RECURRING MENTAL CONFUSION AFTER PORTO-CAVAL ANASTOMOSIS

BY

L. J. HURWITZ, M.D., B.Sc.

AND

R. S. ALLISON, M.D., F.R.C.P., D.P.M.

(From the Department of Neurology, the Royal Victoria Hospital, Belfast)

Alterations in the level of consciousness varying from light clouding to stupor and coma have been described after the operation of porto-caval anastomosis by McDermott and Adams (1954). Their patient had been so treated because of suspected carcinoma of the head of the pancreas, and "episodic stupor" could be induced readily by feeding with various nitrogenous substances. Earlier, Gabuzda *et al.* (1952) and Philips *et al.* (1952) noted that diets rich in nitrogen reduced many of their patients with cirrhosis of the liver to a state bordering on hepatic coma, and their findings are linked with the experimental work of Baló and Korpássy (1932), who produced "meat intoxication" in dogs with Eck fistulae. The mechanism is believed by Walshe (1951) and Riddell and McDermott (1954) to involve ammonia metabolism and the utilization of glutamic acid by the brain cells.

The electroencephalographic changes in developing hepatic coma have been reviewed by Adams and Foley (1953), who believe that constant although non-specific changes occur at first. These are paroxysmal, bilateral, and synchronous theta waves at $1\frac{1}{2}$ –3 c/s on a background of normal frequencies; gradually, with increasing mental confusion, the slow activity becomes dominant.

The following case is reported for its clinical interest and because the confusional episodes occurred spontaneously. They could also be induced by high-protein feeding and relieved by the reverse procedure.

Case Report

A Merchant Navy officer aged 52 was first seen on March 13, 1954. There had been excessive indulgence in spirits since 1923, but, apart from intermittent epigastric pain, no illnesses occurred until 1943, when he had jaundice. He recovered after some weeks, but in 1944 contracted syphilis, for which he was treated energetically with neoarsphenamine, the blood Wassermann reaction becoming negative. In 1952 there was a small haematemesia, and in February, 1953, a more severe one with melaena.

He was admitted to the Royal Victoria Hospital, Belfast, under the care of Dr. Robert Marshall, the chief physical findings being a firm palpable enlargement of the liver and spleen. On March 27, 1953, Professor H. Rodgers did a laparotomy. A cirrhotic liver was found, and a portal phlebogram showed gross intrahepatic distortion. A porto-caval shunt operation was performed. The post-operative period was marked by a low-grade pyrexia and slight jaundice, but on discharge on April 29 he was feeling fairly fit and had no symptoms or signs apart from the firm palpable liver, two fingerbreadths below the costal margin.

From that date until his readmission a year later, he had at least five attacks of "confusion," of which he had a hazy recollection. He readily admitted that most of the details had been furnished by his wife. The attacks described had a similar pattern, but varied a little in their effects. The first symptoms included "shakiness in the hands," noted especially when eating, writing, or dressing himself, and blurring of vision. He would feel "stupid" and unable to concentrate, and was difficult to waken in the morning. The

most striking episode occurred in November, 1953. Late one evening, just before retiring, he wanted to pass water but could not find the lavatory. He wandered all over the house, and then eventually went to bed unrelieved. Some hours later he got up and renewed his search. This time his wife noticed his peculiar behaviour and showed him the way: but after relieving himself he found he did not know how to unlock the door. His wife eventually had to go outside and climb in through the window to let him out. The following morning he was awakened with difficulty and then proceeded to dress himself, but, in his own words: "I could not get my clothes on properly. They were either inside-out or upside-down." His wife watched, amazed at his performance and his persistence in trying to dress, but when she went to help him he resented interference, and nearly one and a half hours elapsed before he had his trousers on properly. In the other episodes he was noted to be querulous and unreasonable at times, and on one occasion he micturated on the floor of the sitting-room. The patient himself did not relate his attacks in any way to increased ingestion of food.

He was readmitted in March, 1954, to the neurological department, having been referred to us by Professor Rodgers. He was fully orientated and co-operative, and displayed no definite signs of impaired mental function on formal testing. The tendon reflexes were symmetrically increased, but the plantars were flexor. There was a fine rapid tremor of the outstretched hands. No other abnormal signs in the central nervous system were elicited. The blood pressure was 170/100 mm. Hg, and there was a precordial systolic murmur, but no diastolic murmur was heard. The breath at times had a peculiar odour, difficult to describe—like fresh meat or concentrated liquid extract of vitamin B. The liver was firmly enlarged to two fingerbreadths below the costal margin and was slightly tender. There was no evidence of ascites.

The results of recent chemical and radiological tests are compared in the Table with those of a year previously.

Investigations

	February and March, 1953 (Pre-operative)	May, 1954
Blood W.R.	Negative	Negative
Bromsulphthalein excretion	3% retention	17% retention
Plasma proteins	6.8 g.%; A/G ratio 1.8	5.8 g.%; A/G ratio 3
Thymol turbidity	4 units	1.0 unit
Serum bilirubin	0.6 mg. per 100 ml.	0.8 mg. per 100 ml.
Alkaline phosphatase	8 units K.A.	12 units K.A.
Urinary chromatogram	Slight excess in amino-aciduria of a general pattern	Slight excess in amino-aciduria of a general pattern
Blood group	AB, Rh-positive	
Haemoglobin	56%	94%
Colour index	1.0	1.0
White-cell count	7,200/c.mm. (normal differential)	6,500/cmm.
X-ray chest		No significant lesion
Barium swallow	Suggestion of oesophageal varices	No evidence of varices
Barium meal	Normal	Normal
Serum copper		228 µg. per 100 ml. (normal 99–111 µg.)
Urinary		0.230 mg. in 24 hours
Lumbar puncture		Pressure, 90 mm. C.S.F.: cells, 1; protein, 20 mg. per 100 ml.; W.R. negative
Glucose-tolerance test		Lag storage curve
Insulin-sensitivity test		Some resistance to insulin

Methods of Investigation.—The patient was given a basic diet containing 70 g. of protein daily. Additional protein was given by mouth in the form of "casilan." Electroencephalograms were taken at regular intervals and the mental state was assessed by observing the behaviour and applying simple tests for his ability to concentrate (counting forwards and backwards), to register and recall (name and address), to calculate, and to grasp simple problems (Kohs blocks) (see Fig. 1).

On a diet containing 170 g. of protein, the E.E.G. showed excess slow activity, he was unable to concentrate well, and his performance with the Kohs blocks was impaired. Within

24 hours of giving 270 g. of protein daily, both the E.E.G. and the mental state became grossly abnormal, the behaviour corresponding to that of his condition previous to admission. Thus on one occasion he wandered around the ward looking for the bathroom, and was quite indignant when told that another patient's cubicle was not the lavatory. He was observed to have considerable difficulty in dressing himself, and he complained of blurring of vision and "shaking." The fetor of the breath was striking. The tremor of the hands became more coarse with flexion and extension movements at the wrist, giving the "flapping" appearance emphasized in most reports, and recently by Sherlock *et al.* (1954). It is of interest that it was more pronounced in the right hand. He was disorientated in place and time, and was unable to draw the points of the compass, in doing which at other times he was accurate.

Examination of the cerebrospinal fluid at this stage gave normal results, the blood-sugar values being also in the normal range. The injection intravenously of 50 ml. of 50% glucose had no effect. However, as the daily protein intake was reduced so both the mental state and the E.E.G. returned to normal. Two values of the blood ammonia were taken, using the technique described by Conway (1935), and were found to be significantly raised.

Discussion

Other possible explanations for the symptoms considered in this case were neurosyphilis and hypoglycaemia, but the blood and cerebrospinal fluid were quite normal and there was no alteration in the state of the reflexes or in the pupils. Insulin sensitivity was investigated and the effect on the blood sugar of physical exertion noted, but the results were against any association with hypoglycaemia. Further, there was the convincing manner in which the symptoms and abnormal electroencephalographic findings could be reproduced by a high-protein diet. If this is the explanation, it is somewhat surprising that such quantities of protein were necessary to produce them. The patient's wife had no doubt that he did not eat comparable amounts at home, where the same symptoms were first noted. However, when the protein intake was reduced the symptoms were reversible

within 24 to 48 hours. It is possible that at home some added factor, such as alcohol or an intercurrent infection, combined to produce symptoms with a lower intake of protein, but we could not obtain any confirmation of this suggestion.

The normal pressure and the cellular and protein content of the cerebrospinal fluid at the time when confusion was maximal are in agreement with other workers (Adams and Foley, 1953). In spite of the clinical evidence of cirrhosis, except for the bromsulphthalein excretion liver-function tests were normal, so that it is likely that the presence of the shunt itself is significant in producing the disordered metabolism as suggested by Singh *et al.* (1954). The E.E.G. abnormality also proved reversible, the slow bilaterally synchronous waves giving way to a normal alpha rhythm (Fig. 2).

We would like to emphasize that we found the E.E.G. an extremely reliable and sensitive guide in predicting mental changes. Thus the most abnormal record preceded by 12 hours the development of severe confusion. The dressing dyspraxia was interesting. Experience with this case suggests that the symptom, although often a feature of parietal lobe disease (Critchley, 1953), is without localizing value and depends to some extent on a general lowering of the level of consciousness.

Summary

The case of a man aged 52 with cirrhosis of the liver is described. Following porto-caval anastomosis for portal hypertension, several episodes of mental confusion occurred which could be reproduced by high-protein feeding. Reversible E.E.G. changes were also seen giving way to a normal alpha rhythm. A high-protein diet is contraindicated in such patients.

Acknowledgments are due to Professor H. Rodgers for giving us the opportunity of investigating this patient. We thank Dr. J. H. D. Millar for the E.E.G. reports and Miss A. Coey, senior electroencephalographer, for technical assistance. We are also grateful for the advice Mr. D. Neill, of the biochemical department, gave us in planning tests and for the copper and ammonia estimations.

FIG. 1

FIG. 1.—Results of investigation. Normal electroencephalographic record before increased feeding: grade 3, 3 c/s waves, main activity; grade 2, moderate excess; grade 1, slight excess, slow activity; grade 0, normal. Mental state: grade 3, disorientated, dressing dyspraxia, etc.; grade 2, tremor, blurring of vision, drowsy; grade 1, impaired concentration; grade 0, normal.

FIG. 2.—E.E.G. recordings taken, from top to bottom, on May 27, 29, and 31, and June 2, 4, 11, and 17, 1954.

FIG. 2

ADDENDUM

We have seen another case through the courtesy of Professor G. M. Bull in which dressing dyspraxia was a prominent feature.

Case Report.—A man aged 59 was first seen in September, 1953, with oedema of the legs, ascites, and hypertension (210/120). A continuous venous hum was heard in the epigastrium (Cruveilhier-Baumgarten syndrome). A biopsy of the liver showed multiple nodular hyperplasia. He was treated with a high-protein diet and kept well until August, 1954, when his doctor reported: "Yesterday the patient became rather confused, and attempts to dress himself were unsuccessful." He was also reported to have melaena. On admission there was jaundice, and he was apathetic and disorientated. On examination there was enlargement of the liver and spleen, and ascites, and the venous hum was very marked. With treatment by low-protein diet he made a good recovery.

An annotation in the *British Medical Journal* (1954) refers to the dual role of liver damage and the effects of a porto-caval shunt in producing mental symptoms. It seems to us, however, that a third factor, not mentioned by the annotator, is important. In the first case described, alcohol and intercurrent infection, and in the second, gastrointestinal bleeding, may have played a part in precipitating the confusional episodes. One of us (Allison, 1952) has emphasized how often anoxia, dehydration, alkalaemia, the injudicious use of drugs, and electrolytic imbalance lead to psychiatric disturbances in later life. In both our cases the possible ancillary action of some such factor cannot be excluded.

REFERENCES

- Adams, R. D., and Foley, J. M. (1953), in *Metabolic and Toxic Diseases of the Nervous System*, p. 198. Ass. Research in Nervous and Mental Disease, Baltimore.
- Allison, R. S. (1952). *British Medical Journal*, 2, 1286.
- Baló, J., and Korpásky, B. (1932). *Arch. Path. (Chicago)*, 13, 80.
- British Medical Journal*, 1954, 2, 859.
- Conway, E. J. (1935). *Biochem. J.*, 29, 2755.
- Critchley, M. (1953). *The Parietal Lobes*. London.
- Gabuzda, G. J., Phillips, G. B., and Davidson, C. S. (1952). *New Engl. J. Med.*, 246, 124.
- McDermott, W. V., and Adams, R. D. (1954). *J. clin. Invest.*, 33, 1.
- Phillips, G. B., Schwartz, R., Gabuzda, G. J., and Davidson, C. S. (1952). *New Engl. J. Med.*, 247, 239.
- Riddell, A. G., and McDermott, W. V. (1954). *Lancet*, 1, 1263.
- Sherlock, S., Summerskill, W. H. J., White, L. P., and Phear, E. A. (1954). *Lancet*, 2, 453.
- Singh, I. D., Barclay, J. A., and Cooke, W. T. (1954). *Ibid.*, 1, 1004.
- Walshe, J. M. (1951). *Quart. J. Med.*, 20, 421.

MUSCULAR DYSTROPHY OCCURRING IN IDENTICAL TWINS

BY

A. G. BECKETT, B.M., M.R.C.P.

Senior Medical Registrar, Royal Free Hospital, London ;
Late Medical Registrar, Addenbrooke's Hospital,
Cambridge

Since the second half of the nineteenth century muscular dystrophy has been recognized as a hereditary disorder (Gowers, 1879 ; Erb, 1891) although there has been disagreement about the way it is inherited. Much difficulty was experienced in the classification and genetics of the many varieties described. Recently further attempts were made to introduce simpler classifications, but, owing to the variability of expression of the defective gene and the similarity of the genetic types, difficulties remain.

After studying 1,228 cases from the literature and 113 case records from the National Hospital, Queen Square, Bell (1943) divided the dystrophies into three clinical groups : group A, the pseudo-hypertrophic form characterized by the enlargement of certain muscles, wasting of others, and progressive weakness in all affected muscles ;

group B, cases with wasting and weakness of the affected muscles, no history of enlargement, and no affection of the facial muscles ; group C, all cases in which the facial muscles were affected. She considered that there were three genetic groups—recessive, dominant, and sex-linked—and that the same gene could produce any of the three clinical types. This theory was supported by Boyes *et al.* (1950), who studied the history of an English and Canadian family in which both group A and group C occurred, the family distribution indicating a simple dominant type of inheritance.

More recently Tyler and Stephens (1950, 1951) suggested making only two groups : the childhood and the facio-scapulo-humeral groups. For the first type they preferred the term "progressive muscular dystrophy of childhood" to the more usual one of "pseudo-hypertrophic muscular dystrophy," as pseudo-hypertrophy may sometimes be absent in this group and present in the second one. This illness runs a steadily progressive downhill course, terminating fatally in adolescence or young adult life. It occurs only in males and is transmitted by females, the gene being a sex-linked recessive. The facio-scapulo-humeral type is inherited as a simple dominant affecting both sexes and half the offspring with a wide variability of expression and penetration. It starts usually in young adult life and runs a very variable course. Tyler and Stephens studied a large family in Utah founded by an affected emigrant born in 1775. In six generations there have been 1,249 descendants, of whom 159 have been affected with dystrophy of the second type. A similar classification was favoured by Ramsey and McCarroll (1952).

After studying 71 cases at Massachusetts General Hospital, Brown (1951) was unable to make a rigid classification but considered that the cases fell into three main groups : group 1, cases with pseudo-hypertrophy ; group 2, cases with generalized muscular atrophy starting in the thighs ; and group 3, cases with generalized muscular atrophy starting in the scapulo-humeral muscles.

Stevenson (1953) studied all the known cases of muscular dystrophy in Northern Ireland together with their families. There were 72 cases in 51 families. He concluded that there are only two groups : (a) the pseudo-hypertrophic variety occurring in boys and transmitted as a sex-linked recessive disease. For this he suggested the clumsy but more accurate title, "Duchenne type rapidly progressive muscular dystrophy of young boys" ; (b) the second group consists of all the other types which he believed to be variants of the same condition determined by single autosomal recessive gene inheritance. For this group he suggested the term "autosomal limb-girdle muscular dystrophy."

The occurrence of a disease in twins is helpful in studying its heredity. Few twins, however, have been affected with muscular dystrophy, and so far there has been no report of the variety without hypertrophy occurring in identical twins. Stephens and Tyler (1951) described male identical twins who had the pseudo-hypertrophic form. The disease ran an identical course in each, being first recognized at the age of 6 years, causing complete incapacity at 11 years, and death, within a few months of each other, at the age of 25. No other member of this family was affected. The occurrence of progressive muscular dystrophy (without hypertrophy) in a male twin but not in the corresponding female has been reported by Milhorat and Wolff (1943) and Karnosh and LaTona (1947).