**Diabetic coma / by Balthazar Foster and Robert Saundby.**

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# DIABETIC COMA.

BY BALTHAZAR FOSTER, M.D., F.R.C.P.,
PHYSICIAN TO THE GENERAL HOSPITAL, BIRMINGHAM;
AND
ROBERT SAUNDBY, M.D., M.R.C.P.,
ASSISTANT PHYSICIAN TO THE GENERAL HOSPITAL, BIRMINGHAM.

OUR attention has for some years past been directed to the phenomena of diabetic coma, and in previous papers* we have tried to elucidate some points in this interesting subject. We therefore desire to record the following case as a further contribution to this discussion, and as an illustration of those views which we have formerly advocated on the pathology of this condition.

F. W. A., 17, jeweller, presented himself as an out-patient at the General Hospital, on Thursday, Oct. 19th, complaining that he was rapidly losing strength and flesh, and passing a very large quantity of urine. He looked very ill, and his urine, on examination, contained a large quantity of sugar, was of sp. gr., 1,040 but gave no reaction with ferric chloride. He was recommended for admission, and the following history was obtained. There has been no known instance of diabetes in the family; his mother

* Foster. On Acetonæmia. British Med. Journal. Jan. 19th, 1878.
Saundby. Diabetic Coma. Birmingham Med. Review. 1881. p. 193.
Saundby and Barling. On Fat Embolism. Journal of Anat. and Phys. July, 1882.

died of phthisis three months ago, and this circumstance had been a source of great grief to him. His previous health had been good, with the exception of bilious attacks, to which he was subject. Five weeks ago, he began to feel ill and to pass water during the night, and for the last fortnight he has been passing very large quantities both in the day and night, altogether, he estimated, about two bucketsful of what he described as "hay-smelling" urine. For the last two weeks he has suffered from constant frontal headache, and great thirst; his appetite has continued good, but not inordinately so. His bowels during the same period have been open every other day. Five days ago he vomited, and had to give up his work. His penis became a little sore, and he noticed that his urine left a sticky stain on his shirt. He had been taking medicine from a chemist for four days before admission.

*Present condition*, Oct. 20th, *11 a.m.* (the day after admission):—Patient complains of frontal headache, weakness, constant desire to pass water, and great thirst. He is an emaciated looking lad, with dilated pupils, dark rings under his eyes, his alæ nasi are working, but his lips are of a good red colour. Expression anxious; skin dry and rough; Temp., 98°; pulse, 112; respirations, 24. No œdema of legs. Teeth glazed; gums red and slightly spongy; throat covered with thick mucus; fauces reddened; tongue very dry, and its centre coated with a grey fur; appetite fair, no vomiting. Bowels were opened on the day before admission (Oct. 18th). His breath smells sweet; there is no cough; breathing deeper than in health. The circulatory organs appear normal. During the night he has passed a large quantity of urine, which was acid, sp. gr. 1040, contained ⅛ column of albumen, and a large quantity of sugar. The urine

passed this morning is acid, clear, greenish coloured, sp. gr. 1035, contains ⅛ col. of albumen, a large quantity of sugar, and gives an unmistakeable deep vinous-coloured reaction with ferric chloride. His eyesight is unaffected. On the day of admission the patient took ordinary diet, but all this day he has been on diabetic diet.

The detection of the ferric chloride reaction at once suggested the fear that coma might be imminent, and as the bowels had not been moved for forty-eight hours, two scruples of pulv. jalapæ co. were administered at 12.30 p.m., and he was ordered to be carefully watched.

*3 p.m.*—Patient became very restless, and complained of great pain in his abdomen; his respirations were deeper, and his pulse quick and feeble. The pain in the abdomen was relieved somewhat by hot fomentations. The bowels had not been moved.

*5 p.m.*—Pulse 156, feeble; resp. 34. Ordered a teaspoonful of brandy every half hour.

*5.30 p.m.*—No cyanosis; respirations deep and sighing; pulse very feeble; complains of no pain. Not restless, seemed rather drowsy. Ordered three teaspoonfuls of brandy at once, and a teaspoonful every ten minutes.

*7 p.m.*—Patient quite comatose; thirty minims of ether injected subcutaneously did not rouse him, nor did he appear to feel the operation of having a drop of blood taken from his finger. After a little he roused sufficiently to put out his tongue and to say that he felt short of breath, but no pain. There was no cyanosis; breathing was very deep, 41, pulse (before the ether) 174, extremely feeble. Pupils were dilated, but reacted to light. Breathing very harsh; heart sounds scarcely perceptible. The blood on examination did not contain any fat globules, but the leucocytes appeared slightly increased. An enema

of one ounce of brandy and a drachm of ether, in two ounces of water, was then administered, and he was enveloped in a hot pack.

9 *p.m.*—Patient had been very violent, tossing himself about in the bed; radial pulse not to be felt; pupils dilated and insensible to light. Breathing deep; no cyanosis. He was deeply comatose and could not be roused. Later on his father managed to rouse him by repeated shouting, and on his father saying, "Do you hear me?" patient replied, "Yes! I hear you."

*11 p.m.*—Patient died; eight hours after the onset of the more serious symptoms. The nurse reported that he turned "bluish" and struggled very violently just before his death.

No urine was passed after 6 p.m.; but ten ounces were passed during the previous hour; this was examined by Dr. Windle, and he reports it to have been pale yellow, clear, acid, sp. gr. 1030, containing a trace of albumen, 1·6 per cent. of sugar, ·95 per cent. of urea; chlorides diminished; no trace of indoxyl; a deep vinous red reaction with ferric chloride.

The total quantity of urine passed in the twenty-four hours, from 5 p.m. Oct. 19th, to 5 p.m. Oct. 20th., was 160 ounces. The temperature on the evening of the 19th was 100° Fahr., but fell gradually, being 98° on the morning of the 20th, and 97° at 7 p.m., four hours before his death.

The *post mortem* examination was performed by Dr. Windle, on Oct. 21st, fifteen hours after death.

*External appearances.*—The body was that of a young male, somewhat emaciated; cadaveric rigidity and hypostatic congestion were well marked.

The *Spinal Cord* presented no abnormal naked eye appearances.

*Head.*—The cranial bones were very thin; the dura mater was extremely adherent; there was no clot in the sup. long. sinus. There was increase of the Pacchionian bodies on the arachnoid along the longitudinal fissure. The brain substance was firm, slightly hyperæmic throughout, with numerous puncta cruenta; a small amount of reddish serum in the lateral ventricles.

*Thorax.*—The cavities of the heart contained some dark fluid blood, and a very few soft clots; the valves were normal; the heart substance was rather pale. The lungs, when squeezed, emitted a peculiar sour acetone-like odour, which was also observed on section of them. Their substance was slightly hyperæmic, but otherwise normal.

*Abdomen.*—The stomach and intestines were much distended. There was no unusual smell detected on opening this cavity. The diaphragmatic concavity reached as high as the upper edge of the fifth rib. The liver was slightly enlarged, and on section pale in colour. The gall bladder was almost empty and collapsed. The bile ducts were pervious. The spleen was small and soft. The kidneys were rather large, their capsules stripped readily; substance pale. The supra-renal capsules were normal. The pancreas was small and shrunken in appearance. The stomach was full of pultaceous food; its mucous surface showed patches of hyperæmia. The intestines were loaded with fæces, the sigmoid flexure and rectum being stuffed full of hard grey masses, quite uncoloured by bile. The small intestine was full of pale yellow soft fæces. There was a large mass of tænia in the colon. The solar plexus and cervical sympathetic ganglia appeared normal. The blood nowhere presented any abnormal appearance.

On microscopical examination the liver, spleen

kidneys, and lungs were quite normal. There were no fat embola or any traces of fat in the vessels of the lungs and kidneys, or in the renal tubules. The medulla was also normal, though the perivascular spaces were slightly enlarged. The cells of the pancreas were badly defined, and their contents cloudy. The sympathetic ganglia were unfortunately lost.

Dr. Norris, who examined the blood, reports that the leucocytes were peculiarly large, and the red corpuscles and granular matter slightly in excess, but there was no excess of fat.

The clinical phenomena presented by this case are of great interest. In the first place, the diabetes was apparently produced by nervous shock, the profound grief induced by the death of a near relative, a fact which is in accordance with many previous observations, and which goes with them to support the view of the purely nervous origin of the disease. Secondly, the course of the disorder was remarkably acute and rapid. Thirdly, we were able to trace the development of the whole of the terminal symptoms, and to forsee their approach by the use of the ferric chloride test.

In considering the predisposing causes of this special termination of diabetes, we must place first the *age* of the patient, and the *acuteness* of the disease. The important fact that it is in *young persons* and in *acute cases*, that diabetic coma is mostly liable to supervene is now well established, and is supported by the statistics of Guy's Hospital, adduced by Dr. F. Taylor.*

In more immediate and direct relation to the actual attack was the *constipation*, which the *post mortem* examination proved to have been much greater than we had

* Taylor, Guy's Hospital Reports, Vol. XXV., p. 158.

supposed from the statement of the patient that his bowels had been opened every other day. We were fully aware of the sinister influence of this condition, and it was in the hope of removing it, and averting the danger which we apprehended, that the compound jalap powder was ordered, but unfortunately without effect. In future, we should be disposed under similar circumstances to give a minim of croton oil at once.

Besides constipation, nervous shock, sudden or prolonged muscular exertion, cold, and the fatigue of travelling, have been recorded as predisposing factors, but none of these were present in this case. The patient lived in the town, he had only a short distance to come to the hospital, and there is no reason to believe that that circumstance in itself disturbed him at all.

Fatty degeneration of the muscular fibres of the heart is maintained by Schmitz,* of Neuenahr, to be frequently present in diabetic patients, and he points out that this condition favours the onset of these symptoms by lowering the blood pressure and impairing the circulation in the brain, lungs, and kidneys. The heart's muscle in the present case is reported as pale, but unfortunately no microscopical examination was made.

Among the earliest of the premonitory signs was the alteration of the respiration: in the morning note we find that the breathing was "deeper than in health."

Throughout the report of the clinical symptoms we have repeatedly the note, "no cyanosis," and until just before death, when according to the nurse he turned "bluish," there is not the slightest evidence of any alteration in the function of blood aëration. Undoubtedly cyanosis has been described in other cases,

* Schmitz, Berl. klin. Woch., Jan. 31st, 1876.

but as it is not constant, when present it is probably due to some complication. Its absence indicates that the dyspnœa is purely nervous in origin, and the result of stimulation of the respiratory centre, rather than of any local change in the lungs, and affords an argument against the theory of Sanders and Hamilton* that the dyspnœa is due to interference with the circulation through the lungs, by fat embolism of the pulmonary capillaries.

The *pulse* at the morning visit was 112, and soon rose to be extremely rapid and feeble; this symptom is regarded by Prof. Lépine† as being of great value as an early indication of the onset.

*Abdominal pain* was complained of first at 3 p.m., and may have been partly the effect of the purgative. It is, however, known to be a very constant and early sign in these cases.

Drowsiness was first noticed at 5.30, and by 7 o'clock he was quite comatose.

Death was preceded by convulsions. Senator‡ speaks of twitchings as sometimes supervening, but in the last case under our notice‖ as in this, actual convulsions occurred. Cyr,§ writing five years ago, considered the absence of convulsions afforded a diagnostic distinction between this form of coma and that from uræmia, but this, it is obvious, cannot be maintained.

Among the premonitory signs presented by this case, and which we regard as of great value, were the gradual fall in the sp. gr. and quantity of the urine, and con-

* Sanders and Hamilton, Edinburgh Medical Journal, July, 1879.

† Lépine, Lyon Méd., 1882.

‡ Senator, Ziemssen's Cyclopædia, Vol. XVI., p. 96.

‖ Rickards, A Case of Diabetic Coma.—Birmingham Medical Review, Vol. XII., p. 190.

§ Cyr, Arch. Gén. de Méd., 1877, p. 691, and 1878, p. 37.

sequent diminution of the amount of sugar excreted, which was far too great to be accounted for by the change of diet. In the last sample of urine examined the quantity of sugar was only about seven grains to the ounce, an amount which must have been greatly surpassed in the previous day, when the sp. gr. was ten degrees higher.

The percentage of urea in the last urine was low, being under one per cent., but considering the large quantity of urine passed, the total amount excreted during the final twenty-four hours of life must have been quite seven hundred grains. This disposes of the objection that the toxic phenomena were due to non-elimination of urea. No urine was passed after 6 p.m., but this coincided with the supervention of the coma. Ebstein's* suggestion that necrosis of the renal epithelium causes the retention of sugar and urea in the blood is, moreover, opposed in this case, by the negative results of the microscopical examination of the kidneys.

The state of the liver and pancreas calls for some remark. The gall bladder was found almost empty and collapsed, though the gall ducts were pervious. This suppression of the functions of the liver was probably a late *ante mortem* phenomenon, the result of the collapse. The presence of bile in the small intestine, the absence of jaundice, and the fair quantity of urea in the urine, indicate that the suppression could not have been of long standing. The state of the pancreas is, as is usual in these accounts, not satisfactory. Similar descriptions are not by any means uncommon in the reports of the autopsies of diabetic subjects, but what relation they bear to the disease itself is by no means

* Ebstein, Deutsches Archiv. Bd., 28

clear. Several cases of disease of the pancreas have been reported during the past year, but no mention was made of the state of the urine. Ewald says that he has found the pancreas more often healthy than otherwise in the bodies of diabetic subjects.*

Teschemacher has pointed out the resemblance of the symptoms of diabetic coma to those of nervous shock, and he suggests that the cause is in some lesion of the sympathetic system. It is a matter of regret to us that we are unfortunately unable to supply any facts as to the microscopical appearances of the sympathetic ganglia. From previous observations on the changes in these organs, we believe that it is very difficult to assign any precise value to the pigmentary degeneration of the ganglionic cells, or thickening of the stroma and blood vessels so often met with in such different pathological conditions, and that it is probable that these changes are more often secondary to the visceral lesions in their neighbourhood than evidences of primary diseases of the sympathetic system.

This case illustrates very strikingly the prognostic use that may be made of the ferric chloride reaction, for although we are quite aware that it is not uncommonly found in diabetes without being followed by coma, and is often present in the urine of scarlatina, measles, and other conditions, yet its sudden appearance in the urine, especially in young subjects and in acute cases of diabetes, should be regarded as a sign of grave moment, and should direct attention to the state of the bowels, the respiration, the pulse, and the other prodromata which have been described.

The chemical significance of this test is at present

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* Ewald, Lectures on Digestion, p. 96.

undetermined. The view generally held is that this reaction is caused by ethyldiacetic acid, which splits up into acetone and alcohol. Deichmüller* and Tollens† believe the substance to be free diacetic acid, and Fleischer‖ has shown that diabetic urine giving this reaction, differs from urine to which ethyldiacetic acid has been added by the reaction not disappearing in the former case after fermentation by yeast for twenty-four hours. It is, however, generally admitted, that the substance, whatever it be, is nearly allied to acetone. A sample of the urine, some days old, was sent to Prof. Tilden, F.R.S., at Mason's College, to be distilled for acetone, but he reported that none was found.

We are of opinion that it has been conclusively shown that diabetic coma occurs wholly independently of lipæmia.‡ The entire classical series of symptoms was present in this case, although there was certainly no unusual amount of fat in the blood. In a previous paper§ one of us has shown that true capillary fat embola are not present even when the blood is loaded with fat, while the supporters of this theory have entirely failed to point out any essential symptom depending upon the fatty state of the blood, or which is absent in such cases as the one we have reported, or in similar cases reported by others.¶

The only explanation which adequately fulfils the requirements of the problem, is the theory of a toxæmia, and this, is best denoted provisionally by the term acetonæmia. This is the view taken lately by Prof.

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* Deichmüller, Liebig's Annalen, Bd., 209, p. 22.
† Tollens, ibid, p. 30.
‖ Fleischer, Deutsche Med. Woch., 1879 No. XVIII.
‡ Sanders and Hamilton, loc. cit.
§ Saundby and Barling, loc. cit.
¶ Gamgee, Physiological Chemistry, Vol. I., p. 169.
¶ Taylor, loc. cit.

Frerichs,* and expressed by all the speakers who took part in the discussion in the Pathological Section of the British Medical Association at the Worcester meeting.

A recent anonymous writer† advances the somewhat vague proposition that "the pathology of this peculiar condition will probably be found to be connected with the general exsiccation of the tissues, and more especially of the nervous matter, which is found in diabetic subjects," but he advances no evidence in support of this opinion except a casual reference to some observations of Ranke. We may be allowed to wait until this proposition, and the facts upon which it is supposed to be based, are presented to us in a tangible shape, before we attempt to form any opinion of its value as a contribution to the pathology of this condition.

We desire to express our thanks to our House Physician, Dr. Bond, for his careful observation of the progress of the case during the time we were necessarily absent from the Hospital, and to the other gentlemen who have favoured us with special reports.

We regret the fatal termination, and the want of any satisfactory therapeutic indications; but we believe much may be done to avert this condition by rational prophylaxis on the lines indicated in the course of this paper; and by the early recognition of such cases, it is to be hoped that medical aid may be more powerful in future than it has been in the past.

In the following conclusions we have summarised the principal points which deserve attention :—

1.—Diabetic coma is especially liable to supervene in acute cases in young persons.

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* Frerich's, Report of Proceedings of Berliner Med. Gesellschaft, June 5, 1882.

† British Medical Journal. On Nervous Derangements in Diabetes, December 9, 1882.

2.—Diabetic patients and their friends should be warned of the danger of constipation, muscular exertion, nervous excitement, and cold, as probably predisposing causes of death by coma.

3.—The discovery of the ferric chloride reaction in the urine should be taken as a warning to look out for the premonitory symptoms of coma.

4.—Deep respiration, rapid pulse, and abdominal pain are the earliest premonitory signs of this condition.

5.—Cyanosis may be absent in spite of the dyspnœa, and may appear only just before death.

6.—Convulsive seizures are not an uncommon occurrence just before death.

7.—Diabetic coma, with all its classical symptoms, occurs independently of any excess of fat in the blood, and the pathological value of lipæmia, when present, is yet undetermined.

8.—The toxæmic theory, or poisoning by acetone or some nearly allied substance or substances, affords the best explanation of this remarkable group of symptoms.