The question now arises: Why did 770 out of 800 men escape beri-beri when all had been subsisting on the same deficient food for months past, when, in fact, all were subjected to the same degree of vitamin insufficiency? And why did 101 out of 105 pigeons escape beri-beri when all were fed alike? Presumably because there was in operation in the 30 men who developed it some factor in addition to the vitamin insufficiency which was absent, or failed to affect in the same degree, the 770 who did not develop it. Similarly with the pigeons. If we look at the matter from the point of view of the heart condition alone we are at once impressed by the fact that some additional factor must have been in operation in beri-beri birds which exercised a specific effect on the heart, for vitamin deficiency alone does not cause cardiac enlargement in pigeons, but, on the contrary, cardiac atrophy. Surmise as to the nature of this factor is permissible, since if it is to be found we must have some line of thought along which to work. It is possible that the subjects of beri-beri may have been carriers of some organism whose products exercised this effect on the heart muscle, just as certain of my pigeons were carriers of an invisible virus which exercised a specific effect on epithelial tissue, and the fact that beri-beri arose only in birds obtained from a certain place is presumptive evidence in favour of such a view; or the gastro-intestinal flora of the sufferers from beri-beri may have been of such a nature as caused the evolution of a poison which exercised this specific effect on the heart; or it may be that certain birds were of such a constitution that the disturbed metabolism resulting from the vitamin insufficiency caused a poison to be evolved in those who suffered from beri-beri which was not evolved, or not to the same extent, in those who escaped. Or was it merely a question of individual idiosyncrasy, and, if so, what do we mean by that? Is not individual idiosyncrasy likely to depend on such things as I have just mentioned? But even if this be so, individual idiosyncrasy to disease resulting from deficiency of vitamin B depends in great measure on the degree of the deficiency; the greater the deficiency the less the variation in individual idiosyncrasy; the less the deficiency—provided there be an insufficiency—the greater the variation in individual idiosyncrasy to disease resulting from it. So on a diet such as those used in the experiments I have detailed, and such as that used by the battalion above referred to, the vitamin values of which were in the neighbourhood of 0.6, one would expect many individuals to escape the grosser manifestations of disease (such as polyneuritis) consequent on their use. But whether the poison which imparts to polyneuritis columbarum the characteristics of true beri-beri be an extrinsic or an intrinsic one, I am of opinion that such a poison exists; that it is one peculiar to certain places or which is evolved in persons residing or who have resided for considerable periods in certain places; and that its operation is rendered possible by the insufficient intake of a certain vitamin or vitamins in an otherwise ill balanced diet excessively rich in starch and deficient in suitable proteins. The conclusion which I reached in 1919, that vitamin deficiency is rarely the sole agent responsible for the causation of beri-beri, has been strengthened by my investigations during the past five years.

In the course of my work I have produced in pigeons by means of the rices in common use in India no less than four "beri-beri-like" diseases:

1. Infective polyneuritis, due to infection, but favoured in its genesis by vitamin deficiency.
2. Polyneuritis due to vitamin deficiency alone.
3. Polyneuritis due to vitamin deficiency, but precipitated in its onset by various infections.
4. A malady presenting the characteristics of true beri-beri, and due to an unknown agent acting in association with insufficiency but not complete want of vitamins.

All these have many clinical and pathological features in common, although all have their own distinctive characteristics—easily enough recognizable at *post-mortem* examination if not always recognizable clinically; in all, vitamin deficiency, in association with the usual food faults which accompany it, is more or less concerned, directly or in-

directly, in their causation. If there be this variety of beri-beri-like maladies in pigeons, whose staple diet is rice, there is probably a similar variety of beri-beri-like maladies in man—a surmise which proved to be correct in Mesopotamia during the late war. I am not at all convinced from the literature that when we argue as to the causation of "beri-beri" we are always arguing about the same condition. And so much has this been impressed upon me of late that I look for further progress along clinical and pathological lines which will separate these beri-beri-like states into entities recognizable as such by the practising physician. Only then will the causal factors in their production be capable of accurate determination.

THE USE OF HYPERTONIC SALINE SOLUTIONS IN INCREASED INTRACRANIAL TENSION.*

BY

HENRY COHEN, M.B.,

SENIOR MEDICAL TUTOR AND REGISTRAR, ROYAL INFIRMARY, LIVERPOOL.

In 1919 Weed and McKibben¹ showed that the intravenous injection of hypertonic saline solutions in cats markedly lowered the cerebro-spinal fluid pressure, as determined by a water manometer connected with the subarachnoid space, whilst hypotonic solutions produced an opposite effect. It was shown later by Foley and Putman² that oral or rectal administration of hypertonic saline solutions produced exactly similar experimental results. Since that time a few papers have appeared in which are recorded the application of these experimental results to man. The value and possibilities of the method have not, however, been generally appreciated, and this paper records further observations on what must be considered a valuable therapeutic method.

Relief of Headache in Intracranial Hypertension associated with Tumour and Meningitis.

If 20 c.cm. of a 30 per cent. sodium chloride solution be injected intravenously, within five to ten minutes there is, after a preliminary feeling of burning in the head, an almost complete cessation of headache. Six cases of inoperable cerebral tumour were treated in this way, and in each case relief was obtained. This period of freedom lasted from ten hours to two days, but in most cases an intravenous injection every third day kept the patient free from headache. Two cases of acute meningo-vascular syphilis showed similar relief for a shorter period (six to twelve hours), although the headache was much less severe for a much longer period than prior to injection. The saline solution causes local pain where it comes into contact with the tissues. To avoid this the needle of the syringe should be washed with sterile water and a little of this drawn up into the syringe before injection. On one occasion it was feared that the saline solution had caused thrombosis at the site of injection (median basilic vein). This, coupled with the fact that in some cases there is difficulty in finding a suitable vein, especially in stout women, led us to investigate the effect of salt given by the mouth. Three to six 5-grain tablets of sodium chloride with a keratin coating were given to the patient three times a day. Some relief was obtained, but the effect was much less marked than with intravenous injections.

In three of the cases the cerebro-spinal fluid pressure before and twenty minutes after the saline injection was measured, the patient in each case being in the left lateral position. The pressures were as follows:

	Before Injection.	Twenty Minutes after Injection.
I. D., cerebral tumour ...	780 mm. water	90 mm.
J. C., cerebral tumour ...	940 "	100 "
E. B., cerebellar tumour	840 "	70 "

It is not claimed that the above pressures are anything but approximate values, but they show the marked effect of hypertonic saline solutions on conditions associated with increased intracranial tension.

* Based on a paper read before the Liverpool Medical Institution.

During the course of acute infections, especially influenza, meningeal symptoms may appear, due to "meningismus"—that is to say, an increased formation of cerebro-spinal fluid without infection of the meninges. Professor Abram and others have shown that withdrawal of cerebro-spinal fluid by lumbar puncture rapidly relieves this condition. Wegeforth and Latham³ objected to this procedure on the grounds that if a pneumococcal septicaemia be experimentally induced in rabbits, lumbar puncture increased the incidence of meningitis in animals so treated, apparently by drawing organisms towards the choroid plexus. Though the clinical opportunity has not yet arisen, it is obvious that hypertonic saline given intravenously would be free from this objection in the meningismus of acute infections; in fact, as Weed's later work⁴ shows, there would be a tendency for the organisms to be dragged away from the choroid plexus, for the current would be, not from blood to fluid as in the case of spinal puncture, but from fluid to blood.

Cerebral Herniae.

The first case on which we tried hypertonic saline was a girl who had been operated on, for a tumour of the cerebello-pontine angle, by the subtentorial route. Subsequently a hernia as large as a Jaffa orange developed; it was associated with headache, vomiting, vertigo, and marked ataxia. Not only did hypertonic salines cause disappearance of the headache, but also marked improvement in the other symptoms, especially the gait; at the same time the size of the hernia decreased and it became much softer. This marked amelioration of the patient's condition continued for two months during her stay in hospital, an injection being given every third or fourth day. On discharge her symptoms recurred despite the fact that she was taking 15 grains of sodium chloride by the mouth thrice daily. Four cases of post-operative cerebral herniae have since been treated by intravenous hypertonic salines, with gratifying results as far as symptoms are concerned. It cannot be too strongly emphasized that the treatment is purely symptomatic in these cases, not curative.

Hypertonic Saline prior to Operations for Cerebral Tumour and Allied Conditions.

It has been shown that the lowering of cerebro-spinal fluid pressure resulting from the intravenous injection of hypertonic saline solutions is accompanied by a diminution in the volume of the brain. To those who have seen the bulging of brain substance through the bony cranial defect during a cerebral operation—a bulging which increases the surgeon's difficulties many times and causes unnecessary damage to the brain substance—it is surprising that the pre-operative use of hypertonic salines is not more widely known.

Other Uses.

Further uses for these solutions readily suggest themselves.

A woman, aged 28, was first seen eighteen months ago with one year's history of headache, occasional vomiting, and dystrophia adiposa genitalis. There were no signs of local pressure in the neighbourhood of the pituitary fossa, and no change in the visual fields or fundus oculi. Injections of hypertonic salines failed to relieve her headache. During the last eighteen months no further evidence of a cerebral tumour has developed, and it can probably be excluded.

A girl, aged 18, with a similar Fröhlich's syndrome, but with secondary optic atrophy and definite evidence of a suprasellar tumour, obtained considerable relief from headache when given salt by the mouth.

Whether this points to the use of hypertonic salines in differentiating intracranial from extracranial causes of headache there is not yet sufficient evidence to show.

In cases of cerebral tumour, when cerebro-spinal fluid is desired for diagnostic purposes, but lumbar puncture is feared lest "foraminal crowding" occur, it would seem that hypertonic salines given fifteen minutes before puncture would minimize the risk.

Whilst hypertonic salines diminish both the volume of the brain and cerebro-spinal fluid pressure, hypotonic salines produce the opposite effect; they increase the volume of the brain and the cerebro-spinal fluid pressure. The practical value of this would seem to lie in the use of hypotonic salines in cases of headache occurring after lumbar puncture. In one case the headache completely subsided after the intravenous injection of hypotonic saline.

The respiratory effects—shallowness of respiration and partial failure—seen in experimental animals have not been observed in the cases here recorded. We have been unable to avail ourselves of the opportunity offered to investigate the rate of chloride excretion, the effect on urine output, alterations in blood volume, etc., following the injection of hypertonic salines. The few indications and results here recorded are sufficient to illustrate the uses and great value of this method in rational therapeutics.

REFERENCES.

- ¹ Weed and McKibben: *Amer. Journ. Physiol.*, 1919, xlviii, pp. 512, 531.
² Foley and Putman: *Amer. Journ. Physiol.*, 1920, lvi, p. 464. ³ Wegeforth and Latham: *Amer. Journ. Med. Sci.*, 1919, clviii, p. 185. ⁴ Weed: *Amer. Journ. Anatomy*, 1923, xxxi, p. 191.

SYSTEMIC POISONING BY HAIR DYE.

BY

H. W. NOTT, M.R.C.S., L.R.C.P.,

LITTLE SUTTON, BIRKENHEAD.

It is well known that some phenylenediamine dyes cause irritation and dermatitis when conveyed to the skin of susceptible people by dyed furs, but hitherto I have not seen any reference to the serious consequences which may result to some from absorption of this poison.

The proprietor of a hairdressing saloon, of middle age, looking apparently well and who presented no physical signs of disease, came for examination on account of serious and unaccountable illness, which as a rule came on suddenly—"flooding him with a horrible sensation of sickness, weakness, and a feeling of impending death." He gave his story in a jerky, nervous manner and with an air of puzzled mystery, saying that he had been subject to these seizures for nearly three years; that in the space of a few minutes he would pass from a feeling of good health into a state of pain, palpitation, and exhaustion; "he was going to die"; and on one occasion when he was preparing for bed an attack came so suddenly and with such tumultuous action of the heart that he fell on the bed helpless, certain he was dying, and lapsed into unconsciousness, from which he must have passed into natural sleep, for he awoke next morning perfectly well, to find himself lying across the bed half dressed. He said he had often been diagnosed at sight as a man "very ill with influenza," and had often been sent home to bed with his temperature up. He had had several sojourns of from three to six weeks in bed getting over the "flu," but as a rule he had been treated for "nerves and indigestion."

His story was substantiated by a large packet of prescriptions in which valerian, bromides, bismuth, and magnesia had been ordered. He had also received two courses of vaccines, and once had been threatened with removal to a sanatorium for tuberculous disease. As there seemed no reason to suspect alcoholism he was advised to watch whether any article of food might be poisoning him.

A week later he telephoned at 9 a.m. saying he had gone to bed perfectly well the night before and had wakened that morning to find himself in for another attack. When seen at 3 p.m. the same day he at first sight gave the impression of one who might have had several nights' drunken debauch, but his breath was perfectly healthy. His face was grey, cyanosed, and blotchy. His eyes were watery, the conjunctivae injected, and the eyelids swollen. The lips and ears were violet, the tongue was swollen and covered with a thick yellow and brown fur. The gums were very swollen, standing away from the teeth, and purple. Some of his fingers were stained, apparently with iodine. The pulse was 105, regular, and fairly strong; the temperature was normal.

He was nauseated, and had taken no food all day. He complained of pain, chiefly in the epigastric and hypochondriac regions, and between the shoulders. There was slight palpitation, and he looked anxious and strained. He described some difficulty in swallowing, with a burning sensation in the throat and behind the sternum. When he took a deep inspiration he felt severe pain in the chest, and a choking sensation. As the previous day, Sunday, had been spent in the house, and as all food taken had been prepared at home, it was impossible to resist thoughts of secret poisoning by arsenic, for he somewhat resembled a series of cases seen here twenty years ago when arsenic accidentally contaminated the beer from several breweries in the North of England.

When it was explained that his symptoms resembled some forms of poisoning, and when he began to think of the possibility of some chance method of poisoning, he supplied the clue himself by asking if hair dye could do it, for it was about three years ago when he first used it. He often worked in the fumes of it, and occasionally applied the dye to his customers without wearing gloves, which accounted for the stains on his fingers—the last occasion being about forty-eight hours before this interview.

Two bottles of the dye were sent to an analyst with a note that it was under suspicion for causing mixed symptoms of lead and arsenic poisoning in a man who worked with it, and the following report was received:

"In accordance with your instructions we have examined the two solutions of hair dye which you handed to us.