RAISED INTRACRANIAL PRESSURE IN EMPHYSEMA

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The cerebrospinal-fluid pressure is usually normal in emphysema, but during intercurrent acute respiratory infections symptoms and signs of raised intracranial pressure—headache, blurred vision, papilloedema—not infrequently develop (Simpson, 1948). The observations recorded in this paper throw light on the aetiology of the raised intracranial pressure found in these circumstances. The relationship of intracranial hypertension to mental disturbance occurring during oxygen therapy is discussed.

Experimental Subjects and Method

Lumbar puncture was performed in a series of 12 emphysematous patients (including 3 with papilloedema) suffering from an acute respiratory infection: in 8 immediately following admission to hospital, and in 4 after 4 to 80 hours of oxygen therapy in a tent. In these four patients relief of anoxia was maintained during lumbar puncture by inhalation of 100% oxygen via a B.L.B. mask. In view of the observations of Friedfeld and Fishberg (1934) and Pickering (1934) of the effect of increased jugular venous pressure and severe hypertension in causing raised intracranial pressure, none of the patients studied had either of these complications. The C.S.F. pressure was measured in the horizontal position with a glass manometer (internal bore 2 mm.) calibrated up to 700 mm. The effect of muscular tension and apprehension was eliminated so far as possible by recording pressures at intervals of 30 seconds for 10–30 minutes until a stable basal level was obtained. It was found that when the C.S.F. pressure was within normal limits fluctuations were seldom greater than 20–25 mm. (Fig. 1), but when it was elevated spontaneous fluctuations of much greater magnitude could occur, and a true estimate of the basal pressure might be obtained only after 30 minutes' recording (Fig. 3). Blood was obtained for measurement of oxygen saturation and carbon dioxide content by arterial puncture immediately before lumbar puncture.

Raised Intracranial Pressure in Emphysematous Subjects with Acute Respiratory Infections

Case	C.S.F. Pressure	Arterial O_2 Saturation (%)	Plasma CO_2 Vols.%	Inspired Gas	Comment
1	500–600	40	91	Air	Papilloedema present on admission
	160	83	78	,,	On recovery 15 days later
2	420–460	—	75·1	,,	Deeply cyanosed and disorientated
	160–180	72	75·4	,,	On recovery 12 days later
3	300	52	72	,,	Disorientated and restless
4	360	67·4	79·3	,,	On admission
5	320–360	68·4	95·8	,,	,, ,,
6	270–300	—	—	,,	Bilateral papilloedema;
	420–440	—	—	,,	B.P. 160/100; J.V.P. +6 cm. on admission
	220–260	89	83	Air	27 days after admission
7	280	—	85·5	,,	Moderate cyanosis
8	165–190	69·7	56·2	,,	Plasma CO_2 63 vols. on recovery
9	285–305	94	100	O_2	L.P. after 80 hours' O_2 therapy
	150–160	92·6	64	Air	On recovery
10	300	100	102·5	O_2	Papilloedema present
11	250	94·8	84·3	,,	L.P. after 16 hours' O_2
12	170–200	—	91·5	,,	,, ,, 4 ,, ,,

Details of the C.S.F. pressure, arterial oxygen saturation, and arterial plasma carbon dioxide content are recorded in the Table. In 10 of the 12 subjects C.S.F. pressures above the normal upper limit of 200 mm. were observed, with pressures of over 350 mm. in five. Arterial anoxaemia was present in all cases (O_2 saturation 40–89%) and hypercapnia (plasma carbon dioxide content>66 vols.%) in all except one.

Effect of Anoxia and Hypercapnia on C.S.F. Pressure

The exclusion of patients with raised venous pressure and hypertension narrowed the possible causes of raised intracranial pressure. The almost invariable presence of anoxia, hypercapnia, and dyspnoea suggested that a study of the effects on C.S.F. pressure of breathing pure oxygen, low oxygen and high carbon dioxide mixtures, and of hyperventilation might prove fruitful.

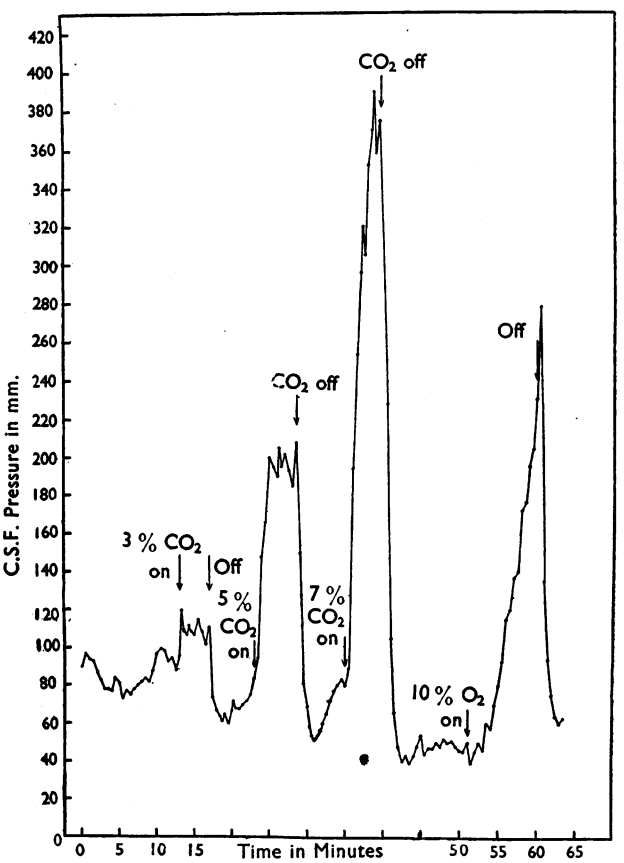

FIG. 1.—Effect of breathing high CO_2 and low oxygen mixtures on C.S.F. pressure in a patient with syphilitic aortitis.

Fig. 1 illustrates the effect of breathing various gas mixtures in a 49-year-old patient with syphilitic aortitis. With 3, 5, and 7% carbon dioxide in oxygen inhaled for five to seven minutes the C.S.F. pressure rose by 27, 133, and 310 mm. respectively. With 10% oxygen in nitrogen the inhalation was terminated before the pressure had finished rising, as the patient became deeply cyanosed and complained of severe headache. Voluntary hyperventilation will consistently produce a fall of 30–50 mm. in C.S.F. pressure (presumably due to washing out carbon dioxide), and if muscular movement has any effect in raising the pressure it is completely outweighed by the effect of hypocapnia and alkalosis. The combined results of inhalation of various combinations of

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carbon dioxide in 29 subjects is presented in Fig. 2. The scatter of individual observations is considerable, especially with the higher concentrations of carbon dioxide. For 3, 5, and 7% CO_2 the mean increases in pressure were 50, 130, and 280 mm. There was no correlation between the magnitude of the rise in C.S.F. pressure on inhaling carbon dioxide

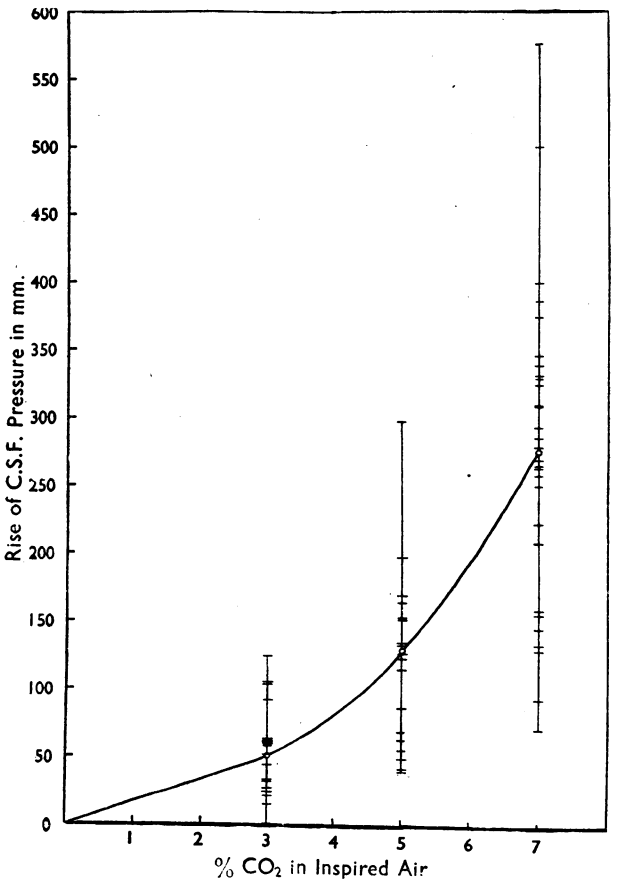

FIG. 2.—Increase in C.S.F. pressure breathing 3, 5, and 7% CO_2 in 29 emphysematous subjects.

and the respiratory response to the same concentration. For example, Case 1, whose ventilation increased by only 4 litres per minute with 7% CO_2, showed an increase of 500 mm. in C.S.F. pressure.

These observations demonstrate that both oxygen lack (low pO_2) and carbon dioxide excess (high pCO_2 and increased H-ion concentration) cause an increase in C.S.F. pressure, and the magnitude of their effect is enough to account for the considerable elevation in intracranial pressure observed in emphysematous subjects during respiratory infections.

Effect of Oxygen on the C.S.F. Pressure in Emphysema

In 10 experiments on normal subjects we have found that inhalation of pure oxygen for 10–15 minutes has no significant effect on the C.S.F. pressure. Davies and Mackinnon (1949) observed that inhalation of oxygen in cases of cor pulmonale with congestive failure caused an immediate and striking increase in C.S.F. pressure. Studies on Case 6 have confirmed their observation and provide an adequate explanation for this phenomenon.

This patient was admitted to hospital in October, 1950, with acute bronchitis. He had been dyspnoeic on exertion for four years and had suffered from severe throbbing headaches for the preceding 18 months. He was found to have advanced emphysema, cor pulmonale with early congestive failure, and bilateral papilloedema with retinal haemorrhages. The blood pressure was 160/100 and the maximum breathing capacity fluctuated between 16 and 30 litres a minute. On the second day after admission the C.S.F. pressure was 270–300 mm. and on the 18th day 420–440 mm. On the 27th day, when the signs of congestive failure had disappeared, the basal C.S.F. pressure breathing air was 220–260 mm. (Fig. 3). The minute-volume of ventilation was 8.03 litres (rate 21×tidal air 382 ml.), the arterial oxygen saturation 89%, and the plasma carbon dioxide content 83 vols.% (normal level 60 vols.). At the 30th minute pure oxygen was administered via a rubber mouth-tube, and over the next 30 minutes a dramatic rise in C.S.F. pressure occurred, reaching a peak of 670 mm. The respiratory minute volume recorded over the last 5 minutes of oxygen inhalation had fallen by 30% to 5.77 litres (rate 20×tidal air 288 ml.), the plasma carbon dioxide content had increased by 9 vols. to 92 vols., and the oxygen saturation had risen to 100%. At this point the patient felt drowsy but did not complain of headache. When inhalation of oxygen was discontinued, C.S.F. pressure fell rapidly and the respiratory minute volume rose to its pre-inhalation level of 8.11 litres

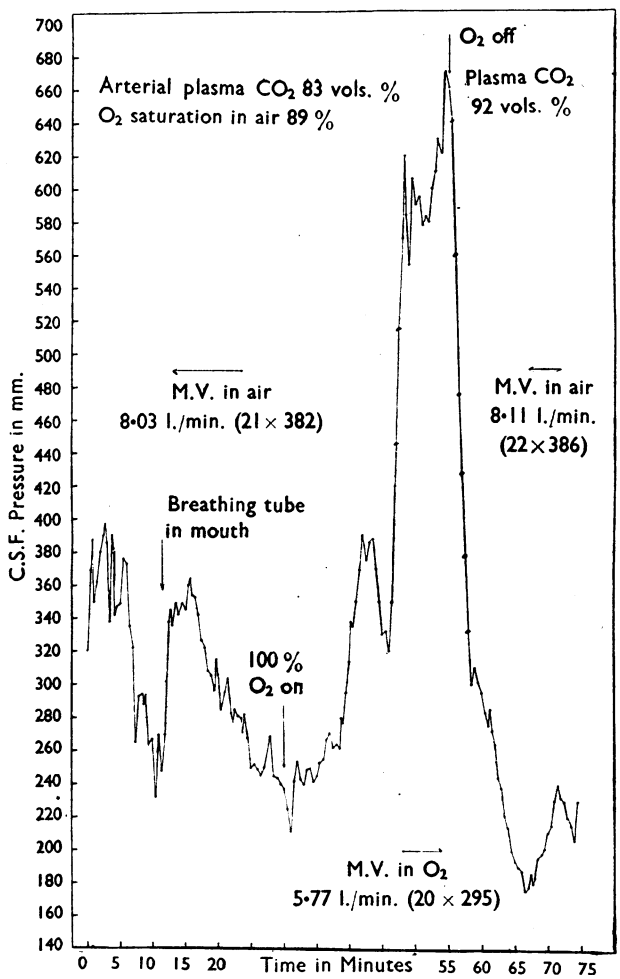

FIG. 3.—Influence of inhalation of oxygen on the C.S.F. pressure, pulmonary ventilation, and arterial CO_2 content in an emphysematous subject.

(22×368). Subsequently papilloedema subsided completely without residual visual impairment. The patient was still alive in July, 1953, and, although completely disabled by dyspnoea on exertion, no longer suffered from headaches and the C.S.F. pressure was normal.

Discussion

Anoxia and hypercapnia might increase C.S.F. pressure by any of the following mechanisms: (1) increase in volume of C.S.F. due to more rapid formation or slower absorption; (2) increase in brain volume due to cerebral oedema; (3) increase in intracranial blood volume due to cerebral vaso-

dilatation ; or any combination of the three. If the rate of C.S.F. formation was increased during the period of gas inhalation it would be expected that the pressure would remain elevated on discontinuing the gas mixture until absorption of the excess had restored normal volume and pressure. In fact, the pressure falls extremely rapidly—usually to 10–50 mm. below the pre-inhalation value (see Fig. 1). Raised venous pressure is thought to slow the rate of C.S.F. reabsorption via the arachnoid villae, and is the presumed cause of intracranial hypertension in congestive failure due to rheumatic heart disease. Inhalation of carbon dioxide does not, however, cause any significant change in venous pressure (Goldensohn *et al.*, 1951). This leaves mechanisms 2 and 3 as possibilities.

Wolff and Lennox (1930), by direct observation of the diameter of the pial blood vessels and measurement of the cisternal C.S.F. pressure in the cat, showed that inhalation of high carbon dioxide and high carbon dioxide plus low oxygen mixtures caused immediate vasodilatation with rise in C.S.F. pressure. Anoxia alone caused cerebral vasodilatation, but this effect was often offset by hyperventilation causing a fall of blood pCO_2. White *et al.* (1942) made quantitative studies on changes in brain volume, cerebral blood volume, and C.S.F. volume in cats. With low oxygen inhalation, brain volume increased considerably, but the cerebral blood volume remained unchanged. This was attributed to the effect of anoxia in causing cerebral oedema by increasing the permeability of cerebral vessels. When carbon dioxide was added to the low oxygen mixture vascular dilatation with increase in cerebral blood volume occurred, but there was no further increase in brain volume. The effect of hypercapnia alone was not studied.

Thus it seems probable that raised intracranial pressure in emphysematous subjects with acute respiratory infections is due to the combined cerebral vasodilator action of anoxia and carbon dioxide retention. The antagonistic effect of low pO_2 and low pCO_2 may explain why the C.S.F. pressure in Case 8 was within normal limits—the vasodilator effect of moderate anoxaemia (O_2 saturation 69%) being offset by the lowered level of plasma carbon dioxide (7 vols. lower than the patient's normal level). The rise of C.S.F. pressure breathing oxygen in Case 6 may be explained as follows: in this patient resting ventilation was largely maintained by the stimulus of anoxia—as is shown by the fact that ventilation decreased by 30% on breathing oxygen. Although relief of anoxia *per se* would tend to produce cerebral vasoconstriction and a *fall* in C.S.F. pressure, this was more than counterbalanced by the increase in blood carbon dioxide content resulting from the fall in pulmonary ventilation. The net effect was a further increase of cerebral vasodilatation and rise in C.S.F. pressure. On breathing air once more ventilation increased, retained carbon dioxide was washed out, and C.S.F. pressure fell to its original (though raised) level.

An increase in blood carbon dioxide content invariably occurs during oxygen therapy in emphysematous subjects (Westlake, 1953) and accounts for the fact that the C.S.F. pressure often remains elevated (cf. Cases 9, 10, and 11) despite relief of anoxia. It is only on full recovery from the acute respiratory infection—when normal or near normal gas tensions are restored—that the C.S.F. pressure also falls to normal.

Is Raised Intracranial Pressure the Cause of Mental Disturbance During Oxygen Therapy?—Oxygen therapy in emphysematous subjects is often complicated by mental disturbance and neurological symptoms—acute mania, disorientation, profuse sweating, salivation, myoclonic twitching, stupor, and coma (Barach, 1937 ; Davies and Mackinnon, 1949 ; Comroe, Bahnson, and Coates, 1950 ; Westlake, 1953). These symptoms are often attributed to raised intracranial pressure, but careful analysis of the mechanism involved makes this view untenable. In cerebral tumour (or other space-occupying lesion) raised intracranial pressure causes drowsiness and coma by decreasing cerebral blood flow, with consequent cerebral anoxaemia. In the emphysematous subject the rise in C.S.F. pressure that occurs during oxygen therapy is due to increased cerebral blood volume from pial vasodilatation. Cerebral blood flow, far from being diminished, is greatly increased (Kety and Schmidt, 1948 ; Patterson *et al.*, 1952). In the absence of any evidence that raised intracranial pressure *per se* (when unaccompanied by reduced cerebral blood flow) has any deleterious action on the function of cerebral neurones, we prefer to regard mental symptoms as manifestations of the direct action of hypercapnia and acidaemia on the brain (carbon dioxide narcosis) and do not believe that lumbar puncture has any therapeutic value.

Summary

Raised intracranial pressure in emphysematous subjects suffering from respiratory infections is attributed to the vasodilator action of anoxia and hypercapnia on cerebral vessels. During oxygen therapy the C.S.F. pressure may remain raised (despite relief of anoxic vasodilatation) owing to further rise in blood carbon dioxide content. Mental disturbance accompanying oxygen therapy cannot be directly related to raised intracranial pressure.

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EARLY TREATMENT OF CLEFT-LIP AND CLEFT-PALATE

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The effective closure of congenital clefts of the lip and palate has presented a challenge which has been taken up by most of the great surgeons of the past century, and considerable ingenuity and daring have been evoked. Many lips and palates were closed without anaesthesia of any kind. To-day, with the help of anaesthesia, electric lighting, suction, and fine instruments and sutures, the surgeon works under improved conditions. Fewer babies with this deformity die than formerly, and actual closure of the clefts can be achieved with certainty. Fairly general agreement has been reached in this country on what procedures are desirable, but there is uneasiness concerning their shortcomings. Any surgeon who operates on these conditions realizes that some of his cases do not turn out as well as he would like. He knows that some will improve with the passage of time, but he will also have the fear that some may become worse. Little is known of the effects of operation on the development of the facial skeleton, and these may be serious enough to prohibit procedures otherwise commendable. Investigation along these lines requires the construction in each case, and with unoperated controls, of a series of models of the dental arches covering the period of growth, and no such survey is likely to be available for a number of years.