

CONCLUSIONS.

The prostate gland is without doubt the cause of the majority of obscure urinary and sexual symptoms and should always be examined where there is any uncertainty as to their origin.

Among the factors that tend to perpetuate a chronic or recurrent gonorrhea a nidus of infection or irritation in the prostate is the most frequent cause. It is in this variety of prostatic inflammation that the largest number of errors are made in the diagnosis.

Palpation, pus and proteid are the three things to rely on in reaching a conclusion as to the condition of the prostate. By palpation through the rectum, the gland, if diseased, may be found enlarged, nodular, irregular, boggy or apparently normal. Pus in the secretion expressed from the meatus or found in the urine or fluid voided after massage, when the urethra and bladder are excluded as possible sources, is positive proof that the prostate is inflamed. Proteid in the fluid passed after massage is equally as reliable as pus in the diagnosis of prostatitis.

1014 Century Building.

THE DIAGNOSIS OF PYELONEPHRITIS

BASED ON THE ABNORMAL RETENTION AND THE DELAYED EXCRETION OF METHYLENE BLUE.*

EDWIN BEER, M.D.

Surgeon to Sydenham Hospital; Assistant Surgeon to Bellevue Hospital and to the Montefiore Home.
NEW YORK CITY.

The following report on what I believe to be a useful differential diagnostic symptom between simple involvement of the pelvis of the kidney and involvement of the pelvis and the parenchyma of that organ, is preliminary to a more detailed publication based on further clinical and experimental data.

There are two types of pyelitis, acute and chronic. In both the parenchyma may be involved, as autopsy of such cases shows. How can we determine whether the parenchyma is involved?

As far as one can judge from the literature there is no symptom which reliably differentiates between pyelitis and pyelonephritis. A patient, without palpable kidney tumor, without tenderness over the kidney areas, is suffering from a chronic pyuria. Despite careful bladder irrigations and in some cases despite drainage of the bladder (3 cases reported by Osler), the pyuria continues. Cystoscopy shows a chronic cystitis and by means of ureteral catheterization it is found that pus is passed from one kidney, whereas from the other the secretion is normal. Examination of the specimen from the diseased side shows a faint trace of albumin and considerable pus. Does this pus come from the pelvis or from the pelvis and the kidney parenchyma? Are we face to face with a chronic pyelitis or a chronic pyelonephritis? That question crops up in every case, and such cases are by no means rare.

In the literature there are no definite aids that I know of to assist in this differentiation. In the two cases that are to be reported, I think I have found a differential sign which will throw some light on this question and probably help us in differentiating between simple pyelitis and pyelonephritis with formation of multiple suppurating foci in the kidney parenchyma.

CASE 1.—History.—Mrs. W., aged 35, married; has two children; was operated on for anal fistula six years ago. She had cystitis for some time, for which she was treated. About March, 1904, she developed an ascending infection of her left kidney with chills, high fever and pains in left lumbar region. No kidney enlargement and only slight local tenderness. Operation was disadvised because of poor general condition. She was treated with the usual measures and for several weeks during this illness was put on methylthionin hydrochlorid (methylene blue). Gradually the patient improved and the fever disappeared. The pains became less and slow convalescence set in. Her pyuria and bladder irritability persisted despite regular bladder irrigations, and ten months after the onset of the acute symptoms, I had an opportunity to make an inspection of her bladder and catheterize her left ureter.

Cystoscopic Examination.—Dec. 29, 1904, the bladder showed marked thickening of the mucosa, which was thrown into folds. Left ureteral orifice red and swollen. Bladder excessively irritable. Urine from left kidney was rapidly excreted and neutral in reaction. It contained pus cells, epithelial cells; no casts, no tubercle bacilli. Colon bacilli were present. As there was no mass in the kidney region and no tenderness on deep pressure, it was assumed that the pus came from the kidney pelvis and that the acute pyelitis of earlier date had become a chronic pyelitis. With this diagnosis in mind, lavage of the left pelvis was determined on and measures were taken to diminish the vesical irritability. At this time every specimen of urine was bottled and labelled in order of voiding. On standing, one-half to one inch of pus almost regularly deposited in a six-ounce bottle. In some bottles there was more pus than in others, and it was observed that occasionally there was very little and again at other times a great deal of pus.

On Jan. 2, 1905, the left kidney pelvis was irrigated with boric acid followed by silver nitrate. No effect was noted.

Jan. 19, 1905: Lavage was discontinued, as patient had her menses and a mild attack of influenza. On this date I noticed that the pus deposited in one of the bottled specimens was stained blue, while the supernatant fluid was yellow and unstained. The appearance of this blue immediately suggested methylthionin hydrochlorid (methylene blue), and to determine absolutely what this was I made various tests and microscopic examinations.

Examination of Pus.—Professor Giess of the department of physiologic chemistry, Columbia University, very kindly examined this blue pus, as well as other similar specimens passed at subsequent times, and reported as follows: "The urinary sediment was very blue, so that the quantity of pigment was relatively large and easily handled. The pus varied considerably in its coloration, many corpuscles appearing to be entirely uncolored. Others were deeply colored. Many of the latter were disintegrated into granular debris. The pigment was undoubtedly methylene blue, as shown very distinctly by its response to reducing and oxidizing agents. It was easy to convert the color to the leuco-methylene blue condition and this in turn to methylene blue. I gave no attention to solubility tests, but aimed directly at the main point. No doubt combinations of the pigment in the pus interfere with the usual solubility tests, but by treatment with acids any such combinations were broken and the tinctorial effects above referred to obtained."

Here, then we have a patient who discharges methylene blue stained pus, eight to nine months after administration of the drug. That there is no question of fraud is self-evident, as the pus alone is stained while the supernatant fluid is unstained. Moreover, the blue stained pus is limited almost completely to one specimen. Both these facts preclude deceit on the part of the patient. Where did this blue stained pus come from?

It is evident that the bladder, as well as the kidney pelvis, could be excluded from our reckonings. The bladder had been irrigated countless times and inspected several times—the pelvis also had been irrigated. The assumption was forced on the patient's physician, Dr.

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Sternberger, and myself, that the pus must come from small abscesses in the kidney parenchyma. The small amount of blue stained pus pointed to a small pus focus. In other words, the diagnosis of chronic pyelitis was inaccurate. The patient was suffering from pyelonephritis. The methylene blue administered during the acute attack had apparently been stored in the developing parenchymatous abscesses. One of these had ruptured into the pelvis and blue stained pus appeared in the urine. This explanation also fitted in with the observation that there was frequently marked variation between the amounts of pus in consecutive specimens without signs of ureteral obstruction.

Subsequent History.—These deductions naturally compelled us to stop lavage of the pelvis and to direct our efforts to the patient's general condition, hoping in this way to obtain a beneficial effect on the diseased kidney. The general health improved markedly, and frequently for several days or even weeks the pus content of the urine was almost negligible.

On the following dates in 1905, to our knowledge, methylene blue stained pus reappeared in the urine, almost all the specimens being examined for the first two or three months, and thereafter only those voided during three to four days of each month.

Pus stained with methylene blue appeared in specimens voided on January 28, 1 specimen; January 31, 2 specimens; February 17, 1 specimen; March 3, 1 specimen; March 17, 1 specimen; July 8, 3 specimens; October 13, 1 specimen.

Second Cystoscopic Examination.—On Jan. 1, 1906, I again made a cystoscopic examination and found that the left half of the bladder near the trigonum was slightly congested and the mucosa thrown into folds. The right half of the trigonum and right ureter were perfectly normal. The left ureteral orifice was irregular in shape, open and rigid. There was no ulceration. Both sides discharged regularly. The urine now contained much less pus, no casts nor albumin, specific gravity 1.010. Total amount for twenty-four hours was about 100 ounces.

In 1906, specimens with blue stained pus appeared repeatedly. I have notes of such reappearance on several occasions. The last reappearance was on Dec. 15, 1906. Throughout this time the patient's general health had improved and she had gained some 20 pounds. She was able to do everything she wanted. The only restrictions placed on her related to diet. The urine toward the end of 1906 still contained small amounts of pus and was almost free from albumin and of low specific gravity, because of the large amounts voided.

On March 19, 1907, the patient was again carefully examined. Cystoscopy showed an almost normal bladder. The ureteral orifices were normal. About the left there was the slightest congestion. Ureteral catheterization was readily done. Dr. Sondern made the following report on the specimens obtained:

The left kidney apparently secreted more rapidly than the right. The urine was less concentrated than the right. There was blood in both specimens and a trace of albumin. There was a small amount of pus in the specimen from the left kidney. Bacteriologically, this specimen was sterile in various media up to ninety-six hours. The phloridzin test was negative on both sides in the first thirty minutes after injection.

In this abstract I have left out all details that do not bear directly on the point in question—i. e., the diagnosis of involvement of the parenchyma in pyelitis cases. In this patient we have seen a recurrent discharge of methylene blue stained pus at various periods after the administration of this drug. There was no regularity in the discharge, as far as time was concerned. The first specimen thus stained that was noted was passed eight to nine months after the primary excretion of methylene blue stained urine had ceased. Again and again other specimens were discharged, stained with the same pigment. The last time such excretion was

noted was 2¾ years after administration of the coloring matter. This phenomenon is in itself worthy of careful consideration, as it is well known that methylene blue administered by the mouth disappears from the urine in three to six days. After such administration the urine holds the methylene blue almost wholly in solution. On the other hand, in this case the methylene blue is not in solution, it is more or less fixed to the pus cells and it has been, so to speak, shut up in the organism for several months, even years.

CASE 2.—History.—Mr. M., aged 45. Had gonorrhea ten years ago, since which time urine had been turbid. Chancre nine years ago. Operated on twice for hemorrhoids. Complained of turbidity of urine, loss of appetite and weight. Had never had pain, no marked increase in frequency of micturition.

Examination.—The general physical examination was negative. There was no tumefaction or tenderness in the kidney regions. The urine contained a large amount of pus. Specific gravity 1.024; alkalin reaction; moderate amount of albumin; no casts; no gonococci nor tubercle bacilli.

Jan. 5, 1907: Five grains of methylthionin hydrochlorid (methylene blue) given. In twenty-four hours the coloration of the urine disappeared. On January 7, cystoscopy showed marked thickening of the mucosa, which was thrown into folds. Swelling of the trigone. Two small hemorrhages close to the right ureteral orifice. Left ureter normal.

Diagnosis.—Chronic cystitis.

Therapy.—Bladder irrigations every day; hexamethylenamin (urotropin), etc.

Jan. 18, 1907: Urine had not improved despite local therapy. On this date, 12 days after methylene blue had disappeared from the urine, it reappeared in one specimen, which contained a deposit of blue pus. On the strength of this, the diagnosis was changed, and I thought that the patient had in all probability suppurative pyelonephritis. I was not absolutely satisfied, as yet, that the condition was more than a chronic pyelitis, though the diagnosis of pyelonephritis was naturally uppermost in my mind, and to rule out chronic pyelitis, the following measures were adopted on Jan. 27, 1907:

Cystoscopy and Bilateral Ureteral Catheterization.—The bladder was somewhat more injected. The hemorrhages about the right ureter had disappeared. The catheterized specimens were as follows:

	Right Kidney.	Left Kidney.
Amount secreted in 5 minutes.....	3 drachms	1 drachm.
Phloridzin test (gr. 1/10).....	Positive in 24 mins.	*Positive in 18 minutes.
Urine.....	Cloudy.	Clear.
Reaction.....	Acid	Negative.
Specific gravity.....	1.026	1.018.
Blood present.....	Positive	Negative.
Albumin.....	Moderate amount.	Negative.
Urea.....	2½ grs. to the oz.	.6 grs. to the oz.
Microscopically.....	Numerous pus cells.	Negative. No casts.
Bacteriologically.....	<i>Bacillus coli communis.</i>	

This examination showed that the trouble was on the right side. Meanwhile the patient's condition remained unchanged. There was no rise in temperature, no pain, and a fresh test with methylene blue was begun. On February 5 I gave the patient for four consecutive days 3 grs. of this drug three times daily, and by February 11 all traces of the methylene blue had disappeared. As the diagnosis still might rest between chronic pyelitis and chronic pyelonephritis, I washed out the pelvis of his right kidney three times in one week without any effect on the pyuria and without recovering any methylene blue. At last lavage I collected a specimen from the left kidney, and in this casts and albumin were found. On the strength of the negative results of lavage and on the fact that the left kidney was beginning to show signs of a probably toxic influence, I decided to do a nephrotomy.

Nephrotomy.—On Feb. 21, 1907, this operation was performed. The kidney was very large and the seat of the multiple small pus foci. The pelvis was full of pus and contained a large coral-shaped calculus. The size of the organ and its adhesions made the operation a difficult and bloody one. The

*First specimen examined.

subcapsular abscesses were yellow. The pus in the pelvis was similar in color. There was no sign of methylene blue in its blue state. The diagnosis of pyelonephritis was thus verified at operation.

After this operation the patient did very well and the nephrotomy wound gradually closed. On March 17, 1907, there reappeared a methylene blue stained specimen. Since February 11 there had been no sign of this coloring matter. During the following week two other specimens of blue stained pus appeared.

Nephrectomy.—As the wound in the kidney closed the patient ran high temperature, which finally, on April 8, 1907, demanded a nephrectomy. The kidney was completely changed. Instead of a large solid organ with multiple small abscesses, the kidney was converted into a large, soft, fluctuating organ full of pus, a pyonephrosis, with a newly formed conglomerate calculus in the beginning of the ureter. In the remains of the kidney there were none of the old parenchymatous abscesses. In the large quantities of pus that were lost during the operation, no blue discoloration was noted. Unfortunately, all this pus was not collected for chemical examination, as it is more than probable that the methylene blue is deposited in its leuco form, and does not betray its presence by its typical blue color.

If this case be analyzed as to the source of the blue stained pus it at once becomes evident that it could not come from the bladder, as that organ had been very frequently irrigated and also inspected with negative results. From the pelvis it could not come, as this, in addition to being irrigated repeatedly, had also been opened by direct incision and drained. The only possible source that is left us is in the multiple small abscesses in the kidney parenchyma.

Before closing there are several points that I wish to refer to briefly. I do not know whether the methylene blue is excreted in these cases in the blue as well as in the white form. I am inclined to think, but am by no means sure, that it may be excreted in either form, for I have noticed that specimens which I looked at shortly after passage were blue and became bluer and bluer on standing, the white or leuco-methylene blue being gradually converted into the blue form. Another peculiarity occasionally noted was the breaking up of the chemical combination in which the pigment was bound and the progressive staining of the supernatant fluid; this conversion of the fixed and insoluble methylene blue into a soluble substance probably resulted from the action of bacteria, as in specimens bottled with chloroform such changes never occurred.

These remarks will give some insight into the difficulty of recognizing the pigment as it is deposited in the tissues. That we can not rely on its blue color alone for its recognition is evident, for it is more than likely that it is fixed in the pus, etc., in its leuco form. In the kidney that I removed in Case 2, the material was so changed that it was unsuitable for the proper elucidation of this point. Up to date my experimental work along these lines is not ready for publication; still this work indicates, as you will see in the specimen later referred to, that the pigment is deposited in great part, if not wholly, in its leuco form.

The last point that I wish to refer to relates to the time and manner of the deposition of the methylene blue. I feel sure that it is not found in all abscesses of the kidney, as I have had occasion to examine some pus from large abscesses after administration of the drug and failed to recognize the pigment. More than likely the presence of methylene blue in the abscesses is the result of the excretion of the renal epithelial cells. One might suppose that the ascending infection in the collecting

tubules leads to a stenosis behind which the methylene blue is excreted and the developing abscess thus receives its quota of pigment.

As evidence in favor of this view, I would show these specimens taken from a dog, in which I had produced an ascending pyelonephritis. Methylene blue was administered daily for several days following the operation and the kidney was removed about two weeks later. This specimen when fresh showed very little pigmentation, but after treatment with oxidizing agents, even after fixation in alcohol, shows, as you can readily see, multiple grayish-blue pus foci throughout the organ. These areas lose their color if treated with reducing agents and regain the same on subsequent oxidation.

On the other hand, as yet, I have not recognized the pigment in the pus of old thick-walled abscesses. If such old abscesses progress and involve adjacent tubules, I naturally would expect to find methylene blue in goodly amounts in them, provided my explanation of this whole phenomenon is correct.

SUMMARY.

If, then, I should summarize the above clinical and experimental data, I would state:

1. There is no differential diagnostic sign between simple pyelitis and pyelonephritis.
2. Pyuria from the upper urinary tract may be due to either of these conditions.
3. By the use of the above described methylene blue test it would seem that a differential diagnosis may be made.
4. Methylene blue is deposited in the parenchymatous abscesses and may be stored in these for years.
5. A late discharge of methylene blue, bound to the pus, is indicative of the rupture of such parenchymatous abscesses into the pelvis of the kidney, and is consequently diagnostic of pyelonephritis.

MENINGOCOCCUS SEPTICEMIA.

DEMONSTRATION OF THE MENINGOCOCCUS IN THE BLOOD SMEAR.

CHARLES E. SIMON, M.D.

Professor of Clinical Diagnosis at the Baltimore Medical College.
BALTIMORE.

The number of cases of meningococcus infection in which the organism has been found in the blood is as yet rather small, and the one described below, in which it could be demonstrated directly in the blood smear taken from the ear, so far as I have been able to ascertain, is the only one now on record.

Patient.—A man, aged 27, whose family and previous personal history contained nothing of importance. He had been in good health until the night of March 19, when he complained of pain in the head and neck and also in the joints and muscles. He was nauseated, but did not vomit. Within the next days the headache became progressively worse and very severe. There had been no distinct chill, but fever up to 104 F.

Examination.—He was admitted to Dr. Fletcher's service at the St. Agnes Hospital at 11:30 p. m. March 23, in a condition of marked stupor, from which he could be aroused only with difficulty. When I saw him, March 24, about noon, he was profoundly unconscious. There was marked dyspnea; the pulse was just perceptible at the wrist. On both feet, over the flexor surfaces of both forearms and the anterior surfaces of the legs there were numerous ecchymoses. The man's face was mark-

1. I am indebted to Dr. Fletcher for permission to use the clinical notes referring to the patient.