URINARY TRACT DISORDERS

The following abstracts conclude the proceedings of the course on Medical and Surgical Disorders of the Urinary Tract presented by the Frank E. Bunts Educational Institute on November 17, 1949. The first portion of these proceedings appeared in the April issue of the Cleveland Clinic Quarterly.

DIETARY MANAGEMENT OF UREMIA

G. M. C. Masson, Ph.D.

A study was conducted to test experimentally the effects of high iso-caloric carbohydrate, fat, and protein diets and the effect of hormones (desoxycorticosterone acetate and free testosterone) on survival times and azotemia (blood urea N) in bilaterally nephrectomized rats. All treatment was begun at the time of nephrectomy. Survival was definitely improved and azotemia greatly diminished by administration of fat or carbohydrate rather than protein.

Treatment with hormones had no significant effect on survival time regardless of diet, and little effect on azotemia. Neither did diets nor hormones effect the evolution of uremia in nephrectomized rats subjected to simulated infection (turpentine abscess).

These experiments substantiate the beneficial effects claimed by Borst for the treatment of uremia by administration of a high caloric diet, composed largely of carbohydrate. They do not confirm the suggestions of others that hormonal treatment is of value after nephrectomy.

CYSTITIS AND INTERSTITIAL CYSTITIS

J. G. Warden, M.D.

The etiologic agents of cystitis may be grouped into 4 main classes: (1) The nonbacterial agents including both chemical and mechanical; (2) Bacterial including chronic, tuberculous, and the rarely luetic lesions; (3) Yeast fungi; (4) Animal parasites.

The symptoms are:

1. As a general rule the patient's attention is directed to the inflamed bladder by varying degrees of urinary frequency and the severity is usually indicative of the severity of the disease. Frequency experienced during the day but not at night generally indicates a physiologic rather than a pathologic process.

2. Pain occurs in varying degrees depending upon the acuteness of the cystitis. Usually pain is more severe during the act of urination or it may be terminal in type.

3. In the early stages of bacterial cystitis the urine is only slightly turbid. Later on there is pronounced turbidity with clumps of pus cells on microscopic examination. However, it cannot be overemphasized that absence of pyuria does not eliminate the presence of organic bladder disease.

4. The pain of complete urinary retention is usually referred to the suprapubic region. In acute cystitis in the male, the pain is referred to the tip of the penis, to the perineum, and along the inguinal ligaments to the rectum and low back region.

5. In the presence of acute cystitis the urine may be tinged with blood and occasionally the bleeding may be diffuse.

A clinical diagnosis is established by a history of frequency, pain, and pus in the urine. Because cystitis often represents a secondary rather than a primary vesical lesion, conservative treatment frequently fails to alleviate the patient's symptoms. Therefore, in cases which do not subside within a period of 10 days to 2 weeks following adequate conservative treatment, complete urologic investigation is indicated.

The treatment of cystitis with the various chemotherapeutic agents is dependent

upon the type of invading organisms. However, without specific diagnosis, the treatment of any extended or recurrent bout of cystitis with an antibiotic chosen at random is to be condemned.

The etiology of interstitial cystitis is not known but foci of infection, circulatory impairment, and lymphatic obstruction have been suggested. Hunner ulcer is predominantly a disease of women, with an occurrence of approximately 94 per cent.

The pathology of interstitial cystitis essentially is pan-mural inflammation, involving the entire vesical wall. Gross inspection of a typical Hunner ulcer resembles a pink, puckered, contracted ridge, on the summit of which is a linear, so-called "ulcer," frequently covered with a faint white exudate. Location is characteristic as it occurs on the movable portion of the bladder. Long duration of clock-like frequency occurring day and night is a characteristic symptom. If the bladder is not emptied immediately, severe urgency and pain will follow.

The diagnosis is made from the history, presence of reduced bladder capacity and by demonstration of the ulcer by cystoscopy. The urine is usually clear. Treatment constitutes one of the most difficult procedures of urology. The ineffectiveness of any one course is tested by the numerous methods being employed. Currently, hydrostatic distention with fulguration of the lesion with silver nitrate or high frequency coagulating units often affords temporary relief. Recurrence of symptoms is unfortunately frequent, the interval period of comfort varying from 3 months to 1 year, when the procedure must be repeated. Surgical approach is not indicated except in a few cases where bilateral ureterosigmoidostomy becomes a necessity.

HYPERPARATHYROIDISM

Robert W. Schneider, M.D.

Kidney damage in hyperparathyroidism may be of two types: nephrocalcinosis and nephrolithiasis. Kidney damage is more common in hyperparathyroidism than is skeletal involvement. Not over 5 per cent of all kidney stones is caused by hyperparathyroidism. A fatal disease when unrecognized, hyperparathyroidism should not be overlooked merely because it is a rare cause of stones particularly since it is curable. Certain cardinal symptoms and signs of hyperparathyroidism will aid in recognizing at least some of the kidney stones that are caused by hyperparathyroidism. Outstanding symptoms are polydipsia, polyuria, nocturia, muscular weakness, dysphagia, anorexia, nausea, vomiting, constipation, skeletal pain, tumor, deformity or fracture.

Signs in hyperparathyroidism are meager and usually absent. Loose teeth, epulides, muscular flaccidity and hyporeflexia are significant. Only 10 per cent of all parathyroid tumors are clinically palpable. Skeletal changes occur in only 30 per cent of all cases. The alkaline phosphatase is elevated only when the skeleton is involved.

Laboratory:

1. Persistently low blood phosphorus.
2. Sulkowitch test (office procedure). Many causes for a positive Sulkowitch test.
3. Normal blood phosphorus in the presence of a reduced urea clearance.
4. Elevated blood calcium which may be intermittently normal. Many other diseases are associated with a high blood calcium and kidney stones.
5. Total blood protein may aid in evaluating the level of ionic calcium.
6. Urea clearance (not always essential; may explain the absence of a low blood phosphorus).
7. X-ray of the teeth for destruction of lamina dura.
8. X-rays of long bones.

9. Alkaline phosphatase (of limited value).
10. Low calcium diet (only of value to aid in preparation of patient for 24 hour urine calcium determination in borderline cases).

The recognition of one case of hyperparathyroidism is ample reward for the effort involved.

DIAGNOSIS AND TREATMENT OF URINARY CALCULI

Charles C. Higgins, M.D.

It is generally conceded that there is no single factor responsible for the formation of all renal calculi. Preoperative investigation should include the following:

1. Infection
   a. Focal infection
   b. Local infection
      (1) Gram stain
      (2) Culture
      (3) Urea splitting
2. Hyperparathyroidism
3. Metabolic diseases
   a. Gout
   b. Oxaluria
   c. Cystinuria
   d. Xanthinuria
   e. Phosphaturia
      (1) Temporary
      (2) Permanent infected
      (3) Permanent noninfected
4. Excess of crystalloids in the urine
5. Hydrotrophic substances and colloids
6. Vitamin A deficiency
7. Vitamin B deficiency
8. Stasis

Errors in the diagnosis are sins of omission. With refinements in diagnostic procedures, i.e., intravenous urography, retrograde pyelograms with contrast media or air, and lateral pyelograms, a diagnosis always can be established. Conservative surgical procedures should be employed. Since the introduction of the newer chemotherapeutic agents, infections involving the kidney, which in the past failed to respond to treatment, now may be readily eradicated. Extensive nephrotomies may be employed to remove stag-horn stones from the kidney, and in other instances a heminephrectomy may be advisable. The majority of calculi confined to the pelvis of the kidney may be removed through the simple linear incision, pyelotomie elargie, or the inferior pyelotomy. incision. The postoperative management consists of:

1. Chemical analysis of the stone
2. Abundance of water
3. Elimination of stasis
4. Eradication of infection
   a. Local
   b. Focal
5. Correction of metabolic errors

6. Treatment of hyperparathyroidism if present
7. Correction of vitamin A deficiency
8. Correction of vitamin B deficiency
9. Dietary adjustment

The diet to be employed is determined by the chemical constituents of the stone and the pH of the urine from the kidney that harbored the calculus. It serves to control the pH of the urine maintaining the crystalloids in complete solution and minimizes the excretion of crystalloids in the urine. In general it has been stated that the incidence of recurrent stone formation following the removal of a calculus from the kidney varied from 10 to 40 per cent. Prior to the use of dietary management our incidence of recurrent stone formation was 16.9 per cent. Since utilizing the diet in conjunction with the other therapeutic procedures employed in the past, the incidence of recurrence has been reduced to 2.9 per cent.

The dietary management is also used for dissolution of renal calculi in a selected group of patients, obviating the necessity of surgical intervention. Patients who have passed a calculus spontaneously or in whom a calculus has been removed from the ureter by manipulative procedures should be placed on the diet to prevent further stone formation. The patients are instructed how to test and record the pH of the urine daily. These reports are presented to their physicians at monthly intervals. If the pH is not being maintained at the correct level, modifications of the constituents of the diet are essential. Complete cooperation among the physician, surgeon, and the patient is required to maintain a low morbidity and prevent recurrent renal calculus formation.

VESICAL NECK OBSTRUCTION IN WOMEN AND CHILDREN

William J. Engel, M.D.

Obstruction of the vesical neck is frequently unrecognized in women. The symptoms, which are similar to those occurring in men, consist of slowing of the urinary stream with hesitancy in starting, frequency and nocturia, and burning and urgency if pyuria is present. Such obstructions are most common during the fourth and fifth decades. Diagnosis is based on the history, repeated checks of the residual urine, cystoscopic findings which include increased coarse trabeculation, (sometimes deep saccules or small diverticula) hypertrophy of trigone, elevation of the floor of the vesical neck similar to that seen in contracture and median bar in men and depression of the bladder behind vesical neck. Atonic dilated ureteral orifices are seen in long-standing cases, and the cystogram may show a sacculated bladder and in late cases bilateral ureteral reflux. Several theories of causation have been proposed: 1. Fibrous contracture resulting from chronic inflammation, accepted by most; 2. Female prostate—glandular elements; 3. Congenital vesical neck contracture, probable factor in some of younger cases. The condition must be differentiated from neurogenic vesical dysfunction associated with spina bifida, multiple sclerosis, lesions of cauda equina, and cord changes associated with such diseases as diabetes and pernicious anemia. Excised tissue generally shows fibrosis, chronic inflammation, and occasionally glandular elements. Treatment includes urethral dilations, which are usually unsuccessful and transurethral resection of the vesical neck, which is preferred. This procedure requires careful resection. A resection of the lower 180 degrees or less is generally adequate, and it is better to take too little and repeat than too much and regret.

In children vesical neck obstruction is seen predominantly in boys. Several types are encountered: 1. Vesical neck contractures; 2. Posterior urethral valves; 3. Imper-

forate urethra. The most common symptoms and signs consist of frequency of urination and enuresis. The bladder may be palpable. Persistent pyuria and recurrent pyelitis are common. Anemia, weakness, and failure to develop properly are often associated. The diagnosis is made on the basis of the presence of residual urine, intravenous pyelogram, and cystourethroscopic examination. Early recognition and correction prevent renal damage. The obstruction can be relieved either by endoscopic resection or occasionally by suprapubic cystostomy. Too often the results are unsatisfactory because the problem has been recognized too late. It is frequently necessary to control the chronic infection with antibiotics and the sulfa drugs.

AZOTEMIA PRECIPITATED BY SODIUM DEPLETION

Robert D. Taylor, M.D.

The recent recognition of the value of sodium restriction in the treatment of heart failure and hypertensive disease, combined with the more generous use of mercurial diuretics, has increased the frequency with which azotemia is observed as the result of sodium depletion. Although the syndrome can be induced in normal people, it occurs much more readily in patients with some pre-existing impairment of renal function.

Symptoms of the condition are: drowsiness, weakness and lethargy; anorexia, nausea and sometimes vomiting. There is progressive oliguria, weight gain and edema formation. The laboratory findings are progressive azotemia and decrease in urinary chlorides and sodium values. There is evidence of dilution of body electrolytes. The plasma chlorides and total base values are sharply reduced.

Explanation for the occurrence of renal deterioration and azotemia because of sodium depletion is not known. However, unless the electrolyte deficit is corrected, uremia will be progressive and death may occur.

Treatment consists in administering enough sodium chloride so that the extracellular water can be restored to its normal tonicity. This can be done only by supplying NaCl in excess. If it cannot be taken orally, hypertonic solutions by vein are necessary to effect diuresis and normal blood electrolyte values.

PRODUCTION OF GASTROINTESTINAL SYMPTOMS BY GENITOURINARY DISEASE

Eugene F. Poutasse, M.D.

The presenting and sometimes only symptoms in about one-fourth of all upper urinary tract disease may be gastrointestinal in nature. Chief among these are nausea and vomiting, pain in any of the four quadrants of the abdomen, and constipation or diarrhea.

The reason for the confusing symptomatology is the analogous autonomic nervous system innervation of the kidneys and ureter with that of the gastrointestinal tract through the splanchnic nerves, celiac and aortic ganglia.

A stone lying in the renal pelvis or at any point along the ureter frequently gives typical symptoms of a gastrointestinal disease such as appendicitis, gallbladder disease, or intestinal obstruction. Other lesions often producing gastrointestinal symptoms are hydronephrosis, renal tumor, uremia, acute urinary infections, seminal vesiculitis or anomalies of the urinary tract.

A careful history and physical examination usually provides some clue pointing to the urinary tract in these cases. The urine should always be examined and in women it

must be a catheterized specimen. Appropriate studies must then be made to ascertain the diagnosis. Many patients are subjected to unnecessary exploratory operations for inadequately studied urinary tract disease causing gastrointestinal symptoms.

PROSTATISM AND PROSTATIC CARCINOMA

Charles C. Higgins, M.D.

Many men consider symptoms due to prostatic hyperplasia as indicative of advancing years and accordingly fail to secure medical attention. The patient may first notice some hesitancy, frequency, and slowness and lack of force of the urinary stream and subsequently nocturia of increasing frequency. An attack of complete retention may follow exposure to the cold or overindulgence in alcoholic beverages. Symptoms of prostatic obstruction are not proportional to the degree of enlargement of the gland. Thus a large gland that does not encroach upon the vesical outlet does not produce obstructive symptoms as pronounced as those caused by a small gland intruding into the vesical orifice.

A complete physical examination is essential, as in the last 600 patients I have operated on for prostatic obstruction cardiovascular complications were present in 210 and other complicating systemic diseases in 78 patients. Instrumentation may prove a dangerous procedure in the elderly individual with a large residual urine for a long time because it may provoke an exacerbation of infection. Determination of renal function (blood chemistry studies) and an intravenous urogram are secured routinely. The urogram supplies information regarding renal function and determines whether dilation of the ureters with coexisting hydronephrosis is present.

No one surgical procedure, in my opinion, is suitable to relieve all cases of prostatic obstruction. If preliminary drainage is required for more than a few days, I prefer to perform a trocar puncture for drainage rather than a urethral catheter. The former prevents the development of an urethritis and minimizes the incidence of epididymitis.

Approximately 70 to 75 per cent of the cases can be treated by a transurethral prostatectomy. When the gland is large and intravesical intrusion pronounced, I prefer suprapubic prostatectomy. By careful selection of cases, excellent results may be secured with both procedures. In a series of 1000 patients with prostatism I operated upon and reviewed a few years ago, the operative mortality was 2.5 per cent.

Carcinoma of the prostate still presents a baffling problem and a challenge to the urologist. The symptoms may simulate those of prostatic hyperplasia, i.e. frequency, difficulty, lack of force of the stream, and nocturia. Early in the course of the disease the patient may be free of symptoms. Carcinoma of the prostate usually has been present for 2 to 4 years before the diagnosis is established. The diagnosis is based upon rectal palpation of the prostate, laboratory data, and roentgenography.

Even if the gland is not stony hard, extensive induration and fixation, especially if the seminal vesicles are involved, suggest carcinoma of the prostate. A small nodule in the presence of hyperplasia of the prostate may be overlooked.

Acid and alkaline phosphatase determinations should be made on each patient. In the absence of metastasis as elicited by roentgenograms, the acid phosphatase was normal in 72 per cent of the cases. The alkaline phosphatase was normal in 70 per cent. In the presence of metastasis the acid phosphatase was normal in 38 per cent and the alkaline phosphatase in 16 per cent. Roentgenograms of the lungs, spine, and pelvis are advisable to determine the presence or absence of metastasis.

Early diagnosis is essential. If a nodule is palpable in the prostate of a patient 50 years of age or over, I believe perineal exploration is imperative. If the nodule is an

adenoma, it may be removed and the incision closed, and the patient leaves the hospital in a few days. If, however, the nodule is malignant, a radical perineal prostatectomy should be performed. At this stage of the disease a cure probably can be secured by this operation. Therefore, for early carcinoma of the prostate, when the malignancy is confined to the gland, a radical perineal prostatectomy is the procedure of choice.

Unfortunately, at the time the diagnosis is established the disease usually has extended beyond the confines of the gland, and endocrine therapy is necessary. Three types of treatment may be instituted:

1. Orchiectomy
2. Orchiectomy plus stilbestrol
3. Stilbestrol

In most instances I prefer stilbestrol alone. The dosage of the drug varies and I usually begin with a dosage of 4 mg. daily. There is accumulating evidence that in the absence of metastasis orchiectomy plus stilbestrol is the preferred treatment. During the past year I have performed orchiectomies in only 7 patients. It must be recalled that endocrine therapy is not a cure, while radical surgery early in the course of the disease may offer hope for a cure by complete extirpation of the lesion.

MANAGEMENT OF ACUTE ANURIA

A. C. Corcoran, M.D.

Management of acute anuria is directed towards supporting the chemical structure of the body until renal function is restored. A second aim is vicarious excretion.

Support is based on giving no more fluid or electrolyte than the patient can excrete, while providing a high caloric, protein-free diet. Control of infection is essential.

Vicarious excretion is accomplished by peritoneal or blood dialysis or by intestinal perfusion. All these procedures require a maximum of chemical control and may do, at times, more harm than good. Especially in anuria must we recall the old axiom "nihil nocere."

PANEL DISCUSSION (Abbreviated)

(*Drs. Taylor, Leiter, Higgins, Corcoran, and Poutasse*)

Dr. Jordan: Here is the first question. In view of the dramatic results in treatment of calculi medically, what would be your indication for nephrolithotomy?

Dr. Higgins: In the majority of instances, when there is a stone in the ureteropelvic junction that is obstructive in nature, destroying renal parenchyma, producing stasis, surgical intervention is advisable. I demonstrated some cases yesterday in which stones formed both in alkaline and acid urine were completely dissolved by dietary means. I do not wish to imply that this can be secured routinely. There is still a missing link in the dietary treatment of calculous disease. The role of diet at the present time is primarily to prevent recurring stones following operation. Frequency of recurrence before we used diet in conjunction with other procedures was 16.9 per cent. Our recurrence rate for stones at present is 2.9 per cent. The patients now forming recurring stones are those in whom we cannot control the pH of the urine due to the presence of a urea-splitting infection. If the stone lies in a calyx and is not obstructive, I think one is justified in attempting dissolution by dietary means. Stones in the kidney pelvis, stones

in the urethrocystic junction I believe are definitely surgical problems at the present time.

Dr. Jordan: Is the serum protein necessary in blood calcium and phosphorus determinations? Is that question clear?

Dr. Leiter: I suppose it involves the question of the relationship between the serum calcium level on the one hand and the phosphate and plasma protein on the other. Essentially the serum calcium concentration exists in two forms, about half in ionized form and about half in some sort of protein-bound form. Now the fraction which is bound to protein will, of course, be determined quantitatively by the amount of protein in the plasma; in conditions with low serum protein, that portion of the serum calcium will be diminished. On the other hand, the ionized calcium may still be perfectly normal and there will be no signs of tetany. Serum phosphate retention will cause a reduction of the ionized serum calcium. That is one reason why in hypoparathyroidism due to the removal of the parathyroids one finds elevated serum phosphate and decreased serum calcium. In certain conditions associated with hypocalcemia certain bone tumors—multiple myelomas—and so on, high levels of serum calcium may develop without elevation of the plasma proteins and without any remarkable reduction of phosphate in the serum because phosphate is coming into the bones along with calcium. There apparently is some sort of special protein fraction that has an unusual binding ability for calcium which comes into the serum presumably from the bones as well.

Dr. Jordan: Is increased acid phosphatase pathognomonic of metastatic prostatic carcinoma?

Dr. Higgins: In a vast majority of cases an increase in a serum acid phosphatase is extremely suggestive of metastatic carcinoma. A normal acid phosphatase does not mean that metastases are not present because we know that a certain group of the carcinomatoid cells undergo anaplasia and lose their power of secreting the phosphatase.

Dr. Jordan: A corollary question is: What acid and alkaline phosphatase determinations do you use and what levels do you consider abnormal?

Dr. Higgins: We use the Bodansky method, 0.1 to 1.0 acid phosphatase and 1.5 to 4.0 alkaline phosphatase.

Dr. Jordan: Dr. Taylor, here is a question that hasn't come up in this course but I know you can answer it. Please discuss lithium salt poisoning.

Dr. Taylor: Lithium intoxication was first described as far as we know in 1913 by a Dr. S. A. Cleaveland, who lives here in Cleveland. He induced it in himself while he was a student at Western Reserve University. He was on an experimental diet which was low in sodium designed to find out how lithium was metabolized in the body. He took about 5 grams of lithium before he went to a football game and in the middle of the game he began to see 33 players instead of 22, became rather foggy about where he was, and had trouble finding his way home. He became drowsy and developed some muscular tremors. He reported this experience in the Journal of the American Medical Association. All the patients we have observed and reported were on a low sodium diet. Apparently lithium is metabolized in the place of sodium in the body when there is a deficit of sodium present. When lithium is metabolized in the place of sodium, cerebral irritation occurs and it gives a unique picture of a severe hyperirritability of all of the reflexes and of all of the muscles of the body. There is a tremor that is gross and uncontrollable. The patients do not have azotemia or hypochloremia. They do not have decreased chlorides in their urine, and they do not have the oliguria that is associated with hyponatremia. In rats which are given a diet adequate in sodium, lithium produces no symptoms but if the lithium is given to rats fed on a low sodium diet, the same syndrome

appears in them as in human beings. It seems clear that lithium intoxication doesn't occur unless patients are on a low sodium diet.

Dr. Jordan: Would you like to add to that, Dr. Leiter?

Dr. Leiter: In our use of lithium at the Montefiore Hospital we were fortunate in not observing any of the gross manifestations of toxicity. After they were described in the literature, we went back and looked over our records and did not find any evidence of the severe forms of intoxication. Perhaps the reason was that we were careful not to use lithium salts in the old patients with arteriosclerotic heart disease, cerebral arteriosclerosis, or renal insufficiency. Most of our cases treated were younger persons with rheumatic heart disease. The amount of lithium was small. We did not add it to the food in the cooking, not in the hospital certainly, chiefly I think because we didn't want to have chloride in the urine which would confuse our chloride determinations. Only a few were allowed to take it at home.

Dr. Jordan: You don't disagree with Dr. Taylor?

Dr. Leiter: No, I don't disagree with his conclusions at all. It is not surprising that low serum sodium has been associated with lithium intoxication since the condition for which lithium is usually given, namely congestive heart failure, and its treatment with a low salt diet is also likely of itself to produce a low serum sodium.

Dr. Jordan: What are the indications for surgery in tuberculosis of the genitourinary tract and when should that surgery be done?

Dr. Higgins: I suppose the question is aimed primarily at renal tuberculosis. Renal tuberculosis is a local manifestation of the general disease. Therefore, if the patient has active pulmonary tuberculosis, has fever which may be due to an active renal tuberculosis, certainly immediate surgery is contraindicated due to the dangers of a miliary tuberculosis. Sanatorium treatment is necessary. If the patient does not have fever, he may be treated on an ambulatory basis and given streptomycin. I personally prefer to give the streptomycin for a period of 2 weeks prior to operation, if the patient has a normal temperature.

Dr. Jordan: What is the present attitude about orthostatic albuminuria?

Dr. Leiter: It is an optimistic one. Making certain that it is only harmless proteinuria is important. The urine should be obtained during recumbency without lordosis. If such a urine is free from albumin and if there is no history of recent or previous acute nephritis or recent acute infection, then the attitude toward posture proteinuria should be optimistic. An intravenous pyelogram might also be done to make sure that there is no vascular anomaly affecting the ureteropelvic junction on one side producing proteinuria.

Dr. Jordan: Dr. Taylor, do you want to make any comment?

Dr. Taylor: What I'm thinking about is not really orthostatic albuminuria. There are some patients who have acute glomerulonephritis and recover from it completely but continue to have an abnormal degree of proteinuria which is not significant of progressive, degenerative renal disease. When there is a moderate amount of proteinuria even up to 0.4 or a half a gram for 24 hours with no abnormal cellular elements in the urine and no decrease in tubular function or glomerular function for 2 or 3 years, I think one can assume that this is a residue of glomerulonephritis and may be present all the patient's life. It need not contraindicate buying insurance, getting married, or having children, but it does occur and it sometimes leads to misunderstanding and mistaken prognosis.

Dr. Jordan: Dr. Poutasse, there are five questions which deal with some of the subjects you discussed. (1) Which is the drug best suited for the various urinary infections? (2) To establish the type of infecting organism is it necessary in men to obtain

a catheterized specimen or is it permissible after cleansing of the glans to have the patient void into a sterile test tube which is being sent to the laboratory for culture? (3) Is there any rationale in using an unabsorbable sulfa drug in repeated recurrences of coli urinary infections? (4) The sensitivity test of the various antibiotics was mentioned. Would you please give in more detail the technic of the test? (5) Is pyelitis mostly blood-borne or ascending (especially in pregnancy)?

Dr. Poutasse: In answer to the second question, a clean voided specimen in a man is often a satisfactory way of obtaining culture. Perhaps the best way is passing a catheter, but this is not always feasible. There is no one urinary antiseptic that is effective against all organisms. As for the first question, there is reason to believe that chloromycetin and aureomycin may act on most urinary infections. However, there are other useful drugs and indications, of course, dependent upon the organism that is infecting the urinary tract. To the third question I should say that if an unabsorbable sulfa preparation proved ineffective, I would certainly switch to something else such as the more expensive drugs—aureomycin and chloromycetin; for a long period of treatment, mandelamine or mandelic acid may prove fairly effective.

The technic for sensitivity testing varies with different laboratories. The procedure that we use here is to take a culture plate and smear the entire surface with the organism, then place on it the little filter papers which have been wetted with the known strength of each drug. Twenty-four hours later the diameter of the clear area around the filter paper gives an index of the antibacterial activity of the agent.

Dr. Jordan: Then the last question: Pyelitis—is it mostly blood-borne or ascending (especially in pregnancy)?

Dr. Poutasse: It is difficult to answer this question. It is usually believed that infection gets to the kidney and urinary tract either through the blood stream or the lymphatics. Sometimes there can be an ascending infection, particularly when there is obstruction at the lower portion of the urinary tract.

Dr. Taylor: I would like to put a word in on that. I don't think there is any such thing as pyelitis exclusively; I think it is always pyelonephritis or nephropyelitis. I don't see how it is possible for a kidney pelvis to be inflamed without the whole kidney being involved with it. I think pyelitis is a term that should be completely discarded. Unless there is definite evidence of obstruction of the free flow of urine such as prostatism, strictures, or tumors, one may assume that there are constant showers of bacteria which come from teeth, tonsils, and the intestinal tract into the blood. There is little evidence to back up lymphatic origin of such infections. It is pyelonephritis or nephropyelitis, whichever you want to call it.

Dr. Leiter: I agree with Dr. Taylor in regard to doing away with the term pyelitis. It certainly should be pyelonephritis. If we learn to think of pyelonephritis, we will recognize these cases much earlier and shall see fewer of the neglected or so-called latent and chronic types of pyelonephritis.

Dr. Higgins: I agree with Dr. Taylor. The modern concept, of course, of pyelitis is that pyelitis per se is an extremely rare clinical entity. It is usually a pyelonephritis. It is always preferable, if possible, to secure a catheterized specimen from the male. One must remember that there are always nonpathogenic organisms in the anterior urethra. If conditions are such that one cannot secure a catheterized specimen, it does not suffice merely to wash the glans. The patient must void, wash out the anterior urethra, and the second portion of the urine must be utilized for the culture. There is one other feature in the treatment of urinary tract infections. In the presence of stasis one must determine if the organism possesses the power of splitting urea because if it does ammonium chlor-

ide (which is the common acidifying agent used) is contraindicated. Giving ammonium chloride aids in the formation of a stone in the kidney in the presence of stasis.

Dr. Jordan: What is alphalin?

Dr. Taylor: Alphalin is a proprietary drug marketed by Lilly Laboratories. It is their brand of vitamin A. We have used it because, whether accidentally or not, we observed that it increased renal function in hypertensive persons and persons with degenerative renal disease. The effect is not due to the vitamin A itself because crystalline vitamin A doesn't have it. Something in the fish oils which contain vitamin A enhances renal blood flow, filtration rate, and tubular secretory capacity—certainly patients feel better and it's easier to take care of them over a long term when they are getting large amounts of this fish oil. Have you used any, Dr. Leiter?

Dr. Leiter: No, I haven't.

Dr. Jordan: Is there an alternative to periodic massage of a prostate in a young man who—or which—presents an expressable bulge on rectal palpation and which, when not massaged, about monthly produces symptoms of urethritis?

Dr. Higgins: About 35 per cent of men past the age of 37 have microscopic evidence of a so-called chronic prostatitis. Now I do not believe that we are justified in massaging the prostate of such a man unless there is evidence that the prostate is acting as a focus of infection. The prostatic massage merely facilitates drainage from the obstructed ducts of the prostate gland. If the man does have a persistent urethritis, I think probably an occasional prostatic massage is indicated. The primary disease may not be the prostate gland. If patients who have a chronic prostatitis do not respond to prostatic massage, a couple of injections of penicillin sometimes help. Always one must examine the teeth by x-ray to rule out the possibility of a dental root abscess serving as the initial focus of infection.

Dr. Jordan: In your use of low sodium diets, do you follow urine chloride excretion, and if so, by what method?

Dr. Corcoran: We actually follow urine sodium excretion. The correlation at low levels of sodium chloride is not too good since chloride at its best is a rough measure of the degree of sodium restriction. Don't you agree, Dr. Leiter?

Dr. Leiter: Yes, and certainly if you are giving ammonium chloride before mercurial diuretics, you can't follow the excretion at all.

Dr. Jordan: When the ureter is hopelessly involved by rectosigmoid carcinoma and the tumor is removed, how is the remaining segment of ureter and corresponding kidney dealt with?

Dr. Higgins: I suppose the question infers that at the time of operation it is necessary to remove a segment of the ureter. If this is a small segment, I would not hesitate to pass one end of the catheter up to the kidney pelvis, the other end into the bladder, and then bring it to the outside by means of a cystoscope. This leaves the possibility of the patient developing a stricture at a later date. There is one other possibility—anastomosing one ureter to the ureter on the opposite side which I reported some time ago. Finally if one has a normal kidney on the side of the lesion, an autonephrectomy can be produced in that kidney merely by ligation of the ureter. This would be satisfactory except that one loses the function of the kidney. The kidney undergoes—first, a slight hydronephrosis, later atrophy. Surgical removal is not necessary in the absence of infection.

Dr. Jordan: Here is a long question. In our Urological Department we do a great many cystoscopic examinations under anesthesia. Apparently normal persons show definite delay in excretion of both indigo carmine and phenolsulfonphthalein under

anesthesia. In other words, the normal excretion time of 3 to 5 minutes, following intravenous administration of the dye, is repeatedly delayed from 6 to 8 minutes. Please discuss the effect of anesthesia upon kidney.

Dr. Corcoran: It depends on the anesthetic. The delay time is contingent on the rate of urine flow. There is a certain amount of urine in the kidney pelvis and ureter and it must flow on before the dye appears. The appearance time can be as rapid as 1 or 1½ minutes but with a slow rate of flow the time increases. Ether anesthesia, for instance, causes an oliguria, and deep anesthesia of any kind is associated with oliguria. This results in a delay in appearance time.

Dr. Higgins: I agree 100 per cent. In the ordinary cystoscopic examination, however, when the catheter to the renal pelvis is placed without an x-ray film there is no way that one can ascertain whether or not the catheter is in the renal pelvis or in one of the upper calyces. Obviously, if it is in an upper calyx, the drainage is not comparable to that in the opposite kidney if the catheter is in the renal pelvis. The other mistake that is frequently made with the phenolsulfonphthalein test is to rely entirely on the amount of excretion from the kidneys. Unless the specimen is taken from the bladder and the phenolsulfonphthalein content of the urine in the bladder determined, that is the urine is passed around the catheter down to the bladder, the test is not accurate.

Dr. Jordan: Is there any scientific evidence to show that renal function or renal pathology is influenced favorably by so-called kidney substances commercially known as nephrotin?

Dr. Taylor: No.

Dr. Jordan: Do you consider the complications of retropubic prostatectomy any more formidable than those of radical perineal prostatectomy, e.g. the various types of fistulas following this latter procedure?

Dr. Higgins: Definitely. I think for the majority of surgeons doing work on prostatic hypertrophy, suprapubic prostatectomy is preferable. A transurethral resection is extremely technical. If it is done correctly, one must extend the operation proximal to the verumontanum so as to be in close proximity to the external sphincter. The ordinary perineal prostatectomy is a completely anatomic approach. There should not be the complications of fistula. The same applies to the radical perineal prostatectomy. Now, of course, one cannot compare the results of retropubic prostatectomy to the radical perineal prostatectomy for carcinoma of the prostate. Two entirely different lesions are involved. As I stated yesterday, the incidence of osteitis pubis is so high that at present I have discontinued the operation until we can definitely determine the causative factors responsible for this complication.

Dr. Jordan: Please give the pathologic physiology of nocturia. Is there an associated diurnal polyuria?

Dr. Leiter: The nocturia, of course, can result from any disturbance from the cerebral cortex on down to the end of the urethra, I suppose, since it involves partly the question of frequency of emptying of the bladder. From the purely medical point of view we usually look upon nocturia as a lag in the excretion of urine during the daytime followed by an increase of excretion during the night and, therefore, also associated with larger urine volumes during the night. That would lead one to think of all conditions in which the excretion of water is delayed, assuming that the individual ingests water during the daytime. Therefore, almost any type of chronic renal disease, almost any type of secretory failure, or conditions such as diabetes insipidus where there is a continuous and large flow of urine with the associated thirst, would be likely to produce nocturia. Dr. Higgins will probably mention some local renal factors which may be important. What was the rest of it?

Dr. Jordan: Is there an associated diurnal polyuria?

Dr. Leiter: As to whether the total 24 hour urine volume is also decreased, or rather the frequency of urination during the day, that will vary with the etiologic factors. If it is something in the way of irritation in the urinary tract, inflammation and what-not, of course there will be an associated diurnal polyuria. If it is chronic nephritis with renal impairment or cardiac insufficiency or any condition associated with edema or tendency to it, there will be less urine put out during the day and the total 24 hour urine volume may not be increased. In fact, it may even be greatly reduced. The most important cause, I think, for nocturia is too much drinking of water before going to bed.

Dr. Higgins: The nocturia which perturbs the urologist is that which is associated with prostatic hypertrophy. Since the back pressure is transmitted up the ureter and the kidney pelvis, the primary impairment of function is tubular in origin, and that is one of the reasons for nocturia. In addition to this, as Dr. Leiter stated, such patients have had too much water or overindulged in alcoholic beverages.

Dr. Jordan: Dr. Corcoran, do you have anything to add?

Dr. Corcoran: No, just that Dr. Taylor has emphasized something that we commonly lose sight of—that nocturia may be one of the earliest evidences of congestive heart failure. Frequently, because the presenting symptom is nocturia, the heart is not given proper attention and the kidneys receive a lot more than they deserve.

Dr. Jordan: Dr. Higgins, what is the role of introduction of a sclerosing agent following aspiration of a solitary renal cyst?

Dr. Higgins: I have never introduced a sclerosing solution following aspiration of a solitary cyst of the kidney. I have on several occasions aspirated the fluid and as yet I have not seen a recurrence. Why this is I do not know. If the fluid is crystalline clear, that is all that is necessary. If, however, the fluid is hemorrhagic in nature, one must suspect a papillary tumor in the cyst and exploration is advisable. The cysts that I have aspirated I have not seen refill.

Dr. Leiter: I should like to ask Dr. Higgins whether he aspirates cysts in polycystic kidneys and whether he cauterizes them or does anything else besides aspiration.

Dr. Higgins: Some cases we have aspirated by open operation—as a matter of fact, cut them right open. Goldstein of Baltimore recommends marsupialization—that is, not to the skin but underneath the skin, so that he can aspirate them at any time he wishes. I think it is a good procedure in failing renal function in polycystic kidney.

Dr. Jordan: What happens in the kidney when respiratory acidosis or alkalosis exists?

Dr. Corcoran: When respiratory alkalosis exists, there is some polyuria and an increase in urinary bicarbonate. I think it is merely an osmotic diuresis. In respiratory acidosis I know nothing of what happens except that there is usually a good deal of associated oxygen lack and consequently oliguria. Can you answer that question, Dr. Leiter?

Dr. Leiter: I think in respiratory alkalosis there is available a temporary excess of sodium to be excreted, and it is if the kidneys are functioning normally. I suppose in emphysema with severe retention of carbon dioxide there would be a reason for disposing of more chloride in order to balance the sum of carbon dioxide and chloride in the blood.

Dr. Jordan: Here is a case question. A boy of 13 shows 4+ albumin during the day and only a faint trace on arising. He shows 3 to 4 white blood cells per high power field not centrifuged. Please discuss possibilities.

Dr. Taylor: The implication is that orthostatic albuminuria has to be considered, but if the 4+ albuminuria means the 6 to 10 grams per 24 hours it should, that is a

great amount of proteinuria for an orthostatic problem. I would think that this boy should be investigated for a chronic renal disease; he is 13; he certainly is in the age group when one could have a glomerulonephritis of an acute or chronic variety, and certainly his filtration rate should be measured promptly by urea clearance or any other methods available. Surely the Addis examination should be performed which will give an estimate of tubular function, if he has no edema, and it will also tell what this 4+ albuminuria means. Unfortunately, one often sees 4+ albuminuria recorded when it means less than a gram for 24 hours, and some technicians' and even some physicians' estimates of 4+ albuminuria are not accurate. A count of the sediment certainly has to be made to see whether or not these red cells, 3 to 4, are normal or whether there is hematuria. My guess is that a boy who puts out 6 grams or 10 grams of protein in a period of 24 hours, and has red cells, has a glomerulonephritis in either the acute, or healing, or chronic phase.

Dr. Higgins: This question states that he shows 4+ albuminuria during the day but only a faint trace on arising.

Dr. Taylor: I don't believe the laboratory.

Dr. Corcoran: Any proteinuria is orthostatic in a degree. A chronic nephritic proteinuria is partly orthostatic.

Dr. Taylor: We don't know anything about the concentration of the urine—we don't know anything. But anybody who has 4+ albuminuria and red cells in the urine has to be considered to have chronic nephritis until proven otherwise—or glomerulonephritis—until proven otherwise.

Dr. Leiter: I don't see the word "red cells" mentioned here. It says white cells.

Dr. Taylor: Oh, it did. I thought they were red cells.

Dr. Leiter: If there were red cells in the urine, I would certainly agree with Dr. Taylor that glomerulonephritis should be excluded. Regardless of what there is in the urine any youngster with a 4+ albuminuria diurnally (unless it can be shown during the day to be subject to complete remission with change of posture) should be investigated for the diseases mentioned and certainly should have an intravenous pyelogram to exclude some urologic anomaly.

Dr. Jordan: Can you tell us about the surgical treatment of hypospadias in children?

Dr. Higgins: Hypospadias is a plastic surgical procedure. One cannot perform a plastic operation on the penis in the absence of erection and then have the patient develop an erection and have the sutures hold. Therefore, the patients should all receive stilbestrol preoperatively until they do not have a morning erection. The plastic procedures are difficult—or they have been in the past, and I finally resorted to using the Ombredanne's technic for all patients. There is a new operation that is now out which I think is the finest technic that I have employed and certainly our results are gratifying. I would have to draw this on the blackboard, and if the doctor who asked the question would come up after we are through, I would be glad to show him the technics.

Dr. Jordan: What are the lesions in the kidney referred to as sulfa intoxication other than those secondary to sulfa crystal urea?

Dr. Leiter: The anatomic lesions in the kidney apart from the actual presence of crystals in the tubules or anywhere in the urinary tract are far more important than the presence of crystals. Granulomas may form about tubules in which I suppose crystals have precipitated at one time, or about degenerating tubular epithelium. These granulomas may be widespread and ultimately lead to fibrosis and uremia or they may lead to acute fatal uremia. In addition to that, there may be lesions which are absolutely

typical for so-called periarteritis nodosa or allergic arteritis with necrosis and inflammatory reaction in and about the smaller arteries which in themselves are a serious form of damage to the kidney.

Dr. Taylor: There is another allergic reaction which occurs in these persons. I think Dr. Castleman in Boston was one of the first to recognize it. It is not unlike the syndrome that occurs in lower nephron nephrosis. There is an allergic response in which the tubular cells just degenerate. Some recover, but the majority die.

Dr. Corcoran: I was going to ask Dr. Leiter if he has seen many instances of sulfa intoxication which resulted in a permanent, prolonged renal disease.

Dr. Leiter: I have seen only one instance in which progressive renal impairment occurred over a period of months. This was in the early days of the use of sulfapyridine in the treatment of pneumonia. At that autopsy the kidney was full of granulomas—enough of them so that renal tissue was effectively destroyed.

Dr. Jordan: Is the Fishberg modification of the Volhard and Farr concentration test sufficient as an office screening test for the presence of glomerulonephritis and nephrosclerosis?

Dr. Taylor: I don't think so. Back in 1944 and 1945 we tried to get a simplified procedure which would combine short periods of dehydration with the antidiuretic effect of pituitrin. Dr. Sodeman in New Orleans suggested that pituitrin alone as stimulus to tubular reabsorption would be enough to measure the ability to concentrate urine, but we were unable to find a substitute for the Addis test which would give equivalent results. Sometimes the results of the Fishberg test were excellent, but if a person had been consuming large quantities of fluids for a day or two beforehand, they were way off. In the summer, when perspiring a lot, we occasionally got concentrations up to 1034. The Addis test is simple; it can be done at home, is a cheap procedure and gives a tremendous amount of information.

Dr. Corcoran: There have been instances, one severe and one probably fatal reaction, from the use of pituitrin. In the latter case I think it was being used to facilitate intravenous urography. Not only is it ineffective but it may be dangerous.

Dr. Leiter: I should like to ask Dr. Corcoran whether he thinks pituitrin is as effective in patients with heart failure on the basis that there already has been an excess of antidiuretic hormone.

Dr. Corcoran: Practically everybody who has oliguria from almost any cause—lymphatic, renal, or heart failure—has already considerable amounts of antidiuretic hormone in the urine and that is probably why they don't respond much to the addition of some test material.

Dr. Jordan: Is the Clinitest method as reliable as the qualitative Benedict's test for the determination of sugar and for acetone?

Dr. Corcoran: I don't know the Clinitest method for acetone, but the Clinitest method for sugar does well if quantitative sugars are done as well.

Dr. Leiter: We have had a little difficulty with the acetone test because I think, depending upon the amount of powder used, it may be too sensitive. One may get 1+ results when there really isn't any acetone at all.

Dr. Corcoran: I might mention that Dr. Rabinovitch, my former chief in Montreal, developed a small tablet for acetone test which obviates that particular error because the tablet has a little depression into which a drop of urine is placed. Thus the ratio of urine exposure to the surface of the reagent is always constant.

Dr. Jordan: What dosage of stilbestrol do you use?

Dr. Higgins: The dosage of stilbestrol to be employed in a given case is influenced first by the presence or absence of metastases, and second by the acid and alkaline phos-

phatase studies. In the past, if metastases were not present, I started with an initial dose of 4 milligrams of stilbestrol a day—a milligram before meals and at bedtime. Now in the absence of metastases I expect to perform an orchiectomy and prescribe stilbestrol. In the presence of metastases it is necessary to use a larger dosage to control the pain and to soften the tumor, and I have no hesitancy in patients with severe pain to increase the dosage up to 25 or 30 milligrams a day. I certainly believe it is preferable to a chordotomy.

Dr. Leiter: May I ask Dr. Higgins if he has ever seen edema developing on these dosages of stilbestrol?

Dr. Higgins: I have seen it develop in patients in whom there is no apparent evidence that the tumor has extended beyond the confines of the gland. But in my experience in most of the patients who developed edema of one leg—and it is usually one leg—it is due to extension beyond the confines of the prostate.

Dr. Jordan: Why do you use urea nitrogen to the exclusion of the nonprotein nitrogen?

Dr. Leiter: It is largely because first of all it is a specific determination of a specific substance—urea. Nonprotein nitrogen, of course, includes a variety of things. Perhaps more important we do urea clearances so frequently that both blood and urine ureas are known and it is therefore not necessary to do a nonprotein nitrogen test.

Dr. Corcoran: That is the answer. I should like to ask Dr. Leiter, now that creatinine can be accurately determined by using a photoelectric colorimeter, whether it wouldn't seem advisable to shift over gradually to plasma creatinine which more closely reflects the level of filtration?

Dr. Leiter: We certainly should do creatinine studies.

Dr. Jordan: Discuss the medical treatment of idiopathic enuresis in childhood and young adults.

Dr. Higgins: As a general rule, I feel that a cystoscopic survey is not indicated. Now that is in direct contrast to the opinion of Dr. Meredith Campbell in New York, who believes he has shown a definite bulging of the sphincter which disappears as the boy or girl grows older. I believe instruction and perseverance on the part of the parents is the correct method to approach this problem.

Dr. Taylor: Dr. Higgins, how about that penile clamp you sometimes use?

Dr. Higgins: Yes, I forgot to mention it. It is an excellent method in the male. You put the small baby Cunningham clamp on the penis. During the night when his bladder is distended, he will waken, take off the clamp, and get up and void. This is an excellent method devised by Vincent O'Connor of Chicago.

Dr. Leiter: I would like to know whether Dr. O'Connor consulted the Psychoanalytic Institute in Chicago before he developed this.

Dr. Jordan: That is going over a difficult subject rapidly enough! What is the dietary management, particularly protein, in chronic glomerulonephritis?

Dr. Taylor: Some older clinicians felt that because there was protein in the urine, protein by mouth was bad. There was a time when it was thought giving protein orally would correct the hypoproteinemia which exists in this disease. As far as I am concerned, I don't think high protein diets have a great influence one way or the other. I think there should be an adequate amount of protein because most of these patients are young and they need it for growth and replacing tissues that are broken down in the body; they certainly ought to have a normal protein intake. But when azotemia appears and begins to be a problem as far as symptoms are concerned, with acidosis and anorexia and all of the things that go with it, low protein diets admittedly make these patients more comfortable, and I think make their lives last longer. If the protein intake is

reduced to approximately a half gram per kilogram per day, the management of the terminal stage of chronic nephritis becomes a much simpler problem.

Dr. Corcoran: Dr. Addis did determine that the major toxic factor in high protein diets was potassium. On the other hand Dr. Masson's rats were given diets of protein, carbohydrate, and fat which were equal and low in their potassium and other electrolyte content. The protein-fed rats died fairly quickly. Therefore, I don't think that the only factor in the toxicity of proteins is the potassium content although that is certainly considerable. We're speaking now of terminal renal failure.

Dr. Leiter: I think diets should not be changed except to alter the nutrition of the patient beneficially if renal function is above 30 or 40 per cent of normal or until it gets down to the really pre-uremic levels. I wouldn't give such patients a high protein diet or perhaps even a normal diet which contains 90 to 100 or more grams of protein, but 60, 70, and 80 grams should be harmless.

Dr. Jordan: How do you feel about doing a one stage suprapubic prostatectomy instead of a two stage?

Dr. Higgins: In most instances I would perform a one stage suprapubic prostatectomy. The lowering of mortality and morbidity, following suprapubic prostatectomy has not been accomplished by refinements in operative technic but rather by a clear understanding of secondary changes occurring in the upper urinary tract following prostatic obstruction. Whether we anticipate performing a transurethral resection or a suprapubic prostatectomy I have no hesitancy in performing the suprapubic puncture. The suprapubic puncture carries a mortality that is practically nil. The first stage prostatectomy in a patient with poor renal function carries a fairly high operative mortality. Therefore, I believe that such patients should be treated by suprapubic puncture.

Dr. Jordan: Please discuss the significance of a positive Sulkowitch test.

Dr. Taylor: A positive Sulkowitch represents a hypercalciuria. The most common condition in which it occurs is in hyperparathyroidism in which the calcium has been mobilized and excreted in the urine and leads to the formation of renal calculi which are made up predominantly of calcium.

Dr. Leiter: I think carcinoma of the breast with metastases may be a more common reason for a positive Sulkowitch.

Dr. Jordan: Discuss the status of the Streptococcus and the etiology of acute glomerulonephritis.

Dr. Taylor: It is the most common organism which causes infections in the nose and throat and such infections are the most common inciters of the antigen-antibody reaction which is responsible for glomerulonephritis. It produces an antigen to which the body produces an antibody and the reaction occurs primarily in the kidney.

Dr. Leiter: In connection with the attempts to prevent this peculiar antigen-antibody reaction which ultimately eventuates in glomerulonephritis, it should be remembered that the use of antibiotics is most effective if given early in the course of the infection itself. Once this reaction has occurred in the kidney a week or 10 days after the original infection, it is questionable whether antibiotics can any longer effect the course.