Lecture.

PYONEPHROSIS, NEPHROLITHIASIS, HEMATURIA, PYURIA; SUBSEQUENT NEPHROTOMY; NEPHRECTOMY; RECOVERY.

A CLINICAL LECTURE DELIVERED AT THE GOOD SAMARITAN HOSPITAL, CINCINNATI, NOVEMBER 1, 1898.

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THE diagnosis in this case is manifest from the symptoms as given in the history.

History.—B. J. P., politician, age forty-two, entered the hospital October 31, 1898. Family history good. Never had any serious sickness except his present trouble. When eighteen or twenty years of age he was struck with a club over the region of the kidneys. Since that time a slight strain from exertion or catching cold would bring on attacks of pain in the kidneys, loins, testicles and ureter, followed by vesical irritation and frequent urination with bloody urine. Two years ago small calculi were found in the patient's urine. Three years ago the urine was found to contain pus. Last August he was seized with pain in the left kidney, radiating down the ureter to the testicle, the bladder also being tender and sore and urination very painful. During the night he passed a quart of red blood; on the second morning following a large amount of black blood clots was passed. On the third morning one-half gallon (?) of reddish-brown pus was passed. Since then his condition has been one of alternate improvement and relapse. He has gradually become very weak and is now subject to fainting spells, having lost twenty pounds.

Present condition.—He is weak and emaciated. He lies in bed all the time, for the most part on the right side, with the legs flexed on the abdomen. The face is thin, the eyes deep sunken, surrounded with a dark halo. The voice is feeble and husky. The temperature ranges from $99\frac{1}{2}^{\circ}$ in the morning to 101° or 102° in the evening. There is pain over the site of the left kidney, following the course of the ureter, and tenderness over the area of the bladder.

The urine is turbid, muddy and gray with detritus. The reaction is neutral or faintly acid. The following is the report of the microscopical examination made by Dr. Malsbary: (1) Pus cells, large number; (2) pus casts; (3) small granular casts; (4) tailed cells, a few. No crystals found.

The salient points in this history are, first, a contusion of the abdomen. Just what importance to lay upon this accident it is difficult to say, but whether *post hoc* or *propter hoc* symptoms set in afterwards which were not present before. The blow may have caused hemorrhage. The pain attending the passage of kidney stones is so severe as to be unmistakable where there is no account to be taken of hysteria. But if there was any doubt about the pain, there could be little about the passage of blood, and none about the passage of the stones. It is always a matter of regret that the patient does not keep the stones and bring them to the physician, and this fact is to be especially lamented in this case because the examination of the urine shows no crystals. It has been a long time since any blood has been discharged, but pus flows now freely all the time. When the blood does not appear to the naked eye it is sometimes evident under the mi-

croscope, and we are led to make this search all the more thoroughly because the presence of blood corpuscles in the urine has been emphasized, especially by my colleague Professor Ransohoff, as a point of especial value in the diagnosis of stone in the kidney. You can understand, however, that blood would be present only when the pelves of the kidneys or ureters were being fretted or torn by a rough stone. A perfectly smooth stone, a sacculated stone, or a stone embedded in pus would not scratch the kidney and would not show blood.

But whether there is a stone present or not, there is pus in quantity and it is necessary to discover its source, that is, whether from the kidney or the bladder. If the pus belonged to the urethra it would appear with the first discharge of urine, preceding the urine, almost, and could be expressed at any time; if from the prostate it could likewise be expressed, especially with the finger in the rectum, where the large mass of the prostate could be felt, usually with manifestations of pain. The difficulty arises as between the bladder and the kidney. My old teacher, Oppolzer, used to maintain that the reaction of the urine would decide it, for if the pus came from the bladder it would be alkaline, if from the kidney acid. This view, however, is no longer tenable, as pyogenic micro-organisms may decompose the urine in the pelvis of the kidney and make it alkaline. Then it must not be forgotten that pyelitis and cystitis may coincide; they usually do in the course of time.

If from the kidney, which kidney? In a woman we may catheterize the ureter to find out. Bergmann, after washing out the bladder in man, makes pressure upon the diseased kidney, and finds that pus is emptied into the bladder and may be discharged from it quicker than after pressure upon the sound kidney. We are led to locate the source of the pus in the kidney in our case because there is so much pain in this region. The patient spares this side in decubitus, and though we can discover no tumor there is considerable tenderness to pressure, both before and behind.

The microscope reveals unmistakable pus cells in great abundance.

Mention is made in the report of tailed cells. These cells belong to the kidney and not to the bladder. However, we lay not too much stress upon the presence of these cells. We have not been helped much by the presence or absence of these cells. All the best modern authorities, especially Ebstein and Fürbringer, declare emphatically that no cells are characteristic of pyelitis and that in the majority of cases of pyelitis no cells are to be found. The cells with tails and multiple nuclei are anyhow not confined to the pelvis of the kidney, but occur also in the bladder and in the anterior portion of the urethra, as well as in the vagina and cervical canal. The pain in the kidney, the tenderness, the continuous fever, the previous attacks of kidney-stone colic with hematuria, fix the disease in the pelvis of the kidney, and in the left kidney.

It is necessary always to eliminate tuberculosis. There is no evidence of tuberculosis elsewhere, and Dr. Malsbary was not able to find the tubercle bacillus in the urine in a two hours' search. He did turn out some diplococci, a few of which seemed to be embedded in the cells, but there are so many diplococci as to make the differentiation of any particular species difficult. But to make assurance doubly sure, I gave this patient a test injection of tuberculin, which did not in-

any way disturb the diurnal range of temperature. I think, therefore, that we may consider the diagnosis to be pretty clearly established as a pyelitis or a pyonephrosis with nephrolithiasis. The disease began probably with a pyelitis, that particular kind of pyelitis which results in the continuous formation of kidney stones. These stones, or the cause which produces them, lead finally to suppuration, and this suppuration has in turn involved the substance of the kidney, so that the disease, beginning with a simple pyelitis, a pyelitis calculosa, has become a suppurative pyelitis, pyonephrosis or pyelonephritis. In the course of time the flow of pus, with the bacteria which produced it, has also irritated the ureter and finally the bladder. The chief complaint which the patient now makes is the burning of the urine and the frequent desire to pass it. Last night, for instance, he was compelled to pass water twenty times—the tally was kept with strokes—so that his night's sleep was broken up.

The pain is characteristic, but by no means pathognomonic, as just as severe attacks of colic occur in a simple pyelitis without stones or blood clot. A marked increase in the acidity or alkalinity of the urine is enough of itself to produce pain as severe as that caused by like conditions in the stomach. The fever is more characteristic of pyuria; but it must not be forgotten that many cases of chronic pyelitis, even though attended with suppuration, run a course without fever. It is not so much the pyelitis as the pyonephrosis which is responsible for the fever. Fever, more or less continuous or remittent, interrupted by chills, and profuse sweats, are signs of great value in the diagnosis in pyonephrosis. The picture is, then, one of sepsis, and the patient succumbs to marasmus with the symptoms of hectic fever, as in the course of advanced tuberculosis. These symptoms are seen more especially after perforation of the kidney substance with the formation of a peri- or para-nephritic abscess.

The urine does not always show this purulent appearance. It may be perfectly normal at times. Thus it may be heavily loaded with pus at one time and perfectly normal and clear at another. This condition occurs with especial frequency in pyelitis of calculous origin, and finds explanation in occlusion of one ureter.

What we want to know now is the condition of the other kidney. Where suppuration exists for any length of time it is liable to induce a parenchymatous nephritis in the second kidney, and, in any event, a long-continued suppuration may lead to amyloid change. This amyloid degeneration, when of long duration, may be appreciated by enlargement of the spleen and liver. We find nothing of this kind here, but an obstinate diarrhea has set in of late which might speak for an amyloid degeneration of the mucous membrane of the intestinal canal.

Having eliminated tuberculosis, the diagnosis rests between a pure pyelitis or a nephritis or the coincidence of both. It is by no means always easy to settle this question. The implication of the kidney usually imparts the graver signs of sepsis, and the profuse pyuria, the emaciation and the great prostration speak for suppurative nephritis in this case. The fact that there is more albumin in the urine than the pus would account for would indicate also involvement of the kidney. The presence of granulated casts lends additional testimony. A peri- or para-nephritis usually shows a high temperature. The pain is also more

constant in these conditions, and sometimes there is edema of the surface indicative of the suppuration beneath.

Where there is a tumor the question may be solved by aspiration, though the presence of pus would not necessarily differentiate a nephritis from an abscess in the vicinity of the kidney, as sometimes the kidney itself is hollowed out to a mere shell or sac of pus.

At the request of the patient an x-ray examination was made by Dr. Taylor, a skilful skiagrapher of this city. Such pictures are usually extremely unsatisfactory, and this is no exception. It is difficult or impossible to secure penetration of the whole body to the x-ray, but in this case penetration was easily secured on account of the emaciation, the body in the region of the kidney being not as thick as the thigh of an ordinary man. Sometimes these stones show as a light spot in the picture. I pass the plate about. You may make out without difficulty the arches of the iliac bones and with difficulty a few of the lower ribs. There is something of a smirch or smudge which might be interpreted as a foreign body, but I would not be willing to accept it as the picture of a kidney stone. Neither does the skiagrapher in this case.

As to the prognosis, it is plain to see. The patient has postponed an operation to the last possible moment. All the remedies of medicine have long since been exhausted. The indication now is to make an exploratory incision and drain the pus sac, wherever it is. The operation may be a success, or it may be too late already. We cannot tell exactly what is the condition of the other kidney, but the quantity of the urine voided, notwithstanding the weak action of the heart, would indicate a pretty sound kidney on the other side.

The patient having finally consented, two weeks after the clinic, my colleague, Dr. Ransohoff, with his assistant, Dr. Freiberg, and with the assistance of the internes, in my presence, opened the abdomen in the loins posteriorly, and soon came upon a kidney enlarged to three times its natural size, whose pelvis was distended with pus, of exceedingly offensive nature, which was evacuated to the amount of perhaps six ounces by incision. It was now seen that the kidney substance had suffered injury. The cavity of the pelvis extended in anfractuositities in every direction. The kidney itself was found so deeply congested and dark that it was deemed advisable to remove it. It had the appearance of the small lobe of the liver—lobulated. The entire mass was accordingly withdrawn from the abdominal cavity, ligated at the pelvis, clamped and excised, after the manner of treating an ovarian tumor. On section of the kidney it was seen that the parenchyma was greatly riddled by suppuration and reduced. In one of the anfractuositities a stone was found about the size of and twice as thick as an ordinary coat button. It was perfectly smooth. Near it was found a smaller stone of the size of a small pea. This stone was also smooth. It was apparent that neither of these stones had done the mischief.

The patient passed urine freely on the night of the same day. The urine was still turbid, but the quantity of pus was notably lessened and decomposition did not set in so rapidly. Urotropin, seven and one-half grains every four hours, was now prescribed, whereupon the urine became perfectly sweet and free from pus in the course of twenty-four hours. There was no fever after the operation, and the patient partook

of food and drink so soon as he had recovered from the effects of the anesthetic, and is now, ten days after the operation, doing so well in every way that we may predict a restoration to perfect health in two weeks.

Dr. Ransohoff promises to detail the particulars of the operation in this case in a report including a number of similar successful cases. The great amount of effort necessary to deliver the kidney, that is, to withdraw it bodily through the wound to the outside of the body, was a surprise to me. I have since seen a comment to this effect made by Dr. Ben Johnson in his report on the Surgery of the Kidney at the recent session of the Mississippi Valley Medical Society.

Original Articles.

VARIATIONS IN PATHOGENIC ACTIVITY AMONG TUBERCLE BACILLI.¹

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In the production of states of disease due to infection we should recognize two main modifying factors—the pathogenic activity or virulence of the infecting organism, and the resistance² of the infected individual.

Variations in the pathogenic power of bacteria are probably the result of prolonged sojourn in slightly different environments. If, for instance, a given tubercle bacillus had successfully invaded a vigorous adult, and had successfully passed from this person to a second, a third, or a long series of vigorous adults, and had then after this prolonged contact with tissues of a certain vitality invaded the body of a child, we are justified in assuming that the virulence of this bacillus with reference to the child has been increased by its successful invasion of vigorous, naturally more resistant adults. Again, if a tubercle bacillus, vegetating in a tuberculous lesion of the skin, through a favorable combination of accidents had produced a series of infections of the skin, we may assume that differences, however slight, between this bacillus and one infecting a series of lungs would become eventually established. A continuation of such series, through fortuitous circumstances, might finally produce two varieties of tubercle bacilli, each incapable of taking the other's place successfully. It is probably in some such way as this that varieties are produced which become restricted as to the territory they are capable of infecting, while at the same time they become especially adapted to infect this restricted territory. The bacillus of bovine tuberculosis illustrates another phase of the same problem. Does it by its continued passage through the bovine body become more virulent to human beings, or does it thereby lose largely its power to graft itself upon the human system? Either alternative may be true, but neither is proven.

I cite these illustrations to emphasize the relativity of the term virulence and its dependence on the character of the host, as well as the relativity of the term resistance, as it depends more or less on the bacterium. These two terms, virulence and resistance, may be compared to the two opposite sides of the same shield.

¹ Presented, by invitation, at the meeting of the American Climatological Association, September 1, 1898.

² This term figures in medical writings chiefly as immunity, although the term is merely relative, since there is no absolute immunity.

They are, as mathematicians would say, functions of one another. They are, however, none the less real when we come to deal with given species, races or types of individuals whom the tubercle bacillus may infect. It takes a long time to modify bacteria, and for the short space of life of the individual their characters are practically fixed. We need here a certain sense of perspective to enable us to appreciate the slow change during long periods of time and the temporary fixity. The evolution of new characters is going on in all living organisms, but all our information concerning them is anchored, as it were, to their temporary stability.

In the laboratory we are able to modify experimentally both the virulence of certain bacteria and the resistance of the host. By passing these bacteria through a long series of susceptible animals of the same species a greatly increased potency of the bacteria, with reference to that species, is noticed at the end. By treating susceptible animals with certain bacterial products or cultures killed by heat or chloroform, the resistance may be increased. Different degrees of induced resistance lead to different clinical and pathological types of the same inoculation disease, so that the etiological relationship between them would hardly be surmised without a definite knowledge of the experimental details.³

Variations in the pathogenic activity have been demonstrated for a considerable number of disease-producing species. In fact, it seems to be the rule to encounter slight variations in the study of series of cultures of the same organism obtained from different sources. I might cite many illustrations in support of these statements, but I shall limit myself to one of general interest. The diphtheria bacillus, which is so well characterized by the production of a specific toxin, may vary in the power to produce this toxin from case to case. Thus bacilli from one source have produced for years just three times the amount of toxin produced by bacilli from another source, when cultivated in bouillon of the same composition. Other numerical relations in the power of toxin production may be cited, but the fact I wish to emphasize is the constancy of the variation under identical conditions.

In their contact with infectious diseases physicians have laid the emphasis now on virulence, now on resistance. With diseases having a rapid course, like cholera, the plague and diphtheria, the relative resistance of individuals is in the background, and the virulence of the infecting agent receives more attention. With diseases of slow progress, like tuberculosis, attention is centred upon the resisting capacity of the individual as expressed by heredity, bodily conformation and environment—the soil, in other words, of which we have heard so much. It may be that the instinct of the experienced physician is quite correct in attributing to the resisting capacity of the individual in the more prolonged chronic infections a more conspicuous influence than in the acute infections, because in the former the latent forces of resistance have had time to develop in the course of the disease. Of these two conceptions, virulence and resistance, I shall confine my remarks to the most neglected one—not

³ I have expressed this relationship between the type of disease on the one hand and the virulence and resistance on the other by the simple equation $d = \frac{v}{r}$ where v = virulence, r = resistance. Increasing v or diminishing r we augment the severity of the disease (d). Increasing r or diminishing v we diminish its severity.