ATTACKS OF CLOSED LIDS

Besides the oculogyric attacks, in which the eyes turn in some direction, there are others in which the lids close and cannot be opened. These are not uncommon. Some patients will tell you that there seems to be something behind the lids which is pulling, and which prevents them opening the eyes. These are probably only a variation of the other more common form. The grounds for such a view are to be seen in the serial pictures from the case of facial palsy (Fig. 3). When the woman is told to open the closed eyes the first thing that happens is not that the lid goes up, but that the eye begins to move down, and until it has reached its proper position the lid does not show any sign of opening. Just as in closure of the eyes, the two parts of the act are not synchronous but consecutive; but now the order is reversed. Until the normal tone of the eye muscles has been resumed the levatores palpebrarum cannot come into action. In the attack of "closed lids" the eyes go out of action when the lids close, and, as in the oculogyric attack, they cannot be brought into position again. Until they are, the eyes cannot open.

Within the walls of this college, many years ago, your great physician Hughlings Jackson no doubt often repeated his famous aphorism: "Nervous centres know nothing of muscles; they only know of movements." The complexity of the muscular actions in the movement of closing and opening the eyes is an excellent example of this great truth.

OCULAR ATTACKS DUE TO INHIBITION

There is, then, a good deal in favour of the view that these ocular attacks are not active muscular spasms, but rather an inhibition of the muscular tone in the eye muscles which normally follows closure of the lids. Its cue is the covering of the pupils by the eyelids. Conversely, the cue for the lids to open is the return of full tone in the eye muscles. The oculogyric and the eye-closure attacks are merely two slightly different modifications of the same local inhibition. In the former the actors hurry off the stage before the curtain falls, in the latter the curtain cannot be rung up because the actors will not take up their proper positions on the stage. In either case it is very disturbing to the management! During the attacks the head is often drawn in the same direction as the eyes, and may change with a change of their direction. This is probably a compensatory action and secondary to the ocular inhibition.

Mention was made earlier of other forms of periodic attacks occurring in chronic encephalitis, particularly affecting the jaws, upper trunk parts, and respiratory acts. As regards the two former, Bonhoeffer⁴ suggests that these also may be dissociated components of sleep. The occasional attacks of yawning, in some cases leading to dislocation of the jaw, and the so-called torsion spasms, which often bear a strong likeness to the stretching of the sleepy person, lend themselves to such a view.

PROGNOSIS IN PARKINSONISM

It would be difficult to paint a darker picture than is presented by chronic encephalitis as a whole. If its acute stage chastised us with whips, truly its chronic stage chastises with scorpions. But it must be remembered that for various reasons it is usually the more severe cases that are recorded in medical papers. I should like to emphasize the fact that there is also a rather less dark side. There are at the present time a large number of Parkinsonians whose lives, at least seven years after infection, are comparatively little interfered with by their disability. Two years ago I followed up 325 of my cases of Parkinsonism, and more than half were able to go

about, look after themselves, and lead more or less ordinary lives. It has not been possible to repeat that follow-up this year, but I see many of these patients from time to time, and, although there are exceptions, I know that most of them are not any worse than they were two years ago. Judged by their rate of movement in the arms as tested by the apparatus described in the *Lancet* in 1927, many of them show no increase of slowness, nor has any serious loss of power occurred.

Among my cases of Parkinsonism in their seventh, and even in some in their eleventh, year of infection, life is not incompatible with activities such as performing full household duties, playing in a football team, active gymnastics, going with boy scouts to camp and sharing fully in the duties, or working as a blacksmith all the week and holding classes for youths on Sundays. One, a married woman, walks ten or fifteen miles every Saturday with her husband. One youth dives and swims in the sea a great deal better than most people; another is a good rifle shot. Some are managing businesses, one holds high military command. Quite a number of young Parkinsonian men and women have married since their disability. What the future has in store for any or all of these, and whether it is only a pause in a progressive disease or a real arrest of the process, there are no precedents to guide us in forming an opinion. Meanwhile, as the years go on, the latter seems more possible.

For valuable help in preparing this lecture I desire to express thanks to Dr. Vincent and his staff at the South Yorks Mental Hospital, to Dr. Rees Thomas and his staff at Rampton State Institution, also to a large number of resident medical officers at the various Sheffield hospitals, both voluntary and municipal, and to the superintendent of the Blind School, for their observations on the eyes in sleep.

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ACUTE SPONTANEOUS HYPOGLYCAEMIA

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Cases of severe acute spontaneous hypoglycaemia have been so rarely reported in the literature that the recognition of the condition in practice is a reasonable excuse for recording the case reported below. Moreover, this case exhibited certain features different from those observed in any other so far described.

CASE REPORT

On the night of May 14th, 1930, a married woman, aged 27, poorly nourished, was admitted to the Mater Misericordiae Hospital in a semi-conscious condition. She was restless in bed, and was unable to give an intelligent account of herself. Her speech was monotonous and slow, and her expression dull. On the following morning she was completely unconscious, slightly cyanosed, and the breathing was deep and stertorous; she frothed at the mouth and passed urine involuntarily, the limbs were so rigid that the tendon reflexes could not be

elicited, and Babinski's sign was bilaterally positive. The skin was moist, there was blepharospasm, and the conjunctival reflex was diminished, but the pupils reacted normally to light. The urine, obtained by catheter, contained a trace of albumin, but no sugar, diacetic acid, or casts. Blood pressure was 90/70; no other abnormal findings were noted on clinical examination.

In discussing the diagnosis the possibility of acute hypoglycaemia was considered, but at the time no information could be obtained about her condition before admission. A fasting blood sugar estimation (Folin-Wu¹ technique) of 35 mg. per 100 c.cm.—the blood was drawn and the estimation made while the patient was unconscious—supported the diagnosis of acute hypoglycaemia; the blood urea, determined at the same time, was 60 mg. per 100 c.cm. A confirmation of this diagnosis was obtained by the intravenous injection of 10 grams of glucose in 20 c.cm. of distilled water; the injection took about four minutes, and before it was ended signs of returning consciousness appeared. Immediately after receiving the injection the patient became quite conscious and rational, she sat up in bed and asked where she was, the rigidity and blepharospasm disappeared, and the positive Babinski sign became bilaterally negative. We considered that the condition (now thought to be undoubtedly hypoglycaemic in origin) was probably not due to the administration of insulin, because it had become progressively worse in the first fourteen hours after admission.

Three hours after the glucose injection the blood sugar was 111 and the blood urea 30 mg. per 100 c.cm. By this time we learnt that the patient had never had diabetes and had never received insulin; she was therefore put on ward diet and glucose drinks. Glucose was not given after the second day in hospital, except once for a glucose tolerance test.

Previous History

The cause of the attack for which she was admitted to hospital in the first instance was undoubtedly acute spontaneous hypoglycaemia. The previous history, obtained a day or two after recovery from the acute attack, showed that her first three pregnancies had been normal, but the last baby, born in May, 1926, had been stillborn, and this delivery had been followed by a leucorrhoeal discharge which disappeared on treatment. Amenorrhoea had been present since the birth of the stillborn child. A year previous to her admission to the Mater Misericordiae Hospital she had complained of frequent attacks of dizziness, with "an inclination to faint," especially approaching meal-time. Because of these sensations she had gone to the out-patient department of another hospital, and had there received, on February 24th, March 3rd, and March 24th, 1930, three intravenous injections of novarsenobillon (0.3 to 0.45 gram), but the blood Wassermann reaction had been continuously negative. Three days before we first saw her (May 14th) she had actually become unconscious for a few minutes, and on the morning of the day before admission she was found hanging out of bed, with a dull, listless expression on her face, unable to recognize her husband and her friends. On the morning of the day of admission she was again found unconscious—with jerky movements of the limbs and frothy saliva round the mouth—and groaning, with an expression of pain on her face; she recovered partially, and was sent into hospital that evening.

Subsequent History

On the morning of May 16th the fasting blood sugar was 56 mg., and the blood urea 22 mg. per 100 c.cm.; the plasma nitroprusside test was negative, and there were no symptoms then, or afterwards, attributable to hypoglycaemia. At 4 o'clock on the afternoon of the same day, after a mixed ward breakfast at 9 a.m. and dinner at 2 p.m., the blood sugar was 122 mg. per 100 c.cm. On May 17th the fasting blood sugar was 66 without hypoglycaemic symptoms, and one hour after a breakfast, taken at 8.30 a.m., consisting of an egg, about 3½ oz. of bread-and-butter, tea without sugar, and 5 oz. of milk, it was 116 mg. per 100 c.cm.; but at noon, without further food since breakfast, it had fallen to 87. For several subsequent days, while on an ordinary ward diet, with cane sugar allowed in moderation, but no glucose drinks, the patient was kept under observation, and the following figures (mg. per 100 c.cm.) were obtained by blood analyses: sugar (fasting) varied from 72 to 76, calcium 9.75, inorganic

phosphorus 1.5, cholesterol 271, uric acid 2.9, creatinine 2.3, non-protein nitrogen 37.5, and bilirubin less than 0.1. During this period no hypoglycaemic symptoms occurred. The blood sugar values obtained after the ingestion of 100 grams of glucose, 50 grams of starch, and 50 grams of levulose are shown in the following table.

Time in Minutes after Ingestion	Blood Sugar in mg. per 100 c.cm. after Oral Administration of—		
	85 grams Glucose	50 grams Levulose	50 (±) grams Starch
0	76 (nil)	74 (nil)	76
15	95 (nil)	—	96
30	125 (nil)	100 (nil)	94
45	112 (?)	—	79
60	130 (?)	75 (nil)	94
90	122 (trace)	72 (trace)	142
120	93	72 (trace)	123

The comments in parenthesis denote urinary sugar determined on a specimen obtained at the same time as the corresponding sample of blood.

A combined liver function and gall-bladder visualization test, after the intravenous injection of 2.5 grams of isiodikon, showed that the dye was removed at the normal rate from the blood, and that the gall-bladder shadow was normal. A fractional test meal showed complete achlorhydria, with no gastric mucus or bile. Routine gastro-intestinal tract roentgenological examination by Dr. J. A. Geraghty merely revealed some degree of ileal stasis, with a spastic caecum and possibly chronic appendicitis. The blood count showed 75 per cent. haemoglobin, 4,000,000 erythrocytes, and 10,000 leucocytes per c.mm., with a normal differential count. The blood pressure readings showed no subsequent significant change from the first figures. The blood Wassermann reaction was negative, and the patient's weight six days after admission was 101 lb. On the tenth day of observation the stools were examined, and found to contain a large quantity of undigested starch, but there were only a few meat and vegetable fibres present, and fat and fatty acid were absent; the diastatic power of the blood and urine was normal. Apart from one intravenous injection of glucose, followed by glucose by the mouth for the first day, no special treatment was given for the first fourteen days of observation, the patient being on an ordinary mixed ward diet. From the fifteenth day, drachm doses of dilute hydrochloric acid (B.P.) and 2 grains of pepsin were given, in a mixture, three times daily after food during the remaining period of hospital observation and for three weeks after discharge. As the faeces constantly contained a large proportion of undigested starch from the tenth day after admission, when the first examination of the stools was made, it was thought that faulty digestion and absorption of starch might partly account for the constantly low level of the fasting blood sugar (62 to 76 mg. per 100 c.cm.), and that possibly these conditions might also have had some relationship to the acute hypoglycaemic attack on admission, when the blood sugar was only 35 mg. per 100 c.cm. The patient was therefore given 7½ grains of taka-diastase (Parke, Davis and Co.) thrice daily, in divided doses before, with, and after meals, from the thirty-second day after admission, starch being still continuously present in large quantity in the stools. After this the starch gradually disappeared, and on the twelfth day after the taka-diastase was started no starch was found in the stools; indeed, none was again found in the faeces at several subsequent examinations. The blood sugar, however, on the forty-eighth day was still only 74 mg. per 100 c.cm. Hydrochloric acid was still absent in all specimens of the fractional test meal on the forty-third day after admission. The patient decided to leave hospital on the forty-eighth day (June 30th, 1930) after admission, as she constantly objected to the various tests during the last few weeks of her stay, but she promised to keep taking hydrochloric acid and taka-diastase as prescribed. She remained at home on ordinary diet for three weeks, taking hydrochloric acid and taka-diastase as directed, and she experienced no further attacks suggestive of hypoglycaemia. At the end of that period, on re-entry

into the hospital for a day for observation, the stools contained no starch, but achlorhydria was still present, and her fasting blood sugar was 75 mg. per c.cm. Refusing to remain longer in hospital, she again returned home, and ceased to take the hydrochloric acid and taka-diastase on July 25th, but on August 8th we obtained a specimen of stools from her for examination, which contained no starch. Another specimen (August 25th) again contained no starch, and no further symptoms suggestive of hypoglycaemia had been experienced. On August 27th the test meal showed the presence of hydrochloric acid in moderate amounts in all but two specimens, and this result was verified by another test meal next day. On September 5th the fasting blood sugar was 78 mg. per 100 c.cm., and 89 mg. three hours after a mixed breakfast. About a month later a nurse called to see the patient, and found her apparently quite well; the patient stated that she had experienced no inclination to faint, and had had no further convulsive attacks.

LITERATURE

The clinical literature on the symptoms caused by acute spontaneous hypoglycaemia is interesting, and confined to comparatively recent years. Harris² in 1924 was apparently the first to suggest that hyperfunction of the islets of Langerhans might, by causing hypoglycaemia, produce symptoms similar to those caused by an overdose of insulin. He reported five cases with comparatively mild symptoms which he considered to be thus explained, and he mentioned the term "hyperinsulinism" in connexion therewith. A review of the literature would suggest that, while spontaneous over-production of insulin does explain many of the recorded cases, certain of them may not be accounted for in this way; hence the descriptive nosological term "spontaneous hypoglycaemia" would seem more appropriate than "hyperinsulinism," the latter being reserved for symptoms caused by true over-production of insulin by the islets of Langerhans. Shih-Hoa and Hsiao³ in 1925 recorded moderate hypoglycaemic symptoms from excessive purgation in a condition of partial starvation. Wilder, Allen, Power, and Robertson⁴ in 1927 studied a case of carcinoma of the islets of Langerhans with severe hypoglycaemic symptoms; extracts of the tumour tissue yielded insulin. Sendrail and Planques⁵ in 1927 stated that hypoglycaemia had been observed by them in starvation, progressive muscular atrophy, and in the pernicious vomiting of pregnancy. Finney and Finney⁶ in 1928 recorded a case of spontaneous hypoglycaemia, and removed part of the pancreas, which was anatomically normal. Schroeder⁷ in 1928 produced hypoglycaemia with symptoms in a woman by lowering the carbohydrate intake. Thalheimer and Murphy⁸ in 1928 described a case of spontaneous hypoglycaemia due to carcinoma of the islets of Langerhans, and Allen⁹ in 1929 described three cases, one of which was due to carcinoma of the islets; in another, part of a normal pancreas was removed, with some improvement. Griffith¹⁰ attributed some cases of convulsions in infancy to spontaneous hypoglycaemia. Howland, Campbell, Maltby, and Robinson¹¹ in 1929 described a case of spontaneous hypoglycaemia, due to a localized carcinoma of the islets of Langerhans, in which removal of the tumour resulted in spontaneous cure; this is apparently the only recorded case in which surgical treatment was successful. In 1929 McClenahan and Norris¹² described a fatal case due to adenoma of the islets of Langerhans. Allen, Boeck, and Judd¹³ in 1930 reviewed the surgical treatment of acute spontaneous hypoglycaemic attacks, and stated that three of five patients with pancreatic tumours, on whom partial pancreatectomy had been performed, showed slight improvement at first, but tended to relapse, and two obtained no relief of their symptoms after this operation. Gannon and Tenery¹⁴ in 1931 reviewed the literature and recorded a further case of spontaneous hypoglycaemia

with attacks of unconsciousness, due apparently to hyperinsulinism. Cushing,¹⁵ Carr, Parker, Grove, Fisher, and Larimore,¹⁶ and Womack, Gnagi, and Graham¹⁷ record three cases of hyperinsulinism due to adenoma of the islets of Langerhans, with successful removal of the neoplasm and disappearance of the hypoglycaemic symptoms in each case. As far as we have been able to study the literature, about twenty-four cases of acute spontaneous hypoglycaemia with severe symptoms and apparently due to hyperinsulinism have been recorded. Several other references can be found to cases of spontaneous hypoglycaemia, acute and chronic, in some of which the symptoms tend to be less severe or absent, and in which the etiology may not always be clear. For example, the attacks have been attributed to liver insufficiency (possibly in relation to disorders of carbohydrate storage), non-pancreatic endocrine insufficiency or dysfunction, muscular dystrophy, renal glycosuria, lactation, and other causes. Wagner and Parnas¹⁸ refer to a severe and acute case thought to be hepatic in origin, and Cross and Blackford¹⁹ described a case of toxic hepatitis following the administration of neoarsphenamine intravenously, with symptoms definitely due to spontaneous hypoglycaemia. Mann²⁰ has shown that marked hypoglycaemia occurs in dogs after removal of the liver. Cammidge²¹ mentions four cases of convulsive attacks due to chronic hypoglycaemia and associated with abnormalities of digestion, but he gives few details.

The symptoms of hypoglycaemia due to hyperinsulinism resemble those due to an overdose of insulin given hypodermically; the attacks may appear at intervals, and recovery may occur spontaneously, or after the ingestion of carbohydrate or injection of glucose, except in severe terminal attacks. The symptoms vary, according to the severity of the attack, from a sense of uneasiness, faintness, or apprehension, with perhaps sweating or great hunger, to vertigo, staggering, mental confusion, and coma, with or without convulsions, which, when present, are usually of the clonic type. Foaming at the mouth may occur, but loss of sphincter control is said to be uncommon.

DISCUSSION

The case of acute spontaneous hypoglycaemia which we now record is, as far as we have seen in the literature, the first to be reported in detail in these islands, and, furthermore, faulty amylaceous digestion does not appear to have been heretofore described in any other case. The presence of a bilateral Babinski sign during the unconscious state, and its disappearance when consciousness returned after the glucose injection, is noteworthy. The cause of the hypoglycaemia in our case is not clear. The persistently low level of the fasting blood sugar, even when the stools contained no starch, would suggest, in the absence of indications to the contrary, hyperinsulinism. The severer degree of hypoglycaemia which was associated with and, as we believe, responsible for the unconscious state, never recurred during the period of observation. It is interesting to speculate as to whether the faulty digestion of starch, or a sudden exacerbation of this condition, when superadded upon the chronic hypoglycaemia, had an etiological relationship to the production of such a low level of blood sugar (35 mg. per 100 c.cm.) as to cause hypoglycaemic unconsciousness, but this question cannot be definitely answered from the information in our possession; we are inclined to the view, however, that possibly some such relationship was operative. This explanation would not account for the usual low level of fasting blood sugar in this case (62 to 76 mg.), for this level still persisted when the stools were free of starch, but without the occurrence of hypoglycaemic

symptoms. As judged by the tests performed, the liver function was normal; however, the possibility of mild liver injury, due to the novarsenobillon injections, might be considered, but does not seem probable. The blood urea figure was somewhat high while the patient was in coma (60 mg. per 100 c.cm.), but it was normal three hours after recovery. The absorption of glucose from the gastrointestinal tract was normal, as judged by the glucose tolerance test. A puzzling feature is that the blood sugar curve, obtained after the ingestion of a mixed meal containing 50 grams of starch but no sugar, at a time when the stool was loaded with starch, did not show any great departure from what one might expect to be normal; apparently, although much starch passed through in the stool, a certain quantity was digested and absorbed. It is regrettable that further study of the starch digestion was not possible. We have no knowledge of the duration of the faulty amylaceous digestion previous to admission, and we find it difficult to appraise the significance, if any, of the transient achlorhydria. We regret that we were not able to study the case more fully, and our failure in this respect was due partly to the fact that we were not prepared to meet with a condition so unfamiliar to us, and partly to the poor co-operation of the patient, who objected to the tests and to being retained so long in hospital. We desire to record the case because it is possible that acute spontaneous hypoglycaemia may be a commoner condition than is suspected. On the other hand, although more than fourteen months have elapsed since we first saw the case, we have not seen another, even though we have been on the watch for one.

The patient was prevailed upon to return to the hospital for one day in July, 1931—that is, more than a year after her first admission. She looked well, and stated that she had had no attack of unconsciousness since we had last seen her (September, 1930), but that she had occasionally felt a little giddy, especially after eating "sweets" (meaning sugar and chocolates). Her fasting blood sugar was 62 mg. per 100 c.cm.; after the ingestion of 100 grams of soluble starch in water the blood sugar was determined every half-hour for three hours, and the figures were as follows (mg. per 100 c.cm.): 1/2 hour, 50; 1 hour, 62; 1½ hours, 67; 2 hours, 82; and 3 hours, 75. The stool contained no starch, meat fibre, or fat, but a few vegetable fibres were present. These findings tend to support the suggestion that hyperinsulinism was the cause of the chronic hypoglycaemia, and that the temporary superadded deficiency of the digestion and absorption of starch was a factor in helping to produce the acute hypoglycaemia responsible for the attack of unconsciousness which necessitated the first admission to hospital.

SUMMARY

A case of acute spontaneous hypoglycaemia with severe symptoms is described; there was also chronic hypoglycaemia, and there was associated transient achlorhydria and faulty amylaceous digestion. The severe acute symptoms were promptly relieved by the intravenous injection of 10 grams of glucose.

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THE TRANSPLANTATION OF BONE*

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The value of bone transplantation in the treatment of fractures is now so well established that it no longer needs argument to support it. As with so many other great operations, however, the development of a perfect technique has been slow, and failures have been frequent enough to prevent the operation from becoming as popular as it deserves. This paper is based on a review of the failures with which I have come in contact, and on a consideration of the errors that most often lead to bad results.

CAUSES OF FAILURE

The chief cause of failure is infection of the wound. In almost every case in which it occurs the graft becomes a sequestrum and the fracture fails to unite. In this operation, therefore, asepsis is imperative. It can be acquired only by painstaking care, constant practice, and by the team work of surgeon and assistants, but the improvement in the results makes the effort well worth while.

There are still a few who fancy that when a piece of bone is transplanted from one place in the body to another it will continue to live, as does a transplant of fascia or skin. This is an idea which must be eradicated if we are to reduce the percentage of failures. It hardly needs repetition that when a piece of bone is cut free from its circulation it dies, and must undergo complete absorption. The cells in the lacunae become necrotic at once, and within two weeks have disappeared. Only those cells live which are free on the surfaces and in the open mouths of the Haversian canals, and so are capable of utilizing a supply of lymph, if such is available. These are the cells, however, which make the bone graft so important in the treatment of non-union, and which must be humoured to the utmost if success is to be attained. Any abuse of them, such as boiling, immersion in strong antiseptics, and burning with a hot saw, must be guarded against, and any treatment of the graft that mechanically removes the periosteal and endosteal surfaces and leaves only hard compact bone, such as results from putting a graft through a dowelling machine, must be avoided. I do not suggest that an autogenous dowel is not better than a boiled bone peg or a nail, but it certainly is not nearly so valuable as if its surface cells had not been removed.

The revascularization and replacement of the dead graft are processes which are well known. Within a few days after the operation the capillaries are growing into the open Haversian canals, and masses of osteoblasts are making excavations in the dead bone. A few days later they are plastering the walls of the excavations so made with layers of new bone. As the blood vessels spread

* Read in opening a discussion in the Section of Orthopaedics at the Annual Meeting of the British Medical Association, Eastbourne, 1931.