TWO FATAL CASES OF AN UNUSUAL FORM OF NERVE DISTURBANCE, ASSOCIATED WITH DARK-RED URINE, PROBABLY DUE TO DEFECTIVE TISSUE OXIDATION.

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By bringing the following cases before the profession, I desire to draw attention to a certain morbid nerve condition which, from being somewhat rare, has up to the present time been very imperfectly studied, and in consequence its nature is still obscure. And I do so all the more readily seeing that every item, however small, is of value in helping to unravel the mystery of a disease which, from not presenting any definite physical signs, might by some be called a mere functional derangement, notwithstanding its leading to a rapidly fatal result.

The abnormal condition about to be illustrated by the narration of two cases is characterised by grave nervous symptoms—in-somnia (total or partial), diminution of the reflexes, with marked muscular prostration, followed by coma, rapidly ending in death; these symptoms being associated with ichuria, and the urine containing abnormal colouring substances related to the chromogen group.

The first case is one I had the opportunity of seeing while in Edinburgh, and for its history I am indebted to the kindness of Dr. John Wyllie, under whose care it was.

Mrs. T., aged 27, admitted into the Royal Infirmary April 4th, 1890. Complained of sleeplessness and pains all over the body. Her previous health appeared to have been good, until five weeks before her admission, when she married, and a week afterwards became nervous and sleepless, without any assignable cause. The sleeplessness and nervousness rapidly increased, and at the same time she began to be troubled with a painful feeling of weight over her thorax and abdomen. Dr. Matheson, who was first called to see her, tried hypnotics (sulphonal and chloral), but without benefit. She soon became very listless, and began at times to talk in a wandering manner.

On admission she was somewhat emaciated and pale, with a vacant expression. She complained of a want of power in her limbs, and on the first night could not move them at all. On the following day she was able to move them slightly, but with great lack of energy. Her muscles, though somewhat flabby, were not atrophied, and there were no signs of paralysis beyond the weakness just referred to. Besides complaining of a sense of weight on her chest and abdomen, she said she felt at times a sensation of pressure on her head. Her sight was normal, but she said that at one time during this illness she had been blind for three days. Although she seemed perfectly conscious of what was said to her, she replied sluggishly, and wandered at times.

On careful physical examination nothing was found abnormal in either chest or abdomen. Pulse 114, weak and soft. She had no appetite, but considerable thirst. Her bowels were constipated. In spite of hypnotics, quiet, and darkness, sleep was practically in abeyance. She remained in much the same condition, only getting more and more exhausted, from the want of sleep, till the third day after admission, when she somewhat suddenly died in a state of collapse. She only lost consciousness for about ten minutes before death. No necropsy was allowed. During her stay in the hospital her urine was of a port wine colour; the quantity being from 8 to 12 ounces *per diem*. Specific gravity, 1028 to 1032. It contained no albumen, sugar, or bile, and no blood could be detected in it either chemically, microscopically or spectroscopically. It had a slight deposit of triple phosphates.

For the notes and analysis of the urine in the next case I am indebted to Professor Sophus Torup (Christiania) in whose physiological laboratory I am at present working.

E. O., married, aged 54, was admitted into Diakonisse Hospital, Christiania, under the care of Dr. Unger Vetlesen, June 3rd, 1890. The patient being unable to give her own history, the following particulars were obtained from her sister. Her father, who was an inebriate, and insane, died from cancer, her mother from cerebral apoplexy.

The patient, who was somewhat weak minded, had always suffered more or less from sleeplessness, for which she had been in the habit of taking chloral and sulphonal. Four years previous

to her admission, she had been confined to bed for two months, the cause of this being, according to her sister, an over-indulgence in hypnotics.

At the end of March she became weak, and on one occasion fell down in a state of syncope, during which she was unconscious. She, however, quickly recovered. From this time she gradually became weaker and weaker, and at length remained entirely in bed, conscious, but without speaking, and for the most part sleepless. She complained of pain throughout the whole body, and took very little nourishment. There was neither sickness nor paralysis at any time observable. She was sent to the hospital as a "neurasthenic."

On June 6th she was found to be anæmic, but not emaciated. She lay in bed with a vacant expression, and on being spoken to, although quite conscious, replied slowly and almost unintelligibly. She complained of feeling cold, although she was well covered with bed clothes, and bathed in perspiration. Her limbs lay limp in bed, as if they were paralysed; but it was not so, as she was able to move them, and had, even on the previous day, quitted her bed of her own accord. Her pupils were (equally) dilated, and contracted to light, though somewhat slowly. Her reflexes were feeble, and sometimes absent. Respiratory system normal. The heart's first sound was slightly rough and prolonged, but without any murmur. Pulse 80, small and soft. Abdomen normal. Bowels constipated. Urine very small in amount, and at first had to be drawn off with a catheter. On the last day of her life she passed it involuntarily along with the fæces.

She was very apathetic, and although evidently understanding what was said to her, did not always reply. In the evening of the sixth day after admission she suddenly, like the former case, fell into a state of collapse, and, in spite of stimulants, died at 10.45 p.m. No necropsy could be obtained.

The urine (which was examined by Professor Sophus Torup) was small in amount, strongly acid, and contained no albumen, blood, sugar, or bile. It was, when fresh, of a dark-red wine colour, and gradually, by exposure to the air, became of a deeper and deeper tint. On spectroscopic examination, although giving no spectrum of either meta- or oxy-hæmoglobin, it nevertheless gave a very characteristic pigment spectrum.

The acid solution, that is, the urine just as it was, gave three distinct absorption bands, with the following positions: α a very marked narrow band, position $\lambda = 562$ (middle); β a pronounced and larger band at $\lambda = 526$ (middle); γ a very pronounced and large one at $\lambda = 482$. There was also a feeble absorption in the violet. See Fig 1 in woodcut.

Fig. 1.—Spectrum of absorption; urine acid. Three bands α at $\lambda = 562$, β $\gamma = 526$, γ at $\lambda = 482$ (1).

Fig. 2.—Urine ammoniacal; two bands: α at $\lambda = 564$; β at $\lambda = 535$.

Fig. 3.—Filtrate after precipitation with lead acetate; three bands of absorption; α at $\lambda = 578$, β at $\lambda = 539$, γ at $\lambda = 487$.

Fig. 4.—Solution of precipitate by ammonium sulphate; one band of absorption at $\lambda = 499$.

$^1 \lambda =$ wave lengths expressed in millionths of a millimetre. Fraunhofer's lines correspond to A, $\lambda = 780.4$; B, $\lambda = 687.4$; C, $\lambda = 656.7$; D, $\lambda = 589.4$; E, $\lambda = 527.3$; F, $\lambda = 486.5$; G, $\lambda = 431.0$; H, $\lambda = 396.8$.

In an ammoniacal solution the band γ disappeared, and the other two were not only feebler, but had slightly changed their positions: α at $\lambda = 564$ (middle); β at $\lambda = 535$ (middle). There was also, as before, a slight absorption in violet. (Fig. 2.) The urine gave none of the reactions of urobilin.

By oxidation, that is, on being carefully heated with fuming nitric acid, the urine became of an almost black colour, and at the same time gave off small bubbles of a colourless gas (probably CO_2). On carrying the oxidation yet a step further it became of a paler red colour, which gradually passed into a rose, then to an orange, and lastly it returned to the yellow colour of normal urine, and while in this condition it gave the reaction of urobilin, and that, too, very markedly.

By reduction with powdered zinc and sulphuric acid (nascent hydrogen) the red urine became yellow—almost colourless—but reassumed its original red colour on oxidation.

The red pigmentary matter was precipitated from the urine by basic lead acetate as a salmon-coloured deposit; and on the excess of lead being removed by filtration, the filtrate had a red colour, and yielded, on spectroscopic examination three absorption bands: α somewhat feeble at $\lambda = 578$; β more pronounced, but narrow at $\lambda = 539$; γ wider and pronounced at $\lambda = 487$ (Fig. 3.)

On being reduced by means of zinc and sulphuric acid, the above red solution gave a pale yellow, almost colourless, liquid, which, on being filtered and freed from the zinc yielded, with basic lead acetate, an orange precipitate. This precipitate, on being in its turn oxidised with fuming nitric acid gave a garnet-red colour, and showed the same absorption bands as the above spoken of red filtrate from the basic acetate of lead (Fig. 3). On still further oxidation the garnet-red precipitate became almost black, and on the oxidation being carried still a stage further, it became of an orange and then of a yellow colour, and gave, as in the case of the urine before precipitation, the reactions of urobilin.

The original colouring matter in the urine, when precipitated by ammonium sulphate, was of a brownish black hue, and was soluble in water as well as in alcohol (80 per cent.), but insoluble in ether, chloroform, and oil of turpentine. A watery solution of this precipitate gave only one broad absorption band, at $\lambda = 497$. (Fig. 4), while the filtrate from it (which was of a garnet-red colour) gave in addition a very broad band at $\lambda = 499$ (middle).

As will have been noticed, the two cases narrated bear so striking resemblance to each other, both as regards their symptoms and modes of termination, as well as regards the clinical condition of their urines (in as far as their respective examinations went) that one is forced to look upon them as having a common pathology. And the question naturally arises: How can the symptoms be explained and what is their probable pathogenesis? Although it is no doubt to be regretted that no necropsy was obtainable in either case, the loss is perhaps in reality insignificant, for as the physical signs manifested were, for all practical purposes, little better than *nil*, a *post-mortem* examination would probably have revealed no tangible or characteristic structural lesions. Be that as it may, I think I shall be pardoned if I attempt to explain the cause of the symptoms by the facts learned from the analyses of the urines, which, as far as they go, are sufficiently explicit.

To begin with, I think it will not be considered too much if I say that the symptoms in both of the cases closely resemble those met with in what is called auto-intoxication (self-poisoning). For as pointed out there was in each of them a notable absence of appreciable physical signs, associated with well-marked and even grave nerve disturbances—to wit, insomnia and excessive prostration, disordered intellect, and coma, ending in sudden collapse and death. At the same time, in both cases, ischuria was present in a well-marked form, along with decided chemical alterations in the colouring matters of the urine, of a character which unmistakably pointed to a faulty oxidation. For instead of the urine containing normal colouring matter it contained (in the case specially examined) two abnormal pigments. One was a red substance, precipitable by basic lead acetate and ammonium sulphate, possessing characteristic absorption bands, this pigment being by oxidation convertible into urobilin, and by de-oxidation transformed into an almost colourless yellow substance, likewise precipitable by basic lead acetate. Again, from this almost colourless precipitate a red substance could, by oxidation, be obtained, which, by still further oxidation, was in its turn equally convertible into urobilin.

Besides this, as was previously mentioned, the urine contained a

chromogen,² which, like the precipitate just spoken of, was by oxidation transformable into a red colouring matter, which on a still further oxidation was also changed into urobilin.

These transformations can be graphically represented as follows, if we let U represent the urine, C chromogen, and R the red colouring matter.

From these facts it is seen that the abnormal colouring matter is nothing else than a precursory state of the normal urinary pigment, being, in fact, merely a lesser oxidised stage of it. Consequently there must have been a default of oxidation; and if this occurred in the pigment of the urine, we may infer that there equally existed a deficit in the oxidation of the other substances throughout the body. The auto-intoxication then one might suppose would be produced by a default of oxidation—more especially in those substances which originate in the body. As to the cause of this defective oxidation, it would be injudicious in the present state of our knowledge to attempt to theorise. It is, however, I think, by no means too much to expect that when more cases of a similar nature have been met with and carefully investigated, a reasonable explanation of the cause of this faulty oxidation will be found.

THE VALUE OF HYDRONAPHTHOL AS AN ANTISEPTIC.

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Hydronaphthol has been before the profession for some time, but, so far as I am aware, its value as an antiseptic has been tested by only one series of published experiments detailed by Dr. Edington, of Edinburgh, in a paper published in the *BRITISH MEDICAL JOURNAL* of last year. It is said to be non-poisonous, non-corrosive, and non-irritant, and, moreover, a powerful antiseptic agent. I had the opportunity of seeing it tried as a clinical antiseptic by Dr. Renton of this city, and his disappointment with the results led me to investigate its claims. The fact that the following experiments seem to place an agent which certainly has powerful antiseptic qualities on a surer, if on a narrower basis, is my excuse for laying the result before the profession.

Hydronaphthol is one of the naphthol series, being a derivative of β -naphthol, and occurs as a whitish powder of fine flaky crystals. The preparation I used was that of Messrs. Seabury and Johnston, sold by the chemists as hydronaphthol powder. The powder is freely soluble in alcohol, but is, unfortunately, very insoluble in water. It is not wholly soluble in 2,000 parts of cold water. In hot water (above 70°C .) it is much more soluble, but after cooling there is a considerable deposit.

Preliminary experiments conducted in the manner afterwards detailed with a saturated solution, and also with a boiled and subsequently filtered solution (that is, strongest solutions which could be got in water) proved that each, after one hour's exposure, failed to kill *staphylococcus pyogenes aureus*, though the boiled solution was effective after twenty-four hours. It therefore became necessary to obtain a solution stronger than could be obtained in water alone, and to this I attributed the clinical failure of the antiseptic.

I then tried mixing a spirituous solution with water, but the hydronaphthol was at once thrown out when the solution was stronger than 1 to 20 of spirit, while the precipitation occurred more slowly when a solution of 1 to 40 was mixed with water. Glycerine, however, if added to the spirituous solution in excess,

² Of a slight yellow colour, probably due to another colouring matter in the urine.