facial lesions cleared up, but the scalp lesions were not influenced to any extent. Five cases were greatly improved, and one, a case limited to the scalp, remained uninfluenced.

I am therefore able to record 22 per cent. cures, 66 per cent. improved, and 11 per cent. uninfluenced. These results do not compare favourably with those reported in Germany by Martenstein in 1922 (66.5 per cent. cures, 14.5 per cent. improved), Ullmann, Fried, and other workers. Schamberg has recently published success up to nearly 50 per cent. in twenty-five cases treated with sodium and gold thiosulphate (sanocrysin). It is quite possible that my series differs both in their selection as suitable cases and in the relatively small amounts of the drug administered.

The striking preponderance of either a tuberculous history (three cases) or a strongly positive von Pirquet reaction (four cases) in a series of nine, one of which was not examined from this point of view, lends considerable support to the theory advanced by Schaumann and those who favour the tuberculous etiology of lupus erythematosus.

In conclusion I desire to state that in my opinion krysolgan has established itself as a most valuable remedy in the treatment of lupus erythematosus, and that if it really has a specific action on tuberculous foci its effect lends further support to the theory of a tuberculous origin of the disease.

THE TREATMENT OF RINGWORM OF THE SCALP BY THALLIUM DEPILATION.*

BY

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ÉPILATION of the whole scalp is generally admitted to be an absolute necessity in all cases of ringworm of the scalp, with the single exception of kerion, which does not require this treatment.

While x-ray depilation has been the customary method of treatment for about thirty years, and on the whole a very successful method, there are certain objections to it which are obvious and well recognized.

1. X rays can only be employed with safety by those who are highly skilled and constantly employed at the work, for the dose must be very exact. A small margin of error on either side will result either in failure to produce complete defluvium or, on the other hand, in some degree of permanent alopecia. The possibility of the latter accident is the most serious objection to the method.

2. X-ray depilation is impracticable, or at any rate very difficult, for children of 3 years of age and under, for the reason that they cannot as a rule be made to keep still for the time necessary for a depilatory dose. Dr. J. M. H. MacLeod has overcome this difficulty by means of a special apparatus which he has invented, but it is a method which at present, at any rate, cannot be applied universally.

3. A very unpleasant, though temporary, inflammatory reaction of the scalp occasionally follows irradiation, while any inflammation already present is invariably aggravated, so that cases of inflamed ringworm (I do not refer to kerion) are not suitable for immediate x-ray depilation.

Any reliable alternative method of producing defluvium would therefore undoubtedly be a welcome addition to the already existent methods of attacking the disease.

The depilatory action of thallium acetate has been well known for many years, and about thirty years ago Sabouraud attempted to use the drug for the treatment of ringworm. He came to the conclusion, however, that the method was unsafe; in all probability the doses he gave were too large. At all events it was given up. After Sabouraud's therapeutic failures no attempt to make use of thallium for its depilatory action appears to have been made until quite recently, and it is due entirely to the experimental researches of A. Buschke that the method has at last attained a degree of practical usefulness.

The advantages of making use of this property of

thallium are obvious, but a dose had to be found that would be effective and at the same time non-toxic. So, about twenty years after Sabouraud had abandoned his therapeutic trials in this direction, A. Buschke, at first alone and afterwards in collaboration with L. Peiser, undertook the experimental work on animals which eventually resulted in establishing the minimal dose that could be relied upon to make the scalp depilate. This was established to be 8 mg. per kilo of body weight. An effective method of administration was found to be a single dose by the mouth, dissolved in sweetened water. Buschke obtained imperfect epilation when the drug was given mixed with food.

The therapeutic value of the treatment has been tested on a large scale in Mexico by Cicero, and on a somewhat smaller scale by Buschke in Germany, by others on the Continent, and more recently in England. A very large number of cases, altogether approaching 1,000, were reported in 1926, and the results were stated on the whole to be remarkably successful.

My own experience has been 90 cases, of which 10 are still under treatment—a sufficient number to warrant some definite conclusions concerning its value. The technique advocated by Buschke has been followed. I have given 8 mg., 8.5 mg., and 9 mg. per kilo of body weight, dissolved in about 2 oz. of sweetened water; 8 mg. has been found rather too small a dose, and I have generally used one or other of the larger doses, using 9 mg. only in certain circumstances, to which I will refer later.

I have employed two preparations of thallium acetate—one made by May and Baker, the other by Kahlbaum of Berlin, which is the preparation used by Buschke. I have not been able to observe any obvious difference in the depilatory action of the two drugs. Kahlbaum supplies the drug in tablets containing 1 decigram, 1 centigram, and 1 milligram, so that it is a simple matter to convert the weight of the child in pounds to kilograms, multiply by 8.5 or 9, and administer the required number of tablets in water.

The effect of this single dose of thallium acetate is well known; about the seventh day the hair begins to loosen, and by the fourteenth day it comes out in a most dramatic fashion. By the nineteenth day depilation is complete, except for some sparse, fine, unpigmented but quite long hairs of the lanugo type, scattered over the scalp, but found mainly near the hair margin, particularly in the frontal region. These hairs never come out, and incidentally they appear never to be infected with ringworm. The eyelashes and eyebrows do not fall, though the outer third of the eyebrows thins out occasionally, reminding one of the appearance of the eyebrows in thyroid insufficiency. In adults the pubic and axillary hairs and the beard do not come out with a dose sufficient to make the scalp depilate. The infected stumps, though absolutely loose, do not fall with the readiness of the uninfected hairs. In actual fact most of the fall appears to be the result of slight traction—for example, by the hair brush. The stumps, being very short, naturally escape this kind of traction.

The same failure of the stumps to fall out spontaneously also occurs not infrequently with x-ray depilation, when adjuvant measures have to be used, such as the application for some minutes of adhesive strapping followed by sudden withdrawal. This is a very important point, for although these loose infected stumps may come out eventually, and their persistence for a few days or even several weeks after depilation does not necessarily mean that the case will not be cured, yet it is necessary to use a fungicide treatment all over the scalp with some thoroughness to guard against reinfection of the new hairs, which begin to appear almost immediately. This injunction of the whole scalp must not be stopped until it is certain that not one of the infected stumps is remaining.

Occasionally this difficulty does not arise, for the stumps come out with the rest of the hair. This is particularly the case in inflammatory ringworms. But as a general rule it may be stated definitely that the stumps do not come out as readily as the normal hair, except in inflammatory cases, or so well as in a good x-ray depilation. The procedure, then, is as follows: A single dose of thallium

* Read in the Section of Dermatology at the Annual Meeting of the British Medical Association, Edinburgh, 1927.

acetate—8.5 or 9 mg. per kilo of body weight—is given in sweetened water. From the first day a fungicide ointment is rubbed twice daily all over the scalp. At the time of depilation (seventeenth to nineteenth day) the scalp is examined carefully for infected stumps. As many as possible are removed by means of adhesive strapping in the manner already described, or with epilating forceps. However thoroughly this is done it is certain that some stumps will be left behind. In many cases these will come out spontaneously in the course of time. It is advisable, however, to make a daily examination for stumps and to epilate with forceps, as well as to continue local treatment in all cases for a good fortnight after a careful examination of the scalp has failed to reveal the presence of any evidence of infection. I should like to refer to Dr. Roxburgh's method, which he has recently exhibited, of testing for cure by means of an ultra-violet beam—a method which I am sure will be adopted eventually by all skin clinics.

Regrowth after thallium depilation begins very early; the actual time varies a good deal, but, generally speaking, it begins within a fortnight or less of the defluvium. The point I would like to emphasize is that the chief practical difficulty in the thallium treatment is that the hair grows again so rapidly that particular care must be taken to get at all the infected hairs as quickly as possible and to protect the new hairs with fungicide treatment applied vigorously. This entails a considerable amount of trouble on the part of the doctor or nurse.

The local treatment is of the greatest importance; Buschke advocates the use of 10 per cent. sulphur ointment from the first day of treatment. Then at the time of defluvium ointment and tincture of iodine are applied on alternate days. I regret that I did not follow these suggestions of Buschke until recently, and I attribute some failures to this omission. I used at first either mercuric ammonium chloride ointment with 2 per cent. of salicylic acid, or Whitfield's benzoic and salicylic acid ointment. Buschke's treatment has been carried out in the last ten cases that have undergone full treatment, and all of these have been cured.

The weighing of the patient and of the drug must be scrupulously accurate. The difficulty of weighing the drug to the nearest milligram may be overcome by buying it weighed up in decigrams, centigrams, and milligrams.

The urine should be analysed in each case. Sulphur ointment (10 per cent.) is rubbed twice or three times daily all over the scalp, and at the time of defluvium this treatment is combined with application of tincture of iodine twice daily on alternate days, and the daily removal of as many loose stumps as possible. It is better to keep the children in bed during the treatment, though most of my cases have of necessity been ambulatory cases.

Results.

I have divided my own cases into four classes: (1) Children aged 3 years and under and for whom x-ray treatment would not be available; 16 cases, all cured. (2) Children over 3 years of age; 46 cases—35 successes, 11 failures. (3) Four of these cases had already been treated with x rays without success. All these were successfully treated. One of them was still completely bald, except for the patches which had resisted epilation. The thallium was administered two months after the x-ray treatment. An interesting feature of this case was that regrowth all over the scalp commenced within a fortnight of the defluvium due to thallium—earlier, I thought, than would have occurred had he been left alone. (4) Six cases were treated with two-thirds of a depilatory dose of thallium and either half or two-thirds of a depilatory x-ray dose; depilation either failed absolutely or was incomplete in all these cases, except one, in which I am inclined to attribute the depilation to thallium alone. This appears to prove that x rays and thallium act in different ways and that they cannot be used to supplement one another. Twelve patients ceased to attend for further observation and treatment after varying periods or attended irregularly. Some of these may have been cured eventually, for they were all supplied with ointment for local treatment. They are excluded from further consideration. Ten patients

have been treated within the past four or five weeks, and are still attending for treatment.

Other observations which appear to me to be of importance are these: Children with stout, coarse, usually black, hair resist thallium depilation more than those with fine hair. I consider that these cases require the larger dose, 9 mg. per kilo. I have noticed that the crown depilates rather less readily than the rest of the scalp, so for ringworm of this area also I consider 9 mg. advisable.

Thirty-seven cases have been treated with May and Baker's thallium, 25 with Kahlbaum's preparation. The results have been 29 successes and 8 failures with the first preparation, 22 successes and 3 failures with the second. Ten children have been treated locally throughout with sulphur and iodine, all with success, and though I cannot be certain that all cases treated by this method will be successful, the results are suggestive. Of 62 cases fully treated and observed throughout, 51 have been successful, 11 have failed; this excludes patients who have not attended for full treatment or have attended irregularly, and the cases in which x rays have been combined with thallium, so that a possible 18 further cases must be added to the failures, though some few of these may have eventually cleared up. Of 10 remaining cases still under treatment 7 have already epilated: they are undergoing sulphur and iodine treatment, and I expect them to be cured.

Toxic Effects.

I do not think sufficient stress was laid upon the toxic side of thallium treatment by those who published the first cases, or, I must confess, by myself in a small series that I published six months ago. Further experience has proved to me that these are not negligible.

There has been great variability in the degree of toxic effects, but very few patients have been entirely free from them (12 cases out of 90). The commonest symptoms are undoubtedly joint pains, particularly in the lower limbs. These pains usually begin about the eighth or tenth day, but occasionally earlier. They pass off by degrees, usually disappearing altogether in three to four weeks. There is in addition frequently loss of appetite, drowsiness, and irritability. These manifestations pass off more gradually than the pains in the joints. In some cases these general manifestations have been almost totally absent, the joint pains being the only trouble. Two of my cases, and possibly more, have unfortunately been seen by practitioners who, unaware of the facts of the case, have diagnosed acute rheumatism. The fall of hair has taken place, regrowth has occurred, and the new hair has become infected. I do not know the explanation of the joint pains, but it is possible that the drowsiness may be due to temporary damage of the thyroid gland. At any rate, it has been shown experimentally by Buschke and by Curtis that this gland suffers severe damage in animals that are given repeated poisonous doses of the drug.

It has been found also that children develop a temporary hypochlorhydria or achlorhydria during thallium treatment. With this information I have attempted to counteract the general symptoms with small doses of thyroid extract and of dilute hydrochloric acid. I have observed, apparently as a result of this, a rapid recovery to their normal condition of the children who have received this treatment. I should add, further, that in spite of this alarming list of symptoms no child that I have treated appears eventually to be any the worse in general health. This is substantiated by the experimental fact that rats and rabbits remain healthy after a depilatory dose of thallium.

Finally, it must be added that very young children are much more tolerant of thallium than older children. This may be because older children require a larger dose, but I do not think this is entirely the reason. My youngest patients have been 1 year old, and have shown no toxic symptoms whatever.

Pharmacological Action.

The very remarkable action of thallium acetate in producing alopecia is, so far as is known, shared by no other substance. The exact mechanism of its depilatory action is not absolutely known, but certain established facts appear to show that this action is upon the sympathetic nervous

supply of the follicles, and not directly on the follicle or hair bulb itself. Applied locally, thallium acetate has no depilatory action. The endocrine glands are clearly concerned in the action of the drug. By means of thallium feeding Buschke was able to keep animals (rats and mice) permanently bald. The *post-mortem* examination of animals which had undergone prolonged thallium feeds revealed in all cases changes of an atrophic nature in the suprarenal glands, the thyroid, and testes. By such feeding the animals developed a condition like cretinism. Buschke noted that only hairs which have a sympathetic nerve supply were affected; vibrissae supplied by motor nerves were not affected.

A recent paper read by Professor W. E. Dixon to the Section of Dermatology of the Royal Society of Medicine shed some light on the subject of thallium alopecia. The experimental work described proved that thallium heightened the excitability of the sympathetic system, and he compared its action to the heightening of the reflex excitability of the spinal cord by strychnine. For example, if the cervical sympathetic is stimulated with an electric current of certain strength specific effects are produced: erection of hair, dilatation of pupil, etc. If a subminimal current is used these effects are absent. If, however, a dose of thallium has been previously injected, the same subminimal current now produces a marked effect. He stated further that the action of thallium was probably upon the cell stations along the course of the sympathetic nerves, and not on the nerves themselves. This appears to narrow the field of inquiry enormously. It remains to be shown whether the fall of hair is due to a heightening of sympathetic excitability, so that reflex impulses which should normally be blocked at the cell stations can now pass through, or whether the alopecia is due to a further action of the drug of the opposite kind—that is to say, a blocking of sympathetic impulses for the time being, resulting in a temporary cutting off of the nutritional nervous supply. The latter appears at least as probable, considering that the intensity of reflex impulses passing along the sympathetic must vary greatly from time to time,

whereas the actual effect of a particular dose of thallium on the hair is absolutely constant. Professor Dixon added that it had been demonstrated histologically that the effect of thallium was to inhibit the transition of the polygonal cells of the follicles to the flattened cell of the hair.

Summary.

I will end by summarizing what appear to me to be the advantages and disadvantages of thallium depilation compared with x-ray treatment.

The advantages are that:

- (1) This treatment is extremely simple and costs almost nothing.
- (2) It can be used for children under 3 years of age.
- (3) It can be used in country districts where x rays are not available.
- (4) It can be used for cases where x rays have proved unsuccessful.
- (5) It may be used for cases of inflamed ringworm.
- (6) There is no danger whatever of permanent alopecia.

The disadvantages are:

- (1) Its toxic effects.
- (2) It is not as certain to cure as a good x-ray depilation, though this difficulty may, I think, be overcome by very careful local treatment.

In conclusion I would say that were thallium absolutely non-toxic I would use it on all cases, because I am convinced that, apart from these effects, all the difficulties can and will be overcome, but in view of the fact that it is toxic, particularly in children over 4 or 5 years old, I would reserve its use for very young children of 4 years and under, and for cases in which x rays have already failed, or are not available, or are contraindicated for one or more of the reasons I have mentioned. Regarded from this aspect I believe that thallium has found a permanent place in the treatment of tinea of the scalp.

I wish to acknowledge my indebtedness to Dr. G. C. Millis for his valuable assistance in the treatment of this series of cases.

THALLIUM ACETATE DEPILATION FOR RINGWORM OF THE SCALP: ITS ADVANTAGES AND DANGERS.

BY

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As it has been customary to treat cases of ringworm as in-patients at Booth Hall Infirmary there has been considerable scope for the use of the thallium acetate method of treatment and observation of its effects.

Mode of Administration.

A preliminary examination of the urine should be made for albumin and casts, since the presence of these, even in small quantity, is a definite contraindication to the treatment. The child is then weighed nude, and the dose reckoned at the rate of 8 mg. of thallium acetate to each kilogram of body weight.

We have found it convenient to make a solution of 0.5 gram of the drug in 5 c.cm. of distilled water; 1 c.cm. of this contains 0.1 gram, 0.1 c.cm. contains 0.01 gram, and so on. Satisfactory results have been obtained by reckoning the dose to the nearest centigram (that is, the nearest 0.1 c.cm. of the solution). A little sugar is put in a teaspoon, and the suitable dose of solution, accurately measured by means of a Record hypodermic syringe graduated in cubic centimetres, is added. This is readily taken by even the smallest child, and should be followed by a drink of water.

Further Treatment.

This single dose of thallium acetate ends the treatment by the mouth. The period of treatment where the closest medical observation is required is then, however, only

beginning, as the case must not be left to itself. Further measures may be classed under three heads:

1. *Treatment during the Pre-depilation Period.*—During the pre-depilation period every child should wear a cotton bonnet to prevent spread of infection, and it is desirable to apply a germicidal ointment to the affected areas. The pre-depilation period is very intimately associated with

2. *Observation for Toxic Signs.*—These may be manifested either as albuminuria (existing kidney disease is a contraindication to the treatment), or as bone and joint pains. One case excepted, symptoms have, in our experience, occurred in the second week. We have not noticed any roughening of the skin of the extensor aspects of the arms and legs, nor to any extent a dermatitis of the scalp. (See BRITISH MEDICAL JOURNAL, June 18th, 1927, p. 1097.) The importance of daily routine examination of the urine for albumin over a period of at least two weeks after administration must strongly be insisted on.

3. *Supervision and Cleansing of the Scalp.*—Loosening of the hairs has been observed as early as the seventh day, but the best time for epilation by forceps is about the fourteenth day after dosage. This operation should be completed by the nineteenth day. Epilation of the longer hairs which are unaffected is an easy matter, but the short, broken stumps of the diseased hairs require special handling. After the former have been removed, the ringworm areas are strapped with rubber adhesive plaster, which is allowed to remain in position for several hours; it is then stripped off and will bring away the stumps with it. New growth commences very soon, so it is essential to get epilation and strapping completed as soon as possible after the fourteenth day. We should mention that in two cases the scalp became reinfected with multiple patches of ringworm, probably because spores were left in the hair follicles. Further experience may detect in this a possible flaw in the method, but in the cases referred to the condition quickly cleared up with simple fungicidal applications.