CAROTID SINUS EPILEPSY AND ITS TREATMENT BY DENERVATION*

BY

SIMON BEHRMAN, M.R.C.P.

AND

GEOFFREY KNIGHT, F.R.C.S.

*From the Regional Neurosurgical Centre, South-East
Metropolitan Regional Hospital Board, Brook General
Hospital, London*

Unilateral digital compression of the carotid bifurcation can cause immediate loss of consciousness in a few individuals. These cases fall into four main groups: (1) Those in which, because of pre-existing occlusion by disease of the contralateral internal carotid artery, compression causes cerebral anaemia. This effect cannot, of course, be abolished by procainization of the carotid sinus. All cases of unconsciousness following carotid compression were, until Hering's discovery of carotid sinus reflex in 1927, regarded as caused by cerebral anaemia (Roseman *et al.*, 1945; Webster *et al.*, 1955). (2) Those associated with a marked slowing of ventricular rate. (3) Those associated with a significant fall in blood pressure. (4) This is the least common group, and the main concern of the present communication. Loss of consciousness is not attended by bradycardia or a fall in blood pressure, and occurs in the absence of carotid artery occlusion.

A number of patients in group 4 were studied by measuring the flow of blood through the internal jugular vein (by means of a Gibbs thermoelectric recorder), and by measuring at the same time the oxygen content of the blood leaving the brain. From a comparison of the data obtained during states of consciousness and unconsciousness, neither Ferris *et al.* (1935) nor Lennox *et al.* (1935) could detect any significant change in cerebral blood flow in the induced attacks. Lennox *et al.* concluded that "the fact that pressure on carotid sinus in certain persons will bring unconsciousness without preliminary cerebral anaemia points to the existence in man of a non-circulatory, probably neural mechanism by which unconsciousness can be produced."

This syndrome is very uncommon, though among 1,000 epileptic subjects Robinson (1939a) discovered two such cases. An analysis of the case histories of patients whose cerebral blood flow had been measured, as mentioned above, indicates that spontaneous or induced attacks may be preceded by an aura usually described as "dizziness," or consciousness may be lost without any warning. A few patients may have unilateral or generalized convulsions during the period of unconsciousness. The following case presented similar features.

Case Report

About 1952 a man aged 47 had five "black-outs" in fairly close succession, each one preceded by a momentary spinning sensation and followed by severe headache. In September, 1954, he started a series of "black-outs," and these also were preceded by a momentary "whirlpool" sensation. Attacks were occasionally provoked by rotating the chin to the left with the head in the position of extension, as when reclining in an easy chair. The period of un-

consciousness was usually of a few minutes' duration and there were no convulsive movements. He sometimes remained seated with eyes staring, but more usually he fell down. On two occasions he had an attack while cycling. During the attacks which were observed he remained flaccid without any detectable change in pulse or breathing. Immediately on regaining consciousness he complained of intense headache, and as a rule passed into a deep sleep.

Compression in the region of the right carotid bifurcation provoked within 15-30 seconds the familiar "whirlpool" sensation usually preceding his attacks of unconsciousness. There was no associated change in pulse rate or blood pressure. Pressure in the region of the left carotid bifurcation, as also pressure on either of the common carotid arteries, gave rise to no abnormal symptoms. The electroencephalogram showed generalized paroxysmal theta dysrhythmia on hyperventilation.

Since denervation of the right carotid sinus on November 30, 1954, he has remained free from black-outs, and it is no longer possible to induce vertigo by pressure in the region of the right carotid sinus.

Electroencephalographic Changes

The E.E.G. changes during unconsciousness have been the subject of several studies, which comprised a total of 16 cases. Two main types of E.E.G. changes have been described. Romano *et al.* (1940) and Forster *et al.* (1942) noted a varying degree of fast beta activity during the period of unconsciousness. In some cases the slight shift in energy to the fast side could be established only by a comparison of interictal and ictal cortical spectrums. Forster *et al.* stated that "the acceleration is sufficient in some cases to be comparable to that which occurs at the outset of a grand mal epileptic seizure." This led them to conclude that these cases represented "a special type of trigger zone epilepsy with only slight evidence of cortical involvement."

The second type of E.E.G. change is characterized by the appearance of slow waves, 3-6 per second, of moderate or high voltage during unconsciousness (Engel *et al.*, 1944). Even the nosographic purist is unlikely to cavil at the epileptic label being attached to a syndrome comprising a state of unconsciousness which can be induced rapidly without a demonstrable change in the cerebral blood flow, and associated with the appearance of a delta rhythm. The term "carotid sinus epilepsy" therefore seems to be justified in at least some cases. It may even be applied to some cases in which Stokes-Adams syndrome can be induced by carotid sinus stimulation. A case reported by Rabwin and Merliss (1950) illustrates this. The patient was a man aged 51 in whom asystole and generalized epileptic convulsions associated with typical grand mal E.E.G. discharge could be induced by stimulation of the left carotid sinus. However, asystole could be entirely abolished by preliminary intravenous injection of atropine without affecting the epileptic phenomena. On the other hand, lowering the blood pressure by 50 mm. Hg by inhalation of amyl nitrite failed to provoke conclusions.

Glossopharyngeal Neuralgia

Since 1932 a number of cases of Stokes-Adams syndrome provoked by paroxysms of neuralgia, occurring spontaneously or induced by appropriate peripheral stimulation, have been reported. It must be regarded as significant that, with but one doubtful exception, the neuralgia has always been of the glossopharyngeal type—the one exception being a case of superior laryngeal neuralgia, also perhaps a variant of the larger group of glossopharyngeal-vagal neuralgias (Flaum and Klima, 1932). Some of the published case records also indicate that carotid sinus stimulation was ineffective, and that Stokes-Adams syndrome could be abolished by atropine or by division of the glossopharyngeal nerve (Ray and Stewart, 1948; Richburg and Kern, 1953). Without entering into a discussion on how the Stokes-Adams syndrome is

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induced in these cases of glossopharyngeal neuralgia, it can be reasonably inferred that the fibres of the carotid sinus nerve, conveyed by the glossopharyngeal nerve, are implicated in some way. Several explanations suggest themselves, but need not be considered here.

If the suggested involvement of the fibres of the carotid sinus nerve is accepted, and the Stokes-Adams syndrome in these cases is regarded as being due to abnormal activity of these fibres or their ganglionic connexions, however engendered, the following rare cases assume some added significance. Wilfred Harris (1926) described a case of glossopharyngeal neuralgia in which paroxysms were repeatedly followed immediately by epileptic seizures. He mentioned that the patient had been subjected to trephining on this account. An exactly similar case was reported by Thomson (1954). His patient had repeated generalized epileptic seizures lasting 10 to 15 seconds immediately following paroxysms of neuralgia. During the fits there was no significant fall in pulse rate or blood pressure. Pain and convulsions ceased after section of the left glossopharyngeal and upper two filaments of the vagus nerve.

It would appear that glossopharyngeal neuralgia, like hyperactive carotid sinus, can be associated with Stokes-Adams syndrome or with epilepsy, the latter without any demonstrable circulatory changes. The more common cardio-inhibitory reaction can therefore very occasionally be replaced by epilepsy. A few other examples of an epileptic reaction taking the place of the more usual vagotonic response are mentioned briefly.

Oculo-Cardiac Reflex

Moderate pressure on the eyeballs causes slowing of the heart which occasionally is of a degree to cause syncope. Balabane (1935) described two such cases in which the pulse rate fell to approximately 20. Robinson (1939b) has, however, induced epileptic attacks in an epileptic subject by ocular pressure of 12 seconds' duration without detectable alteration in blood pressure or pulse rate.

Deglutition

Weiss and Ferris (1934) described two cases in which transient heart-block occurred during swallowing. Their first case is particularly interesting, since Stokes-Adams attacks could be induced by inflating a balloon placed in the oesophagus, and the case was submitted to a detailed study. The case history is given as follows. "A man aged 64 was admitted to hospital in a stuporous state following attempted suicide with illuminating gas. The cause of this act was dependency because of fainting spells believed to be incurable, from which he had suffered for ten years. The attacks manifested themselves in sudden dizziness or fainting lasting a minute or two and were usually precipitated by swallowing food, particularly sticky food. Sometimes only a sip of water caused an attack. The dizziness and fainting were associated with pains along the lower portion of the sternum, descending towards the stomach." Procaine block of either vagus nerve in the neck abolished repeatedly the transient complete heart-block on inflating the balloon. The authors invoke the result of this experiment as proof of the reflex nature of the syndrome.

In the following case consciousness was lost under identical circumstances, but instantly, and without clinically demonstrable circulatory changes.

The patient was a man aged 41 who for the past five years occasionally, when swallowing, had "a choking feeling as though something squeezing through something small." This sensation, first felt in the region of the manubrium, travelled slowly downwards to the xiphoid process. The total duration of these attacks, in which he often remained conscious, was about half a minute. Recurring, transient, simple, non-sphincteric spasm of the oesophagus (McGibbon and Mather, 1937) is the best

explanation for these attacks, in some of which he lost consciousness completely and abruptly, without any warning, for a fraction of a minute. He had fallen on a few occasions, but usually remained seated with eyes fixed into space. He had no convulsions. His wife reported that there was no appreciable change of colour of his face or of pulse rate in these attacks. Carotid sinus stimulation was ineffective. Barium swallow showed no abnormality. He had no other attacks of unconsciousness.

In the light of these observations it appears justifiable to view carotid sinus epilepsy as one example of a wider pathological phenomenon, whereby the stimulation of certain receptors which ordinarily give rise to cardio-inhibitory reaction may instead engender epileptic activity. Sometimes epilepsy and cardio-inhibitory response occur together, and their coexistence can be recognized only by the use of atropine. According to this interpretation, carotid sinus epilepsy is one form of sensorily precipitated epilepsy. Though the provocation of fits at will by stimulation of the appropriate receptors is the cardinal feature of the latter group of epilepsy, many factors determine whether at any given moment stimulation will be effective or not: element of surprise, repetition, and the emotional state of the subject at the time of the experiment (Behrman, 1955).

Focal Phenomena

Focal epileptic phenomena are mentioned in the histories of several well-documented cases of carotid sinus epilepsy, and one of the two cases of Engel *et al.* (1944) might be cited here. When the patient was either recumbent or erect, massage of the left carotid sinus resulted within 15 seconds in the following progression of symptoms: burning, numbness, and tingling of the right side of the face, right arm, and right leg; clonic jerks of the right arm; and a sense of fullness and buzzing in the head. Simultaneously in the E.E.G. high-voltage, irregular slow waves (2 to 5 per second) appeared in the fronto-occipital lead from the cortex on the left side. The patient, who was a physician, had for 20 years been subject to similar attacks on turning his head to the right. Occlusion of the left carotid artery for 20-30 seconds gave rise to neither symptoms nor E.E.G. changes.

Vertigo was the aura in the case we have presented, and it was also a feature of a case fully described by Turner and Learmonth (1948). For 12 years spontaneous attacks occurred when turning in bed and at other times, and consisted of a sensation of falling to one or other side. Light pressure over either carotid sinus produced immediate cardiac asystole and symptoms he had experienced in the spontaneous attacks. Following bilateral denervation of the carotid sinus the attacks ceased during the one year's follow-up. Smith (1947), reviewing the Mayo Clinic material of 85 cases of hyperactive carotid sinus, mentions that "vertigo was a prominent feature." Vertigo in some of the cases mentioned might be regarded as another focal epileptic manifestation, and the regional differences in seizure susceptibility described by French *et al.* (1956) in the monkey cortex might provide an explanation.

Summary

In a few individuals a state of unconsciousness can be induced rapidly by stimulation of an overactive carotid sinus. During the period of unconsciousness there is no demonstrable change in cerebral blood flow, and a transient delta rhythm may make its appearance. After carotid sinus denervation this response is no longer obtainable.

It is concluded that this evidence points to an epileptic causation of unconsciousness, and that the syndrome should be classed with sensorily precipitated epilepsy.

A case of carotid sinus epilepsy relieved by denervation is described.

It is concluded that carotid sinus epilepsy is one example of a wider pathological phenomenon whereby the stimulation of certain receptors which ordinarily give rise to cardio-inhibitory reaction may instead engender epileptic activity.

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TREATMENT OF ACUTE HAEMORRHAGIC PANCREATITIS WITH CORTISONE

BY

J. G. BROCKIS, Ch.M., F.R.C.S.
Senior Registrar

AND

E. T. JONES, B.Sc., M.B., B.Ch.
House-Surgeon

Cardiff Royal Infirmary

Amongst surgical emergencies, acute haemorrhagic pancreatitis remains therapeutically one of the most difficult. The mortality from this condition, including the many mild cases, is still in the region of 33% (Paxton and Payne, 1948). It is now generally agreed that, when a correct diagnosis can be made, it is better to avoid operation in the acute phase of the illness and to institute measures to combat dehydration and circulatory failure. These take the form of correction of protein, fluid, and electrolyte imbalance by transfusion. Gastric suction is also necessary when there is paralytic ileus. Analgesics are given to relieve the intense pain, together with antibiotics to combat infection and propantheline to diminish the amount of pancreatic secretion (Comfort, 1955). In spite of these measures a number of patients (about 11% according to Paxton and Payne) pass into a state of peripheral circulatory failure from which they do not recover.

With this in mind it was decided to try the effect of cortisone in preventing or treating this circulatory collapse. Only one case so treated appears to have been reported previously (Eskwith *et al.*, 1955), and the authors considered their result sufficiently striking to justify further trials. The following two cases are recorded as it seems that this method of combating the severe effects of haemorrhagic pancreatitis is promising.

Case 1

A married woman aged 64 was admitted to Cardiff Royal Infirmary on September 14, 1955, having seven days previously experienced severe mid-abdominal pain and vomiting. Two hours before her admission a particularly severe attack of upper abdominal pain occurred which was constant and did not radiate. She felt faint and lost consciousness for a short period. During the previous five years there had been at least five attacks of abdominal pain, each coming on suddenly with retching and vomiting; none was associated with jaundice.

The patient was found to be an obese woman, cold, clammy, and slightly cyanosed, and retching continuously. Pulse rate, 120 per minute; blood pressure, 230/130 mm. Hg. Tongue dry and coated. Lung fields clear and heart normal. There was gross abdominal distension, with maximal tenderness in the left hypochondrium. Both flanks were dull to percussion. Urine contained sugar, acetone bodies, and a trace of albumin. Serum amylase, 1,600+ Sömogyi units per 100 ml. A diagnosis of acute haemorrhagic pancreatitis was made.

She was immediately given pethidine, 100 mg., and atropine, 0.65 mg., followed by intravenous transfusion of plasma and normal saline containing aureomycin. By the following morning she was very much worse and desperately ill. Blood pressure had dropped to 100/70 mm.; pulse rate was 140, and respiration rate was 40 per minute. Cortisone, 150 mg. twice daily for three days, was prescribed, together with propantheline, 15 mg. twice daily. Intravenous administration of fluids containing aureomycin was continued. Staining in the left flank and around the umbilicus was then noted, and this persisted for three days. On September 16 there was some improvement, the pulse rate having fallen to 120 per minute, though the blood pressure was still low—140/70 mm. The treatment outlined above was continued. At this stage the serum electrolyte values were: Na 130, K 8.2, Cl 95 mEq per litre. Blood sugar, 130 mg. per 100 ml. The raised serum potassium level caused some anxiety, but, as the patient appeared to be better, no treatment for this was instituted. There was further improvement by the 17th, the pulse rate having fallen to 100 per minute, but a tinge of cyanosis still remained about the lips and the respiratory rate was

FIG. 1.—Case 1: Showing the dosage of cortisone and the effect on the course of the illness.

30 per minute. Both lung bases showed signs of congestion. Intravenous transfusion of fluids was discontinued, as water could now be taken by mouth. Progress was maintained on September 19 and the cortisone dosage was reduced. The propantheline was stopped altogether owing to severe dryness of the mouth. At this stage the serum electrolytes were: Na 135, K 7.2, Cl 101 mEq per litre. On September 21 the dose of cortisone was reduced to