

ALOPECIA AREATA: A CLINICAL STUDY

BY

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Alopecia areata is a disease quite commonly encountered in hospital practice. It was present in 2% of the 15,000 new patients seen at this clinic in 1937-41.

This paper is based on a clinical study of 114 almost consecutive unselected cases seen in hospital during the past two years. The series was made up of 81 cases of simple alopecia areata of the type which recovers after a few months, 24 cases of alopecia totalis and universalis (the initial lesions being those of alopecia areata and therefore considered to be the extreme degrees of this condition), and 9 cases of persistent alopecia areata which had been present for a period of years.

Age, Sex, and Colour of Hair

There were approximately an equal number of male and female subjects (59 male, 55 female) and for the most part the disease seems to affect both sexes equally. Brown (1929) found that with increasing age females predominated over males, but in this series there were equal numbers even over the age of 30.

These patients do not represent a true cross-section of the cases of alopecia, as many are treated in a children's hospital in the area. However, the age at which the disease first occurred was recorded; this showed that 50 (44%) were attacked before the age of 21. There were, however, 22 (19.5%) over the age of 40 (Table I). Brown, in a series of 300 cases, found a considerably higher proportion of children (57% under 21) and only 9% over the age of 40

TABLE I.—Age at Onset and Prognosis

| Age at Onset of First Attack | No. of Cases | % Cases in which Disease Persisted or Extended to Complete Baldness |
|------------------------------|--------------|---|
| 0-10 years | 23 | 45 |
| 11-20 " | 27 | 33 |
| 21-30 " | 23 | 19 |
| 31-40 " | 19 | |
| Over 40 | 22 | 23 |
| | 114 | |

The hair colour was recorded in 82 cases; 37 (45%) were dark haired compared with 42 (51%) in a control series of out-patients (Table II).

TABLE II.—Hair Colour

| | Alopecia Cases | Out-patients |
|--------|----------------|--------------|
| Fair | 16 | 20 |
| Medium | 29 | 20 |
| Dark | 37 | 42 |
| Total | 82 | 82 |

Cockayne (1933) stated that the disease is much commoner in dark-haired subjects; in this series, at least, the difference appears to be due to the higher proportion of dark hair in the population of this city.

The Disease

The best descriptions of alopecia areata are probably those of Sabouraud (1936). The pattern that he described was shown well in most of the cases. The disease begins

as one patch, and this may remain single or, after a few weeks, secondary patches may appear on other parts of the scalp. Charting of the position of this first patch revealed a significant difference between the sexes (Table III). Of the males, 35 had occipital patches and 15 fronto-

TABLE III.—Position of Primary Patch

| Position | Present Series | | Kinnear and Rogers Series of Scalp Ringworm; % Incidence | |
|----------|----------------|----------|--|--------|
| | Male | Female | Male | Female |
| Occiput | 35 (60%) | 15 (27%) | 56 | 32 |
| Vertex | 8 | 15 | 6 | 22 |
| Frontal | 7 (25%) | 16 (56%) | | |
| Parietal | 4 (7%) | 9 (16%) | 9 | 17 |
| Beard | 5 | — | | |
| | 59 | 55 | | |

vertical, while the females showed a reversed distribution—15 occipital and 31 fronto-vertical. This has not been previously recorded, to my knowledge, and may indeed be a distortion due to hospital selection (occipital patches in females passing unnoticed). Five male cases had the first patch on the beard area, and the primary patch may presumably occur on any hairy part of the body.

Before dismissing the primary patch it is interesting to compare the figures with those of Kinnear and Rogers (1948) for the position of ringworm of the scalp in 505 boys and 93 girls. The higher incidence of occipital primary infection in boys compared with girls (56% to 32%) was taken as evidence of barber-shop infection. Their figures are strikingly similar to the present series (Table III).

The secondary patches may appear anywhere on the scalp, beard, eyebrows, or body hair. The loss of one eyebrow has not the same bad prognosis as the fall of both eyebrows and lashes in the universalis cases.

Of the 114 cases 81 were those with single or multiple patches which run their course in four to twelve months.

The 24 cases of alopecia totalis and universalis are in no way an indication of the incidence of this condition; they were seen because the patients attended for a Health Service wig. Most of them had been bald for many years and the condition was regarded as permanent. All cases began in the same way as ordinary alopecia areata, but after the appearance of the secondary patches a general fall of the hair occurred, starting with eyebrows and lashes and followed by pubic, axillary, and body hair in most cases. It is interesting to note that areas not actually attacked at this time may grow hair in later life; one female patient without a hair on any of the usual areas had a marked post-menopausal facial hirsutism.

Only one case was followed from the primary patch through all the stages to complete and probably permanent universal baldness. Four cases were followed from their onset through to the totalis stage, but later on hair grew satisfactorily. An interesting point in many of the histories is that in recovery from a severe attack the primary patch is often the last to be covered. It is as if the first area is attacked more severely than the others and the follicles are more permanently affected.

The third type of case is that which may be called persistent alopecia areata. There are nine of these, and it is possible to divide them into: (1) small recurrent patches which heal and reappear continuously over a period of years, and (2) the slowly advancing type, which may be band-like (ophiasis) or round in shape and fronto-vertical in position. This appears to differ little from the ordinary alopecia except in its prognosis. Four of the second type

which have been observed for the past 18 months show little sign of change except for some alteration in the shape of the patches.

Recurrence Rate.—A previous attack of the disease had occurred in 32 cases (28%). Walker and Rothman (1950), in a follow-up of 120 cases for 5 to 20 years, reported an overall relapse rate of 86%, and believe that all cases will be found to relapse if followed long enough.

Family History

In 22 cases (19%) alopecia areata occurred in another member of the family. At first sight this would appear conclusive of a familial tendency; it agrees well with Brown (1929) and Sabouraud (1929), both of whom found a 20% family incidence. However, we could discover no account of the incidence of alopecia in the population as a whole, and in view of this 320 traumatic orthopaedic out-patients were interviewed. Eight had a history of alopecia areata, and it is possible that this incidence of 2.5% may be a little on the low side. One of the parents of the 22 familial cases had been affected in seven and a brother or sister in eight. It would be interesting to compare these figures with the families of normal subjects, as the incidence suggests there may be little difference. In Brown's 135 cases, a parent was affected in only 8 of the 28 familial cases. There was only one case in the present series with a multiple family history (grandparent and father).

It must also be noted that in 7 out of these 22 cases alopecia areata occurred in near relatives at the same time as in the patient. In none of these seven was there an obvious cause which may have affected the whole family. Savill (1944) mentions multiple cases in the family and finds it difficult to explain. It may be said that two other patients had intimate friends who suffered at the same time as themselves.

Precipitating Cause of Attack

The commonest precipitating cause was found to be mental shock or acute anxiety. If alopecia followed a few weeks after such an event then that was taken to be the cause. In 27 cases (23%) the alopecia had been preceded by some form of mental stress. In a control series interviewed by members of the Scientific Advisory Committee of the Empire Rheumatism Council (1950) 9% of 292 subjects reported some form of mental trauma within three months previous to the investigation. A further 26 cases were obviously suffering from various degrees and forms of mental disturbance, or what the patients themselves called "nerves." They had, however, been in this state for years, and it was not related chronologically in any way to the appearance of the alopecia.

It is concluded that the incidence of precipitating shock (23%) is too large to be due to chance. It is interesting to note that the incidence of mental disorder is no higher in cases of severe alopecia than in the series as a whole (Table IV).

TABLE IV

| | Whole Series | Cases of Persistent or Total Alopecia |
|---|--------------|---------------------------------------|
| Total number | 114 | 33 |
| No. with carious teeth | 17 | 4 |
| clinically infected throats | 18 | 4 |
| precipitating shock or worry | 27 | 8 |
| emotional instability not related to attack | 26 | 7 |

In addition to these 53 cases of possibly nervous origin other cases included: (1) Three cases of general infection—

one of influenza and two of measles. (2) One case of local infection: this followed a boil on the scalp, and was true alopecia areata and not the usual type of post-infective alopecia. (3) One case of local trauma: alopecia appeared on the area of trauma to the scalp. (4) One case of pregnancy: patches recurred at each pregnancy. (5) Four cases in which the patient felt unwell before the onset, nothing was found physically, and the cause was not apparently mental in origin.

It may be as well here to mention focal sepsis: 15% showed some degree of carious teeth, a figure which does not suggest that it is a frequent cause of the condition, and 16% had clinically infected throats. The incidence of these conditions is no higher in the severe alopecia cases than in the whole series (Table IV), and I cannot believe that they play a big part in the aetiology.

Thirty-one cases (27%) were found both physically and mentally to be in perfect health.

Prognosis

The prognosis of a case of alopecia areata seen in the early stages is difficult to judge. It seems that most cases recover, but to give a definite opinion is impossible. Later in the course of the disease a generalized fall of hair with complete loss of eyebrows and whitening or loss of eyelashes is grave, and when this generalized loss is rapid the case very rarely recovers. Cases of alopecia totalis without loss of body hair may recover even after a year or more, but alopecia universalis appears to be nearly always permanent. Even if there is some recovery it is rarely lasting and the condition relapses. Two factors in the history have been said to have an adverse effect on the outlook. A positive family history is the first of these. Yet in this series there were 19% with such a history in the 33 severe and persistent cases, compared with 20% for the 81 simple cases. Even if we accept the familial tendency it does not seem to influence the prognosis. Age of onset is another factor mentioned by some, and it will be seen from Table I that the disease appears to have the graver prognosis in children. Walker and Rothman (1950) also found that the prognosis was less favourable for children than adults (50% went on to total baldness, compared with 23% in adults). Of the 32 cases with a previous history of alopecia 6 became generalized, and of the 82 with no previous history 18 took a similar course.

From wigs provided it is estimated very roughly that the incidence of complete baldness in this district must be at least 1 in 5,000, and, presuming a disease incidence of 2-3%, we arrive at the possibility that 1 in 150 patients with alopecia areata can look forward to a permanent disability. The figures given in Table I are purely comparative and are probably far in excess of the true prognosis. Walker and Rothman (1950), however, believe that even in adults 23% of the cases proceed to total baldness, and that 75% of these remain permanently bald. I can account for these high figures only by presuming that they were dealing exclusively with very severe cases from the start.

Of persistent alopecia areata I can say little. I feel that patients with small recurrent patches usually eventually recover, while some of the ophiasis type progress to permanent complete baldness.

Associated Conditions

Five out of the 114 cases had associated vitiligo. The presence of that condition among the population is uncommon, and this incidence of 4% may, I feel, be significant. Roxburgh (1929) found no association with vitiligo

in his series of cases. Nail changes seen in alopecia are interesting and quite common: 13 out of the 24 totalis and universalis cases showed them, and three other cases with simple patches had them in a minor degree. Leuconychia was not included, as this is not uncommon in normal subjects.

Nail changes fall into two groups: (1) longitudinal striations with a serrated nail edge, and (2) the pitted nail not unlike that of psoriasis. Sabouraud (1936) described these changes and said that when they are present the prognosis is hopeless.

Discussion

The aetiology of alopecia areata has been and still is the centre of considerable speculation. Early writers attempted to find one cause for all cases, which, as seen in this series, is a difficult task. There seem to be two likely causes.

The first, and probable, explanation is that the alopecia represents the reaction of the body to stress—i.e., it is, in modern terminology, a disease of adaptation. Barber (1950), in a discussion of psoriasis, included alopecia areata in the same group as psoriasis and thought that they were examples of diseases of adaptation. Stresses which may result in alopecia in a person with the hair as a "target area" are trauma, mental stress, and infection.

The other explanation, a possibility which we must still consider, is that of a virus infection. Since Sabouraud, opinions have been much against infection, but alopecia would agree well with a virus disease. We might visualize a virus which, like herpes simplex, remains dormant in the scalp and which with stress multiplies to cause the primary patch, this being followed in some cases by a general infection and an attack on all hairy parts and the nails. Attempts to infect subjects with alopecia have always failed, but I doubt if this can be taken as conclusive evidence. Epidemics of so-called alopecia areata have also been largely discounted in recent years.

For the present we must content ourselves with the knowledge of the precipitating causes only.

Summary

Alopecia areata was found in 2% of the 15,000 skin out-patients seen in a five-year period, and 2.5% of 320 orthopaedic patients had a past history of the condition.

The present series of 114 cases consists of 81 of simple alopecia areata, 24 extensive cases, and 9 of persistent areata.

The incidence seems to be the same in both sexes, and was not related to the colour of the hair. The disease occurs at all ages but is commonest in the younger age group.

There appears to be a difference in the position of the primary patch between the sexes—male: 60% occipital, 25% fronto-vertical; and female: 27% occipital, 56% fronto-vertical. A previous history of the disease was found in 28%.

A positive family history was present in 19%, but it is doubted if this is really significant of a familial tendency. Other members of the family were affected at the same time in 6% of cases.

Mental trauma was a precipitating cause in 23%. Focal sepsis is thought to play little part in the causation and was no more prominent in extensive cases than in those which recovered. In 27% the health, both physically and mentally, was excellent.

Vitiligo was present in 4% of cases. Nail changes are common in extensive alopecia.

The prognosis is difficult to give in an individual case, but probably less than 1% suffer permanent ill effects. The prognosis is graver when the disease occurs before 10 years of age, but is little affected by other factors in the history.

The aetiology is unknown; alopecia could be either a disease of adaptation or possibly a virus disease.

I wish to thank Dr. H. R. Vickers, Dr. I. B. Sneddon, and Dr. Doris Fletcher for permission to publish this series.

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TREATMENT OF THYROTOXICOSIS WITH 2-MERCAPTOIMIDAZOLE

CLINICAL IMPRESSIONS

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The use of antithyroid drugs of the thiouracil series is undoubtedly established; however, as with all other treatments of thyrotoxicosis, relapse occurs in some cases and there is also the possibility of toxic effects. In many cases relapse is due to an aversion to continuing adequate treatment with a potentially toxic substance or to accepting its permanent use in maintenance doses in the same way as with thyroid substitution therapy in myxoedema. Thyrotoxic subjects treated with antithyroid drugs should be under supervision at regular intervals by units organized for long-term follow-up, with all the necessary facilities and attention, as with diabetes. In this way the patients would benefit from better control, and an opportunity would be provided for careful and concentrated study of thyroid disease.

With the use of some of the more recently introduced antithyroid drugs the toxicity factor has been much reduced, but not eliminated, and Stanley and Astwood (1948), by employing radioactive iodine tests, have been able to compare the potency of these newer drugs in man. They claim that 2-mercaptoimidazole is approximately five times more potent than methyl thiouracil; and Astwood (1949—personal communication) reports that methyl mercaptoimidazole is about 10 times more potent than 2-mercaptoimidazole.

Stanley and Astwood (1948) have briefly reported the efficacy of treatment with 2-mercaptoimidazole in a series of 20 patients with thyrotoxicosis; they found that 40–100 mg. daily was an adequate therapeutic dose. Even in severely thyrotoxic subjects a dose of 20 mg. sometimes produced nearly complete inhibition of hormone synthesis lasting as long as 11 hours. In others a dose of 20 mg. was only partially effective.

In May, 1949, 2-mercaptoimidazole became available for clinical trial in this country, and this paper reports the results of treatment of a small series of cases.