one hour. Deficient chloride elimination was observed also. Sellards has one case; Baetjer has four (also with deficient chloride elimination) in which he also noted the fluid balance, the elimination of lactose and potassium iodide, and the percentage of rest nitrogen in the blood. Baetjer adds, however, that a high excretion of phthalein may justify a good prognosis in these, as "none of them have yet come to autopsy."⁵ A very comprehensive study in relation to this point was made by Thayer and Snowden,⁶ who recorded the complete results in 54 cases of chronic nephritis right up to the necropsy, and declared that in not a single instance did they fail to find a material diminution of the phthalein. The progressive diminution of the phthalein excretion with the advance of the disease was definite and striking. They observed, however, that cardiac disease with chronic passive congestion often causes a considerable reduction of the phthalein output. This point is important. I have found a reduced phthalein elimination in cases presenting want of oxygen, howsoever induced, or in which the alveolar carbon dioxide tension was low. Kendall,⁷ in a suggestive paper, records experiments which seem to show that oxygen protects the dye, and that it is destroyed by the reducing substances of the body. So far as trench nephritis is concerned, high excretion of the dye has never been encountered in cases which did badly. On the contrary, they all made good recoveries. The elimination of chlorides and sulphates was normal in all such cases examined.

The cases in the second month of the disease showed phthalein elimination varying from 15 to 50 per cent. or over in one hour. Needless to say, the early high percentage cases do well, and some, though by no means all, also lose their albumin quickly. For the others, which form the great majority, the third month is rather critical. It may be best to summarize the matter, and indicate a classification which is the outcome of long-continued observation of the cases.

1. If, within three months from the onset of the disease, the phthalein excretion rises to 40 per cent. or over in one hour, recovery will be good, even should albuminuria continue for another two months or possibly longer. For part of this time casts may also be present.

2. If, at the end of the third month, the phthalein excretion be under 30 per cent. in one hour, notwithstanding a slight degree of albuminuria, or with intermitting albuminuria, recovery will be protracted, and in some of the cases unsatisfactory.

3. If, at the end of four months, the phthalein excretion reaches 40 per cent. or over, ultimate recovery is the rule, even should the albuminuria last for several months longer.

4. If the excretion remains persistently low (15 to 30 per cent.) up to the fourth or fifth month, the prognosis is unfavourable without reference to the presence or degree of albuminuria. Several such cases which reported themselves after eight to nine months still presented a low index of elimination and slight albuminuria. As to the final issue, it is difficult to say, but the fact that they all had either normal blood pressures, or slightly over, seems to presage in some of these a favourable result.

As regards the distribution of the cases, if we include in Class 1 those showing high elimination in the second month, a total of about 50 per cent. would be represented in this class. The cases in Class 2 proceed either to Class 3 or Class 4, between which the remaining 50 per cent. were fairly evenly distributed, if anything a slightly higher percentage being in Class 3.

A good many cases admitted were relapses after being sent back to active service from other centres. No doubt in these the albuminuria had disappeared at the time, but it is doubtful if the phthalein test (had it been made) would have been satisfactory. Even had it been, one is compelled to doubt if a return to active service is in any case warrantable. It is very probable that in a goodly percentage of the cases some antecedent kidney disability, or a tendency thereto, existed.

The phthalein test also serves as a very good guide to dieting. An excretion under 30 per cent. indicates a milk and vegetable diet; 30 to 35, the addition of fish or chicken; and over 35, ordinary diet with extra milk, provided the albuminuria is moderate and not increased by the diet, and blood is absent. All cases appear to derive benefit from an iron mixture.

Considerations as to the Pathology of the Disease.

What may be termed the clinical impression given by trench nephritis differs materially from that of ordinary parenchymatous nephritis. The subjective feeling of well-being, and the absence of the symptoms of ill health in the

vast majority, are characteristic. The disease may present two very puzzling features. One is the intermittence of the albuminuria which occurs in a few cases, even where the albuminuria is of a high grade. Complete absence of albumin may be recorded one day, and on the next or a few days thereafter perhaps as much as 1 to 1.5 per cent. may be present. Care, of course, must be taken lest an alkaline urine be present which fails to react with heat. The other curious condition is a persistent high degree of haematuria without albumin latterly (except such as is due to the blood). On these conditions speculation is perhaps better avoided. The long persistence of a high grade of albuminuria, with casts in some cases, might seem to create a need for revision of our ideas as to their significance. Again, except in the early stages, the blood pressure is nearly always within normal limits (110 to 135 mm. Hg), and, as we have seen, the kidneys may perform their functions perfectly as soon as the acute stage is over. The disease is doubtless due to an infection. Certain microscopical findings by Dunn and McNee⁸ can hardly be regarded in an etiological sense. I venture to suggest a comparison with acute pneumonia. Just as an entire lung may be involved in the acute stage, so, doubtless, the entire kidney is at first inflamed. When resolution occurs, a district or districts of kidney fail, just as may occur in a section of lung, which continues in the state of delayed resolution—that is, an epithelial overgrowth and desquamation. Such a lung may, of course, be perfectly competent to carry on normal respiration even under average conditions of exercise, and recovery of the damaged area may ultimately be complete. This view of the kidney lesion explains the presence of albumin and tube casts alongside a normal functioning power and a normal blood pressure. As regards the abundant secretion of urine, this would seem to depend on vaso-dilatation of the renal vessels, due to metabolic products.

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THE OCCURRENCE OF SPIROCHAETES IN THE URINE.

BY

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A WIDESPREAD interest in the increasingly numerous group of diseases known to be caused by spirochaetes, and the consequent desire for a rapid and sure means of diagnosis, have brought forward the possibility of recognizing such cases by finding the spirochaetes in the urine.

I.—INTRODUCTORY.

That spirochaetes may actually be excreted by the kidney in diseases of spirochaetal origin is a fact resting on the reliable experimental evidence of the workers on spirochaetosis icterohaemorrhagica. Their animal experiments have demonstrated that spirochaetes occur in the urine which have the same pathogenic effect on guinea-pigs as the organisms found in the blood. Obviously a similar excretion may occur in other diseases, and thus afford an easy means of diagnosis.

Certain observations made recently at this hospital, however, show a source of error in a procedure of this kind. It was found, in brief, that:

1. Spirochaetes are not uncommon organisms in the urethra of men without history or symptoms of relapsing fever.

2. Many different varieties are found.

3. Some of the varieties seen are morphologically closely similar to pathogenic varieties.

4. The spirochaetes occur so definitely within the urethra that they are an obvious source of contamination in uncatheterized specimens of urine.

5. They are a sufficiently dangerous source of error, even in catheterized specimens, to deserve attention in careful work.

6. It is possible that a staining reaction or some other morphological character may be discovered to differentiate microscopically the common and harmless from the patho-

genic spirochaetes. Since the pathogenic spirochaetes are still in the process of discovery, such methods are not universally applicable.

The facts summarized above are possibly known to a few workers, but they are not to be found in the publications at our disposal. They are new to us, and probably to a majority of those who are likely to make use of them. That a source of error in diagnosis may be pointed out, and possibly time saved for prospective workers in these diseases, the observations made are given herewith.

II.—FREQUENCY.

The work was initiated by the finding of spirochaetes in centrifugized specimens of the urine of a nephritic patient with relapsing fever. The urine was divided into two portions, and the sediment of the first portion passed found to contain ten to twenty times as many spirochaetes as the later portion passed. The obvious intraurethral or periurethral source was investigated by films made with a platinum loop, and spirochaetes of the same variety found in great numbers. It seemed probable that such spirochaetes were a common saprophytic organism rather than a localized evidence of a general spirochaetosis. Consequently other patients with and without relapsing fever were investigated similarly. Spirochaetes were found in the urine and in urethral smears from five out of fourteen men. In only one case were spirochaetes found locally, but not in the urine. That the spirochaetes do not have their ultimate origin in the urine seemed probable because by passing the urine in successive portions a part toward the last could be obtained in which no spirochaetes could be found. Such methods cannot be depended upon, however, to eliminate the intraurethral parasites.

When it was evident that spirochaetes of intraurethral origin could frequently be found in the urine, a study was made of 100 men without history or symptoms of any fever of a relapsing type. Fifty of these, given below in Series I, were hospital patients with miscellaneous medical and surgical conditions; many of them were gassed cases. They were selected entirely haphazard. The other fifty, called Series II, consisted of U.S.A. men who came to France from America in early June or the latter part of July.

In each case films were made with a platinum loop from the distal one-third inch of the urethra and from the region about the urethral orifice. In making the urethral smears as a rule the meatus was parted and the loop introduced with as little contact with the orifice as possible. In several cases the anatomical conditions were such that contamination from extraurethral sources undoubtedly occurred, and in other cases faults in technique may have been present. Consequently no rigid separation of sources is possible. The occurrence in several cases of spirochaetes in the urethral but not in the other smears is evidence of their intraurethral origin, in these particular instances at least. In any case they are an evident danger in urine sediment examinations. Notes were made of the presence or absence of spirochaetes, of the morphology, and of the approximate numbers.

In the following summary of the figures, each series is considered separately, then the 100 men as a whole. The percentage occurrence in urethral films is given first, for the urethra is the most definite source of contamination. In a certain additional number of cases spirochaetes were found near but not in the urethra. It is evident that these also might get into the urethra or prove a contamination in other ways. Figures are therefore given for the total incidence of spirochaetes either in or near the urethra.

The spirochaetes similar in type to those found in the urine of patients with "trench fever" or to Noguchi's description of *Spirochaeta icterohaemorrhagiae* are grouped with other spirochaetes obviously not similar to *S. refringens*. Figures are then given for all spirochaetes, including *S. refringens*. The latter figure is not as significant, for the *refringens* type is so different from the others as to cause little confusion.

In all figures, cases where only a few doubtful organisms were found are excluded.

Series I.—In this first series, consisting of 50 hospital patients, spirochaetes (excluding the *refringens* type) were found in 46 per cent. of the urethral films. If *S. refringens* is included, the total incidence of all kinds of spirochaetes amounts to 56 per cent.

Series II.—In the second series, of fifty well U.S.A. men, intraurethral spirochaetes (excluding *S. refringens*) occurred in 20 per cent. of the cases. The total incidence of all spirochaetes, including *S. refringens*, was 22 per cent.

It is our belief that the smaller percentage in the U.S.A. men is due to the better health and hygiene of the subjects. It is very probable that saprophytic organisms increase on these as on other mucous surfaces in conditions of low vigour (or hygiene). That this is the explanation here is suggested by the correspondingly smaller percentage of occurrence of the *refringens* types.

Since these differences are probably not of great significance, it is of interest to average the figures of the two series to get the incidence in the whole series of 100 men. When this is done it is found that spirochaetes of all types but *S. refringens* occur in 33 per cent. of the cases. Including *S. refringens*, spirochaetes are found in 44 per cent. If the figures for the spirochaetes present near but not in the urethra are added, the percentage of spirochaetes in either one or the other situation becomes 38 per cent. If *S. refringens* is included, the incidence is 46 per cent.

In a large proportion of cases the spirochaetes were present in the film in considerable numbers.

The comparative figures give no conclusive proof as to the real source of the spirochaetes—that is, whether in or near the urethra. They occurred, however, more frequently in the urethra by 50 per cent.

III.—MORPHOLOGY.

In regard to the morphology of the spirochaetes, studies were made principally with the tannic acid carbol-fuchsin method, but the Fontana, the India-ink, Giemsa, and the Leishman and Wright modifications of the Romanowsky methods were tested. As a rule, the stain with carbol-fuchsin was definite, but some slender spirochaetes were found which stained with difficulty. The Fontana stain was usually definite and clear. Loeffler's methylene-blue stained not at all, or very faintly. Carbol-fuchsin, without previous mordant, heated as for tubercle bacillus (but not decolorized), stained moderately well, but less satisfactorily than the mordanted stain. Flagella were not made out, although there was frequently extremely fine tapering of the extremities.

No noticeable difference could be made out between the spirochaetes found in the urine of patients with trench fever and those found in the urethral smears of other individuals.

The smears from the periurethral region were more apt to contain a greater proportion of spirochaetes of the *refringens* type, while slender, closely-coiled spirochaetes were perhaps more apt to be predominant in the urethral smears.

It was soon evident that many different varieties exist. It is not proposed to make an exhaustive study of the different kinds, but merely to point out the limits of variation found, and to describe a few common varieties.

Length.—From $3\frac{1}{2}$ to 22μ . The most common length is $6\frac{1}{2}$ to 9μ , but 11μ is not uncommon.

Spirals.—Closely coiled, rather flat to moderately deep spirals are most common. The organisms may be moderately thick or extremely slender. The length of the spiral is $\frac{1}{2}$ to 1μ . Spirals also occur flatter and longer, averaging $1\frac{1}{2}$ to $3\frac{1}{2}\mu$, but occurring up to 4μ . A frequent type has a spiral of $\frac{3}{4}\mu$ in an organism $7\frac{1}{2}\mu$ long—that is, about 11 turns in $7\frac{1}{2}\mu$. In some cases the spirals were exceedingly close and fine, and almost impossible to count.

Ends.—Often taper, but may be blunt; often end in a hook, such as is described for the spirochaete of infectious jaundice.

Regularity of Spirals.—Very often the spirals are irregular. Flat or close coils may be present in the mid part, while deeper coils may be distinct near the ends. In portions, especially toward the middle, coils may be absent. There may be deep narrow, or deep wide spirals, or flat narrow and flat wide, intermingled in various ways in one organism.

Flexibility.—Almost all the organisms seen were evidently quite flexible, being seen in U or S or other contortions.

Capsule.—In a few, especially some very fine and closely coiled spirochaetes, there is a stain of substance by the carbol-fuchsin method, which lies about the organism in such a way as to simulate a capsule. It seems more probable, however, that it is an artefact.

In one film many different varieties are often present, including frequently organisms similar to the description of *Spirochaeta icterohaemorrhagiae*.

IV.—SUMMARY.

A series of 100 men without history or symptoms of relapsing fever showed intra-urethral spirochaetes in 33 per

cent. of the cases. If spirochaetes of the *refringens* type are included, the incidence rises to 44 per cent.

The spirochaetes occurred in about 1 in 2½ men sick of miscellaneous medical and surgical conditions, and in 1 in 5 of healthy men. This difference is probably to be ascribed to differences in hygiene, and to the variations in amount of flora of mucous surfaces familiar in other regions, in conditions of varying vigour.

The variety of organisms makes it improbable that the mere finding of spirochaetes in the urine can have any diagnostic value in relation to the relapsing fevers until definite morphological or other differences are established between the various normal and pathogenic varieties.

TABLE I.—Incidence of Spirochaetes in 50 Hospital Patients.

	In Urethra.	In Urethra or near Orifice.
	Per cent.	Per cent.
Spirochaetes (excluding <i>S. refringens</i>)...	46	52
Spirochaetes (including <i>S. refringens</i>)...	56	62
Spirochaetes (<i>refringens</i> type only) ...	6	10

TABLE II.—Incidence of Spirochaetes in 50 U.S.A. Men.

	In Urethra.	In Urethra or near Orifice.
	Per cent.	Per cent.
Spirochaetes (excluding <i>S. refringens</i>)...	20	24
Spirochaetes (including <i>S. refringens</i>)...	22	32
Spirochaetes (<i>refringens</i> type only) ...	2	6

TABLE III.—Incidence of Spirochaetes in the Whole Series of 100 Men.

	In Urethra.	In Urethra or near Orifice.
	Per cent.	Per cent.
Spirochaetes (excluding <i>S. refringens</i>)...	33	38
Spirochaetes (including <i>S. refringens</i>)...	44	48
Spirochaetes (<i>refringens</i> type only) ...	11	10

I wish to express my thanks to Lieut.-Colonel R. U. Patterson, M.C., U.S.A., for his aid in enabling me to get a complete series, and to Major R. I. Lee, M.O.R.C., U.S.A., for his suggestions.

SPIROCHAETES OCCURRING IN THE URINE OF CASES OF "PYREXIA OF UNKNOWN ORIGIN."

(Preliminary Note.)

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DURING the past few months I have examined the urine of cases of P.U.O. (pyrexia of unknown origin) for spirochaetes, using a modification of Renaux and Wilmaers's technique.¹ The results are so suggestive that I venture in this preliminary note to call attention to the necessity for a systematic examination of the urine in certain clinical types of P.U.O. which may ultimately turn out to have a common etiological origin.

Since in March, 1917, Garnier and Reilly² suggested that in certain cases of icterohaemorrhagic spirochaetosis the chief incidence of the disease may be upon the kidney, I have examined a number of cases of trench nephritis and found a spirochaete in a fairly large proportion. Further, in what I regard as a definite clinical type of P.U.O. (appendicular, or abdominal—described below), which is probably a mild form of icterohaemorrhagic spirochaetosis, I have found a spirochaete almost constantly present in the urine. Again, in the relapsing type of P.U.O. (trench fever) a spirochaete can frequently be found in the urine during and immediately after the exacerbations of temperature.

Methods.

The method I have been using is as follows:

At first the specimens of urine were obtained in the ordinary way, and brought to the laboratory in clean

bottles; but later precautions were taken to try to avoid contamination of the samples. After drawing back the foreskin, the prepuce and meatus were swabbed with a 1 in 1,000 mercury perchloride solution; the patient then passed urine, and a sample towards the end of the act of micturition was caught in a large sterile test-tube. The urine was centrifuged and at first, after pouring off the supernatant fluid, the deposit was washed with sterile water and recentrifuged. Control experiments showed, however, that the spirochaetes seemed to be of comparatively low specific gravity, requiring, therefore, prolonged centrifuging (ten minutes at least, and the longer the spinning is kept up the greater the number found), and care not to remove the lowest layer of supernatant urine before recentrifuging. So it was easier, once one learnt the morphology of the organism, to pick it out in greater quantity even amongst a certain amount of debris, rather than to hunt for isolated spirochaetes on a comparatively clean slide; and the deposit was not washed.

Dark-ground illumination not being available, the following methods of dealing with the deposit were adopted:

1. Indian Ink.

Some of the deposit was mixed intimately with a drop of "Chin-Chin" liquid pearl ink (Watson) on a clean slide, and a film made by drawing along the slide a small piece of cigarette paper wetted in the drop. The film so made soon dried and could be examined directly with the oil-immersion lens. Spirochaetes, if numerous, showed up readily by this method, but the debris of the urinary deposit sometimes caused confusion and difficulty. This method, however, probably shows the spirochaetes in a more natural condition than when mordants and dyes are used.

I. Spirochaetes of Type 1, abdominal P.U.O.
II. Type 2, relapsing P.U.O.
III. Spirillar form from urethra.

2. Tannic Acid and Carbol-Fuchsin (Renaux and A. Wilmaers).

Films are made of the deposit and fixed for ten minutes in absolute alcohol; then covered with 5 per cent. tannic acid solution and warmed till steaming; then well washed with distilled water, and, without drying, stained with carbol-fuchsin, steaming for half a minute, washed, dried, and examined. This is a very simple and rapid method, but does not give such a clear-cut picture as silver nitrate.

3. Tannic Acid and Silver Nitrate (Fontana).

The films are fixed with repeated washes of fixing fluid (acetic acid 1 c.cm., formalin 20 c.cm., aq. dest. 100 c.cm.), then washed well with distilled water; flooded with mordant (tannic acid 5 grams in 100 c.cm. carbolic acid solution 1 per cent.) and warmed for thirty seconds; then well washed with changes of warm distilled water, flooded with 1 per cent. silver nitrate, and warmed gently for half a minute, washed and mounted in balsam.

Spirochaetes.

The spirochaetes have the following characters:

They are about one to one and a half times the diameter of a red blood corpuscle, and are very thin, the ends tapering.

They show five to eight more or less regular turns, and may be straight, bowed, or lying in a semicircle.

The spirals are not so fine as in *Spirochaeta pallida*, nor so coarse as in the spirochaete of Obermeier.