Comment

Apart from the successful control of hyperpnoea, the following points in the above case history are considered to be significant.

At the time when intermittent positive-pressure respiration was instituted copious mucopus was present in the trachea. With our form of treatment, however, tracheo-bronchial toilet could be performed with ease, and bronchial aspiration was prevented. Thus one of the major hazards of coma was eliminated. Another advantage was that intra-gastric feeding could be continued in safety.

Following the institution of our form of treatment, the raised temperature and pulse rate moved rapidly towards normal, suggesting that they were caused by the heightened respiratory muscular activity.

The response of this boy to the inhalation of carbon dioxide shows that it has no place in the treatment of salicylate intoxication.

Tetany in our patient was a manifestation of alkalosis, and was not related to the level of ionized calcium in the blood, as this was within normal limits. It is therefore not surprising that the administration of calcium gluconate had no beneficial effect.

Summary

Salicylate intoxication causes an appreciable number of deaths among children. Gross hyperpnoea is one of the more serious toxic effects of salicylate poisoning; it is caused by reflex stimulation of the respiratory centre through the afferent fibres of the vagus nerves. The hyperpnoea gives rise to respiratory alkalosis and this may be accompanied by tetany and convulsions.

A case is described in which the hyperpnoea of salicylate poisoning was treated successfully by neuromuscular block and manually controlled intermittent positive-pressure respiration. It is believed that this method of treatment contributed materially to the patient's recovery. In addition, the administration of intravenous fluids is essential in order to conserve the body's water balance; milk can be given by gastric drip with impunity, as aspiration of fluid is prevented by a cuffed endotracheal tube.

The inhalation of carbon dioxide and the administration of calcium gluconate were not found to be effective therapeutic measures.

We are indebted to Dr. R. W. Brookfield for permission to treat and publish this case; we thank him and Professor Norman B. Capon for their advice in the preparation of this paper. We are also grateful to Mr. J. T. Ireland for the biochemical estimations; and to Dr. K. M. MacWilliam, the resident students, and Sister Ismay and her staff for their part in the management of this patient.

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USE OF HYPOTHERMIA IN NON-VASCULAR INTRACRANIAL TUMOURS

BY

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During recent years the value of hypothermia as an aid to certain types of surgery has become established. In cardiac surgery when temporary occlusion of one or more of the great vessels is required, and in cerebral surgery when the main arteries supplying vital structures are occluded, or when a period of prolonged induced hypotension is desired, hypothermia has been found to be of undisputed value (Lougheed *et al.*, 1955; Botterell *et al.*, 1956).

One mechanism by which reduced body temperature safeguards vital organs is known to be that of metabolic depression with resulting reduced vulnerability to anoxia, and where arterial occlusion is practised this mechanism is clearly the prime one (Ralston *et al.*, 1955; Rosomoff, 1956). Where no deliberately induced ischaemia of this type is involved, however, hypothermia would still appear to have certain benefits, the exact mechanism of which is less clearly understood, although the basic theory of reduction of susceptibility to anoxia is still no doubt a major consideration (Lundberg *et al.*, 1956).

The use of hypothermia in the management of head injuries has had recent publicity and is an example of this "non-vascular" indication for a lowered body temperature. We have recently gained the impression that reduction of temperature is also of value when operative procedures involving the hypothalamus, diencephalon, and brain stem are contemplated, even though neither carotid occlusion nor prolonged hypotension is to be employed as part of the technique. Operative intervention in the brain-stem region is known to carry a high post-operative mortality, and the reasons for such deaths are not always clear. It is suggested that the commonly seen post-operative coma and hyperpyrexia are due, in part at least, to tissue-swelling resulting from trauma with consequent cellular damage, in which case it is probable that anoxia plays a not unimportant part. Indeed, such anoxia might conceivably result from operative retraction itself, as the arteries supplying the midline structures are often end arteries. It is not at all unknown for an actual thrombosis of the lenticulostriate artery to occur on one or other side during the course of such an operation.

Whatever the causes of such injury may be, however, whether they be anoxia or indirect or direct trauma, we have come to the opinion that hypothermia protects cells of the brain stem and diencephalon during operative procedures.

This is obviously a point which would require statistical proof, and such will not be possible until large numbers of cases are available; even then advances in other directions render a control series almost impossible. No further comment can therefore be made than to say that it is now our routine to use hypothermia in all cases

where operations on the brain stem are required, and that we have been favourably impressed with results. It has been our opinion that cases so managed have had fewer post-operative complications in the form of prolonged unconsciousness and hyperpyrexia. Some patients have survived who would, we think, have died without the method. The introduction of hypothermia has been the only change in method that we have made in the period in question.

Method

The hypothermia in this series has been induced by surface cooling, using the Birmingham hypothermia unit previously described (Inglis *et al.*, 1954). Briefly this unit consists of a pair of tubulated blankets through which refrigerated ethylene glycol is circulated by means of a pump. The temperature of the glycol can be predetermined and the patient can be rewarmed as soon as the vital operative period is over. Anaesthesia has been in all cases by means of nitrous oxide and oxygen with intravenous thiopentone and pethidine, while chlorpromazine has been used to facilitate the fall in temperature. Corticotrophin or cortisone has been employed as a routine, so maintaining a standard management for all such cases operated upon in the past five years.

Two cases of craniopharyngioma are described. They were two consecutive examples of the condition; both had a large craniopharyngioma completely removed under hypothermia, with survival. They serve as examples to show our present favourable impression, and to encourage others to try a method which may help in a rather difficult surgical field.

Case 1

A boy aged 5 was admitted in July, 1956. Three months previously a change in his personality had been noted—from a quiet, placid child he had become excitable, careless, dirty in his habits, and rather irritable. A month before admission he had begun to complain of headaches, and from that time to his admission he had occasional morning vomiting, with increasing apathy, which gradually progressed to drowsiness and finally to stupor. On examination he was found to be lightly stuporous. He could be roused temporarily to co-operate in examination, and it was then found he had an increase of tone with some spasticity in all four limbs and a frank left hemiparesis. Both plantars were abnormal, the left being more frankly extensor than the right. There was bilateral ptosis and the pupils reacted sluggishly to light, the right one being slightly larger than the left. No papilloedema was present.

FIG. 1.—Ventriculogram of Case 1 showing elevation of the floor of the third ventricle.

A ventriculogram showed gross elevation of the floor of the third ventricle by a mass protruding into it from the suprasellar position (Fig. 1). At operation under hypothermia to 29° C. a right frontal craniotomy was performed and the frontal lobe was elevated until the right optic nerve was seen. Medial to it a mass protruded forwards between the two optic nerves. This mass proved to be partially cystic, and 30 ml. of golden glistening fluid was aspirated. The base of the cyst was firmly fixed to the suprasellar region, but the superior wall was gently coaxed downwards and pulled off the hypothalamus by gentle blunt dissection and removed through the aperture below the chiasma. The solid portion of the tumour was now thoroughly scraped off the dura, and the diaphragma sellae and any vestiges of tissue in this situation were thoroughly treated with diathermy. The operation was completed and the patient was then gradually rewarmed to 36° C. over the course of four hours, when consciousness returned. Although he was drowsy for a few days, his post-operative progress was extremely smooth. From the day of operation he received corticotrophin in physiological doses; this was gradually changed to cortisone.

A fortnight after the operation he was shown to have a progressive anaemia. A blood transfusion was given and thyroid was added to the hormone medication. At this stage he made a dramatic improvement, and from being drowsy, somewhat spastic, tremulous, and rather irritable, he became in the course of a few days a normal boy for his age—intelligent, co-operative, with only a mild bilateral ptosis to be remarked upon in his general appearance. Histology had confirmed that the cyst was lined with squamous epithelium overlying collagenous fibrous tissue. In a few places the lining consisted of lipogranulomatous tissue infiltrated with chronic inflammatory cells. The solid nodule was composed of squamous epithelium. The appearances were those of a craniopharyngioma.

During the post-operative period there had been a fairly brisk diuresis to about two to three times the normal, with a corresponding increase in thirst: no special measures had to be employed to counteract this mild diabetes insipidus. His further progress has been satisfactory, and he was instructed to go back to school in October, as he did not require further hormonal treatment.

Case 2

A boy aged 15 was admitted in September, 1956, because of progressive and latterly alarming impairment of vision. In the month before his admission visual acuity fell from 6/9 to 6/60; he was obviously in great danger of losing his sight.

On examination he was obese, with small extremities and markedly tapering fingers, and the genitalia were

FIG. 2.—Ventriculogram of Case 2 showing upward displacement of the third ventricle.

undeveloped. His intellect was well above average; indeed, he had passed his school certificate at the age of 15 years, some three months previously. The fields of vision showed a right homonymous hemianopia which was not quite congruous. A ventriculogram showed the third ventricle grossly displaced upwards. The upward displacement included a posterior part of the third ventricle, so that there was no obvious concave impression of a globular tumour (Fig. 2).

Operation was performed under general anaesthesia together with hypothermia to 28.6° C. A left frontal craniotomy gave access to a large craniopharyngioma, which when tapped yielded 40 ml. of fluid, the last 10 of which contained typical glistening crystals of cholesterol. The cyst seemed to be firmly fixed to its surroundings, but, in view of the experience of the previous case, the same manoeuvre was attempted—namely, the pulling downwards of the part attached to the hypothalamus and dissecting it off first. This manoeuvre was again successful in separating the cyst from the thinned-out floor of the ventricle, to which it was lightly adherent. Again it was possible in the terminal stage to remove the solid portion at the base. Post-operative progress was astonishingly smooth. The patient recovered consciousness three hours after operation; the maximum elevation of temperature was 102° F. (38.9° C.) and the blood pressure was steady. The only sign the chart showed of the usual hypothalamic disturbances that punctuate the post-operative course of these patients was a persistent tachycardia running up to 160 and lasting 48 hours. The pulse was regular. The skin throughout was well coloured and showed no sign of cyanosis. Electrolytes were normal, and, though there was again a mild degree of diabetes insipidus, it was easily controlled by the administration of larger quantities of fluid than normal.

The patient was very well four to five days after his operation and his visual acuity and visual fields returned to normal within 18 days.

Summary

A preliminary note is put forward to suggest an extension of the value of hypothermia in neurosurgical cases. In addition to the accepted advantages of lowered metabolism when arterial occlusion or prolonged hypotension is employed, there would appear to be a *prima facie* case for reducing the patient's body temperature when operations on the brain stem or diencephalon are contemplated.

Two consecutive cases are described of large craniopharyngioma completely removed; they illustrate the smooth post-operative course to be expected in operations under hypothermia.

We are indebted to Dr. Gilbert Hall, under whose care the second case was admitted, and to Mr. W. H. Biffen for technical help with the hypothermia.

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The industrial advisory committee of the Ross Institute has issued a bulletin (No. 11) on iron-deficiency anaemia, prepared by Dr. R. FORD TREDRE, and its bulletin on tropical ulcer (No. 4) has been rewritten. These bulletins, and all other publications of the Ross Institute, may be obtained from the secretary, Mr. L. G. PONSFORD, London School of Hygiene and Tropical Medicine, Keppel Street, London, W.C.1.

IMMUNITY TO DIPHTHERIA EVALUATION OF SCHICK TEST AS A PRELIMINARY TO IMMUNIZATION

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An investigation was carried out to determine the immunity to diphtheria of R.A.F. recruits, to assess the value of Schick-testing as a routine Service procedure, and to correlate the results of Schick tests with circulating antitoxin titres.

A total of 991 recruits from five recruit centres were Schick-tested in a survey which took place in March and April, 1956. Nearly all the men were 17½ to 18½ years old and belonged to the 5–6 years age group in 1943, when most children were immunized against diphtheria by local authorities. There was no geographical selection of the recruits at the different centres, though some selection by trade. It is just possible, therefore, that there may have been a slight social selection at the different centres. It is felt that the group as a whole was a reasonable cross-section of the young men of this country. Each volunteer had 5 ml. of blood taken by venepuncture and then a Schick test. All the Schick tests were performed and read by one person (P. J. S.).

The Schick Test

The materials used were Schick test toxin and Schick control fluid (a heated diluted toxin) prepared by Evans Medical Supplies, Limited. The dose of each was 0.2 ml., and this was administered intradermally, the test dose being put into the anterior aspect of the right forearm and control into the left. The Schick tests were read after 48–72 hours (first reading) and on the fifth, sixth, or seventh day (second reading). On each occasion the reactions to both test and control were recorded in the following way: 0=no visible reaction at all or merely a tiny red spot of 1–2 mm. marking the needle puncture. 1=a faint flush, barely discernible up to 15 mm. diameter. 2=a more definite flush

TABLE I.—Interpretation of First Schick Reading

Test	Control	Result
0	0	Negative (—)
1 or 2	0	Weak positive (w+)
3 or more	0	Positive (+)
1 or more	1 or more	Pseudonegative (ps—)
(both reactions equal)		
2 or more	1 or more	Pseudopositive (ps+)
(test reaction greater than control)		

TABLE II.—Interpretation of Both Schick Readings

First Reading	Second Reading	Schick Status
—	—	Negative
+	—	"
w+	—	"
w+	+	Positive
+	w+	"
w+	w+	"
+	+	"
—	w+	"
—	+	"
Either or both ps+ or ps—		Pseudoreactor