Neosynephrin acts upon both heart and vessels in an extremely favourable ratio. It improves the filling of the heart, it adds to the strength of the beat, and while increasing the heart output often causes slight bradycardia. Though it shows a relatively brief action after intravenous injection into an animal, yet when given intramuscularly, as it very frequently is under clinical conditions, its length of action (30 to 40 minutes) is not greatly different from that of ephedrine or pholedrine (40 to 60 minutes) by the same route. It may be injected repeatedly with no loss of activity. After the administration of neosynephrin the patient rarely complains of even slight discomfort.

Phedracin appears to act almost entirely upon the vessels. It loses its pressor action upon repetition and, like ephedrine, its length of action is reduced. Owing to severe constriction of the skin vessels it may produce an unpleasant feeling of tightness.

Summary

The importance of using a substance which acts directly upon the cardiovascular system, when it is desired to restore a low blood pressure, is stressed.

Pholedrine, neosynephrin, and phedracin are compared with ephedrine in a series of animal experiments.

It is suggested that neosynephrin as well as pholedrine should be adopted clinically as a substitute for ephedrine.

The results obtained with phedracin do not favour its possible therapeutic use, although it might with advantage be given a further clinical trial.

Neosynephrin may be of value as an alternative to adrenaline in local anaesthetic preparations.

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A DEPRESSION-HYPOSEXUAL-ALOPECIA SYNDROME

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Some years ago one of us (C. A.) treated a case of complete alopecia in a man of middle age. This man complained of deep depression, with very marked hypochondriacal trends, accompanied by absolute loss of sexual interest. The alopecia was complete and all hair-bearing areas were denuded, so that it was impossible to find any remaining hair. The lack of sexual interest occurred synchronously with the fall of hair, and the patient not only was impotent but showed no interest in his wife or other women. Nor had he developed any abnormal form of sexual interest. This case progressed in spite of treatment, and when last heard of the patient had entered a mental hospital, as his depression had become severe enough for him to contemplate suicide. (Unfortunately, owing to the exigencies of the war, his notes are not available to us, nor is it possible to follow up his case.)

Record of a Recent Case

The present case is that of a man aged 33. He came from a normal family. His father died at the age of 64 from a perforated gastric ulcer, and still retained his hair at that age. His mother is still alive, is healthy, and has normal hair. She suffers from occasional attacks of migraine, but has no other symptoms of illness. He has five brothers; one died from a gastric ulcer, and another was operated on for the same reason. (One might suspect from this, and the fact that the patient also has gastric symptoms, that the family is an anxious one and that emotional disturbances tend to cause malfunction of the intestinal tract.) He had five sisters, but one died from pneumonia and one was murdered by her husband. The patient himself has had little other than the usual children's illnesses, except that he has suffered from typical migraine ever since he can remember: his eyes "half black out," then he sees bright lights and zigzags, and finally develops a severe headache which ends with nausea and sometimes actual vomiting. After the attack his head feels sore, but there is a general sense of well-being.

The patient was called up in November, 1940, and joined the R.A.F. He felt well and passed Grade I. A week later he was vaccinated, and seems to have reacted allergically to this. The first night he felt very chilled and his arm was excessively painful. He was faint next day and noticed that both arms had swollen—the oedema reaching down to his hands. He reported sick; but his condition was evidently not considered serious, and his arm was merely re-dressed. Then he complained of a sore throat and feelings of general malaise. This lasted about 14 days and then gradually passed away, although he never felt as well as he had done before. At the beginning of January, 1941, the hairdresser drew attention to a small area on the vertex of the head where there was no hair, and about the same time he himself noticed that there was a diminution of his sexual interest. Eleven weeks after the vaccination he attempted intercourse, but although he had been sexually deprived for some time he had an excessively delayed orgasm—so much so that his wife commented on it. He did not feel depressed at that period. With the passage of time the baldness developed in a patchy way, mainly over the posterior of his scalp. It then spread to the sides, and over the frontal regions the hair grew more and more sparse. He became quite bald. His eyebrows disappeared and he noticed large bare areas on his face, starting on each side of the chin and slowly spreading all over the lower face to coalesce with glabrous areas on the opposite side. This became so pronounced that he had to shave only once weekly instead of twice, as was his custom. The hair on his chest dropped out and a large amount of the pubic hair disappeared also. (This was mainly over the "male" abdominal distribution.) The only area unchanged appears to have been the axillary hair, none of which seems to have been affected even at the worst period. Simultaneously with the appearance of the extensive alopecia he felt depressed. That this was not the result of brooding on his condition but was related to his general feeling of malaise is shown by the fact that he stated definitely: "I felt depressed because I felt ill."

By June, 1941, he had reached the climax of his condition: his hair was absent except in the axillae, he was extremely hypochondriacal, was depressed, and was devoid of all sexual feeling. At this time he had an attack of abdominal pain, which he described as heartburn, but for which no organic cause was discovered. His sleep was poor and he ate little. He was transferred to an R.A.F. hospital in August, 1941, and has slowly improved since then. He was allowed home on short leave at intervals during September, October, and November, 1941. He felt little sexual desire with his wife, and when he did attempt intercourse—he felt he should do so to "prove his manhood"—his orgasm was delayed. The depression was sufficient to make him weep frequently, and he was unable to concentrate on anything. He could not write letters, and eight holes at golf exhausted him. He became excessively worried over his condition and has remained anxious about it ever since.

The condition appears to have followed his vaccination, but psychological factors may be important also—these being the fact that he was in some financial difficulty when he was conscripted into the R.A.F. and while away from home his wife developed a trivial mental ailment; but he was given a wrong idea of her state, and seems to have thought she was in danger of her life. Curiously enough, during his illness he suffered less from migraine than usual, having only three attacks during the whole of his service in the R.A.F.

In February, 1942, this man was still suffering from considerable alopecia and depression, and, as it was considered

that it might be another year before he recovered, he was invalided, since it was unlikely that he would be of much value to the Service during this period.

Laboratory Investigations.—The patient's urinary malesterone excretion was found to be 10.6 mg. a day, which is within normal limits. It is felt that this may not be significant either way, since he is now definitely recovering. The Wassermann reaction was negative.

Discussion

It appears to us that this patient is suffering from a syndrome, and since similar cases exist it is possible that it has not been recorded owing partly to the rarity of such extensive alopecia and partly because such cases fall into the hands of dermatologists who are not particularly interested in the concomitant psychological symptoms. The syndrome we would suggest consists of (1) wide-spread or complete alopecia; (2) depression with strong hypochondriacal features; and (3) diminution or complete lack of sexual desire, together with (4) diminished or absent capacity to fulfil the sexual act.

Alopecia.—The alopecia itself presents several problems. Is it directly dependent on the nerve supply or is it an endocrine deficiency which causes the fall? The distribution of the bald patches is not markedly symmetrical, so the suggestion is that the cause is endocrine rather than nervous. Again, there is no pattern suggestive of nerve or root distribution. Moreover, the delay between the causal factor and the onset of the loss of hair suggests an endocrine rather than a nervous mechanism at work. If it is an endocrine matter, then it would seem that there must be two endocrines—one which causes the growth of ordinary hair and one which stimulates the growth of sexual hair. The work of Broster and his collaborators (1938) on adrenal virilism has thrown considerable light on the endocrine factor—the adrenal cortex—and its relation to sexual hair. It seems probable, although there is no proof, that both hormones originate in the adrenal and complete alopecia is due to absence or diminution of them. The actual cause of the glandular damage, whether psychogenic or toxic, must be purely speculative. There is considerable evidence for the toxic origin. The amount of reaction evoked by vaccination, the loss of the feeling of well-being, and the fact that it is well known that alopecia commonly follows acute specific fevers, particularly if pyrexial, all suggest a toxic factor at work. On the other hand, there is the fact that this patient was in financial straits and was very anxious regarding his wife's health before he became ill. There are several well-authenticated cases in which anxiety has caused a fall of hair. For example, Spiegler (1918) recorded a case of a soldier who lost all his hair following the explosion of a shell close by him. Similarly, Pusey (1928) noted the loss of hair ten days after an emotional shock. Stern (1922) has suggested that the fall of hair is the extremity of the process which usually appears as greying of the hair. He, too, recorded alopecia following psychic trauma—the excitement of a barrage. Hurst (1940) describes cases of sudden greying of the hair within a week of strong emotional strain due to war-time experiences, also of permanent erection of the hair on the scalp and body, but does not appear to have seen any cases of alopecia.

Loss of Sexual Feeling and Power.—This lowering of sexual feeling and ability to carry out the act is very suggestive of endocrine disease. The attempts made by our patient seem to have had their origin in a psychic effort rather than a fundamental desire. It is a great pity that we were not able to arrange for investigation of his urinary male-sterone excretion during this time. On the other hand, he did not respond very strongly to injections of testoviron, so possibly the basic factor is a polyglandular one.

Depression.—The depression is accompanied by a heightened self-interest, which shows itself in hypochondriacal symptoms. The patient complains continually of his sad plight. He constantly draws attention to his terrible appearance and his miserable feelings. There is no retardation, and in neither of the cases seen has there been any delusional construction or hallucinosis. It might be tempting to explain the patient's reaction as a real response to his condition. There is no doubt that he does look bizarre with no hair or eyebrows, and he has some reason to complain and feel miserable. We would point out firmly that this is very unlikely to be the basic cause

of his symptoms. We have seen pilots, air-gunners, and others who have suffered severe burns so that their faces were scarred and disfigured, but these men did not moan or complain. On the contrary, they were inclined to joke about themselves and were usually cheerful, although much more disfigured and more permanently scarred.

Prognosis.—The prognosis usually given by dermatologists is a hopeful one. Nevertheless the hair may take a year or even two before it grows again. Presumably the other symptoms, also disappear with the reappearance of the hair, but we have had no opportunity of confirming this. That the prognosis is not always favourable is shown by the first case we saw. On the other hand, these cases must usually have a favourable termination, since wide experience in a number of mental hospitals has not brought us in contact with any further cases.

Treatment.—It would seem logical to treat these cases by psychotherapy, and this has been advocated by Hingston (1939), who claims favourable results. She also states that small doses of thyroid (1/2 to 2 g.) appear to have influenced the result. It seems more probable that testosterone propionate would be of value, but we are unaware of any really extensive and convincing experiments with it.

Conclusions

This combination of depression, alopecia, and lowered sexuality at once suggests some relationship, although doubtless a distant one, with Simmonds's disease. This illness, which is a polyglandular syndrome, is characterized by emaciation, anorexia, asthenia, precocious ageing, and general depression of glandular activity. It is usually accompanied by atrophy of the genitalia, cessation of the menses and sterility in women, and impotence and loss of sexual interest in men. There is in most cases a fall of the hair—so that the pubic and axillary hair may be absent. If the case is an early one the hair is found to be brittle and sparse. It is of interest to notice that Cahane and Cahane (1935, 1936) have described cases of diencephalic origin and suggested that these are related to Simmonds's disease. We feel that it would be unwise, on such slight clinical grounds as we possess, to make any suggestion as to the causation of the syndrome which we have described, except to point out its similarity to some of the other characteristics of endocrine disease and to suggest that it seems also to be of endocrine origin, although the cause of the damage to the glands is yet to be determined.

We have to thank Dr. Jocelyn Patterson for investigation of the sterone content of the patient's urine.

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The effect of acute loss of blood on normal persons has recently been investigated by R. V. Ebert, E. A. Stead, and J. G. Gibson (*Arch. intern. Med.*, 1941, **68**, 578). Between 760 and 1,220 c.cm. of blood was removed from each of 6 persons within 6 to 13 minutes; this was estimated to amount to from 15.5% to 19.7% of the total blood volume. Five out of six collapsed with weakness, nausea, blurred vision, sweating, and fall in blood pressure. Before the onset of collapse the pulse rate increased from 14 to 30 beats a minute, and at the height of the collapse the rate became slow (between 30 and 40 beats a minute). Restoration of the plasma volume began immediately after the bleeding and continued for the subsequent 72 hours, at the end of which it was approximately equal to the volume before bleeding. The authors observed that during the first two hours after venesection the increase of volume was contributed by a protein-poor fluid, so that there was decrease in the concentration of serum protein. After this, fluid and protein entered the blood stream simultaneously. At the end of 72 hours approximately one-quarter of the plasma protein was protein which had entered the blood stream after the bleeding. The proportions of the albumin and globulin fractions were unaltered. The authors conclude that loss of blood acted as a physiological stimulus to the production of normal protein.