soaked to capacity in the solution; this in turn is covered by a sheet of waterproof material and fixed on by a binder or bandage. The compress is applied 6 hours before the operation, and is removed on the operating table.

Bacteriological Tests.—These were carried out on 38 consecutive cases prepared for abdominal section. In each case, when the compress was removed, a platinum loop was made to streak the prepared skin surface and was then streaked on the surface of human blood-agar in a Petri dish. Four such streaks were made from different parts of the prepared area and were streaked on four different areas of the plate. As a control, four similar streaks were taken from an area of skin just outside the prepared area and streaked on the surface of another blood-agar plate. Multiple streaks enable a judgment to be made between growth indicating permanent diffuse infection and growth indicating chance contamination or loop-holes in the preparation.

Results

Prepared Areas.—Of the 38 plates from the 38 prepared areas, 29 showed no growth at the end of four days' incubation and 9 showed growth. Of these 9, one exhibited it on 3 of the 4 streaks, four on 2 of the 4 streaks, and four on 1 streak only. No plate had growth on all 4 streaks. Moreover, the bacterial colonies were few and isolated, except on the plate which showed growth on 3 streaks, and in this case there were other reasons to believe that the preparation had not been carried out thoroughly. As regards the growth on the other plates, these too were probably due to imperfect preparation, though in lesser degree. The effect of the antiseptic, however, is best displayed by comparing the number of sterile streaks with those not sterile; for of the total 152 streaks made from the prepared areas only 15 showed growth. From these the following organisms were identified: *Staph. aureus haemolyticus*, from 9 streaks; non-haemolytic *Staph. aureus*, from 1 streak; and *Staph. albus*, from 9 streaks.

Controls from Unprepared Areas.—All the 38 plates from the 38 unprepared areas showed growth at the end of four days' incubation. Growth occurred on all four streaks in 36 of them, and on three out of four streaks in 2. Counting the number of streaks instead of the number of plates, it is seen that of the 152 streaks made from the unprepared areas 150 showed growth and only 2 remained sterile. The growths in most cases were profuse, and the following organisms were identified: *Staph. aureus haemolyticus*, from 118 streaks; non-haemolysing *Staph. aureus*, from 10 streaks; *Staph. albus haemolyticus*, from 17 streaks; non-haemolysing *Staph. albus*, from 86 streaks; *Str. haemolyticus*, from 1 streak; non-haemolysing streptococcus, from 16 streaks; *Staph. citreus*, from 4 streaks; and diphtheroid organisms, from 30 streaks.

In addition to these tests one of us (S.A.), in order to ascertain the depth to which the antiseptic effect reached, on 13 occasions took cultures from the cut edge of the skin after the incision was made. In 12 cases no growth occurred, but in the remaining case *Staph. aureus haemolyticus* grew. This was the same case in which 3 of the 4 streaks taken from the prepared area showed growth and in which there was a strong suspicion that the area had not been properly prepared.

Discussion

It is to be noted that *Staph. aureus haemolyticus* was by far the commonest organism recovered. It occurred in 35 of the total of 38 plates taken from the unprepared areas, and the frequency on the skin of an organism so potent for mischief gives all surgeons cause to think furiously. The danger to surgical achievement which lurked in unsterilized skin, and the need to abolish it, were taught by the great thinker Lister. Then, in reaction, arose the soap-and-water school, headed by Lawson Tait, which asserted that simple cleanliness was enough: that good surgical results can be so attained is true, for healthy tissues have strong resisting powers. Later still, another school of thought emerged which, recognizing the difficulty of completely sterilizing the skin, employed as the chief line of defence cotton or rubber sheeting to cut out the skin—and this remains the usual practice to-day. But, although the soap-and-water school as such has disappeared, there remain some persons who, believing that swabbing with an antiseptic immediately before the operation sterilizes the skin,

unknowingly depend on what its adherents depended on. The bacteriological investigations carried out in connexion with violet-green showed quite conclusively that such brief applications do not effect sterility, though they do enfeeble the organisms so that growth on the agar plate is delayed as compared with that on the controls. Iodine is the best of these perfunctory applications, because it has superior power of penetrating organic material—a quality made use of in the sterilizing of catgut.

Organisms entrenched in the skin are very stout enemies, and to knock them out a vigorous and, above all, prolonged attack is required. Those who do not appreciate this fact ascribe the satisfactory healing of the wounds they make to the perfunctory measures they have taken, though in reality they owe it to that natural tissue resistance which enabled the soap-and-water school to make good its claim. But every now and then the enemy gains a foothold, and failure of the wound to heal kindly leaves the operative result something less than perfect and the surgeon with his pride hurt—and sometimes worse things happen. Surgical success depends on so many factors that the share taken by rigid antisepsis cannot be assessed in figures, though it can be perceived by anyone who studies attentively over a number of years the results of different surgeons practising different degrees of antisepticity. But whatever the share is, everyone must agree that operative infection arising from the skin is a theoretical possibility, and it is the duty of a surgeon to close all doors against all possibilities, theoretical or otherwise. To ensure, as far as may be, initial sterility of the skin should be the first line of defence against infection from the skin, and sheeting the second line, in case the first fails. For those who object to violet-green on the score of staining, the solution we describe, if used in the manner set forth, efficiently and inoffensively sterilizes the skin.

Our thanks are due to the pathological department of Cheltenham Hospital for the work it has done for us.

PITUITARY CACHEXIA TREATED WITH CORTICOTROPHIC HORMONE

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Panhypopituitarism, not the result of pituitary necrosis following pregnancy, has been regarded as a clinical entity (Fraser *et al.*, 1941). We (Hemphill and Reiss, 1940, 1942) have described cases in which severe melancholic depression associated with clinical pituitary cachexia—namely, emaciation, asthenia, loss of hair, desiccated skin, and low output of 17-ketosteroids—developed after the menopause. Although there was usually evidence of polyglandular insufficiency, where the skin was dry, hair brittle, and 17-ketosteroids low with subjective complaints that the “bowels did not operate,” adrenocortical failure seemed the most important endocrine disturbance. On this hypothesis a number of such cases have been treated with corticotrophic hormone. This treatment was on the whole promising, and early results have been recorded already (Hemphill and Reiss, 1940, 1942). The case described below showed such extreme emaciation that the picture was that of advanced Simmonds's disease. Complete physical recovery followed treatment with two courses of corticotrophic hormone. The mental condition cleared up some time later.

Case Record

A woman aged 41 was admitted to the Bristol Mental Hospital on Dec. 21, 1940. She was married, but had never been pregnant. There was no history of antecedent mental or physical illness. The menses ceased abruptly at the age of 39 without hot flushes or other subjective menopausal disturbances. About six months before admission she became depressed, lost appetite, and imagined that her viscera were deranged and the bowels “stopped up”; she attempted suicide. This was the mental condition on admission. Physically she was thin, weak, and frail-looking; height 5 ft. 6 in.,

weight 6 st. 3 lb. The skin was sallow, with an extremely dry "desiccated" texture; sweating was entirely absent, and there was a marked sensitivity to cold. The blood pressure was 90/60 mm. Hg. There were no respiratory, cardiac, or renal abnormalities. The breasts and mons veneris were atrophied; the hair of the head was brittle and lustreless, that of the pubis and axillae scanty; muscle bulk was very much reduced. There was no assayable output of gonadotrophic, corticotrophic (method of Reiss *et al.*, 1936), or thyrotrophic (method of Heyl and Laqueur, 1935) hormones in the total urine of 96 hours; the output of 17-ketosteroids was 2.6 mg. per 24 hours. The patient (Figs. 1 and 2) displayed none of the

delusions of alimentary malfunction and gain in appetite, there was at first little mental change. Even the posture and expression were unaltered in spite of the improvement in physical state. There has been a change recently. She is now less retarded and seems to be emerging from the depressive state.

FIG. 1

FIG. 2

restless activity seen in anorexia nervosa. There was a low concentration of intercellular water, as shown by the diurnal electrical resistance of the skin, which, normally now and steady after the menopause (Hemphill, 1942), was high and fluctuated widely. Attempts at fattening failed in the next ten months; the weight dropped to 4 st. 11 lb.

Corticotrophic hormone, 40 sudanophobic units daily for 24 days, was administered. There was an immediate improvement in appetite and some return of the sense of well-being. The desiccated appearance of the skin had gone, and within four days the electrical resistance fell to the normal low level, at which it remained steadily. Two months later a further course of 14 daily injections of 25 units was given. The weight rose steadily and has continued to do so (Fig. 3). It is now two years since any hormone treatment has been

FIG. 3

given, but the improvement has been maintained. The breasts have developed and there has been a normal deposition of fat and restoration of hair loss (Figs. 4 and 5). Menses have not returned, and the vaginal smear, as before treatment, is of the post-menopausal atrophic type. The 17-ketosteroids rose to 8.3 and later improved to 10 mg. per 24 hours. Apart from an immediate loss of the

FIG. 4

FIG. 5

Discussion

In this case the physical condition was that of pituitary cachexia, and conformed closely to the picture of Simmonds's disease. Although there was no history of antecedent pregnancy the emaciation and asthenia, dry skin, loss of hair, and subnormal output of anterior pituitary hormones may be attributed fairly to adrenocortical insufficiency secondary to hypopituitarism. This was corrected by treatment with corticotrophic hormone. Improved adrenal performance would be accompanied by improved water and fat storage with more normal salt retention, and therefore better metabolism and alimentary function. Objective evidence that this took place was provided by the gain in weight and strength, loss of the desiccated quality of the skin, restoration of the normal electrical resistance behaviour, rise in output of 17-ketosteroids, and loss of delusions of alimentary inadequacy, which, as we believe, are a secondary derivation of the physical illness. The mechanism of cure was at first replacement therapy. Either atrophy or suppression of function of the adrenal cortex for want of trophic stimulation produced at least a large part of the clinical picture. Stimulation of the adrenal cortex by injected corticotrophic principle of the pituitary at first corrected the deficiency. It is reasonable to suppose that with an approach to normal water and fat metabolism other endocrines behaved in a more normal way, so that to some extent their insufficiency was adjusted. That the patient was able to remain well and even to improve further when corticotrophic hormone was no longer administered indicates that once the anterior-pituitary-peripheral-endocrine system was set in motion, there being no destruction of anterior pituitary substance, it could continue to function satisfactorily without aid.

It is believed that menopausal symptoms in many women are due to a temporary rise in gonadotrophic hormone output from hyperactivity of the anterior pituitary (Nathanson *et al.*, 1940). We have noticed in this and similar cases that the menopause came abruptly and there was a complete absence of menopausal symptoms. Assays in such cases showed a very

low or a negligible output of gonadotrophic hormone. This suggests that in this type of case there is a sudden functional reduction in pituitary activity to be followed later by the physical symptoms of hypopituitarism. The suggestion that the picture of pituitary cachexia without structural changes in the pituitary itself can follow the menopause is supported by the resumption of normal pituitary function observed in this case after treatment. The physiological properties of corticotrophic hormone have been studied in hypophysectomized rats. It is known that sugar storage is much reduced after hypophysectomy, for the combustion of fed sugar is much higher than in normal animals. This condition has been corrected by corticotrophic hormone (Reiss *et al.*, 1938). The cholesterol and fat content in hypophysectomized rats can also be increased by corticotrophic hormone (Reiss *et al.*, 1937). No doubt there were comparable actions in the case we have described.

Summary

A case of clinical pituitary cachexia in a nulliparous woman has been described. Clinical and hormone studies indicated extreme hypopituitarism. Treatment with corticotrophic hormone resulted in complete restoration of weight and cosmetic features. This was not a case of anorexia nervosa. The psychotic depression was not relieved until a considerable time after physical improvement was complete. The origin of this condition has been discussed.

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Medical Memoranda

Effect on the Nutrition of School-children of adding Vitamins and Minerals to the Diet

The purpose of this experiment was to discover if the addition of minerals and vitamins to the diet of school-children would make them gain weight at an increased rate.

THE INVESTIGATION

The experiment was carried out between Oct., 1940, and May, 1941, in an industrial area on the south bank of the Thames. For three months 300 children were weighed fortnightly; half of them were then given vitamin supplements for five days a week for three months, and the fortnightly weighings were continued. The ascorbic acid and vitamin B, contents of the urine of the "vitamin children" were determined before and after the administration of the supplement; a few vitamin A tests were performed with the photometer. The incidence of colds in the groups was recorded.

The daily supplement given contained 360 mg. of calcium, 552 mg. of phosphorus, 4,000 units of vitamin A, 300 units of vitamin D, 200 units of vitamin B, 12 mg. of available iron, 20 mg. of ascorbic acid, and some trace of minerals.

Results.—The average gain in weight of the vitamin children was no greater than that of the controls. The initial urinary estimations suggested that the intake of vitamin B, and of ascorbic acid was low, but there was no gross deficiency. Very few of the children showed increased excretion of the vitamins at the end of the experiment. (It should be noted, however, that the vitamins were estimated in single specimens of urine.) The few photometer tests carried out did not show any marked deficiency at either the beginning or the end of the experiment; there was no difference between the two groups in incidence of colds.

DISCUSSION

The experiment, though limited in scope, seems worth reporting, for it was carried out earlier than the other vitamin-feeding tests, in a different part of the country, and minerals as well as vitamins were added to the diet.

The fact that the children did not gain weight at an increased rate while having the supplement may be explained in several ways. The tablets might not have been taken regularly, no vitamin shortage may have been present initially, or a vitamin deficiency may have been present which was so severe that the supplements were not adequate to deal with it. Or a moderate deficiency might have existed, but vitamins given in tablets might not have been so effective as they would have been if

given in fruit and vegetable juices. Or a moderate deficiency might have been present, capable of being dealt with by the supplements but accompanied by a deficiency either of first-class protein or of calories. Finally, the children might have been on optimum diets at the beginning of the experiment, and so could not be expected to gain at an increased rate.

There is not space to discuss these points fully. It seems probable that a mild vitamin deficiency existed, accompanied by a shortage of protein. It is possible that the vitamin tablets were not so effective as fruit and vegetable vitamins; it is probable that the children were not on optimal diets. (This last conclusion was arrived at by comparing the average weights of the boys who took the supplements with those of public-school boys.)

This experiment merely corroborates the findings of several workers in this field. Feeding of vitamins in tablets to school-children has had no appreciable effect on weight.

It would be interesting to see the effect on the weight of English school-children of the diet recommended by Brown and Robertson of Toronto as late as 1942. Who could help thriving on food such as the following: (1) A quart of milk daily (32 oz.)? (2) One generous serving of orange, grape-fruit, tomato, or raw cabbage, fruit at another meal, and two vegetables besides potato. (3) One serving of whole-grain cereal with wheat germ. (4) One serving or more of meat, eggs, fish, or fowl, with eggs three or four times a week, and liver or kidney once a week. (5) One regular dose of a good source of vitamin D during at least the six colder months of the year.

I should like to thank Vitamins Ltd. for supplying the tablets free of cost, and also all those who helped me with the experiment.

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Herpes Simplex Corneae in Malaria

Herpes simplex corneae is said to be the commonest ocular complications in malaria (Duke-Elder, 1943). Low and Fairley (1941) state that iritis, retinal haemorrhage, and optic neuritis also sometimes occur. In a series of 4,000 European cases of malaria in West Africa herpes simplex corneae was the only ocular complication noted. Rings of the malignant tertian form of malaria were demonstrable in 35% of the cases. The remainder were diagnosed on clinical grounds as malignant tertian malaria. Corneal lesions developed in the following four cases:

CASE HISTORIES

Case 1.—This patient had three attacks of malaria. In the second attack he developed herpes of the lip on the second day and herpes of the right cornea on the eighth day. The eye was red and painful and corneal sensitivity was diminished. Staining showed multiple fissures in the corneal epithelium. The eye settled in ten days, leaving one nebula. After the third attack, two months later, the nebula had faded and sensitivity had returned to normal.

Cases 2 and 3.—One patient developed herpes simplex corneae in his first and fourth of five attacks of malaria. Dendritic ulcer followed in both instances. The first herpes developed on the sixteenth day, in the left eye, and was rapidly followed by a spreading dendritic ulcer. Treated with atropine and heat, the ulcer healed in 40 days, leaving a scar. The second herpes occurred on the seventh day of a later attack of malaria. A dendritic ulcer, in the shape of a lion rampant, developed on the site of the old scar, and spread rapidly. The whole corneal epithelium was removed with a strong solution of iodine (7% iodine and 5% potassium iodide in alcoholic solution). The eye improved rapidly and was quiet within ten days, leaving the old scar and impaired corneal sensitivity. Another attack of malaria with herpes labialis three months later provoked no eye complications, although the corneal sensitivity was still impaired. The original corneal scar was then less pronounced.

Case 4.—This patient developed herpes of the left cornea on the tenth day of his second attack of malaria. A small ulcer formed near the limbus, which was slow to heal. Treated with atropine and heat, it became vascularized and quiet in five weeks.

COMMENT

In four cases of uniocular herpes simplex corneae among 4,000 cases of malignant tertian malaria corneal lesions occurred between the seventh and the sixteenth day of illness. The best result followed removal of the corneal epithelium with strong iodine solution.

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