ref. 2). To further clarify this question we have studied the appearance of enzymic activity in the urine after injection of catalase in the cystic cavity.

A human polycystic kidney was initially washed with cold Fresenius^{R}-solution and subsequently connected to the Gambro-Perfusion-System and hypothermically perfused for 8 hours. A solution of catalase was injected in the individual cysts and the enzyme activity was determined 2 hours later in the urine collected from an ureteral catheter.

Neither in the cysts, nor in urine nor in the perfusate was any catalase activity detectable before injection. 2 hours after injection only the urine contained enzyme activity, but no catalase could be demonstrated in the perfusate. Since catalase is a high molecular weight protein (240.000 daltons) which at the temperature of perfusion neither diffuses nor can be reabsorbed by the cystic wall, we believe that the appearance of enzyme activity in the urine can only be explained by assuming the existence of an especial continuity between the cysts and the renal pelvis.

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The Role of the Lymphatics in Hydronephrosis. An Experimental Study in Dogs.

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Ureteral obstruction causes pyelolymphatic as well as pyelovenous backflow (1). The reabsorbed amount of urine from the renal pelvis was determined in acute and chronic hydronephrosis to elucidate the role of the lymphatics.

Methods
In 23 dogs the ureter was ligated. Lymph studies were performed after 3 hours (n = 13), 6 - 12 days with (n = 4) and without (n = 4) induced infection and 34 days (n = 2). Following injection of ^{99m}Tc pertechnetate into the obstructed pelvis the reabsorbed amount of urine was determined (2). Its concentration in renal hilar and/or subcapsular lymph was followed and the fraction reabsorbed through the lymphatics calculated.

Constant intravenous infusion of ^{125}I iothalamate and ^{131}I iodohippurate was administered to determine glomerular filtration rate and effective renal plasma flow in the experimental and the control kidney.

Results
Reabsorption of urine from the occluded renal pelvis was between 0,06 ml/min (in acute obstruction) and 0.1 ml/min (in chronic obstruction). Hilar lymph represented less than 0,5% of reabsorbed urine.

Conclusion
Increase of lymph flow following ureteral occlusion is only caused by urine reabsorption to a very low degree but is mostly due to an increase of plasma filtrate.

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Experimental Investigations of Core and Shell of Urinary Calculi.

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This work tries to answer the question, if the core and shell of urinary calculi show a variance in their chemical or phase composition and as to how far they coincide with the findings of Prien and Frondel, which show that in most stones, with exceptions of the uric-acid and cystine-stones, only calcium-phosphate was found in the cores. Lagergren found in addition uric-acid in oxalate-stones.

Material and Method
Our stone-material consists of 200 urinary-stones, which were obtained operatively. The stones were halved trough the centre with help of a thin thread-saw. Under binoculars, samples of 20 mg were removed with the help of a fine needle from the regions of the stone-cores and also from the shell-areas for X-ray analysis.

Results
In our material for investigation which necessarily concerned large urinary stones seven different mineral-phases as core substance could be determined. They were: 3 Phosphate-phases: Apatite, Struvite and Whitlockite. 2 Oxalat-phases: Whewellite and Weddellite.

There were uric-acid as well as cystine-cores. We found also many different phase compositions of the shells.

Discussion
We conclude that every crystal-phase formed and retained in the urinary tract can function as a nucleus for the following stone formation, and this is important for the medical therapy of the urinary calculi.

Human Prostatic Carcinoma in Cell Culture: Preliminary Report on the Development and Characterization of an Epithelial Cell Line (EB 33).

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This work has been published in Urol. Res. 2, 111-121 (1974)

Chromosomal Studies of Human Prostatic Tumors in Vitro.

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Chromosomal studies were performed on primary cultures from human prostatic adenomas and carcinomas. All cells from both tumor types showed diploid chromosomal counts with a normal human karyotype.

Chromosomal analysis was also performed on cells of the permanent epithelial line called EB 33 which was derived from a human prostatic carcinoma in this laboratory. In contrast to the primary cultures hypotriploid chromosome numbers were found during a continuous culture period of more than one year. The range of chromosome numbers increased with time in culture and was reduced to the original modal number of 64 by only one animal passage ("nude mice").

Feulgen-fluorometry on different passages of the permanent cell line EB 33 showed tetraploidy. This discrepancy to the hypotriploid chromosome number can be explained by variant Feulgen-hydrolytic properties of different cell types.

The complete text of this paper will be published in the next issue of Urological Research.

Heterotransplantation of Human Prostatic Carcinoma into "Nude Mice".

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In spite of many attempts in several laboratories, successful heterotransplantation of human prostatic carcinoma into a laboratory animal has never been accomplished. The "nude mouse", an athymic genetic variant of the Balb C mouse has been shown to tolerate heterotransplants of human skin and several human malignant tumors without immunosuppression for indefinite periods of time.

Fresh tissue fragments from 6 adenomas and of 19 carcinomas were transplanted into 110 "nude mice" subcutaneously. The wet weight of the transplanted tissue decreased with time proportionately. However, after transplant periods up to 100 days intact and histologically recognizable tissue was found from 6 adenomas and 7 carcinomas. The carcinoma tissue was in all instances identical to the original tumor by histological means. Studies on the hormonal dependence of such transplants are in progress.
Cells from the permanent prostatic epithelial cell-line EB 33 were also transplanted into "nude mice" by subcutaneous injection. Tumors become palpable after 2 weeks and grow to the size of several grams. Histological examination reveals solid carcinomas. Dependence of growth of such tumors on steroidal hormones could not be shown.

This paper has been accepted for publication in Investigative Urology.

Xenogeneic Transplantation of Human Prostatic Tissue on Newborn Thymectomized Rats.

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Xenografts of human BPH as well as of carcinomas of the prostate were implanted into newborn thymectomized rats to determine how long the transplants could be maintained in the animals.

New born Sprague Dawley rats were thymectomized at birth by the sternal approach. At the same time freshly prepared small fragments (1-2 mm^3) of prostatic tissue obtained from BPH or carcinoma of the prostate were implanted subcutaneously in the region of the buttock. 10, 14 and 30 days after transplantation the explants were removed for histological and histochemical examination. Autoradiographic studies were done to study the incorporation of H^3-thymidin into the transplants.

82 animals were reexamined after transplantation. In all of them the transplants were to be seen macroscopically. They had however not increased in size. Most of the transplants revealed microscopically necroses or inflammatory destruction. In one instance the xenograft of BPH could be maintained viable for 10 days in the host.

The study was discontinued since thymectomy alone seems to be insufficient for achieving generalized immunosuppression of the animals.

Ultrastructural Observations in Prostatic Carcinoma Before and After Castration.

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With the electronic microscope we examined cellular alterations of prostatic carcinoma after castration. Different responses to antiandrogenic therapy and modes of involution are observed.

Four different types of cells are regularly seen in prostatic cancer:

1) Most frequently cells are dark with a cytological glandular pattern. Nuclei are rich in heterochromatin and cytoplasma is rich in organelles.
2) There are clear cells containing nuclei rich in euchromatin and cytoplasma which shows no secretion.
3) Vacuolized cells with an abnormally increased secretion.
4) Small basal cells poor in organelles.

Four weeks after castration clear cells show the least change. The nuclei become dispersed and there is often an accumulation of lipid vacuoles.

The nuclei of dark cells become smaller accompanied by a vacuolar cytoplasmic degeneration in which endoplasmatic reticulum, mitochondria, golgi apparatus, and probably cytoplasmic basic substance take part. Secondary lysosomes and large autophagic vacuoles are involved in cytoplasmic degradation.

The vacuolar cells show a decrease of enriched secretion products.

The ultrastructural examinations of prostatic cancer cells before and after castration have shown:
1) Carcinoma of the prostate consists of different cell types which differ morphologically as well as functionally.
2) The cell types show different behaviour after castration.
3) Since we found all cell types and their various

reactions in any prostatic tumor, we concluded that the carcinoma of the prostate is not sufficiently treated by antiandrogenic therapy alone.

A Comparative Ultrastructural-Morphometric Study on the Ventral Lobe of Rat Prostate.

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While the correlative biochemical investigations of the prostatic gland do offer quantitative data, the current morphologic information is restricted to descriptive findings obtained subjectively. In recent years there has been made available a quantification of findings as yet only known by qualitative description (Weibel, Rohr). The aim of the present paper is to report on the development of a quantitative model of the ventral lobe of rat prostate.

Method
Tissue of the ventral lobe of the prostate of 200 g male, adult Wistar rats was according to the strict criteria of randomisation sampled in three steps of magnification. The first step (magnification 30 x) was done with the Wild sampling microscope, the second and the third step (magnification 1.300 x and 4.100 x) was done with the electron-microscope (Zeiss EM9A). The calculation of all data obtained from the various magnifications was done with a small computer (Olivetti Programma 602). A special program was devised by Rohr, which permitted fully automated evaluation.

Results
The study shows that a quantification of the prostatic cellular organelles involved in the secretion and enzyme synthesis is possible. The data show that the ventral lobe consists of 24% of extracellular space (blood vessels, connective tissue, smoth muscle-fibers) and of 76% of prostatic acini. Dividing the prostatic acini into the acinar lumen and functional parenchyma, the last one was calculated to be 22,5%, whereas the sum of all acinar lumina represents 53,5%. The volume density of rough endoplasmic reticulum (related to 1 cm^3 prostatic tissue) is very high and was calculated with 54%; also the Golgi apparatus (17%) and the lysosomes (1%) are well developed in the prostatic cell, whereas the mitochondrial fraction (5,5%) is low.

It is hoped, that our studies have served as a basis of numerous morphometric analyses of the prostatic cell which should give us a better insight into the physiology of the prostate.

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Systematic Study of Testosterone in Benign Prostatic Hypertrophy (BPH): In vitro and in vivo Results.

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An in vitro system for testing steroids which might be effective in treating BPH has been developed based upon the transformation of H^3-testosterone in dihydrotestosterone and 3α, 5α-androstanediol. In scrutinizing the influence of the amount of BPH-tissue, time, and pH, 300 mg of tissue incubated for 2 hours at the physiologic pH of 7.4 were used in the standard experiment.

The H^3-testosterone concentration was varied from .17-100 x 10^{-8}M. Plotting the resulting 5α-reduction products as a function of testosterone concentration a hyperbolic pattern of enzyme kinetics ensued. Performing a double reciprocal plot of 4 experiments with double determination of each value regression lines could be computed. Those two regression lines most different in their slopes were considered "normal" limits. Thus the effect of steroid pharmaca can be studies and the results are comparable and reproducible.

These in vitro results were compared to those obtained in vivo. For this purpose five patients undergoing prostatectomy received 400 - 600 mcCi H^3-testosterone IV. The radioactivity recovered within the enucleated prostatic adenomas measured 20 times as much as in rectus muscle. Pretreatment with 200 mg gestonorone caproate lead to a suppression of prostatic radioactivity from aprox. 20 000 to less than 1 000 dpm/g. The same is held true in regard to the 5α-reduction products declining to less than 5% as compared to the untreated control. Since these 5α-reduction products are essential mediators of testosterone action, this finding may provide a clue as to a possible mode of action of gestonorone caproate.

Female Mastomys as an Experimental Model for Prostatic Disease.

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A well developed prostate gland consisting of two lobes is present in all female praomys (Mastomys) natalensis. Previous reports suggest the occurrence of hyperplasia and adenocarcinoma in the prostate of old female mastomys. In this report the hormonal behaviour of this prostate and the possibility of using this animal as a suitable model for investigating pathological conditions of the prostate is presented.

At 2 hours after the injection of tritiated testosterone, the uptake by the urogenital tract, as well as non-target tissue, was significantly less than that by the prostate ($P = 0.001$). Prolongation of the time after injection to 16 hours resulted in a sharp decrease in the uptake of tritiated testosterone by kidney and liver, whereas prostate retained tritiated testosterone more than any other target or non-target tissue. Administration of 100 µg of unlabelled testosterone prior to injection of labelled testosterone caused a significant decrease in the uptake of labelled testosterone by prostatic tissue. The uptake of labelled oestradiol by various tissue of female mastomys was also studied.

These studies show that the prostate in the female mastomys is androgen dependent and has identical hormonal behaviour to that of the male mastomys. It is suggested that this animal is suitable as a model for further investigation into prostatic disease.

Prostate Scintiscanning by Zinc Radioisotopes.

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Zinc radioisotopes have been used in attempts to obtain prostatic scintiscans, but basic data concerning zinc radioisotope uptake rates by tissues are incomplete and there is no information concerning the optimum conditions that should be used for scintiscanning. We have examined the uptake rate of ^{65}Zn by human and rat prostate and used these results in a study of prostate scintiscanning with ^{62}Zn.

20 rats each were given 50 µCi ^{65}Zn chloride i. v. and killed at 2, 8 and 20 hours. Radioactivity was measured in various tissues and expressed as counts/min/mg wet tissue. Uptake studies were carried out with 20 µCi ^{65}Zn chloride in 12 patients and tissues (muscle, bladder and prostate) were obtained at open prostatectomy between 2 - 24 hours after injection.

The rat studies showed that at 2 hours the highest radioactivity was in the kidney, liver, pancreas and prostate: at 20 hours, the concentration in the prostate, seminal vesicle, testis and bone had increased, whereas the concentrations in other tissues had decreased. In human studies the maximum contrast between prostate and periprostatic tissues was between 12 - 24 hours.

As a result of these uptake studies, prostate scintiscans were carried out in patients using 1 mCi ^{62}Zn. Although uptake by the prostate was detected it was not adequate for clinical use and uptake by pelvic bones appears to be the main limiting factor.

The Effect of Procainhydrochlorid on Tumor-Bearing Rats. An Animal Experimental Study.

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In radiation of healthy plants and animals procainhydrochlorid has proven to be a radio-protective and radio-therapeutic substance. There is little knowledge about radiation sensitivity or radiation resistance of tumors under therapy with procainhydrochlorid together with radiation. It is also unknown whether there is a repair of radiation damages.

1 ml steril suspension of tumor-cells (5 mill. cells of Yoshida-Ascites-Hepatom AH 130) was injected i. p. into female Wistar rats. Procainhydrochlorid was given per os in a dosage of 5 mg/kg body weight. Radiation was done by a Gammatron in various experiments (whole body and local radiation).

All animals with procainhydrochlorid showed a decrease of tumor-production between 45 - 90% in comparison with control groups. A repair of radiation damages and radio-protective screen seems to exist.

It is possible that procain operates on immunological reactions so that the organism is building up a better protection against tumor-specific-transplantation-antigens. Procainhydrochlorid is well known in human medicin. The use of procain together with radiation of human tumors seems to be justified one should examine the effect of procain together with radiation on malignant tumors of the bladder in order to reduce predominant somatical radiation damages.

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Simple Procedures for Long-Term Preservation of Kidneys in Experiments with Minipigs[1].

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Experiments were done using technically simple procedures for long-term preservation of kidneys over periods of 24 hours and above. Three different methods of preservation over periods of 24 and 48 hours were attempted in 14 minipigs.

Following removal, the organs of the 14 animals were primarily perfused with a modified Collin's solution (free of heparin and phenoxybenzamine) at a temperature of 0 - 2°C, and implanted in donor animals after preservation. The contralateral organs were removed at the time of reimplantation, or later. Primary perfusion in the first group (n = 4) was followed by cooling the kidneys to 2°C in a preservation unit for 24 hours, and exposing them to 5 atmospheres excess oxygen pressure. The same procedure was followed in the second group (n = 4), but without excess oxygen pressure. In the third group (n = 6), the preservation time was extended to 48 hours. Following primary perfusion, the kidneys were cooled to 2°C and exposed to 5 atmospheres excess oxygen pressure for 24 hours, perfused once more, and stored at 2°C for another 24 hours. The contralateral kidneys were removed three weeks after reimplantation.

Urea-N/creatinine values 3 - 4 weeks after preservation averaged 15.5/1.3 mg % for the first group, 22/1.4 mg % for the second, and 61/3.8 mg % for the third (3 weeks after removal of the contralateral kidney). 24-hour urine excretion was 5500 ml for the first group, 2800 ml for the second, and 3430 ml for the third. The compensatory weight gain of the kidneys 6 month after preservation was 130 % and 103 %, respectively, for the first and second groups, and only 18 % for the third experimental group.

It appears from the results that continuous perfusion of the organ, which is more complicated technically, can be dispensed with renal preservation times of up to 24 hours. Substantial loss of function must be accepted if the preservation time is prolonged to 48 hours.

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Hypothermic Kidney Preservation with a SO_4^- Solution.

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Acquatella et al. (1, 2) proposed a hypertonic SO_4^{--} containing solution for kidney storage as alternative method to preservation perfusion or storage with Collins intracellular solution (3). To investigate this possibility left kidneys of bastard bitches (n = 6) were autotransplanted into the right iliac fossa after 24 h storage in this solution at 4°C. The kidneys were flushed out by gravity with 500 ml of the same cooled solution (100 cm water pressure). 14 days after transplantation contralateral nephrectomy was performed.

The vascular reaction to the washout showed great variability (extreme values 100 ml/min/kg - 24 ml/min/kg). Immediately after the anastomosis homogeneous blood flow was constantly observed - exceptionally transient vasoconstriction was of little duration. In all except one case urine production intra operationem could be stated. Kidney structures were apparent in one case 4 days after transplantation by X-rays, and in two more cases 8 days after transplantation. In the other three cases the i.v. pyelography was negative. All contralateral kidneys showed increased GFR 14 days after the transplantation of the left kidney while the transplanted kidneys in 3 cases had decreased filtration and in 3 cases no filtration. After nephrectomy of the contralateral kidney, improved GFR of the filtrating kidneys could be seen while in the three other cases no filtration could be induced. Unlike kidneys that had been preserved by hypothermic plasma perfusion, the SO_4^{--} preserved kidneys showed no compensatory hyperfunction even 90 days after neprectomy of the contralateral kidney. The tubular function of the SO_4^{--} preserved kidneys as checked by glucose transportcapacity after high plasma glucose levels and Na^+ transport showed no qualitative difference to the normal kidneys. The main impairement of the renal function in the SO_4^{--} preserved kidneys is assumed to be at the glomerular level.

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Qualitative and Quantitative Functional Studies with the Anger Camera in Conserved and Transplanted Dog Kidneys.

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Kidneys are evaluated by scintigraphy with Gamma-camera during preservation. After application of 250 µCi ^{131}J-hippuran outside of the machine we count the impulses and compare them with the results of controls after 2 to 18 hours.
This is an easy and perfect information about organ vitality and function.

Reabsorption of Glucose in the Transplanted Dog Kidney.

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To investigate possible changes in the nephron glucose transport capacity of transplanted dog kidneys experiments with high glucose plasma levels were performed in dogs after autotransplantation of the left kidney in the right iliac fossa and contralateral nephrectomy. All kidneys were preserved before transplantation by 24 h hypothermic plasma perfusion or cold storage after flush with SO_4^{--} containing solution. Glucose (20%) was given i.v. and the GFR as inulin clearance and tubular glucose transport as difference between glomerular filtration and urinary excretion were determined. 155 clearance periods from non transplanted kidneys and 107 clearance periods from transplanted kidneys were analysed for the present investigation. The GFR in all transplanted kidneys was reduced. The degree of impairment was greater in the kidneys with simple flush out and cold storage than in the plasma perfused kidneys. The glucose load as a function of the GFR decreased proportionally to the degree of filtration impairment. At a plasma glucose concentration under 200 mg% significant glucosuria was observed neither in the normal nor in the transplanted kidney (reabsorption rate of the transplanted kidney 98, 81 $\pm$ 2, 6 % of the load; reabsorption rate of the normal kidney 99, 38 $\pm$ 1, 6 % of the load). At glucose plasma levels above 200 mg % (maximum values in the transplanted dogs 1023 mg % and 1085 mg % in the normal dogs) glucosuria was registered. The maximum relative transport capacity of the normal kidney was 233 $\pm$ 57 mg/100 ml GFR (n = 99) and 230 mg/100 ml GFR (n = 69) for the transplanted kidneys. These results indicate that in the transplanted kidney the glomerular filtration function is impaired but the tubular transport capacity for glucose is not affected.

Ion Changes in Dog Kidneys After Continuous Hypothermic Perfusion with Homologous Plasma.

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At low temperatures, cells lose K^+ and gain Na^+. Leaked K^+ is transported from the near cell area by the plasma perfusion while Na^+ is continuously apported; thus the ion gradient at the cell membrane is maintained at its greatest value and the diffusion processes are facilitated. Total Na^+, K^+ and H_2O has been measured in the cortex and medulla of perfused canine kidneys at 6°C after 24 and 48 h perfusion time. The kidneys were perfused with homologous filtered plasma. The perfusion pressure was fixed before the experiment at 90 mm Hg and maintained at this value throughout. Changes of flow were not corrected.

After 24 h perfusion Na^+ gain ($p \leq .001$) and K^+ loss ($p \leq .001$) are found in the renal cortex while the water content is unchanged. In the medulla the Na^+ content shows no change, the K^+ content diminishes ($p \leq .001$) and the water increases ($p \leq .01$). After 48 h persusion time, additional Na^+ gain and encreased water content is observed in the cortex ($p \leq .02$); while the K^+ content shows no further change compared to 24 h.

Consistently with the results of this investigation plasma perfusion preservation at 6°C fails to maintain the intracellular K^+ concentration. Consequently to keep this ion at its normal level, K^+ rich perfusion fluids should be employed. To protect cells against K^+ loss, simple cold storage without perfusion might be preferable to plasma perfusion.

The Possibilities of Energy Supply of the Isolated Perfused Kidney.

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In long term preservation experiments with the isolated perfused kidney it is necessary to offer substrate for oxidation. Burg and Orloff demonstrated for isolated tubulus cells, that even at 0°C

there are still active energy consuming transport processes (1). Huang et al. perfused a kidney for 24 h at 10°C and measured a decrease of total kidney lipids of 35%; they postulated that only a part had been oxidized, while the main portion had been released into the perfusion medium (2).

In our experiments we compared the oxidation rate of some substrates in the isolated perfused kidney in order to find, which of these substrates was the most convenient energy yielding compound. We used the normotherm isolated perfused rat kidney (the experimental conditions were identical in: flow rate, O_2-uptake, Na-net transport, inulin clearance) and offered each of the following ^{14}C-U-labelled substrates: D-glucose 3.75 mM, and fructose, lactate, pyruvate, acetate, propionate, palmitate, glutamate, alanine, and tyrosine 2 mM (in the presence of unlabelled glucose 3.75 mM). We measured the $^{14}CO_2$-production; the oxidation rates of the substrates were: pyruvate 66%, lactate 45%, acetate 34%, palmitate 30%, glutamate 25%, fructose 18%, propionate 12%, alanine 10%, and tyrosine < 1%.

It is concluded that pyruvate, offered in the presence of glucose, can yield 2/3 of the total energy in the isolated perfused rat kidney. Under our con ditions it is a better compound for substrate oxidation than the fatty acids, known as the physiological substrate for the energy supply of the kidney (3).

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The Effect of Platelets-Anti-Aggregating Drugs on the Rejection of Allotransplanted Canine Kidneys.

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In chronic rejection of allotransplanted kidneys thickening of small artery walls is observed. This is thought to be caused by aggregation and organisation of platelet and fibrin thrombi (Kincaid-Smith). The influence of the platelet-anti-aggregating drug acetylsalicylic acid (Colfarit-Bayer) and the pyrido-pyrimidine derivate SH 869-Thomae on the rejection process of allotransplanted canine kidneys was studied.

The kidneys of 30 mongrel dogs were crosstransplanted. Histology of the rejection process was graded (grade 0 - III). 12 dogs of group II received 3 g acetylsalicylic acid per day, 10 dogs of group III 5 mg/kg SH 869.

The control group survived 8,6 days (group I), the animals of group II 9,1 days, and those of group III 7,3 days. All animals excreted urine postoperatively. BUN and creatinine were equally increased in each group postoperatively. Platelet aggregation was reduced in all groups (method of Jakobi). Three cases of group I showed an excessive rejection reaction (grade III), three cases of group II a grade 0, three cases grade I, and one case a grade II rejection reaction. In group III there was no rejection twice, once a grade I, and twice a grade III rejection process. Two cases of each group presented with an ischemic necrosis of the kidney due to renal artery thrombosis.

The platelet-anti-aggregating drugs investigated did not prolong life of the animals. The rejection process however was found to be significantly reduced histologically in the kidneys of those dogs treated with acetylsalicylic acid. The cellular immune response in these animals appeared to be suppressed.

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Sperm Collection by Vasostomy. Experimental Studies.

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The possibility of sperm collection within a period of several months following vasostomy (terminal-cutaneous implantation of the vas deferens) was studied in 10 Beagles. The vas deferens was dissected and the end of the proximal segment implanted at the cranial angle of an inguinal incision. This was found to be the optimal vasostomy technique in dogs (Lunglmayr et al., Andrology, in press). After surgery the stomata remained patent for a maximal period of one year.

The study was productive of the following results:

1. Morphology and motility of sperms obtained by vasostomy and suspended in PBS buffer

(pH 7,2, 37°C) were not found to differ from normal ejaculates.
2. Inseminations of 4 females with sperm suspension were productive in 2 cases with 2 definite litters.
3. Testicular blood flow measurements by intratesticular injection of 133-Xenon did not show any significant changes after vasostomy.
4. Immunfluorescence studies for identification of any circulating auto-antibodies to sperms were negative.
5. Histologic and histochemical studies (histochemical demonstration of alkaline-phosphatase, acid-phosphatase, DBNH-diaphorase) of the testis and epidydimis gave no evidence of pathologic alterations due to vasostomy.

Histometric and Enzymatic Histochemical Studies on the Puberal Testis of the Dog in Experimental Unilateral Cryptorchism.

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Is the recently advocated early treatment of cryptorchism (Hösli, Hecker, Mengel, Brandesky) justified? The question was examined whether, in unilateral cryptorchism (C.), both originally normal testes underwent pathological changes. In two groups of 2.5 month old Beagle dogs, the left testicle was placed in the abdominal cavity. After 3 month, castration was performed and the diameters of the tubules were measured in histological preparations. The values for both testes in the experimental animals were compared with those of the control animals. In another morphological test some demonstrable enzymes were examined.

In group 1 the data of 6 of the 7 orthotopic testes were significantly below the mean value of all the control animals. A statistically significant growth deficit of 14% was found for all the orthotopic testes and 32.5% for all dystopic testes. In group 2 the data of all 5 orthotopic testes were significantly below the mean for all the control animals. The significant growth deficit was 18.4%, that of the dystopic testes 38.5 ($p = 0.001$).

The acid phosphatase shows an irregular reduction of activity in the epithelium near the lumen of the dystopic testis. The LDH lost its activity in the seminal epithelium of the orthotopic testis. Dystopia increased this loss of activity still further. The glucose-6-phosphate dehydrogenase and the steroid-3ß-ol-dehydrogenase show an increase in activity in the Leydig cell complexes of the orthotopic testis and a still greater increase in the dystopic testis.

From histometric and histochemical changes in the orthotopic and dystopic gonads in experimental unilateral C., later fertility disorders can be considered to be acquired in some of the patients. The need for early operation is supported.

Adrenergic Innervation of the Ureter: Electron Microscopic Evidence with a "False" Sympathetic Neurotransmitter.

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Adrenergic nerves can be demonstrated by electron microscopy and further identified with 5-hydroxydopamine (5-OH-DA), a "false" sympathetic neurotransmitter which has proven to be useful as a marker for adrenergic nerve endings (1).

Specimens consisted of 4 human ureters removed during surgery and incubated 30 min at 37°C in a Krebs-Ringer solution containing 1 mg/ml of 5-OH-DA before fixation for electron microscopy. In addition, 4 rabbits received 5-OH-DA intravenously (10 mg/kg) 30 min before sacrifice and after pretreatment with α-methylmetatyrosine (200 mg/kg i.p. 20 and 4 h before the experiment); the ureters were removed and fixed for electron microscopic examination.

This ultramorphological study demonstrated the existence of a rich sympathetic innervation of the rabbit and human ureteral musculature. This was confirmed after treatment with 5-OH-DA which filled the vesicles of adrenergic nerves with electron dense material and allowed their selective ultrastructural identification.

Cholinergic nerves were unaffected by the "false" transmitter and since numerous nerve endings remained empty, it suggested the existence of a parasympathetic innervation too. These results allowed to present a model of the autonomic innervation of the ureter at an ultrastructural level.

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Animal Experimental Studies on the Pharmacological Treatment of Ureteral Colics.

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Would it be possible to obtain by drugs spasmolysis of ureter during acute colic due to calculi, and to relieve the kidney this way?

By means of a small incision into the kidney, concrements were inserted into the upper ureter, the renal pelvis and the congested ureter was perfused with a constant pressure of 30 mm Hg. Measurements of the volume of the perfusion per minute and of the usual parameters below the concrement were done on 36 narcotised bastard dogs.

The spasm of the ureter on the level of the stone is of great urodynamic importance. After administering a dose of epinephrine the well known positive inotropic and chronotropic effect is obtained. By restriction of the ureter the perfusion is diminished. After having applied some alpha-blocking-substances as well as some beta-receptor-provoking substances, a distension of the ureter via spasmolysis and an increase of the volume of the perfusion is gained. The increase of perfused volume after a dose of 0,4 mg/kg Phenotolamin and 0,02 mg/kg Orciprenalin is statistically highly significant (p below 0.001).

As an alternative or addition of the usual analgetic and antiphlogistic therapy of ureteral stone colic spasmolysis with alpha blocking substances or stimulating beta receptor substances can be obtained. Alpha blocking substances are to be preferred because of the smaller secondary effects.

Optimal Parameters of Electrical Stimulus in the Urinary Bladder.

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The effect of changing the different parameters of the electric stimulus on the urinary bladder was studied in 20 male rabbits.

When the voltage was increased gradually - with a constant frequency and pulse width - a concommitant rise in intravesical pressure and drop in urethral pressure profile were obtained. The best result was reached with 5 V.

Increasing the voltage above that level was without any effect.

When the frequency was increased - with constant amplitude and pulse width - the maximal rise in intravesical pressure and drop in urethral pressure profile were reached at 20 - 30 Hz. Increasing the pulse width - with constant amplitude and frequency - the strongest effect on the intravesical and intraurethral pressure was obtained with 3 - 8 msec. We conclude, that the optimal parameters of the electric stimulus for rabbit bladders are 5 V, 3 - 8 msec and 20 - 30 Hz.

Electrical Bladder Stimulation.

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Electrical bladder stimulation under different polarities in a complete electrical field was performed in 30 male rabbits. The intravesical pressure was registered by a suprapubic canula. Wire electrodes were applied circulary around the bladder neck and fundus. With stimulation of 3 V, 1 msec, 30 Hz, an intravesical pressure of 200 mmH_2O was obtained.

The negative electrode was positioned at the bladder neck and the positive electrode at the fundus (Position I). When the negative electrode was at the fundus and the positive electrode at the bladder neck (Position II) the pressure did not exceed 100 mmH_2O. After extending the pulse width to 5 msec in Position II, the intravesical pressure rose to 200 mmH_2O.

In our opinion, the electrical stimulus has the same direction as normal efferent nervous impulses in Position I. In Position II, the stimulus is against the direction of normal efferent impulses.

To prove the hypothesis that detrusor contractions in Position I are similar to normal neurogenic and in Position II similar to myogenic stimulation, electrocystography is essential.

Changes in Urethral Pressure Profile by the Pressoreceptor Reflexes in the Rabbit.

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Investigations regarding the anatomy, automatic innervation and action of drugs on the bladder neck encouraged us to investigate the influence of pressoreceptor stimulation on the urethral pressure profile. Stimulation of pressoreceptor of the aortic arch and carotid sinus causes an increase of the parasympathetic tone and a decrease of the sympathetic tone. Striated muscular tone is also decreased. Pressoreceptor stimulation was simulated by electrical stimulation of the depressor nerve in the rabbit. Urethral pressure profile studies were performed according to Brown and Wickham (5 F., infusionsrate 0,4 ml/min catheter withdrawal rate 8 mm/min). In the

control studies (n = 22) the maximum urethral pressure was 33.2 ± SE 2.8 mm Hg, the mean urethral pressure 19.4 ± 1.2 mm Hg. Depressor nerve stimulation caused a drop of these values to 27.4 ± 2.1 and 16.0 ± 0.87 mm Hg respectively ($p < 0.001$, n = 22). The intravesical pressures during the recording of the urethral pressure profile did not show statistically significant differences in the control studies and with depressor nerve stimulation.

We conclude that the interpretation of the action of parasympathicomimetic, sympathicomimetic and sympathicolytic drugs on the bladder neck has to take into consideration the cardiovascular effects of these drugs and therefore the effect on the pressoreceptors.

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Morphological Studies of Rabbit Renal Arteries after Instrumental Compression.

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The reaction of the renal artery after temporary compression was studied on 40 normal cholesterinemic rabbits. For this purpose in one sitting both renal pedicles were clamped for 10 sec, 15 and 45 min with Overhold forceps, one protected with rubber and the other unprotected. The histological examinations of the arteries were carried out after 3 hours to 8 weeks. The applied pressure was measured with the help of a special power-pressure-machine. It has been proven that the renal artery responded with a total necrosis of its wall which showed no difference between the clamping methods. The necrosis of the vessel wall depends purely on the pressure of the forceps and not on the duration of the compression.

Renoportal Shunt.

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Problem
If a renal tumor has invaded the vena cava, a radical nephrectomy can be performed only if the vena cava can also be resected. The procedure requires the diversion of the venous return from the other kidney.

Method
A left nephrectomy with a right sided renal vein to superior mesenteric vein end-to-side-anastomosis was performed in seven mongrel dogs. The ischemia time averaged between 15 and 30 min.

Results
The dogs were sacrificed in monthly intervals up to five month. The urograms were normal. Angiographically the anastomosis was widely patent and a smooth outflow of contrast medium from the peripheral intestinal veins was present. Pathologically no obstructive changes were present in the small intestine, kidney or liver.

Conclusion
With these results (which agree with the work of other authors) it seems possible in selected patients with vena cava tumor invasion without distant metastases to resect the vena cava and divert the venous return of the remaining kidney over the portal system.

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Cyanoacrylates: Identifying in Renal Tissue by Scanning Electron Microscopy.

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The reaction of the host-organism on foreign implant - as they are the cyanoacrylate tissue adhesives (1) - is not only dependent on the chemical characteristics but also on it's surface properties.

As an ideal technique for the microscopic study of surfaces the scanning electron microscope (SEM) was applied to demonstrate the fate of acrylates in renal tissue (2).

In 15 rabbits pole-resections and nephrotomies were performed by the aid of iso-butyl-2-cyanoacrylate[1]. Immediately after the procedure and on the 1., 20. and 45. p.o. day specimens were obtained. They were fixed in formaldehyde, dehydrated, air dried and coated with gold.

[1] Ethicon GmbH., Hamburg, Robert-Koch-Straße

In contrast to light microscopy the SEM demonstrates a firm polymer-film which covers and follows all unevenness of the cut surface. A thick film consists of two or more layers which are more brittle than a single layer. After 3 weeks the film desintegrates, and by shrinking of the wound the acrylate particles seem to be arranged like flakes of ice.

The unfinished studies have shown till now that there is a good adhesion between wound surface and acrylate. There are no sharp edged polymer particles. All structures have a very smooth outline. Thick polymer films delay wound healing and are less strong as they consist of several layers. Studies up to one year p.o. are in preparation.

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Experimental Study on the Influence of Plastic Splints in the Production of Epithelial Tubes from Buried Strips.

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Introduction
The practice of the Denis Brown technique is well established for reconstructing the urethra in the treatment of hypospadias and urethral stricture. Polymerized plastics well known for their tolerant attitude to tissue are frequently used more in plastic-surgery. The aim of the present study was to show whether epithelium is attainable by splinting the epithelial tubes. On the other side we want to test the tolerance to the tissue of polyvinyl (PVC) tubes in the production of epithelial tubes from buried strips.

Method
In 3500 g adult rabbits the skin of the abdomen was shaved closely and a measured strip (10 mm wide and 50 mm long) was isolated by two parallel incisions. The skin was undermined lateral to the incisions so that these flaps could be mobilized and secured together by a subcuticular absorbable stitch, thus covering the ntact strip. In 22 rabbits a polyvinyl tube (10 French) was deposited on the buried strips for 10 days. In 6 rabbits the buried strips were excised together with the polyvinyl tubes after 10 days. In another group (20 animals) the polyvinyl tubes were removed after ten days and the epithelialized tubes were excised in 6 animals after 20 days, in 6 animals after 40 days and in 4 animals after 100 days. In 6 other animals the polyvinyl tube was inserted for 20 days. The control group consisted of 6 animals without splinting of the epitheliased tubes with polyvinyl tubes.

Results and Summary
The tolerance to tissue of the PVC-tubes was excellent; except of one subcutaneous inflamatory infiltration near the epithelialized treat, we have not seen any disturbance in wound-healing in the other 31 animals. Cross sections, obtained from the middle of the tubes demonstrated that complete circumferential epithelialization occurs in 10 days and that the newly formed epithelium comprises one fifth to one third of the total circumference of the new formed skin tube. In the group of epithelialized tubes, which have been splinted by a PVC tube and the group where the PVC tube was removed after 10 days the total circumference of the epithelialized tube was 150% more than in the unsplinted ones. In 6 animals, where the PVC tube was removed after 40 days, the newly formed epithelium comprises a lesser portion of the circumference, but there was still an increase of epithelium of 80% in comparing it with the unplinted skin tubes.

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