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## THE PSEUDOMALARIAL TYPES OF PYELITIS\*

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The diagnosis of pyelitis (non-calculous and non-tuberculous) appears forty-seven times in the histories of 2,500 private patients examined by me during the past five years, an incidence of approximately 2 per cent. Of these forty-seven patients, twenty-one had been treated for malaria.

In most cases of infection of the pelvis of the kidney, constitutional symptoms arise that may closely simulate malarial fever. About one-half of the cases present local signs on the part of the kidney or bladder, or urinary disturbances manifest themselves in such a way as to direct attention to the existing lesion. In the other 50 per cent. of the cases, however, neither the history of the illness nor a thorough physical examination reveal any clues suggestive of an infection of the genito-urinary tract. As a result, pyelitis may remain unrecognized for long periods of time. Furthermore, the insidious onset without pain or local symptoms, the characteristic intermittent or remittent temperature curve, and chills occurring with peculiar regularity, all suggest malaria very strongly. The rigors in such cases are probably

associated with a temporary blocking of the ureter-drain with inflammatory products, as the urine during the fever may be clear and free from pus, while at the termination of the paroxysm turbid urine loaded with pus is voided. Pyelitis in early childhood is much more common than is usually supposed, and is the cause of many unexplained fevers. One such instance is included in the report of cases below (Case 2).

Instances of pyelitis of the pseudomalarial type can be divided roughly into two groups, acute and chronic. The acute cases may be of very short duration and subside with sudden alacritty (Cases 3 and 4), or may last for weeks while the patient continues to be dosed with quinin. The chronic cases are not so frankly septic, but give rise to lesser symptoms, such as periodic aching in the extremities, chilly feelings, night sweats, etc. In one such case, reported below (Case 6) these symptoms had recurred every summer for fifteen years. The urinary findings in these chronic cases may be almost insignificant, and in women it is absolutely necessary to secure a catheterized specimen for microscopic examination, in order to exclude contaminating cellular elements from the external genitalia. The real difficulty in these chronic cases of pyelitis does not lie in disproving the diagnosis of malaria, as that can be readily accomplished by careful search through a stained blood-smear, but consists in excluding pulmonary tuberculosis, as the clinical history always suggests this latter possibility.

The diagnosis of pyelitis depends on the interpretation of the microscopic cellular elements present in the urinary sediment, correlated with the constitutional symptoms. Urethritis and cystitis, in the absence of local disturbances, can only be excluded by endoscopic or cystoscopic examination. It is not the purpose of this article to discuss the differential diagnosis of pyelitis from other pyogenic infections of the genito-urinary tract, but simply to emphasize the close clinical resemblance of pyelitis to malarial fever. In acute pyelitis the paroxysms may be identical with those of malaria, presenting hot, cold and sweating stages, with fever-free intervals. Chronic pyelitis gives rise to general symptoms that are commonly attributed to chronic malaria, although, as a matter of fact, the malarial parasite is so susceptible to the action of quinin that actual chronic malaria is an extremely rare condition and only arises in individuals who harbor the parasite and remain untreated. A great number of conditions masquerade under the name of chronic malaria, and not the least of these is a chronic low-grade infection of the genito-urinary tract.

The following six cases are reported in brief abstract from my histories of patients suffering from pyelitis.

CASE 1.—*Patient*.—A professional man, aged 53, who had always enjoyed excellent health, with the significant exception of an attack of acute prostatitis one year previously, developed chills and fever in September, 1906, while on a vacation at Hot Springs, Va.

*Clinical History*.—After having two shaking chills at an interval of forty-eight hours, he was told that he had malaria and returned to his home in Richmond. For over three weeks he continued to have hard chills followed by high fever and profuse sweating. The chills occurred every day, although on a few occasions he went two days without a rigor. After the chill his temperature often reached 104 F. Except for the chills, fever and sweats, he was free from symptoms, complained of no pain in any part of the body and had no symptoms on the part of the bladder or kidneys. Quinin was administered in full doses from the beginning of the illness, and at the time this note was made he had been taking 40 grains of quinin daily for a week.

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**Examination.**—On Oct. 3, 1906, I was asked to see this patient. Physical examination was entirely negative. Examination of the blood was as follows: red blood-cells 4,472,000, white blood-cells 12,000, polymorphonuclears 75.2 per cent., small mononuclears 15.6 per cent., large mononuclears and transitionals 7.5 per cent., eosinophils 1.3 per cent., mast cells 0.4 per cent. Stained blood-smear: negative for malaria. Widal reaction: negative. A specimen of freshly voided urine was slightly turbid, acid, specific gravity 1.014, albumin good trace, no sugar, no bile. Microscopically, there were present many pus-cells, an occasional red blood-cell and a moderate number of hyaline and finely granular casts. Diagnosis: Acute pyelitis.

**Treatment.**—It was suggested that the quinin be discontinued at once. The patient was given hexamethylenamin (urotropin) and urged to drink large quantities of water. His recovery was remarkably rapid, and in one week he was out of the house. In the spring of 1908, he was examined for life-insurance and the urine was absolutely clear and his blood-pressure normal.

**CASE 2.—Patient.**—A girl, aged 3½, was brought to me Aug. 10, 1909. She had been subject at irregular intervals to attacks of vomiting, fever and abdominal pain. Three months previously she was thought to have swallowed a safety pin. For two weeks previously she had been running an irregular temperature which had reached 103 F. There had been no periodicity in the temperature curve, and no chills. The appetite was poor and bowels constipated.

**Examination.**—Complete physical examination was negative, and there was no reaction in thirty-six hours from a tuberculin ointment test. The chest and abdomen were x-rayed to determine if the safety pin was within the body. There was no evidence of the pin, and the skiagraph of the lungs showed no areas suggestive of tuberculosis.

**Blood:** Polymorphonuclears 53 per cent., small mononuclears 28 per cent., large mononuclears and transitionals 16 per cent., eosinophils 3 per cent. Negative for malarial parasites.

**Urine:** Amber, clear, white mucoid sediment, acid, albumin a good trace, sugar negative. Microscopically it showed moderate number of epithelial cells, very many pus-cells, an occasional red blood-cell, mucus strands, one hyaline cast was seen, no crystals. Stool: Well digested, no ova or parasites present. Diagnosis: Acute pyelitis.

**Treatment.**—Bland diet, forced water consumption, free catharsis, and hexamethylenamin 2 grains three times a day.

Aug. 27, 1909: A letter from the patient's mother stated that the child has had only one spell of fever since leaving for her home in another city. A specimen of urine, forwarded by express, showed no albumin and only an occasional epithelial and pus-cell under the microscope.

This patient was last heard from in March, 1910, and at that time was said to be in perfect health.

**CASE 3.—Patient.**—A medical student, aged 24, while apparently in the best of health, had a severe shaking chill on the afternoon of July 6, 1907. A second similar rigor occurred the next forenoon.

**Examination.**—That afternoon at 3:00 p. m., when I saw him, his temperature was 103.2 F. A specimen of blood was carefully examined for malaria but no parasites were present.

**Urine:** amber, slightly cloudy, slight white granular sediment, acid, albumin a distinct trace, sugar negative. Microscopically an occasional epithelial cell, a moderate number of pus-cells and about an equal number of blood-cells, no casts.

Diagnosis: Acute pyelitis.

**Treatment.**—He was sent to the hospital and his temperature on admission at 5:00 p. m. was 104 F. He then began to drink large quantities of water, and was given hexamethylenamin and his temperature steadily fell to normal by the following morning and remained so.

He returned for observation Oct. 3, 1907, and said he had had no recurrence of the symptoms, and an examination of the urine showed it to be perfectly normal. When last seen, during the summer of 1911, he said that he continued to remain in the best of health.

**CASE 4.—Patient.**—A business man, aged 60, had a hard, shaking chill during the night of Feb. 11, 1909, and this was

accompanied by diffuse pain in the abdomen. For several months he had had some difficulty in voiding at times and had frequently suffered with some abdominal pain after urination.

**Examination.**—He saw me the following afternoon and his temperature was 100 F. at 4 p. m. Physical examination revealed no abnormality to account for his fever, and his blood-pressure was 135 mm.

**Blood:** Polymorphonuclears 82 per cent., small mononuclears 8 per cent., large mononuclears and transitionals 9 per cent., eosinophils 1 per cent. Negative for malaria.

Urine showed a trace of albumin together with the presence of a moderate number of epithelial and pus-cells, otherwise negative.

Diagnosis: Acute pyelitis.

**Treatment.**—Patient was given hexamethylenamin and advised to consult a genito-urinary specialist, as his symptoms were regarded as an acute exacerbation of a chronic lesion secondary to hypertrophy of the prostate.

The following morning his temperature was 98.8 and he felt well. A letter from him three weeks later said that he had had no recurrence of his symptoms.

**CASE 5.—Patient.**—A traveling salesman, aged 30, formerly a resident of Baltimore, had been treated for malaria every summer since he came to Virginia six years previously. He consulted me Sept. 4, 1907, and had been suffering since the middle of June in exactly the same way that he had been afflicted during the preceding five summers. The chief complaint was that of chilly feelings and night sweats which would occur every second or third day. He had had no shaking chills at any time, no cough, no increased frequency of urination, but had lost 15 pounds in weight in the past three months. Each summer he was told that he had an obstinate malaria, and was given quinin persistently and in large doses.

**Examination.**—Complete physical examination was negative. Temperature at 3 p. m. was 99.3 F.

**Blood:** white blood-cells 11,800, polymorphonuclears 77 per cent., small mononuclears 15 per cent., large mononuclears and transitionals 5 per cent., eosinophils 2 per cent., mast cells 1 per cent. Stained blood: negative for malaria. **Urine:** amber, clear, slight white mucoid sediment, acid, albumin a faint trace, sugar negative. Microscopically many strands of mucus, moderate number of epithelial cells, a few pus-cells, an occasional red blood-cell, no casts, no crystals. The following day a specimen of fresh urine was obtained after urethral irrigation, and carefully examined for tubercle bacilli with negative results. Diagnosis: Subacute pyelitis.

**Treatment.**—Sept. 14, 1907: Patient had been drinking large quantities of water and had been taking hexamethylenamin in full doses. The chilly feelings and night sweats had entirely left him, and he said he was feeling well.

Sept. 24, 1907: Remained well. Examination of urine showed no albumin, and no pus, blood or casts.

On June 23, 1908, patient had a slight recurrence of the pyelitis and complained of feeling tired and of an occasional chilly sensation. These symptoms entirely cleared up in about a week's time. When he was last seen, in the fall of 1911, he stated that there had been no further recurrence of his former symptoms and that he remained in the best of health.

**CASE 6.—Patient.**—A railroad conductor, aged 56, was seen March 1, 1911, and complained of chilly feelings with aching in the extremities for the past fifteen summers. Gave a history of chills and fever thirty years ago, and had gonorrhea many years ago, otherwise his past history was unimportant. Every summer for the past fifteen years he had suffered with aching, at times over the whole body, but chiefly in the legs. This aching was accompanied by chilly feelings, followed by a burning and a feeling as if he had fever, but he had not taken his temperature. Bowels were always regular. He had had to void with increased frequency and generally had to rise four or five times at night. Occasionally had burning on urination. No loss of weight. He had been treated for the past fifteen years for malaria, had taken a great deal of medicine and had also tried homeopathy, osteopathy and kindred cults.

**Examination.**—Physical examination was negative except for slightly suspicious signs of pulmonary involvement in the

left back. Blood-pressure was 126 mm.; temperature 98; rectal examination negative; prostate not enlarged.

Blood: polymorphonuclears 63 per cent., small mononuclears 24 per cent., large mononuclears and transitionals 11 per cent., eosinophils 2 per cent. Negative for malarial parasites.

Sputum: i.o. blood, negative for acid-fast bacilli.

Urine: amber, clear, white flocculent sediment, acid, specific gravity 1.021, albumin, a trace, sugar negative. Microscopically occasional epithelial cell, many pus-cells, singly and in small clumps, no blood, no casts, calcium oxalate crystals.

Diagnosis: Subacute pyelitis.

Course.—Patient's symptoms did not respond to internal administration of hexamethylenamin, salol, creosote and other urinary antiseptics. The urine continued to show the presence of pus-cells. On three occasions the urinary sediment was stained for tubercle bacilli, but none could be demonstrated. On May 3 a percutaneous tuberculin test was applied and there was no reaction observed in twenty-four and forty-eight hours. The patient was then referred to Dr. L. T. Price, who found on cystoscopic examination an hypertrophy of the median bar of the prostate, with two ounces of residual urine. Local treatment was then instituted by Dr. Price, and when patient was last seen during the latter part of October, 1911, he said that he felt very well and had been free from all symptoms for the first summer in fifteen years.

#### SUMMARY

Forty-seven patients with pyelitis have been seen during the past five years, of whom twenty-one had been treated for malaria. The clinical features of these two affections may be almost identical. The differentiation, however, is not difficult, but the confusion of the two conditions will continue until physicians realize that quinin is a specific in malaria, and that it is useless to continue this remedy if the febrile disturbance persists. Furthermore, quinin, even in moderate doses, is irritating to an infected kidney. The constitutional symptoms of a low-grade chronic infection of the genito-urinary tract simulate pulmonary tuberculosis, but in the absence of cough the condition is often regarded as a chronic malaria. The urinary findings in these cases may appear almost insignificant, but a urine that is apparently clear on gross inspection will show the presence of a few pus-cells, often accompanied by an occasional red blood-cell. Pyelitis is the cause of many unexplained fevers, and this is especially true in the case of young children.

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### THE GERMICIDAL ACTION OF BASIC FUCHSIN \*

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#### GENERAL CONSIDERATIONS

"Fuchsin (rubin) is obtained by the oxidation of a mixture of anilin, ortho- and paratoluidin, by means of arsenious acid or nitrobenzol in the presence of iron chlorid, which acts as the means of carrying over the acid. . . . It is soluble in water, alcohol and amyl alcohol. Rubin is basic dyestuff and serves for the staining of cell-nuclei, fuchsinophil granulations and bacteria."<sup>1</sup>

A convenient classification of the anilin dyes, that of Krieger,<sup>2</sup> places the three salts of fuchsin in the resanilin

group. The members of this group, as given by Krieger, are:

Methyl violet 6 B.  $C_{25}H_{30}N_3Cl$   
Malachite green  $C_{25}H_{26}N_2Cl$   
Rosanilin acetate  $C_{20}H_{20}N_3C_2H_3O_2$   
Rosanilin hydrochlorid  $C_{20}H_{20}N_3Cl$   
Rosanilin sulphate  $(C_{20}H_{20}N_3)_2SO_4$

It is only with the last three members of this group, rosanilin acetate, hydrochlorid and sulphate, that I shall be concerned. These three salts are generally known as the fuchsins. The acetate is the most basic, and the sulphate most acid in reaction, and it is the acetate which is furnished us as basic fuchsin and the hydrochlorid and sulphate as acid, or ordinary fuchsin. This difference of chemical reaction in the salts is of importance, since Krieger<sup>2</sup> has shown that the greater the degree of basicity of the dye, the greater is its germicidal action. My experiments confirm these findings, with the exception that the results, when testing the germicidal action of the acid salts on bacteria, have been uniformly negative.

#### METHODS

There are many technical difficulties in the handling of the problem and many observers have attempted to work out a technic which will not be open to criticism. Ainley Walker and Murry<sup>3</sup> added such dyestuffs as Grubler's methyl violet, fuchsin and methylene-blue, in 0.2 per cent. solution, to culture mediums (principally plain agar-agar), sterilizing the mediums in the ordinary way. They often noted the precipitation of the coloring matters to the bottom of the tubes. They then inoculated the tubes with the bacterium under investigation and their experiments proved that very interesting morphologic and biologic changes occur in bacteria which are grown on culture mediums so prepared. They found that the motility of the *Bacillus typhosus* was lost; that the bacillus was replaced by a thread-like organism, twenty to thirty times as long as the original bacillus. No segmentation was noted, though branching forms were frequently encountered. With the work of Walker and Murry as a basis, many observers accepted it as a proved fact that the bacilli were dead. This I believe to be an error, since the tubes were not under observation for a sufficient length of time. I have noted growth after seven or eight days in tubes, in which no growth had been observed after forty-eight and seventy-two hours. This phenomenon is readily explained by an inhibitory, rather than a germicidal, action of the dye (as proved by Geppert,<sup>4</sup> quoted by Krieger).

Further, I have noted a very great difference in the germicidal action of the dye, when the inoculations were made into warm or cold solutions, cold solutions being for the most part non-germicidal, while warm solutions are uniformly active. Again, I have noted many times that solutions from which all pigment had been precipitated by careless sterilization had completely lost their power to kill bacteria. Because of heat applied during the sterilization of solutions of the dye, chemical changes occur in the dyestuff itself, perhaps new and entirely different chemical compounds are produced, and these are apparently more active than the original dyestuff.

Koch used what is known as the silk-thread method. He placed sterile silk threads in emulsions of bacteria and then allowed them to dry for twenty-four hours. They were then introduced into sterile solutions of various dyes and tested. Krieger dismisses the technic

\* From the Pathological Laboratory of the Cincinnati Hospital.  
1. Rohman: *Biochemie*, Berlin, 1908, p. 482.  
2. Krieger: *Centralbl. f. Bakteriologie*, 1911, lix, No. 4, p. 481.

3. Walker and Murry: *Brit. Med. Jour.*, 1904, ii, 16.  
4. Geppert: *Berl. klin. Wchnschr.*, 1880, No. 36, p. 37.