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CEREBRAL BLOOD FLOW IN PARAPLEGIA

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INTRODUCTION

PATIENTS with spinal cord transection above T6 segment are prone to suffer from symptoms of orthostatic hypotension (OH) (Guttmann, 1953; Guttmann, Munro, Robinson & Walsh, 1963). Symptoms are worse in the first few weeks after injury, but after the initial period of mobilisation these patients are able to sit without symptoms for as long as they wish to do so. This suggests that a number of adaptive mechanisms may have been called into play. One possibility is the development of reflex control of blood pressure at a spinal level as shown in animal experiments (Beacham & Kunze, 1969; Andrews, Andrews & Orbach, 1971), and in spinal man (Guttmann & Whitteridge, 1947; Gilliatt, 1948; Gilliatt, Guttmann & Whitteridge, 1948; Corbett, Frankel & Harris, 1971*a*, *b*). Another possibility is that there may be a return of vascular tone (Sharpey-Schafer, 1961) which might be due to an increase in absolute levels of, or of sensitivity to, circulating humoral agents (Johnson, Park & Frankel, 1971; Johnson & Park, 1973; Debarge, Christensen, Corbett, Eidelman, Frankel & Mathias, 1974). A further explanation of why patients with high paraplegia do not have symptoms of OH is that their interruption of sympathetic pathways does not interfere with the ability of cerebral blood vessels to maintain adequate blood flow even though blood pressure may fluctuate widely.

NORMAL CONTROL OF CEREBRAL BLOOD FLOW (CBF)

Cerebral blood vessels maintain a constant blood flow despite moderate changes in blood pressure. This autoregulation maintaining constant tissue perfusion has been thought to be due to intrinsic myogenic and metabolic factors (pH and pCO_2, etc.) (reviewed by Lassen, 1974). More recently a 'neurogenic' hypothesis has been advanced suggesting that the autonomic innervation of cerebral blood vessels (Dahl, 1973) has an important role in maintaining normal CBF during blood pressure changes (James, Millar & Purves, 1969; Ponte & Purves, 1974). Harper (1974), however, has suggested that it is *only* the extra-parenchymal cerebral blood vessels that are influenced by the autonomic nervous system and that the intracerebral vessels are under metabolic and myogenic control.

MEASUREMENT OF CEREBRAL BLOOD FLOW

CBF has been measured using a modification of Veall's Xenon 133 inhalation technique (Mallett & Veall, 1966). A mixture containing air and xenon at a

specific activity of 1 mCi./litre was breathed in a closed loop system for two minutes. After a further 30 seconds, during which time the arterial concentration of xenon falls rapidly, the clearance from the head was monitored using a gamma camera. Thirty-two consecutive scintiphotos, each of four seconds' duration allowed the clearance rate of xenon from the head to be computed for each region within a 16×16 matrix. A fraction of the expired air was pumped through a Capnograph for carbon dioxide analysis and subsequently through a well-type scintillation counter in which the end-expired air concentration of xenon was recorded. This is proportional to the arterial concentration and it enables the clearance rate of xenon from the head to be converted into blood flow in ml./100 g./min. The method has been described in detail by Wyper and Rowan (1974). The patients were studied in the supine position initially. Blood pressure was measured at one-minute intervals using a sphygmomanometer. When a steady blood pressure reading was obtained on at least three measurements CBF was measured. During this procedure blood pressure was monitored as before. After an interval of five minutes the subject was sat in a chair to effect a fall of blood pressure. The CBF measurement was again made when a steady blood pressure had been achieved. Care was taken to avoid a fall of systolic blood pressure below 70 mm. Hg. by straightening the legs at the knees if necessary. Next, the response to hyperventilation was studied at least 10 minutes after the patient had returned to the supine position. The subjects were asked to maintain the end tidal pCO_2 below 21 mm. Hg by altering their ventilation as necessary. Hyperventilation continued for five minutes and cerebral blood flow was measured during the last two minutes.

The reproducibility of CBF measurements by the technique used in these investigations has been estimated by studying the repeatability of results obtained in 16 normal subjects aged 20 to 50 years. A change of 7 ml./100 g./min. between any two CBF results on the same subject was significant at $P = 0{\cdot}05$. The mean value obtained from these subjects during normocapnia was 47·25 ml./100 g./min., which agrees closely with results from the intracarotid injection xenon method (Høedt-Rasmussen, Sveinsdottir & Lassen, 1966; Wilkinson, 1972; Fieschi & Bozzao, 1972).

CEREBRAL BLOOD FLOW IN PATIENTS WITH IDIOPATHIC ORTHOSTATIC HYPOTENSION (IOH)

An opportunity to investigate CBF during change in blood pressure is provided by patients who have poor control of blood pressure. This occurs in patients who have IOH which develops due to a failure of part of the nervous arc involved in baroreceptor reflexes. The reflex depends upon the activity of carotid arch and aortic arch baroreceptors which are innervated respectively by the glossopharyngeal and vagus nerves. The reflex passes through the brain stem and efferent pathways lie in the spinal cord and peripheral sympathetic nerves. We have studied CBF in seven patients with IOH. Five patients had evidence of a block of the baroreceptor reflex on the afferent side. Evidence included orthostatic hypotension with a fixed heart rate, and a blocked Valsalva response with normal sweating and a normal vagal response to intravenous atropine. Two patients had a block of the baroreceptor reflex on the efferent side, probably in postganglionic sympathetic nerves as evidenced by absent sweating,

both thermal and chemical, absence of a 'renin-response' to orthostatic hypotension (Love, Brown, Chinn, Johnson, Lever, Park & Robertson, 1971) and absent vagal response to injection of atropine. CBF was measured in the supine position first and then with the patient in a sitting position. The change of posture caused a significant fall of blood pressure. Nevertheless, CBF was unchanged in the two positions and we concluded that patients with IOH had normal cerebral autoregulation to a fall of blood pressure (fig. 1). Contrary views have been expressed: Gotoh, Ebihara, Toyoda and Shinohara (1971-72) and Meyer, Kunio, Fukunchi, Ohuchi, Okamoto, Koto and Ericsson (1973) have reported several patients with IOH in whom CBF autoregulation was impaired. However, the reductions in blood pressure effected in some of these patients may have been to a level below

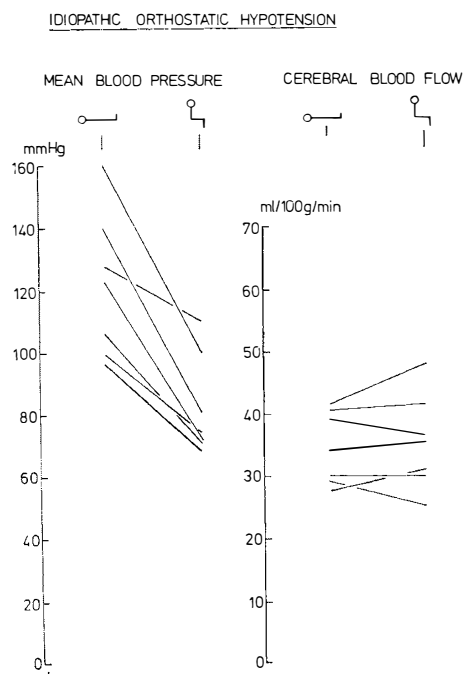

FIG. 1

Mean blood pressure and cerebral blood flow (ml./100g/min.) in seven patients with idiopathic orthostatic hypotension in the supine and sitting positions. No significant change in cerebral blood flow occurred with the fall of blood pressure.

that at which the cerebral vessels can normally compensate (60-70 mm. Hg) (Harper, 1974). Skinhøj, Olesen and Strandgaard (1971) reported one patient with IOH with normal CBF autoregulation and response to change in arterial carbon dioxide ($PaCO_2$); Caronna and Plum (1973) studied four patients with IOH. Three of them with preganglionic lesions had intact autoregulation and response to hypocapnia. The fourth patient with postganglionic denervation had impaired CBF autoregulation but an intact response to $PaCO_2$ changes. Part of the problem exemplified by the last patient reported by Caronna and Plum (1973) is that there cannot be a definite statement of the level of autonomic lesion in patients with lesions due to progressive disease. One group in which the site of lesion is clearly understood is that comprising patients with traumatic paraplegia affecting the cervical spine. These patients have a definite preganglionic sympathetic lesion.

CEREBRAL BLOOD FLOW IN SPINAL CORD TRANSECTION

Our subjects have included six male and one female, aged 25-39 years. They had suffered trauma to the spinal cord 5-12 years previously. Apart from one subject who had a T2-3 lesion and one who had an incomplete C4-5 lesion, all had physiologically complete lesions at C5-7 spinal segments. All subjects had indwelling bladder catheters on free drainage. CBF was measured in the supine position, sitting in a wheelchair and during hyperventilation in the supine position. Before and during a CBF study, blood pressure and pulse rate were measured at one-minute intervals.

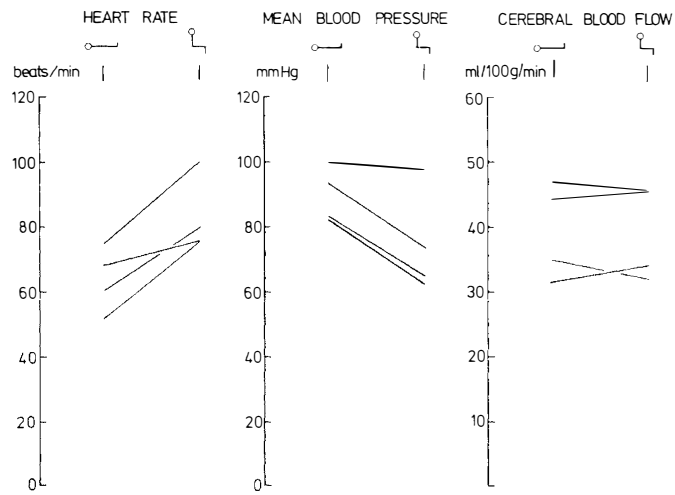

FIG. 2

Heart rate, mean blood pressure and cerebral blood flow (ml./100 g./min.) in four patients with complete cervical spinal cord transection in the supine and sitting positions. No change in cerebral blood flow occurred with the fall of blood pressure.

The four patients in whom the blood pressure fell in the sitting position showed normal autoregulation of cerebral blood flow (fig. 2). In one subject with a complete C5-6 lesion, blood pressure was raised by elevating the legs. This too was compensated in the cerebral circulation by normal cerebral blood flow autoregulation (fig. 3). Six subjects who hyperventilated satisfactorily to produce a significant fall in end-tidal carbon dioxide concentration showed a decrease of cerebral blood flow. This was similar to the cerebral blood flow response to hyperventilation examined in ten normal control subjects (fig. 4).

Eidelman, Corbett, Debarge and Frankel (1972) reported an absence of cerebral vasoconstriction with hyperventilation in tetraplegic man. Hoff, Sengupta, Harper and Jennett (1972) failed to substantiate in baboons the observations previously reported in man by Eidelman *et al.*, and we think that the results of Eidelman *et al.* are possibly erroneous due to the limitations of their CBF measuring technique.

Our observations in chronic paraplegia suggest that CBF autoregulation is

complete to posturally induced hypo- and hypertension. Further, the cerebral vasoconstriction in response to hypocapnia is not mediated by the cervical sympathetic outflow. It is possible that these responses of CBF are not present in the acute phase of traumatic paraplegia and that they develop at a later stage. Our

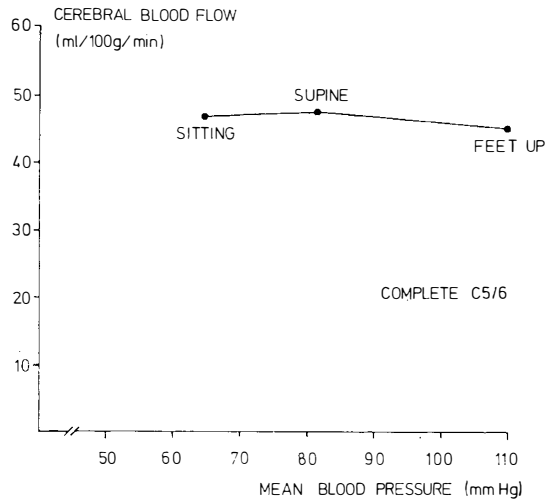

FIG. 3

Cerebral blood flow (ml./100 g./min.) in one patient with a complete spinal cord transection (C5-6 level) in the supine, sitting and feet up positions. Cerebral blood flow remained constant in spite of the changes in blood pressure.

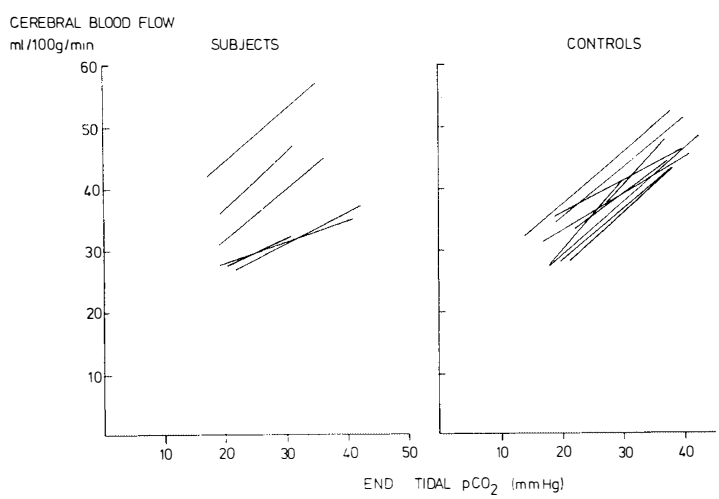

FIG. 4

Cerebral blood flow (ml./100 g./min.) and end tidal pCO_2 during hyperventilation in seven subjects with paraplegia and ten normal controls. There was no significant difference between the two groups.

observations imply that one reason patients with chronic paraplegia are able to change their posture without developing dizziness and fainting as signs of cerebrovascular insufficiency is that they have unimpaired autoregulation of their cerebral blood flow.

SUMMARY

Cerebral blood flow has been measured by a Xenon 133 inhalation technique in patients with chronic high spinal cord injuries and neurological disorders affecting the sympathetic pathways supplying intracranial vessels. These included patients with idiopathic orthostatic hypotension and also patients with a physiologically complete cervical cord transection. Cerebral blood flow and arterial blood pressure were measured in the supine position and then in the sitting position. Patients in whom the mean blood pressure fell in the sitting position to 70 mm. Hg had no change in cerebral blood flow during the period of hypotension. In all subjects the response of cerebral blood flow to hyperventilation for five minutes was measured in the supine position and compared with that in normal 'control' subjects.

Hyperventilation resulted in the same decrease of cerebral blood flow in the controls as in the subjects with paraplegia or other neurological disorders. It is concluded that the responses of the cerebral circulation to hypotension and to hypocapnia were normal in all patients studied, including those with high spinal cord transection. The mechanisms involved in these responses are therefore independent of control via sympathetic pathways.

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