despair, since there is, I believe, a perceptible upward trend in our journey towards the goal of enlightenment. Comfort springs invariably from the labours of defining what we know and what we do not know, and many gloomy fears vanish in facing up to the unknown. My endeavour has been to define some of the problems of tumour spread which I believe would repay further investigation. I would plead, especially, for a change in attitude towards matters which are dismissed as insoluble. Why should we throw aside the problem of metastasis as hopeless? Why not strive to find ways of circumventing the growing tumour, by inhibiting or suppressing its powers of growth, by turning it aside into less innocuous channels, perhaps by throwing obstacles in its pathways of spread or even sacrificing healthy tissues in order to hold up the neoplastic invader by means of a "burnt earth" policy?

The search for effective chemotherapeutic measures must go on with the same enthusiasm and imagination displayed by Dr. Blair-Bell throughout his pioneering efforts in this great city of Liverpool. Ideas must be sought after and cultivated. We must not be afraid to attempt the impossible; no device or technique that holds out the faintest hope of discovery can be put aside without proper reference to the work in hand. Above all, I maintain that we teachers have a special duty to perform in firing the imagination and carefully fanning the flame of enthusiasm so that our young men and women may demand an entrance into the domain of cancer research. Perhaps it will be a supreme, audacious flight of youthful genius that will bring the answer to the riddle of neoplasia.

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TOXIC REACTIONS AFTER INTRAVENOUS SACCHARATED IRON OXIDE IN MAN

SUGGESTIONS FOR IMPROVED PREPARATIONS

BY

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It is six years since saccharated iron oxide was introduced for intravenous administration in patients refractory to or intolerant of oral iron (Nissim, 1947). Saccharated iron oxide may be said to have gone through the first critical years of its life with greater success than expected, and as regards the incidence of serious reactions following its administration it compares favourably with blood transfusion. Mild or moderate side-effects, however, have been reported rather too frequently. Holt (1953) made a plea for an assessment of the general toxicity of saccharated iron oxide. It is the object of this paper to give an account of my clinical experience with this preparation, albeit limited, and to submit the findings of various authors to careful analysis in the hope of shedding light on the type, incidence, and possible causation of these reactions. This is followed by suggestions of possible procedures to eliminate or minimize the incidence of such reactions.

Toxic Reactions in Animals

Toxicity studies of intravenous saccharated iron oxide in four species—namely, mice, rats, rabbits, and guinea-pigs—have shown conclusively that the observed toxic effects are associated with precipitation (Nissim, 1949, 1953a; Nissim and Robson, 1949). This iron preparation does not precipitate when mixed in any concentration with plasma or blood *in vitro*, but undoubted precipitation occurs *in vivo* above threshold doses, depending on the species. In the mouse and rabbit this threshold is around 45 mg. Fe per kg. body weight, above which *gradual* precipitation of the compound occurs. The iron precipitates in fine particles rather than clumps as occurs after colloidal ferric hydroxide (Nissim, 1949, 1953b). For this reason the toxic effects of saccharated iron oxide after such doses occur only after an interval when enough iron has precipitated. Precipitation occurs particularly in the lung capillaries.

Plasma iron and histological studies show that at a second and higher threshold—namely, 180 mg. Fe per kg. in the rabbit—saccharated iron oxide is followed by *abrupt* but partial precipitation, and is therefore capable of producing toxic reactions immediately after the injection of unusually large doses—for example, 360 mg. Fe per kg. The toxic effects are those of multiple embolism. No toxic reactions have been noted which could not be explained on the basis of pulmonary or systemic precipitation.

Types of Toxic Reactions in Man

My experience with saccharated iron oxide includes 28 patients, 19 in the first series (Nissim, 1947) and 9 in the second (Nissim, 1949). The total number of injections was 90, and the dose per injection varied from 10 mg. to 1 g. Fe. Two samples of saccharated iron oxide were used, one with an LD_{50} in white mice of 180 mg. Fe per kg. body weight, the other with an LD_{50} of 300 mg. Fe per kg. With the latter sample, which was used in the second series, doses of 200–300 mg. were given on 20 different occasions without toxic reactions of any kind. Only four mild or moderate reactions were encountered, all of which were in

the first series and followed doses of 1, 0.5, 0.5, and 0.25 g. Fe respectively. All these reactions came on 15 minutes to several hours after the injection, the interval being shorter with the larger doses. The reactions consisted of pyrexia with headache, pain in the back with weakness, or some degree of collapse with shivering and diarrhoea.

A review of papers on the clinical use of intravenous saccharated iron oxide, however, shows that toxic reactions fall into two groups, early and late. Early reactions usually occur immediately after injection, and certainly within the first ten minutes, while late reactions occur usually one-half to six hours after the injection. The reactions so far reported by the various authors are listed in Table I under the headings of early and late. A number of observations regarding the two types of reaction can be made.

TABLE I

Early Reactions	*Late Reactions*
Symptoms of pain:	Dizziness, lightheadedness, vertigo, and difficulty in standing upright
Headache	Weakness
Pain in arms and shoulders	Cold feeling, chilliness, rigors
Pain in chest (anginoid)	Temperature—103° F. (39·4° C.)
Pain in lumbar regions	Sweating
Pain in sacral regions	Nausea, vomiting, anorexia
Pain in front of thighs or back of legs	Diarrhoea
Symptoms suggestive of sympathetic stimulation:	Generalized urticaria or papular rash (in children)
Tachycardia and palpitation	Vague discomfort, tight feeling of skin all over body
Pallor	Tightness in chest
Faintness	Headache
Symptoms suggestive of para-sympathetic stimulation:	Pains over stomach
Feeling of heat or intense burning all over body	Pain in abdomen: may be associated with rigidity
Sweating	Pain in chest (pleuritic)
Lacrimation	,, ,, lumbar regions
Nausea	,, ,, arms
Irritation of throat and coughing	,, ,, legs and feet
Bronchospasm	Collapse, with grey colour, tachycardia, pulselessness, and subnormal temperature in severe cases
Dyspnoea	
Symptoms of circulatory collapse:	
Cyanosis	
Low blood pressure	

Early Type

Reactions of the early type are by far the more common, and occur even after relatively small doses—under 100 mg. Fe (Kartchner and Holmstrom, 1950). The late reactions are infrequent and occur particularly after large doses, their frequency increasing with the size of the dose (Ramsey, 1950). Only once was a delayed reaction reported after a dose of 100 mg. Fe (Mooney, 1950). From publications which record the time of onset of reactions, the incidence of early toxic effects varies from 0 to 10% of all injections (Govan and Scott, 1949; Briscoe, 1952) and seems to depend on the sample used. Thirteen cases of delayed reaction have so far been reported in this country (Table II), only three of which occurred after doses of less than 300 mg. Fe. Nine were reported by Ramsey, who attempted massive single injections of 300–900 mg. Fe. One delayed reaction occurred after a slow infusion of 1 g. Fe (Slowik, 1950). In America, Briscoe reported only "a few" reactions of delayed onset out of a total of 57.

It is of interest that in both my series of cases (Nissim, 1947, 1949) and that of Slack and Wilkinson (1949) the incidence of reactions was far less than that reported by later authors using commercial samples. In all three series "analar" sucrose was used in the preparation of the iron-sucrose complex, and the samples were fresh—that is, the period of time from manufacture to injection was short. It seems quite possible that both factors are responsible for increase in incidence of reactions, but the purity of sucrose seems to be a particularly important point (see below).

A woman who was treated at Guy's Hospital with 100 mg. Fe of one commercial sample of saccharated iron oxide responded with a typical anginose type of pain in the chest, down the arms, and also in the small of the back after each injection. The pain came on immediately at the end of the injection and lasted two to three minutes. When the same dose of saccharated iron oxide prepared from "analar" ingredients was given on a following day, there was no toxic reaction whatever. On the third day the patient was given another commercial preparation, prepared in the same way as the second sample (Nissim and Robson, 1949), except that the sucrose was not this time of "analar" standard. Exactly the same reaction supervened, and this painful effect thus appears to be due to impurities present in commercial preparations.

Precipitation of Iron Oxide

As already pointed out, toxic reactions in animals are accompanied by precipitation of the compound in capillaries, a precipitation which may be abrupt or gradual. Although no histological evidence of precipitation is available in man, it seems reasonable to presume that the delayed toxic reactions occurring after large doses are due to precipitation, particularly as the clinical superiority of samples possessing high LD_{50} and high threshold of precipitation (Nissim, 1949, p. 138) seems to be established. Further, this type of delayed reaction (Table II) appears to be in no way different from that described by Goetsch *et al.* (1946) and

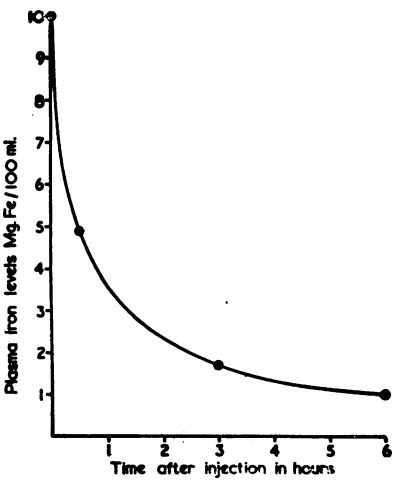
TABLE II.—*Incidence and Type of Reactions Following Intravenous Saccharated Iron Oxide*

Author	Preparation	No. of Cases	No. of Injections	Systemic Reactions			Doses in mg. Fe	Doses Causing Reactions in mg. Fe
				Early	Late	Total		
Briscoe (1952)	Feojectin	94	660	Most of 57 reactions	Few	57	30–200	—
Mitchell (1949)	Ferrivenin	Several	50	—	1	1	—	—
Mooney (1950)	—	24	—	—	1	1	—	100
Nicholson and Assali (1952)	Feojectin	16	203	?2	?1	2	150–400	200 and 400
Ramsey (1950)	Ferrivenin	11	16	3	9	12	300–900	300–900
Slowik (1950)	—	1	1	—	1	1	1,000	1,000
Barritt and Swain (1953)	Ferrivenin	1	1	1	—	1	160	100
Govan and Scott (1949)	,,	25	—	10%	—	10%	30–100	30–100
Hawkins *et al.* (1950)	,,	6	130	3 pts. on several occasions	—	3	20–100	—
Horrigan *et al.* (1950)	Feojectin	18	146	13	—	13	100–600	100–600
Kartchner and Holmstrom (1950)	,,	26	193	Most	—	35%	100–1,000	100–1,000
Librach (1953)	Ferrivenin and neo-ferrum	2	—	Several	—	Several	5–100	5–100
Scott and Govan (1951)	Ferrivenin and 2 other preps.	125	—	10–20%	—	10–20%	30–100	—
Sinclair and Duthie (1949)	Ferrivenin	23	—	1	—	1	50–200	200
Brown *et al.* (1950)	Feojectin and 2 other preps.	10	—	—	—	1	40–200	100
Cameron *et al.* (1951a)	Feojectin, ferrivenin, and 1 other prep.	6	52	—	—	0	50–200	—
Sinclair and Duthie (1950)	Ferrivenin and iviron	28	—	—	—	Occasional	50–400	—
Slack and Wilkinson (1949)	Own prep. and ferrivenin	60	—	—	—	1	25–200	200
Dickstein *et al.* (1952)	Feojectin	80	198	—	—	21	25–100	25–100

* In children.

by Nissim (1947) after colloidal ferric hydroxide, a preparation known to precipitate in the plasma. If these toxic reactions following doses of 0.3–1 g. Fe (Nissim, 1947; Ramsey, 1950) are assumed to be due to precipitation, then the threshold of precipitation in man is considerably smaller than in the mouse and rabbit—namely, about 4–10 mg. Fe per kg. in the former as compared with about 45 mg. Fe per kg. in the latter.

The common early reactions in man described by many authors are largely different in type from late reactions and are not believed to be due to precipitation. Plasma iron levels in a 60-kg. patient following the injection of 300 mg. Fe gave figures of 10, 4.9, 1.7, and 1 mg. Fe per 100 ml. at 0, ½, 3, and 6 hours (see Chart), and conformed to the type of curve obtained in rabbits. There was even and total distribution of saccharated iron oxide in the plasma immediately after injection, and the iron showed a slow decline in the plasma according to a recognized semi-logarithmic pattern for the uptake of colloidal substances by the reticulo-endothelial system (Halpern *et al.*, 1953; Biozzi *et al.*, 1953). Thus there is no evidence of precipitation in man following such doses normally, though this may perhaps occur in certain conditions—for example, severe reduction of the pulmonary capillary bed. Those factors present in certain samples which give rise to early toxic reactions in man cause no detectable toxic effects in animals, so that the superiority of samples regarding these early toxic reactions are not shown by their LD_{50} or by the absence of some typical toxic response.



Plasma iron levels in a 60-kg. patient after intravenous injection of 300 mg. Fe as saccharated iron oxide.

The anginal type of pain as well as the pain in the back seen among the early reactions, particularly in elderly patients, suggest ischaemia of poorly supplied viscera. The ischaemia may be caused directly by spasmodic action of the material on the coronary or renal vessels. Alternatively, it may be caused by dilatation of vessels in the splanchnic area with diversion of the blood thereto. The list of early reactions shows that sometimes the responses suggest sympathetic stimulation, at other times parasympathetic stimulation. It is of interest, however, that the injection of tetraethylammonium chloride in one case simultaneously with saccharated iron oxide did not prevent this painful type of reaction, but the injection of calcium gluconate in another diminished its intensity (Horrigan *et al.*, 1950). Only a proportion of people (10–20%) seem to be susceptible to these early reactions.

Perhaps the strongest support for the dual mechanism of the reactions is obtained from the paper of Ramsey, who gave doses of 300–900 mg. Fe to 11 patients. Delayed reactions, which are extremely rare in doses under 300 mg., occurred here in 9 out of 16 injections (56%). Early reactions, on the other hand, occurred only in three out of 16 injections (19%), a frequency not much higher than that reported after the usual smaller doses. More interesting still is the fact that two of the latter three patients, having recovered from their transient early reactions, showed the delayed type of reaction several hours later, after a period entirely free of symptoms between the two episodes.

Toxic Reactions in Tuberculous Patients

Librach (1953) described two cases of toxic reactions to intravenous saccharated iron oxide in patients with pulmonary tuberculosis and discussed the possible mechanisms of iron intoxication in detail. It is pointed out here, however, that a different mechanism may have operated in these two cases, both of which had a severe involvement of the lungs with the tuberculous process. One was described as a case of chronic pulmonary tuberculosis complicated by amyloid disease and massive albuminuria; the other had tuberculous bronchopneumonia. In both cases severe limitation of lung capacity was likely, with marked diminution in the lung capillary bed. This may be an important point in the consideration of the mechanism of toxicity of intravenous saccharated iron oxide. Animal studies show that saccharated iron oxide is most likely to precipitate in the lung capillaries after intravenous injection (Nissim, 1953a), since it is through these capillaries that the iron passes before being adequately diluted in the blood. Another favourite site of precipitation is the kidney (Nissim, 1953c), because of the increase in iron concentration following plasma filtration through the glomeruli. Saccharated iron oxide can precipitate both immediately and gradually above certain threshold concentrations, and it seems reasonable to suppose that such precipitation is more likely to occur with small doses when there is severe diminution in lung reserve. This is a point worth bearing in mind when intravenous iron is considered for such cases. Although in Librach's cases the early reaction may have been due to impurities, as discussed previously, the epileptiform fit and pain in the chest lasting for 24 hours in Case 1 and the dyspnoea and cyanosis in Case 2 are compatible with reaction of the second type, in this case due to abrupt precipitation. The restriction in the lung capillary bed may have been made worse by the previous two injections given without untoward effects.

Librach invoked the iron transport mechanism of the β-globulin-fraction iv–4(8) of Cohn, or siderophilin, as being partly responsible for the occurrence of iron reactions in these subjects. The work carried out on plasma iron following saccharated iron oxide throws doubt on this hypothesis. Klopper (1951) found that toxic effects arose only when the iron-binding capacity is exceeded in the individual injections. It is pointed out here that siderophilin cannot be involved in the transport of the iron of saccharated iron oxide to any extent, since calculation shows that the iron-binding capacity of the total plasma in an adult is only about 16 mg. Of this total a third is already bound to iron, so that doses in excess of 10 mg. should give rise to toxic reactions. This is evidently not so, as shown by the plasma iron levels of 5–10 mg. Fe per 100 ml. maintained for a period of hours without the slightest toxic manifestation.

Saccharated iron oxide is a colloidal compound the iron of which is not split off easily. Its estimation in plasma requires the use of much larger quantities of HCl than is usually employed (Nissim, 1953b), and this accounts for the much lower plasma iron figures obtained by previous workers following intravenous saccharated iron oxide (Cameron *et al.*, 1951b). The proportion of plasma iron estimated by the usual methods—for example Laurell's (1947) method—after injection of saccharated iron oxide is not greater than the proportion before injection (20%), suggesting that little splitting of the compound, if any, takes place *in vivo*. It is possible that certain preparations of saccharated iron oxide contain a small proportion of diffusible or ionic iron as impurities, but until this is shown to be the case toxic reactions due to oversaturation of siderophilin remain hypothetical. Cameron *et al.* (1951a) found that following injections of saccharated iron oxide the total iron-binding capacity of serum was reduced but never approached zero, so that the belief that saccharated iron oxide remains unsplit in the plasma finds additional support here.

Allergy

Librach further believed that the question of allergy is important. Evidence for natural hypersensitivity to impurities in certain commercial samples exhibiting itself in the early and usually transient type of reaction has already been presented. These impurities may have the nature of histamine releasers, as suggested by the bronchospasm reported in some patients (Sinclair and Duthie, 1949). Acquired allergic hypersensitivity to a component or impurity in the preparation, however, is another matter. The repeated injection of saccharated iron oxide in animals has never resulted in allergic manifestations (Cappell, 1930; Nissim, 1953). In man the incidence of reactions of the early type is not greater after later injections than after first injections. The incidence of the delayed type of reactions decreases if anything with repeated injections (Ramsey, 1950) apparently owing to hypertrophy of the reticulo-endothelial system (Cappell, 1930). The occurrence of a reaction in a patient following an injection of saccharated iron oxide when previous doses were well tolerated may possibly be due to differences in batches of the preparation (Dickstein *et al.*, 1952). However, the occurrence of isolated instances of acquired hypersensitivity—for example, the case of Sinclair and Duthie (1949) and the two cases of Librach—cannot be ruled out, but on account of their rarity other possible causes must be considered—for example, change of batch—before such a hypothesis is accepted.

The suggestion put forward by Ramsey for the late reactions is interesting. He noted that they resembled in a striking manner those symptoms of paroxysmal haemoglobinuria from cold, and believed that they "may well be caused by sudden increased activity of the cells of the reticulo-endothelial system." To what extent overactivity of the reticulo-endothelial cells is by itself capable of producing toxic symptoms is a problem difficult to answer. The injection of colloidal dextran in *relatively* large doses or of vital dyes which are taken up by the reticulo-endothelial cells seems to be devoid of toxic effects. Saccharated iron oxide is certainly taken up by the reticulo-endothelial system, but it is also known that, in animals, saccharated iron oxide precipitates above a threshold level, and this seems the obvious mechanism responsible for the toxic effects in man after large doses. Other hypotheses lack experimental evidence.

Librach (1953) discussed "iron poisoning" in rather general terms, and included in his discussion cases of toxicity after intravenous saccharated iron oxide and after oral ferrous sulphate (Prain, 1949) without adequate distinction. It cannot be too strongly emphasized that, apart from completely ionized ferrous and ferric compounds, many iron preparations are in fact non-ionized complexes with entirely different mechanisms of toxicity, mechanisms which depend on the chemical reactivity and other properties of the whole molecule (Nissim, 1953d). Indeed, some preparations show different mechanisms in the causation of death at different dose levels. Discussion of toxicity must therefore be confined to the compound in question, unless it is shown that the compound is ionized either partly or wholly, when the mechanisms of toxicity for either ferric or ferrous ions may be invoked.

Reaction in a Fatal Case

In the fatal case reported by Barritt and Swain (1953) it seems fairly clear that the reaction was of the early type without evidence of precipitation. The absence of multiple emboli at necropsy and in the toxicity tests carried out on samples before and after injection seems to rule out this possibility satisfactorily. It seems likely that the mechanism of ischaemia discussed previously was responsible for the fatal outcome, especially on account of the post-mortem evidence of calcification of both coronaries with complete occlusion of the right artery. It is difficult, however, to assess the seriousness of the part played by intravenous iron, as such a patient may succumb to an attack of coronary occlusion even after a relatively mild reaction. It becomes obvious, nevertheless, that particular care should be observed with such cases.

Infants and children seem to tolerate saccharated iron oxide in relatively large doses—25–100 mg. Fe (Bramham, 1952; Dickstein *et al.*, 1952), in contrast to elderly patients, who tolerate it less well than normal adults (M. R. Jeffrey, 1952, personal communication). Reactions in children are mild. In a series of 198 injections in 80 infants and children, Dickstein *et al.* reported three cases of generalized papular rash, which suggest an allergic response. The rash lasted only for one day. All of nine febrile reactions were associated with one sample of the preparation and ceased when a fresh batch was used. Although these febrile reactions were delayed in onset (appearing in about two hours) and lasted some two to three hours, it is difficult to attribute them with certainty either to allergy-producing impurities or to precipitation.

Conclusions

Sucrose and other substances used in the preparation of saccharated iron oxide should be of high standard.

There is evidence from histological studies in animals injected with two- to three-year-old solutions of saccharated iron oxide that the character of the compound undergoes slow alteration in solution with increase in diffusibility, and its uptake by fibrous-tissue elements becomes marked. This change may be associated with increase in toxicity or allergy-inducing properties in man and may be prevented by keeping the compound and ampoules in powder form just as practised with intravenous barbiturates. If this reduces the incidence of toxic effects the additional cost of the procedure would be justified.

It may prove possible to separate impurities from solutions of saccharated iron oxide by dialysis. Further, saccharated iron oxide may consist of colloidal particles of various sizes, and fractional ultrafiltration may give a more uniform preparation of reduced toxicity.

The extent to which these suggestions are compatible with the cost of manufacture can be decided only by the various firms engaged in the preparation of saccharated iron oxide. The use of analar ingredients seems to be the easiest step, and this is believed to have been already adopted by some drug firms.

Summary

The frequency and type of toxic reactions following intravenous saccharated iron oxide are discussed. A review of the incidence of these reactions in the hands of various workers is presented.

Reactions are of two types, early and late; a list of the toxic effects in the two types is given. Early reactions are believed to be due to individual hypersensitivity to impurities apparently present in commercial (*B.P.*) sucrose and may be allergic in type. Particular care should be taken in patients with arteriosclerosis, as the frequent transient anginal type of pain and back pain suggest ischaemia of the myocardium and kidneys.

The majority, at least, of delayed reactions are believed to be due to the gradual precipitation of the compound as occurs in animals following large doses. Some precipitation of saccharated iron oxide may possibly occur immediately after injection if the capillary bed in the lungs is greatly reduced by disease or the preparation injected too rapidly.

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MANAGEMENT OF THE COMMON VARIETIES OF SCALP RINGWORM*

BY

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The differential diagnosis of the various types of scalp ringworm is of importance, since good treatment follows accurate mycological diagnosis. It is not necessary to have the result of mycological culture before treating any individual case. Considerable accuracy in clinical diagnosis can be achieved when one has, as a background, full knowledge of the various types of fungi which are endemic or epidemic in the area. One can simplify diagnosis and arrive at sound practical treatment by concentrating on the three, four, or five fungi which occur in the locality (Table I). In the North of Ireland there are four important fungi (Beare and Cheeseman, 1953), which accounted for 99% of 1,157 cases of tinea capitis seen between May, 1948, and December, 1952, and from which the responsible organisms were identified. These four fungi are *Microsporum audouini* (889 cases), *M. canis* (178 cases), *Trichophyton sulphureum* (55 cases), and *T. discoides* (24 cases). Three other fungi were encountered during this period—namely, *T. mentagrophytes* (8 cases), *T. equinum* (2 cases), and *T. schönleini* (1 case).

TABLE I

Fungus	Animal	Inflammatory Reaction	Wood's Light	Outbreaks	Treatment
M. audouini	None	None	Green fluorescence	Large epidemics often occur	*X*-ray epilation
M. canis	Kitten	None or moderate	Green fluorescence	Usually small outbreaks affecting about 5–15 children	Fungicidal ointments
T. sulphureum	None	None	Nil	No very large outbreak so far reported, but general incidence is apparently increasing	*X*-ray epilation
T. discoides	Calf	Severe	Nil	Individual cases or 3–4 in a family	Starch poultices; extraction of loose hairs with forceps; soothing local applications

An easy and useful practical classification of the four common types of tinea capitis is by division into Wood's-light-positive and Wood's-light-negative cases, and subdivision of each of these two groups into human and animal types of fungi, as follows. Wood's-light-positive: human, *M. audouini*; animal, *M. canis*. Wood's-light-negative: human, *T. sulphureum*; animal, *T. discoides*. These four main groups are discussed in turn.

M. audouini Infections of the Scalp

Recently there has been considerable discussion regarding the possible effectiveness of local ointment treatment for cases of tinea capitis due to *M. audouini*. Among the best results are those obtained by Schwartz *et al.* (1946), who, in a carefully conducted and very practical trial, claimed 274 cures out of 445 children treated with local medications within a 16-months study period (61.6%). Similar results were obtained by Barlow *et al.* (1950). It would be fortunate indeed if we could cure this type of scalp ringworm by local application of a simple ointment, but the conservative treatment of this variety requires certain ancillary measures which the average general practitioner or school medical officer would find extremely difficult to carry out.

Treatment with Ointment.—The disadvantages of local ointment treatment for this condition, even assuming that this treatment is really effective and that cure is not spontaneous—and this is still in debate—include the following. (1) Treatment has to be carried out by reliable trained persons and not left to parents or friends. (2) During the time that the child is having treatment, unless supervision is very close, he will be infectious. (3) The failure rate over a reasonable period, such as six months, is considerable, as can be seen from an examination of the various clinical trials so far reported. (4) Some of the cures seem to have acted by producing local kerion-like reactions. I have seen these "artificially produced kerions" leave permanent scarring. (5) It is usually necessary to shave the children's scalps. (6) *X*-ray therapy centres are still required to deal with those children who fail to respond to ointment therapy.

Advantages of X-ray Epilation.—(1) *X*-ray epilation for this form of scalp ringworm offers an almost 100% certain cure within a period of four to six weeks. The treatment can be carried out in less than an hour, it is completely painless, and from all practical points of view it is safe if used by people who have been thoroughly trained in this method of treatment. Hair regrowth in boys is complete in six months. (2) The amount of co-operation required between hospital staff and parent is reduced to a minimum. One has only to get written consent, have the child for an hour, and then, no matter what the parents do subsequently, that child will almost certainly be free of infection in a month. (3) Unruly and obstreperous children can be conveniently managed under a light general anaesthetic.

Steps Taken in a Series of Cases

In 1948 it was estimated that there were about 1,000 cases of *M. audouini* scalp ringworm in the North of Ireland. The following steps were taken to deal with this campaign. (1) Examination of all schoolchildren within the affected areas by a nurse using Wood's light. In Belfast 50,000 such examinations were made and 225 cases found; 100 further cases were discovered among relatives of non-school age. (2) General practitioners and school medical officers were encouraged to refer their cases to a ringworm centre. (3) Wall maps were made out and coloured pins inserted to denote the homes of infected children. (4) An adequate

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