certain amount of office work after January, 1920, and the improvement in his mentality as the result of having some occupation was obvious. It was noticed, however, that he was very shaky and inclined to be "jumpy," and it was apparent that he was about reaching his limit of toleration of injections. During the whole time of the patient's association with the Institute his observation and treatment were entrusted to Dr. J. H. Harvey Pirie.

The patient left Africa on April 29th, 1921, and arrived in London on May 17th, 1921. He came direct to the Hospital for Tropical Diseases, where he has been off and on to the date when this paper was written (November, 1921).

On admission there was little, if anything, to note: no fever, no enlargement of glands, no splenic enlargement—in fact, no definite signs of the disease. It was resolved then to stop all treatment and watch very carefully the results, the patient in the meantime living an ordinary life, going and coming from the hospital from time to time, just like an ordinary person. Blood examinations were uniformly negative for trypanosomes and malarial parasites, and inoculations into guinea-pigs and rats gave negative results. The only thing that one could say was wrong was that the patient did not feel as strong as he used to, and there was a fine tremor just visible in the hands.

In July, 1921, during one of his spells in hospital, he complained one day of the sight in one eye; he was examined by Colonel R. H. Elliot, who reported that there was a patch of paracentral choroido-retinitis in the right eye, a condition, as far as we know, only twice before reported in human trypanosomiasis (a case of Sir Patrick Manson's, the first case of trypanosomiasis at the London School of Tropical Medicine, in 1902; and one by Morax in 1910 associated with cyclitis¹). This observation is of very great interest, as it records a third case of this condition, though other eye lesions (for example, cyclitis) are not uncommon and have been described by Daniels and others. Whether the condition has existed from the beginning of the infection or came on later in the course of the disease is not clear.

The question now arises, Is the patient cured of his infection? It is difficult to say definitely whether this is so or not. One point against it is that the tremors of the hands seem to be definitely increasing and the general condition, though very good, on the whole does not appear in some ways to be perfect.

During the autumn months the patient was in the country and kept well, with no complaints. He stated on his return that he had had no fever whilst he was away, and had been able to play a hard game of tennis without in any way getting exhausted. He returned to hospital for another examination in November, and we got Dr. Gregg to do a lumbar puncture in order that an investigation of the cerebro-spinal fluid might be made.

The fluid obtained was perfectly clear, with no increase of pressure. Microscopically the cells were normal in number, a few lymphocytes were present, and there were no signs of trypanosomes. The Wassermann reaction of the fluid as well as of the blood was negative.

This would seem to indicate that cure has taken place, but it does not absolutely prove that this is so. All that remains, then, is to observe the case for a longer period of time before definitely coming to the conclusion that he is really free from his infection, and we propose to do this and not to give any more treatment for the present.

As the patient's home is in South Africa he is going to return there, and he will notify the authorities at the Institute for Medical Research at Johannesburg if any further symptoms develop. His future progress can also be controlled there, and it will be of great interest to see what that will ultimately be.

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ACCORDING to the records of thirty-seven leading American insurance companies, the year 1921 was the healthiest in the history of both the United States and Canada. It is stated that during that year influenza almost disappeared from the United States and Canada, and that pneumonia decreased by 50 per cent. as compared with 1920. On the other hand, the mortality due to automobile accidents showed an increase of 15 per cent.; the number of deaths from this cause was in round numbers 10,000. Homicides and suicides also showed large increases, being four times more frequent than in 1920.

THE SIGNIFICANCE AND TREATMENT OF SOME ABNORMALITIES OF THE URINE IN CHILDREN.*

BY

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WHEN we are called upon to give a diagnosis in the case of a child, and to follow this up with prognosis and treatment, we seek for assistance from family and personal history, we study symptoms, and we determine facts. History may be elusive, is often imperfect, and sometimes unreliable; the recognition and valuation of symptoms is largely a matter of experience and opportunity, and, lacking these, perspective is imperfect. But the determination of facts is in the hands of every medical graduate, and one important means of search for facts is thorough examination of the urine. Certainly, in any doubtful or continuing illness general examination is incomplete without chemical and microscopical examination of the urine. In this paper I wish to discuss certain facts in urine examination and certain difficulties in the determination of their significance.

Bacilluria.

The first is a fact determined by microscopic examination of the urine—the finding of pus cells and motile bacilli. What is the significance of the fact? In the cases of healthy children, are motile bacilli and pus cells commonly present in catheter specimens of the urine? We may certainly answer, No.

But points of clinical difficulty arise in attempting to advance a step further. In apparently healthy children we rarely feel called upon to use the catheter for obtaining a specimen of urine for examination. If careful precautions as regards cleanliness, retraction of parts, asepsis, etc., are taken, do we find pus cells and motile bacilli present in the urine of healthy children? The answer here must be guarded, because we do sometimes find, in cases of perfectly healthy children, rare cells resembling pus cells and a scanty number of various micro-organisms, which in many, if not all, cases are probably present because of unavoidable contamination. But we may safely say we never find large numbers of pus cells and immense numbers of motile bacilli. While, however, this is true of perfectly healthy children, it is not true of certain children apparently in fair normal health.

I have at present under observation seven children whose mothers consider them in fair average health, who are, in the ordinary acceptance of the term, well, and whose urine, on regular microscopical examination, is found to be swarming with motile bacilli and to contain a distinct amount of pus. I also have reports of four other children, seen in private during the past year and not within the past three months, and who were carefully, thoroughly, and apparently successfully treated for acute pyelitis, and on recent examination of the urine I find that in one out of the four pus cells and motile bacilli are present in large numbers, although the child is apparently well.

It is quite certain that there must be a considerable number of children—probably mainly girls—who are "well" or "fairly well," or, it may be, "out of sorts," who are going about, with or without medical attention, and in whose urine motile bacilli and pus are present in quantity. What exactly is the condition? Why is it present? By what dangers, if any, is it attended?

The condition is not tuberculous and it is not due to calculus. There may be no urinary symptoms of any kind, but enuresis sometimes occurs. Renal efficiency is good. The urine is acid; it may show perceptible haziness with cold nitric acid, or it may not. When a fresh drop of urine is examined under the high power of the microscope, pus cells are seen in considerable or large numbers, and along with them great numbers of motile bacilli. If a catheter specimen is obtained and a report prepared by a laboratory, these bacilli are determined to be of the "coli" group, or "para-coli" or "meta-coli" or "pseudo-coli" group! In some cases cocci are also present. No casts are present, and usually no blood cells and no crystals. The general nutrition

* A paper read before the Liverpool Medical Institution, October 27th, 1921.

is fair, but the child is not fat. There is no fever. Constipation is, I think, always present, and it is often most intractable. There is often extensive caries of the teeth. The children, as a rule, are not undersized. All my cases have been girls.

We have to deal with a chronic infection of the urinary tract by bacilli of the nature of some form of the colon type. Catheterization of the ureters in young children cannot be carried out, and, consequently, it is not justifiable to define more accurately the locality of infection.

Important points we must bear in mind are these:

In 90 per cent. of cases in which the urine of healthy female infants under 2 years of age is drawn off by catheter under complete aseptic precautions, bacteria are found in it, mainly bacteria of the coli group.² Similar examination in cases at a greater age shows the urine to be sterile.

A temporary bacilluria is not uncommon in critical, acute, and continued illnesses accompanied with marked prostration.

Acute pyelitis occurs twice as often in babies as in older children.

A great deal of importance is laid on the relation between full control of the bladder sphincter in girls and bacilluria. The frequency of urinary infection by *B. coli* in female infants and the frequent occurrence of the symptom of enuresis in older girls in whom this infection can be noted is striking.

There has been much discussion as to the method of infection of the urinary canal. In female infants it may be impossible always to prevent an ascending infection, but obviously digestive disorder and diarrhoea must favour the passage. In older children, likewise, all marked digestive disturbances must favour infection by one means or another.

In many of the cases of the type of which I speak—chronic “colon” urinary infection—no definite history of an attack of acute pyelitis can be obtained. We do not know whether many of the cases have commenced acutely or not. In some probably a chronic course is run throughout with eventual cure. In some, acute pyelitis first attracts attention. In none is the general health really satisfactory, though it is often impossible to tell from consideration of the general health and physical examination whether bacilluria and pyuria are present or not. Microscopic examination of the urine alone shows, and such examination should be made in the case of every ailing child with doubtful or continuing disability.

If the condition is found to be present and the child “well” she may be considered “merely a carrier” or the type of bacillus present “non-pathogenic.” But a child with long-standing continuance of pus and coli-like bacilli in the urine is one in imperfect health, who may at any time develop acute urinary inflammation as a sequel to comparatively trivial affections in practically any part of the body. We know little of the interaction of bacteria, and a chronic “coli” urinary infection can be powerfully influenced by totally different infections elsewhere. Further, it is possible that a reverse train of events may occur in some cases and the urinary infection produce far-reaching secondary effects.

When we turn to treatment we must of necessity divide it into two categories: (a) preventive, (b) therapeutic.

Preventive treatment consists in such dietetic and general hygienic measures as will ensure good digestion, a healthy mouth, normal evacuation of the bowels, and the absence of irritation or excoriation in the region of the perineum. The importance of such treatment from every possible medical point of view is of course self-evident, as it must form the basis of healthy childhood. Its proper carrying out, however, requires attention to many details, none of which should be neglected by the medical man. Its essence is correct diet and no septic foci.

Therapeutic treatment is at present greatly influenced by two conditions—namely, the infrequency with which urine is examined microscopically except in acute cases or cases with marked urinary symptoms; and, secondly, the prominence given in cases of acute pyelitis to treatment by alkalies, urinary antiseptics and vaccines.

The importance of microscopic examination of the urine I have already emphasized.

Acute pyelitis in infants, in the absence of pyelonephritis, can almost always be cured by sufficient dosage of alkali; urotropine and salol are useful in some cases, and autogenous vaccines are sometimes of value in cases of older children and in relation to acute attacks or relapses.

But in the cases of which I speak—the chronic cases with few and indefinite general symptoms—all such methods of treatment are extremely unsatisfactory. The only means of

eradication of the firmly installed bacilli is the restoration to health of the various bodily functions. By all means let us use the above remedies as they may seem indicated in the individual case, but, above all, let us employ scrupulous care in our search for focal sites of infection, for the nature of disturbances of digestion, and for any other abnormalities whatsoever in the child. Let us devote our first attention to the securing of healthy orifices, healthy mouth and healthy intestinal canal, and we have taken the first secure step forward in what, even then, is often a long-drawn-out cure.

Presence of a Reducing Substance.

The second abnormality with which I wish to deal is that of the presence of a reducing substance in the urine.

We are examining the urine of, let us say, a thin, rather poorly developed girl of 6 years, and we find a positive sugar reaction. Is she diabetic? From our undergraduate days probably we have remembered and been influenced by the statements—“sugar is rarely found in the urine in children,” and “diabetes in a young child is almost always rapidly fatal.” For the moment, however, let us wash the slate clean and ask ourselves with an open mind—Is it uncommon when testing the urine of a child for sugar to get a positive reaction? The ordinary clinical tests for sugar in this country I take to be Fehling's solution and Benedict's solution. Both in the method of their use and in the interpretation of results there are many possible fallacies. Fehling's solution I have used according to the second method mentioned by Cammidge; Benedict's solution as described by Benedict.

Having for some time been much impressed by the reactions obtained in many cases, I recently took 100 unpicked cases to determine impartially the results of examination. The urine of 50 consecutive out-patients and of 50 in-patients of a hospital were examined, the ages of the patients ranging between 2 years and 11½ years. Of these 100 urines, 19 gave a positive reaction, in all cases very slight with Fehling's solution, and in most, but not all instances, confirmed with Benedict's. In some of the positive cases (9) I proceeded further to a fermentation test with yeast and got positive reactions in 6. In others (6) I sent the specimen to the laboratory, and got reports in 2 cases that the reducing substance was not glucose and in 4 either that it was glucose or was probably glucose.

Thus in 19 per cent. a positive reaction was obtained with Fehling's solution, and in 10 out of 15 of these specimens, on further examination, evidence was obtained of the presence of sugar. In this particular series of 100 cases, then, evidence of sugar in the urine was certainly present in 10.

These results would show that it is not uncommon to find clinical evidence of the presence in small amount of a reducing substance in the urine of ailing children, and that in many of these cases the reducing substance is some form of sugar. In all of these particular 100 cases the amount present was small and consequently the test reactions slight. How are we to account for the textbook statement that “sugar is rarely found in the urine in children”? There are three possible explanations, and I think the full explanation includes all. They are:

1. Lack of systematic examination of the urine for sugar;
2. Variations in sugar content of the urine in different districts; and,
3. Estimation of test results as negligible or “physiological.”

As regards testing for sugar, this is obviously desirable in all cases. The test with Fehling's solution, as also confirmation with Benedict's, is readily carried out, though attended with various fallacies so far as a positive diagnosis of glycosuria is concerned. The tests should not be hurried, and if found positive even in slight degree, definition of the reducing agent present as a sugar or not a sugar can be conveniently made by reaction with yeast in a ucometer tube. In the series of 100 cases just quoted, sugar was found to be the reducing agent present in two-thirds of the cases showing a positive reaction.

Is it likely that the sugar content of the urine varies in different parts of the country? Sugar, we know, is normally present in the blood and in the urine in amount conditioned by complex processes of metabolism. The liver, the pancreas and the thyroid—to mention only a few of the important organs—are closely associated with its absorption, utilization and excretion. The nervous system is intimately affected.

Varying conditions of climate, diet—of hygiene generally—often affect in a degree so marked as to be obvious the grosser results of differing function of these organs and systems—for example, goitre, asthma. We cannot deny the possibility of a difference according to locality in the degree of frequency of excretion in the urine of a reducing substance in detectable clinical amounts.

This leads to the third consideration: Should such minor test results as those I am discussing be considered negligible and physiological or not? I think they should always be noted, however slight and however fleeting they be, and an explanation sought. It is possible that most, if not all, children from time to time may give detectable sugar reaction on examination of the urine, but even so this forms no foundation for an argument that the detection of such a reaction is of negligible significance.

If once found, examination of numerous specimens should be made—of the twenty-four hours' urine and also of morning and evening specimens. In a large proportion of cases the presence of a positive test corresponds with indiscretion in diet or digestive disturbance, and disappears on correction of such. In other children with indigestion and constipation the reaction is completely negative. This point is in itself important, as possibly affording evidence of individual idiosyncrasy in carbohydrate metabolism.

Another important line of consideration is demonstrated by the findings in the following case.

A girl, aged 6 years, has been under observation in hospital for several months suffering from what I suspected might be progeria. The urine was healthy. She developed a large abscess in the face with considerable sloughing, and the urine showed a distinct positive sugar reaction. The abscess is now healed and the urine free from any reducing agent.

Here was a well-marked case of "sapraemic glycosuria." The precise nature of the reducing substance or substances in the urine during the period of suppuration was not determined, but the fermentation test with yeast was positive and the urine after the abscess healed was free from sugar. I am not now concerned with the nature of "sapraemic glycosuria," but with evidence that slight positive urine reactions should lead to search for a septic focus.

The precise nature of the sugar present in a specimen of urine cannot be determined without expert laboratory assistance; and the examination of blood sugar is, in my experience, valueless except in the hands of a skilled worker in constant practice. The fermentation test with yeast is, however, simple, and in the presence of a positive fermentation test we are faced with the possibility that the reducing agent may be dextrose (glucose or grape sugar), or laevulose (fructose or fruit sugar), or both. (I am not here dealing with nursing infants suffering from gastro-enteritis, in whose urine lactose may be present.)

It has been proved that the presence of laevulose in the urine may be regarded as a sign of liver inadequacy. Laevulose often appears in the urine along with dextrose in marked clinical cases of diabetes. It may, however, appear alone and be derived from cane sugar, honey, vegetables, fruits, etc., in the diet. When it appears it is, as stated above, to be regarded as a sign of liver inadequacy. If, with this in mind, we now turn to the clinical aspect of cases in which we find traces of a sugar present in the urine, we find that in many there is definite evidence of attacks of acidosis; in many there is a history of recurrent attacks of "biliousness"; and in most there is what one may term a full fatty diet. In fact, clinical evidence goes to show that in most there is evidence of strain on liver function, and it seems reasonable to conclude that the small amount of sugar in the urine is probably laevulose. This is further borne out by the satisfactory result of treatment by reduction of fat intake and, if necessary, restriction in amount of other elements in the diet.

But in a considerable proportion of the cases in which only a small amount of sugar is present in the urine, and in the great majority of cases in which the sugar is present in large amount, the sugar is dextrose—that is, the patient has glycosuria. What is the significance of this fact? It is outside the scope of this paper to consider cases either of intermittent or of persistent glycosuria in which large quantities of sugar can be demonstrated in the urine. In all such cases we obtain expert laboratory assistance, determine the level of the blood sugar and the nature of its reaction to a dose of sugar, and also the leak-point for sugar. But whatever methods of research we employ, and however favourable the

results we obtain, our treatment must be that of diabetes mellitus.

It is with cases which show minor results on urinary examination that I wish to deal. In the majority of them there is no marked polyuria, and there may be no excessive thirst or wasting.

The presence of glucose in the urine is, we know, the chief sign of the existence of diabetes mellitus, but we also know that a small detectable amount of glucose in the urine may exist in the presence of sound health. Glycosuria is a term the interpretation of which in any individual case lies somewhere in a scale extending from sound health at the one extremity to diabetes mellitus at the other.

Cambridge, speaking of transitory, intermittent, and persistent glycosuria and diabetes, says: "It is important that it should be clearly recognized that each is but a phase of the same metabolic error, and that no hard-and-fast line can be drawn between them." He further speaks of a "preglycosuric stage." The obvious truth would seem to be: watch for the earliest beginning of abnormality and attempt to check it, as otherwise it may develop into uncontrollable disease.

The markedly outstanding lines along which to attempt to check development are dietetic—a well-balanced diet with the avoidance of constipation and intestinal putrefaction—and aseptic, the removal of all discoverable foci of infection.

My subject deals with small things and is mainly concerned with the beginnings of disease. For fuller development it requires blasts of clinical ozone to play around the figurative laboratory frog.

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BLOOD PRESSURE OBSERVATIONS IN FUNCTIONAL BRUITS IN CHILDREN AND YOUNG ADULTS.*

BY

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DURING convalescence from various mild infections children often go through a period in which they exhibit a sustained rise in blood pressure, the development of a systolic apical bruit presenting the usual functional signs, and accompanied by some cardiac dilatation. This phase of raised blood pressure is sometimes present during convalescence even from acute rheumatism, and its possibility must always be borne in mind when judging of the nature of a systolic cardiac bruit in children after pyrexia.

The child is far more unstable in its circulatory equilibrium than an adult, and the heart muscle just recovering from the damage of pyrexia is in no case able to sustain the increased work that a slight hyperpiesis involves. A rise of 10 or 20 mm. Hg, which is often to be observed, makes a far deeper impression than in an adult and can be the cause of the cardiac condition. My contention is proved by the fact that as soon as the blood pressure falls the cardiac sounds become normal, in the absence of an organic endocarditis.

The normal blood pressure in childhood has been very little studied in this country. I find a record of 3,000 repeated observations by Judson and Nicholson¹ in America. The standard of systolic pressure they lay down is as follows:

From 3 to 6 years	...	...	...	90-92 mm. Hg
" 7 to 9 "	...	...	...	up to 94 "
" 10 to 11 "	...	...	...	" 99 "
" 12 to 13 "	...	...	...	" 103 "
" 14 to 15 "	...	...	...	" 106 "

I have found that children are very susceptible to the action of the nitrites, and I have employed them in the following combination for reducing blood pressure in my cases: Sodium nitrite, liquor trinitrini, and spt. aetheris nitrosi in suitable dosage. In adults these are of no use. Appended are some notes of typical cases.

W. E., female, aged 9, had a mild faucial attack of diphtheria in February, 1916. Increasing tachycardia was observed as convalescence advanced, and she was kept in bed; ten days later, in spite of cardiac tonics, the heart had dilated beyond the nipple line, and a systolic bruit, not conducted, and heard in all postures,

* Being abstracts from a paper read before the Bradford Medico-Chirurgical Society, February, 1921.