

The Clinical Significance of Indoxyl in the Urine.⁽¹⁾ By
LEWIS C. BRUCE, M.D., District Asylum, Murthly.

THE clinical study of the physical symptoms of mental diseases has of late years been pushed with energy and originality, not only in this country but also abroad. Advances in the general knowledge of physiological and pathological chemistry and the great doctrine of immunity have had their effect upon the views held regarding mental diseases, and particularly with regard to their causation.

The history of past advances in the science of medicine repeats itself at the present day. Advances in knowledge produce new theories and scepticism on the part of the younger members of the profession as to the correctness of the views held regarding the causes of disease, views which the present holders relinquish with reluctance as they are equally the result of past advances in knowledge.

Such is the present position of the science of psychiatry. There is the younger school who say that the majority of mental diseases are secondary to bodily disorders, and there is the older school who assert with equal confidence that the majority of mental diseases are primary disorders of the brain cortex. Certain bodily disorders are, however, regarded by both parties as certainly present in many cases of mental disease, the point in dispute being, Are they cause or effect? By far the most frequent disorder so recognised is that collection of physical symptoms known at the present day as "auto-intoxication," by which is indicated toxins formed within the body as the result of disordered metabolism.

In opening this discussion to-day I will confine myself to remarks upon one of the known autotoxins, "indoxyl," which is formed in the intestinal tract as the result of putrefaction of the albumens of the food, and is excreted largely by the kidneys.

I take for granted that there is no question as to the existence of this substance indoxyl or to the fact that it is a toxic substance.

Indoxyl as it is excreted by the urine is really indican, or indoxyl-sulphuric acid.

When the albumens of the food decompose in the intestines

the first substance to be formed is indol. After absorption indol is oxidised to indoxyl, and then on excretion combines with the sulphuric acid of the urine and is therefore excreted as indoxyl-sulphuric acid.

To detect indican in the urine it is necessary first to break down the sulphuric acid compound by the addition of strong mineral acids and then to convert the indoxyl into indigo by oxidation.

One-third of a test-tube of urine is treated with an equal quantity of strong hydrochloric acid, 1–2 c.c. of chloroform, and a drop of a one half saturated solution of calcium chloride. The test-tube is corked and repeatedly inverted, when the chloroform takes up the indigo and falls to the bottom of the test-tube. Instead of calcium chloride solution very small quantities of calcium hypochlorite may be used instead. Great care has to be taken on adding the oxidising agent that too large a quantity is not used, as an excess of the oxidising agent discharges the colour. Instead of calcium chloride solution or bleaching powder, a 2 *per cent.* solution of potassium permanganate may be employed as the oxidising agent. I have never got satisfactory results when using potassium permanganate.

When indoxyl is present in excess in the urine, the chloroform becomes dark blue, or even black ; when it is absent the chloroform is colourless. Between these two conditions there exists every shade of colour. Judging from the results of testing the urines of persons in health, I am of the opinion that any shade of blue over medium or cobalt colour is a pathological excess.

The questions before us to-day are :

(1) Is an excess of indoxyl in the urine invariably associated with one mental symptom or one form of disease ?

(2) If so, is indoxyl the causative factor of that mental symptom or form of disease, or is it merely an accidental factor or effect of the disease ?

Townsend, in the *Journal of Mental Science* for January, 1905, published the result of work done on this subject, and his conclusions were :

(1) That in depressed states indoxyl is excreted in excess.

(2) That patients excreting indoxyl in excess exhibit symptoms and signs of toxæmia.

(3) That in states of mental elation there is seldom any increase, the amount excreted being normal or less than normal.

(4) That in some states of mental alteration indoxyl is excreted in excess during both the melancholic and maniacal phases.

(5) That the more severe the mental attack the greater the excess of indoxyl.

(6) The greater the excess of indoxyl the more marked are the symptoms and signs of toxæmia.

(7) That mental recovery was in the cases recorded preceded by the reduction to normal of the amount of indoxyl excreted.

For the past twelve months I have made observations upon the urines of patients admitted to the Perth District Asylum regarding the presence or absence of indoxyl in the urine. The results are as follows :

Out of five cases of acute melancholia, by which I mean the disease characterised by apprehension and depression, and which in every one of my cases had an acute onset, during which the patient was confused, as well as depressed and apprehensive, I only found excess of indoxyl in one. The four cases which showed no indoxyl or only a trace had, however, upon admission had the large intestine emptied by enemata. The fifth case suffered from symptoms of acute toxæmia, and she was so confused and difficult to manage that the nurse was unable to administer an enema. The nurse, however, reported that the patient's bowels moved regularly. This state of affairs went on for three days, and on each of these days the urine gave almost a black reaction when tested for indoxyl. I therefore ordered a large enema, the result of which proved that the intestine was loaded. The day following the enema scarcely a trace of indoxyl was to be detected in the urine, and at the same time the patient passed into almost complete sanity. This patient was admitted one day after the commencement of the acute mental symptoms, while the other four had been ill for a considerable time before being treated.

One case of excited melancholia had only a trace of indoxyl in the urine. In four cases of acute mania, by which I mean the condition of excitement with confusion as distinct from the excitement of the folie circulaire type, there was rarely even a trace of indoxyl in the urine.

In two cases of excitement of the folie circulaire type one showed a trace of indoxyl while the other had an excess which

was immediately removed by the use of large enemata. There was no mental improvement.

In three cases of depression of the folie circulaire type indoxyl was present in slight excess but was removed by the use of enemata combined with a purely milk diet. All these patients improved as the result of treatment.

In three cases of hebephrenia indoxyl appeared in the urine of one coincidentally with the onset of an attack of depression, with symptoms of toxæmia. The indoxyl disappeared the day following the administration of a large enemata and the depression passed off.

In three cases of katatonia, all in the stage of stupor, only one showed an excess of indoxyl which was associated with constipation.

In three cases of delusional insanity, in the early depressed stage, all had an excess of indoxyl which disappeared under treatment and the mental symptoms were alleviated.

In three cases of general paralysis there was no indoxyl in the urine. One of these patients was distinctly depressed.

Out of these 27 patients, 13 presented the mental symptom of depression, of whom 5 had a marked excess of indoxyl and 3 had a slight excess.

All of these cases were benefited by treatment which reduced the indoxyl, but in only one was there absolute and sudden improvement.

Out of the remaining 14 patients who were not depressed, only 2 had an excess of indoxyl in the urine, one being a case of *folie circulaire* in the elevated stage of the disease, and the other a case of katatonia in the stage of stupor. That is to say, out of 13 patients who presented the mental symptom of depression, 8, or 61·5 *per cent.*, had an excess of indoxyl in the urine, while out of the remaining 14 patients who were not depressed only 2, or 14·2 *per cent.*, had an excess of indoxyl in the urine.

As the result of these observations I conclude—

(1) That there is some connection between this symptom of the presence of excess of indoxyl in the urine and the mental symptom of depression.

(2) That, to judge by the result of treatment in one of the cases, the indoxyl may have been the chief causative factor in the mental disease.

(3) The evidence is in favour of the indoxyl being the cause

of the depression rather than the depression being the cause of the presence of the indoxyl.

(4) The fact that four typical cases of melancholia had no indoxyl in the urine appears to be evidence that we cannot regard all cases of melancholia as suffering from indoxyl poisoning. We must remember, however, that many toxins may, by linking themselves chemically to the nerve-cells or otherwise altering their functional activity, produce long-continued mental effect after the presence of the toxin can no longer be demonstrated in the excretions of the body. I believe that this is the explanation of our failure to improve the condition of patients who are not placed under treatment sufficiently early.

(5) That the presence of an excess of indoxyl in the urine means a loaded alimentary tract, which should at once be treated by the use of large enemata—two to three pints of normal saline solution by preference—and the placing of the patient on a purely milk dietary or a milk and farinaceous dietary.

The whole alimentary tract can be rendered free from putrefactive processes by seeing that the mouth is kept clean—by the removal of carious teeth and by the use of antiseptic mouth-washes—by placing the patient on small but frequent quantities of milk diluted with aerated water and washing out the large intestine with enemata. The benefit of this treatment is most obvious, especially in patients who show symptoms of alimentary disturbance and toxæmia, and under such treatment indoxyl practically disappears from the urine.

(¹) Read at the Scottish Divisional Meeting held at Glasgow March 23rd, 1906.

Industry and Alcoholism. By W. C. SULLIVAN, M.D.

AS a preface to the remarks which I propose to submit for your consideration to-day, I wish to recall to your memory the substance of a paper which I had the honour to read before this Association some two years ago(¹). In that paper I endeavoured to establish a distinction between two opposed types of drinking, which, having regard to the chief factor in each form, I referred to as convivial drinking and industrial drinking; and I pointed out that these two modes of drinking differed widely in their relations to drunkenness and to chronic alcoholism, convivial excess producing drunkenness but rarely tending to cause