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## SPOROTRICHOSIS IN IRELAND<sup>(1)</sup>

A REVIEW

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### INTRODUCTION

SPOROTRICHOSIS is a chronic fungal infection that is usually confined to the dermis and subcutaneous tissue, presenting typically with one or more ulcerating, gumma-like granulomas. Its cause is *Sporothrix schenckii*, a mould that has its natural habitat in decaying vegetation, straw, soil and the like, and occasionally on living plants, such as barberry (*Berberis*) and gorse (*Ulex*). The sporothrix enters the tissues through superficial wounds, such as abrasions, or when the skin is penetrated by contaminated spines or thorns of plants. In some cases the initial lesion is followed by ascending ulcerative lymphangiitis (Fig. 1); lymphadenitis seldom results, even in these cases. Disseminated haematogenous ('septicaemic') sporotrichosis and visceral sporotrichosis are fortunately very rare – the mortality of these forms of the infection is very high. Cutaneous sporotrichosis, with or without lymphangiitis, may run a long course but seldom, if ever, puts the patient's life in any danger. Confirmation of the diagnosis is most regularly and reliably obtained by culturing the causative fungus from the lesions, a procedure that is usually straightforward, provided there is no bacterial contamination. Unlike virtually all other deep-seated fungal infections, sporotrichosis can seldom be diagnosed by histological examination: this is because the sporothrix is rarely demonstrable in infected human tissue (Symmers, 1964).

The disease is of worldwide occurrence. It is seen frequently in some lands and very rarely in others. The number of cases in an area may vary remarkably from

(1) The names sporotrichosis for the disease and *Sporothrix schenckii* for the fungus that causes it are used in this paper in accordance with the recommendations in Medical Research Council Memorandum No. 23, *Nomenclature of Fungi Pathogenic to Man and Animals*, 3rd edition (London, 1967: Her Majesty's Stationery Office).

year to year or decade to decade. Factors influencing the prevalence of sporotrichosis include standards of living, occupation, working conditions and climate (particularly changes in climate that favour or discourage saprophytic growth of the sporothrix in the environment [Mackinnon, 1947-49]). The disease has never been other than a rarity or curiosity in the British Isles: including the four cases that are formally reported for the first time in the addendum to this paper<sup>(2)</sup>, I know of only 16 published cases of sporotrichosis diagnosed in the British Isles (Table). In at least five of these the infection was acquired overseas – of the remaining eleven no fewer than six originated in Ireland (three in Dublin, one in Belfast, one in rural Armagh and one in Fermanagh – see Case Reports in the addendum). The predominance of Irish cases has prompted this paper, and the opportunity is taken to present some hitherto unpublished observations on sporotrichosis in Ireland by doctors and laymen whose names will still be known to some readers of the *Journal* at home and overseas.



FIG. 1. *Ascending lymphangitic form of cutaneous sporotrichosis. The lesion at the site of inoculation over the medial aspect of the hand at about the level of the neck of the fifth metacarpal bone had healed when the photograph was taken, leaving a small pigmented scar. The lymphangitic lesions of the forearm and upper arm are at various stages of active ulceration or healing. (From a colour transparency kindly prepared by Dr. A. González Ochoa.)*

#### HISTORICAL NOTE

Sporotrichosis was first recognized in December, 1896, by Benjamin Robinson Schenck, a medical student, while working with Simon Flexner in the pathological laboratory of the Johns Hopkins University and Hospital in Baltimore, Maryland.

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(2) Two of these four cases were described briefly in an account of sporotrichosis presented at the meeting of the Pathological Society of Great Britain and Ireland in Glasgow in July, 1963.

Schenck's observations were published in 1898, the year in which he graduated in medicine<sup>(3)</sup>. He isolated the sporothrix from the lesions of a characteristic case of the ascending lymphangitic form of the disease.

The disease was first recognized in Europe in 1903 by Lucien de Beurmann and his house physician, Louis Ramond, at the Hôpital Saint-Louis in Paris. Their patient presented with multiple subcutaneous nodules, simulating cysticercosis. They consulted Sabouraud, the great French dermatologist, about treatment: he advised them to try potassium iodide, on the grounds that he had often found this drug helpful in cases of another fungal infection, actinomycosis. De Beurmann and Ramond cured their patient with the iodide. They share the credit for introducing iodide therapy of sporotrichosis with Lutz and Splendore (1907) of Sao Paulo, Brazil, whose first patient with this disease had been cured with iodide in 1902. To this day iodide remains the most effective and the safest agent in the treatment of cutaneous sporotrichosis (iodide is usually ineffective in cases of generalized haematogenous and visceral sporotrichosis, which are likely to end fatally unless treated with the antifungal antibiotic amphotericin B).

A most important occasion in the history of this disease was the publication in 1912 of the two volumes of the remarkable monograph, *Les Sporotrichoses*, by de Beurmann and his colleague Henri Gougerot, dermatologist to the Hôpital Saint-Louis, Paris. Between 1903, when the first French case was recognized, and the end of 1911, when their manuscript was completed, over 200 cases of sporotrichosis had been diagnosed in France: these formed the material for the book, which is still the most comprehensive account of the disease that has been written<sup>(4)</sup>. Since the 1914–18 war sporotrichosis has become a rare disease in Europe, including France – the explanation of this change is unknown, for demonstrably pathogenic strains of the fungus are still present in French soil: perhaps it is the improvements in living standards, and in nutrition particularly, that are responsible (Mariat, 1963).

In contrast to the earlier predominance of European cases in the literature, most contemporary accounts of sporotrichosis come from the United States of America, Mexico and other American lands. In Mexico, for instance, sporotrichosis is the most frequent of all the deep-seated fungal infections (González Ochoa, 1954): on one day alone of a visit to a large general hospital in Mexico in 1966 I saw more than forty patients under treatment for confirmed sporotrichosis of the skin.

One of the most remarkable circumstances in the history of this fascinating disease is the recognition of its potential importance as an occupational disease. This has been a feature of the disease right from the first recognized case – Schenck's patient had scratched his finger on a nail while at his work in the iron trade – and ever since there has been a steady flow of reports of sporotrichosis following minor injuries at work, particularly among nursery employees, professional and amateur gardeners and agricultural workers liable to suffer penetrating wounds by spiny and thorny plants or to have other skin wounds contaminated by soil or other materials that may harbour the fungus in its saprophytic state. Brickmakers and

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(3) Schenck became a gynaecologist and practised in Detroit. He died in 1920, aged 47.

(4) There is much in *Les Sporotrichoses* that is regarded today as controversial. This does not detract from the historical merits of the work.

pottery workers, and others who work with straw and the like, are similarly prone to the infection. But the most outstanding instance of occupational sporotrichosis is the outbreak in South Africa among the miners in the Witwatersrand gold mines: with the occurrence of several thousand cases within a period of only a few years it was no exaggeration to state that "the economic well-being of the gold mining industry, and indeed of the whole country, was threatened" (*Sporotrichosis Infection on Mines of the Witwatersrand: A Symposium*, 1947). Luckily, the disease was brought under control following chemical treatment of the mine timbers to render them resistant to saprophytic colonization by the sporothrix: its incidence among the miners is now a twentieth or less of what was the case when the outbreaks were at their height (Pringle, 1963).

#### SPOROTRICHOSIS IN THE BRITISH ISLES

No cases of sporotrichosis that had been diagnosed in the British Isles were published until 1911<sup>(5)</sup>. In that year three cases were identified and reported – one by Norman Walker at the Royal Infirmary in Edinburgh (Walker and Ritchie, 1911)<sup>(6)</sup>, one by Ernst von Ofenheim at St. John's Hospital in Lewisham (von Ofenheim, 1911) and one by H. G. Adamson at St. Bartholomew's Hospital, London (Adamson, 1910–11). These cases are included in the Table. Although these are the earliest published cases, others had in fact been diagnosed in the British Isles – in Ireland – before 1911 and confirmed by isolation of the sporothrix (see below).

#### *Sporotrichosis in Ireland*

The first published case of sporotrichosis in which the infection had been acquired in Ireland was reported in 1918 in the *Dublin Journal of Medical Science* by Wallace Beatty, honorary professor of dermatology in the University of Dublin and physician to the Adelaide Hospital in Dublin. Four years later the second Irish case was published by Adamson of St. Bartholomew's Hospital in London (Adamson, 1921–22). As far as I know, no further cases of Irish origin have been published until now: four Irish cases are recorded in the addendum to this paper. That other cases have been recognized in Ireland is indicated, I believe, by the following reminiscence of a medical student's Sunday in Belfast in 1935.

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(5) It is sometimes said that a case of sporotrichosis was studied in London in 1900 by Alexander Foulerton, then director of the Cancer Research Laboratories and lecturer in bacteriology and public health in Middlesex Hospital Medical School. This is incorrect: Foulerton's study, which was published in 1901, concerned a culture of the sporothrix that had been sent to him from the United States of America by Ludvig Hektoen, professor of pathology in Rush Medical College, Chicago. Hektoen had isolated the fungus in 1899 in cultures of pus from a child with ascending lymphangiitis who was under the care of C. F. Perkins, a practitioner in Shenandoah, Iowa. It was Hektoen and Perkins (1900-01) who gave the fungus the name, *Sporothrix schenckii*, by which it is now properly known. Their patient, it is interesting to note, was still in excellent health when seen in 1964, 65 years after being cured of his infection at the age of seven years (McFarland, 1966).

(6) Walker's secretary, Miss Rae, made a fine cast of this patient's infected arm, beautifully illustrating the typical clinical picture of the ascending lymphangiitic form of the disease. The cast has been familiar to generations of students of dermatology through the coloured reproduction included in Professor Percival's *Introduction to Dermatology* (Percival, 1956).

*A Sunday Round in the North of Ireland in 1935*<sup>(6a)</sup>

It was the custom of Surgeon T. S. Kirk<sup>(7)</sup>, then senior surgeon to the Royal Victoria Hospital, Belfast, to take his son<sup>(8)</sup> and other students<sup>(9)</sup> on his Sunday morning visit to '9 and 10' at the Royal or to the Belfast Hospital for Sick Children. Often we were then taken to his home at 10, University Square, for lunch. On some of those Sunday afternoons Kirk would take one or more of us on his visits to country doctors and their patients. Sometimes the visits provided occasions for assisting at his operations in country hospitals or in patients' homes.

It was on such a round, in the summer of 1935, that I first saw a case of sporotrichosis. On the way to visit the patient, a farmer in County Armagh, Mr. Kirk explained what the disease was. He had been familiar with it since his student days in Belfast in the early 1890s, and had seen in all about six cases in the course of almost 45 years' experience in the North of Ireland. All but one of these cases seem to have been instances of the classic ascending lymphangiitic form of the infection; the exception had presented with disseminated subcutaneous granulomas (a form of sporotrichosis frequent among the cases studied by de Beurmann and Gougerot in France between 1903 and 1911 but otherwise rarely recorded). Most, if not all, of Kirk's patients were countrymen, and about half of them gave a history of running a thorn deeply into the skin at the site of the initial lesion. The first patient whom he saw was a road-mender from near Ligoniel whose ulcers he had attended to over a period of months while a dresser in the Extern Department of the old Royal Hospital in Frederick Street, Belfast: this was before he graduated in Medicine in the Royal University of Ireland in 1893 (Schenck, whose original publication appeared in 1898, saw the disease first in 1896). Mr. Kirk did not discover the nature of the disease until the sporothrix was cultured from the lesions of his third patient by my father "not long after he came to Belfast"<sup>(10)</sup>: this patient was quickly healed with iodide of potassium by mouth.

The case of the patient whom we visited on that Sunday in 1935 is included in the addendum to this paper (Case 1). When seen then he had been on treatment with iodide for two weeks and the lesions were healing well: their distribution along a line of subcutaneous lymphatics in the forearm and upper arm was so striking that it seemed unlikely that the diagnosis would be overlooked when next a patient with this condition was seen. It was 19 years before I again saw such a patient (addendum, Case 2).

After our drive Surgeon Kirk came to my parents' home in Wellington Park for tea. As on most Sunday afternoons after my father's retirement, Professor R. M. Henry<sup>(11)</sup>, then still Professor of Latin in the Queen's University, had dropped in for a chat with my father. On this occasion he was accompanied by his brother,

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(6a) This account is taken from notes made at the time.

(7) Thomas Sinclair Kirk (1869-1940).

(8) Christopher Kirk, now in practice in Dunedin, Otago, New Zealand.

(9) T. T. Baird, now working in Belfast, C. R. Murdock (1914-1968), and I were the most frequent of Surgeon Kirk's guests on these occasions, which gave added reality and purpose to our preclinical years at Queen's University, 1934-36.

(10) William St. Clair Symmers (1863-1937). He came to the Musgrave Chair of Pathology in Queen's College, Belfast, in 1904 and retired in 1930.

(11) Robert Mitchell Henry (1873-1951).

Paul<sup>(12)</sup>, the Irish landscape artist. Conversation turned to the day's surgical round and Surgeon Kirk referred again to the case of sporotrichosis that he and my father had investigated together some thirty years earlier. My father recalled five or six further cases that had been proved by culture or animal inoculation during the 26 years he had spent in the pathology laboratories in Belfast. All but one of the patients had worked on farms or in gardens, and at least three had blamed the infection on deep pricks by gorse or barbery spines: one of these was a gardener who worked for a Queen's University professor living in Gilnahirk and one was a retired military man who lived in Windsor Avenue and was well known as an amateur gardener. The patient who had no particular association with the land was a schoolboy with sporotrichosis of the eye (Case 4 in the addendum).

Although the Henry brothers were not medical men, they had a remarkable knowledge of Irish lore relating to illness and folk remedies. R. M. Henry spoke that afternoon of cases he had seen of a skin disease that exactly fitted the description of the ascending lymphangiitic form of sporotrichosis: this condition had been familiar to him during his boyhood, in the 1880s, as a rare affection among country people, including fishermen on the coast, in parts of the West, North-West and North of Ireland. Paul Henry mentioned that the traditional way to treat this ulcerative disease was to apply compresses of kelp or of boiled seaweeds and to take a decoction of dulse (*Rhodymenia palmata*, the common Irish edible seaweed) internally over many weeks, until healing resulted. The efficacy of such treatment could have been due to the iodine content of the seaweeds, if, as seems to be quite possible, the disease was indeed sporotrichosis.

As far as I have been able to find out, thirty years after that Sunday tea, and three-quarters of a century after the Henry brothers knew of the condition, no disease with such manifestations is now known in any parts of Ireland, either to doctors or among the country and fishing people themselves. It would be interesting to hear if readers of the *Journal* have seen any cases of sporotrichosis in Ireland. The remarkable fall in the frequency of cases of this disease in some lands, e.g., France, has been referred to already: it is possible that something comparable has occurred in Ireland.

#### SUMMARY

Altogether only 16 cases of sporotrichosis diagnosed in the British Isles have been published. In at least 5 of these the infection was acquired in some other part of the world. Of the rest, 6 originated in Ireland, including 4 cases that are reported for the first time in the addendum to this paper. Reference is also made to unpublished Irish cases of which no formal records are now known to exist.

#### ACKNOWLEDGEMENTS

In addition to the acknowledgements that are indicated by the text of the paper and its addendum to be due to my teachers and old friends named here, I want to mention my appreciation of the kindness of the late Dr. Ivan H. McCaw of Belfast and of the late Dr. J. E. M. Wigley of London, who took over clinical care of two of the patients (Cases 2 and 3 respectively) and who permitted publication of their clinical observations. I am also indebted to Professor Raymond Vanbreuseghem of Antwerp and to Dr. Jacqueline Walker of London for advice about the cultures in Cases 2 and 3.

Mr. R. S. Barnett helped with the preparation of the photomicrographs.

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(12) Paul Henry (1880-1958).

## FOOTNOTES TO TABLE OVERLEAF

(a) This table includes only those cases of sporotrichosis diagnosed in the British Isles that have been formally published. The diagnosis has been made correctly in a number of cases that have not been reported, *e.g.*, Surgeon Kirk's and my father's cases of sporotrichosis acquired in Ireland (see text, pages 89 and 90). A more recent case of sporotrichosis acquired in England was recognized by Dr. A. J. Rook at Addenbrooke's Hospital, Cambridge, in 1964. My own unpublished cases include (a) subungual sporotrichosis acquired in Warwickshire by a woman who walked into a hedgehog in the dark while wearing sandals, one of the animal's spines running under the nail, (b) localized cutaneous sporotrichosis acquired in Hertfordshire by an amateur gardener who ran a barbery spine into one hand, and (c) two more cases of cutaneous sporotrichosis originating in Africa (one in the Congo and one in Malawi – the cases included in a published table of African mycoses seen in Britain [Symmers, 1966c]).

I know of only one case of sporotrichotic infection in an animal in the British Isles – a railway rat-catcher's ferret (Symmers, 1964a). Sporotrichosis appears to be rare in animals; most of the published instances have concerned horses (Ainsworth and Austwick, 1959).

- (b) Several of the earlier cases in this table were reported in more or less detail in two or more publications. Only the most important reference is given here in each case.
- (c) The case reported by Greig is the first on record of sporotrichosis acquired anywhere on the African mainland (a case had been reported from Madagascar by Carougeau in 1909). No further South African cases were reported until 1927, when Pijper and Pullinger described the first recognized outbreak in the gold mines (see text, page 88).
- (d) Bass is a traditional name for various hard vegetable fibres used in the manufacture of coarse brushhes, matting, and similar articles.
- (e) It is tantalizing that Gray and Bamber did not enlarge upon the history of their patient's infection. They give no indication about her occupation or where she was when she was bitten by the boa-constrictor. Presumably the animal was in a zoo; they noted that it subsequently died from 'canker' of the mouth. I know of no records of sporotrichosis in cold-blooded animals.
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## CASE REPORTS

### *Case 1*<sup>(13)</sup>

A middle-aged farmer ran a gorse spine into the ball of a thumb while clearing scrub from a field on his home farm in County Armagh in 1935. Part of the spine broke off under the skin and his efforts to squeeze it out failed. A painful, firm swelling formed round the foreign body, with reddening of the skin over it and a constant, thin and slightly bloody discharge from the puncture wound. A fortnight later the farmer went to his family doctor, who opened the sinus with a scalpel and removed the gorse spine. The doctor gave no other treatment, apart from ordering the wound to be dressed with a paste of magnesium sulphate in glycerol. The wound healed after a few days, but a tender nodule persisted deep to it. During the following three weeks or so the patient noticed the development of further nodules in the skin over the radial aspect of the wrist and up the forearm towards the fold of the elbow. These nodules, including the one at the site of the initial lesion, enlarged and became ulcerated, and within three months of the accident there was a series of shallow ulcers extending from the thenar eminence up the lateral aspect of the forearm, across the antecubital fossa and half way up the medial aspect of the upper arm. The ulcers ranged between one and three centimetres across and were a millimetre or so deep, with a moist, red base and a flush

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(13) This is the case of Surgeon Kirk's patient referred to in the text of this paper (page 89).

TABLE

## Published Cases of Sporotrichosis Diagnosed in the British Isles(a)

Chrono-logical Order	Refer-ence(b)	Country where Infected	Sex, Age (yrs.) and Occupation	Means of Infection	Form of Disease	Method of Diagnosis	Duration of Symptoms at Time of Diagnosis	Treatment	Outcome
1	Walker and Ritchie (1911)	England (Cumberland)	M 46 Iron ore handler	Bruised finger with limestone	Ascending lymphangitic	Culture Inoculation of mice	5½ months	Potassium iodide by mouth	Recovery
2	Von Ofenheim (1911)	Not known	F 19	Not known	Subcutaneous abscess (retro-auricular); osteitis (tibial)	Culture	5 months	Surgical drainage	Not known
3	Adamson (1910-11)	Brazil	M 50 Labourer	Injury to thumb	Ascending lymphangitic	Culture	2 months	Potassium iodide	Recovery
4	Adamson (1912-13)	England (London)	F 60	Not known	Disseminated subcutaneous 'gummas', with ulceration	Culture	2 years	Potassium iodide	Recovery
5	Adamson (1913)	U.S.A.	M 60 Publican	Not known	[Synovitis also, possibly a side-effect of iodotherapy] Disseminated ulcerative and verrucose cutaneous (simulating North American blastomycosis)	Culture	6 months	Potassium iodide	Recovery
6	Greig (1917)	South Africa (Vaal River, near Kimberley)(c)	M 39 Diamond miner	Cut finger	Subcutaneous abscess (chest and axilla)	Culture	2¼ years	Potassium iodide	Recovery
7	Beatty (1918)	Ireland (Dublin)	M 15½ Handling African bass (d) in brush factory	Accidentally pricking a pimple with piece of bass (d)	Ascending lymphangitic	Culture	2 months	Not known	Not known



8	Adamson (1921-22)	Ireland (Dublin)	F 37	Not known	Cribriform ulcers of both legs	Culture	6 months	Iodine ('Iodeol') by mouth	Healing
9	Gray and Bamber (1931-32)	Not known	F 43	Bitten on wrist by boa-constrictor(e)	Lymphangiitic	Culture	7 weeks	Not known	Not known
10	Banks (1946)	England	F 11 mths	Not known	Membranous rhinitis and pharyngitis (simulating diphtheria); conjunctivitis; ulcerative keratitis	Culture	6 weeks	Potassium iodide; sulpho- amides	Toxaemia and death
11	Symmers (1966b); Case 11	France	M 48 Farmer and veterinary surgeon	Contact with infected horse. No remembered injury	Lymphangiitic	Culture. Sporothrix asteroid in histological sections	4 weeks	Potassium iodide	Recovery
12	Symmers (1966b); Case 12	Kenya	M 2	Not known	Facial granulomas with early ulceration	Sporothrix demonstrated in histological sections by specific immunofluorescent staining	1 year	Potassium iodide	Recovery
13	Symmers: this paper, Case 1	Ireland (County Armagh)	M Middle-age Farmer	Spine of gorse ( <i>Ulex</i> ) ran into thumb	Ascending lymphangiitic	Culture	3 months	Potassium iodide	Recovery
14	Symmers: this paper, Case 2	Ireland (County Dublin)	M 24 Student of law	Wound by rose thorn	Ascending lymphangiitic	Culture	3 years	Potassium iodide	Recovery
15	Symmers: this paper, Case 3	Ireland (Co. Fer- managh)	M Young adult Poacher and labourer	Wound by hook used in catching song-birds	Solitary ulcer of skin	Culture. Sporothrix asteroid in histological section	4 months	Potassium iodide	Recovery
16	Symmers: this paper, Case 4	Ireland (Belfast)	M 12	Injury to eye by sago or similar pellet	Panophthalmia	Culture	6 weeks	Removal of eye	No recurrence

(See page 91 for footnotes)

or slightly raised edge. There was induration of the tissues immediately deep to and around the ulcers, and the adjacent skin had a cyanotic appearance. It was at this stage that Mr. Kirk had been asked to see the patient and made the diagnosis of sporotrichosis. This was confirmed by the isolation of the sporothrix from the ulcers by Dr. J. C. Rankin<sup>(14)</sup>, whose many practical interests in addition to being head of the Electric and V.D. Departments at the Royal Victoria Hospital, Belfast, included medical mycology (he kept a fascinating collection of fungal cultures in a small laboratory in his home on University Road, opposite the University).

Mr. Kirk's initial treatment was to dress the ulcers with urea crystals and to give the patient compressed tablets of normal horse serum by mouth. When this proved to have little effect he prescribed large doses of potassium iodide by mouth, and within a month the lesions were well healed, leaving conspicuously pigmented scars.

*Comment.* This was a classic case of the ascending lymphangiitic form of sporotrichosis (see also Case 2), starting with a puncture wound by a spine of a plant, initial healing of the primary lesion being followed by recurrence at its site and the formation of nodules along the course of the subcutaneous lymphatic vessels and the eventual ulceration of these secondary foci. It is noteworthy that the lesions of sporotrichosis of a limb seldom extend right up to the axilla or groin. Clinically apparent involvement of the lymph nodes is exceptional in sporotrichosis of a limb although not infrequent when the initial lesion is on the trunk or head.

The source of infection in cases such as this is clearly the penetrating foreign body, presumably contaminated by the sporothrix which is present in the environment in its saprophytic state. Infection seems as likely to result from the injury whether or not the foreign body remains implanted in the tissues.

Once the diagnosis is suspected it is quite easily confirmed, culture of the fungus seldom presenting much difficulty provided bacterial contamination can be avoided. Swabs of the ulcers are usually contaminated and therefore material aspirated from unulcerated nodules is preferable. Serological tests and skin tests have little place in the diagnosis of sporotrichosis. Even histological examination – so often the means to the diagnosis of other fungal infections of the dermis and subcutaneous tissue – has little to offer because of the rarity with which the sporothrix can be demonstrated in sections of infected tissues.

Untreated, the disease may persist indefinitely, its tendency to heal balanced by reactivation of the lesions. In most cases the full extent of the infection is reached within a comparatively short time of its onset: however long the condition remains active thereafter it has little or no tendency to spread farther. Treatment with iodide in large doses by mouth is immediately effective in most cases and results in rapid and permanent healing, provided the treatment is continued for several weeks after clinical cure has been achieved. When iodide fails or when the individual patient is unable to tolerate the treatment other methods may be tried. Some authorities still advocate parenteral administration of organic arsenicals – neoarsphenamine or oxophenarsine. Neither sulphonamides nor the antibacterial antibiotics are effective against the sporothrix, and those cases that do not respond to other drugs must be treated with the antifungal antibiotic, amphotericin B, a drug that has to be administered with particular discretion on account of its potentially dangerous side effects.

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(14) John Campbell Rankin (1876-1954).

## Case 2

A law student, aged 24, cornered a pathologist at a party in London and quickly overcame the latter's reluctance to listen to a socially inopportune story of ill-health by giving such a typical account of sporotrichotic lymphangitis that even from the history alone the nature of the condition could scarcely be doubted. He described how, three years before, in 1951, he had torn the skin of the medial edge of his right hand on a thorn while pruning rose bushes in a relative's garden in County Dublin. The wound was about three centimetres long and no more than skin deep, except at the end where the thorn had dug well into the tissues. He painted the site at once with 'tincture of iodine'. After a few days it began to fester and induration developed in a zone about a centimetre and a half wide on each side. By the end of a week the wound had become a linear ulcer with a bright red floor and a soft, slightly undermined, purplish margin that bled easily when touched. The ulcer enlarged slowly and three or four small nodules appeared in the skin between it and the wrist. One of these nodules developed into an ulcer like that at the site of the wound; the others disappeared.

During the nine months following the injury a succession of nodules formed in the subcutaneous tissue along the line of the lymphatic vessels of the extensor and medial aspects of the forearm and in the antecubital fossa and for a short distance above the elbow along the medial aspect of the arm. The nodules broke down, discharging a small amount of blood-stained matter and becoming transformed into chronic ulcers. There was considerable induration of the tissues between the ulcers. Pain was not troublesome and the patient suffered little physical discomfort. He lost seven kilograms in weight during the first year or so of the illness but after that his weight was steady. His general health was scarcely disturbed. By the end of the first year the disease had reached its greatest extent: there was little change in the lesions during the following two years, apart from a tendency to heal over, with some scarring, and then break down again. From time to time he noticed transient enlargement of lymph nodes in the right axilla.

The patient saw a succession of doctors during these three years. Various diagnoses were suggested, including syphilis, tuberculosis, angiosarcoma, malignant melanoma and mycosis fungoides. One surgeon considered the lesions to be self-induced, the result of stubbing lighted cigarettes on the skin; he recommended psychiatric treatment, but the psychiatrist referred the patient back with the dry comment that a physical cause should be sought for a physical malady. Biopsy specimens were taken on three occasions: each time the histological picture was merely that of a simple, unspecific, ulcerative inflammatory reaction; no micro-organisms were seen either in the sections or in stained films of the exudate from the ulcers. Swabs from the lesions were cultured on several occasions: these yielded growths of various bacteria, among them *Staphylococcus aureus*, *Proteus vulgaris* and *Pseudomonas pyocyanea*, but treatment with appropriate antibiotics never had more than a slight and transitory beneficial effect on the condition. Two of the biopsy specimens were also cultured: both were reported as sterile, although the laboratory records were later found to include a note that one of the specimens gave a growth of a "peculiar yeast-like fungus, presumably a contaminant" that was not investigated further.

By the time when the patient was introduced to the pathologist at the party he

had begun to regard his disease as beyond both diagnosis and cure. A week later the diagnosis of sporotrichosis had been confirmed by isolation of *Sporothrix schenckii* from an unulcerated nodule freshly excised from the forearm. Three weeks after this, following administration of 300 grams of sodium iodide by mouth (5 grams thrice daily), all the ulcers had become completely covered by epithelium and the inflammatory induration was subsiding. Treatment with iodide was continued for a further month at the same dosage, and then withdrawn by progressively reducing the dose during one more week.

There has been no recurrence of the disease during the period of almost 14 years since the diagnosis was made. The site of the lesions is marked by extensive and very unsightly scarring and pigmentation of the skin.

*Comment.* The initiation of this patient's disease by a wound while working in a garden, with the subsequent development of ulcerating nodules along the lymphatics, ought to have indicated the diagnosis at once. The only condition clinically simulating sporotrichosis that might arise from a similar 'garden' wound is the rare lymphangiitic form of infection by *Nocardia brasiliensis*, an actinomycete of tropical and subtropical lands that ordinarily causes mycetomas resembling 'Madura foot' and that has not been recognized as occurring naturally in the British Isles. The long failure to recognize the presence of sporotrichosis in this patient's case can be explained only by his doctors' unfamiliarity with the disease.

The various bacteria grown from the ulcers are to be regarded as secondary invaders. The 'peculiar yeast-like fungus' that was grown from one of the biopsy specimens may well have been no more than what it was at the time considered to be, a contaminant – but it may have been the sporothrix itself. It is always advisable to regard any fungus isolated from any specimen as possibly pathogenic until the opposite has been adequately established after consideration of all the clinical circumstances.

In view of the efficacy of oral administration of sodium iodide in the treatment of the infection it is of interest that the use of an iodide-containing iodine solution as a first-aid application to the initial wound seems to have had no inhibitory effect on the development of the infection. However, it is relevant that nothing is known about how iodotherapy works in overcoming sporotrichosis – it is possible that the effect of iodide is primarily on the infected tissues of the host rather than on the infecting organism itself.

### Case 3

An Irish labourer was referred to hospital in London for treatment of a chronic ulcer on the right side of his chest. The ulcer had been present for almost four months. It began while he was living in County Fermanagh: he was catching black-birds on lines of baited hooks laid among bushes when he was spied by a party of bird-watching Boy Scouts – while running away from them through shrubbery he got entangled in one of his lines and a hook lodged in his side. That evening he removed the hook, a barbed one, in the traditional way, cutting its haft and pushing the point onward and out. The resulting wound did not heal: after about two months it had become an ulcer, some three centimetres in diameter and two or three millimetres deep. The ulcer was at the centre of an indurated area about seven centimetres across. Having reached these dimensions the lesion did not change appreciably in size or appearance.

The disease was well established when the patient left Ireland for the first time and went to work in England, a month before he was seen at the hospital. He took a job on a building site in London: as it was outdoor work in warm autumn weather he stripped to the waist. Other men on the site, seeing the ulcer, took him to have some sort of venereal disease, refused to work alongside him, and downed tools. He left the job. A few days later he went to a doctor who sent him to hospital with the clinical diagnosis of carcinoma of the skin.

Clinical and serological investigations at the hospital showed no evidence of syphilis or other venereal diseases. A wedge of tissue was excised from the edge of the ulcer: histological examination showed chronic suppuration, tuberculoid foci, suppurating pseudotubercles (Symmers, 1960) and fibrosis – the possibility of sporotrichosis was indicated by the finding of a characteristic sporothrix asteroid in the pus at the centre of a suppurating pseudotubercle (Fig. 2); there was no

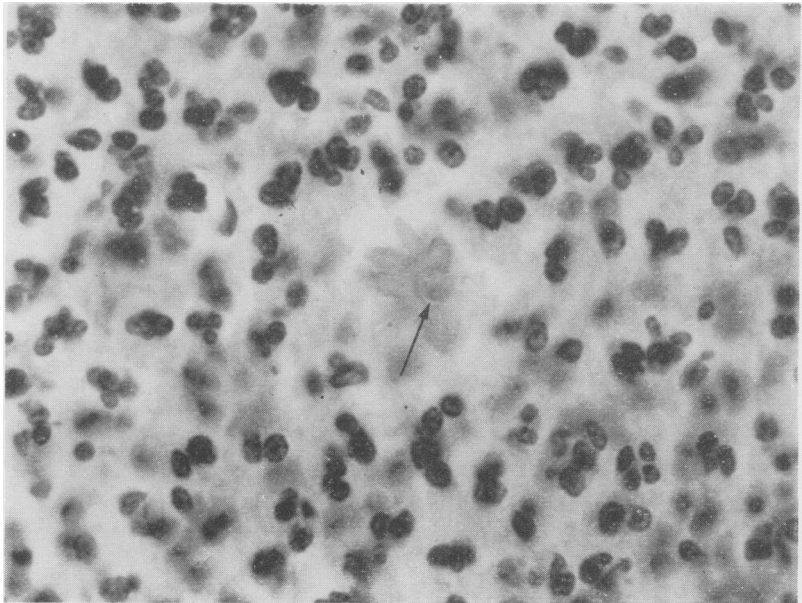


FIG. 2. *Sporothrix asteroid*. The fungal cell is arrowed, lying almost buried in a cup in the hyaline, palely stained deposit of radially disposed coagulum occupying the clear centre of this collection of neutrophil leukocytes. Haematoxylin-eosin.  $\times 1,000$ .

evidence of any neoplastic condition. Only diphtheroid bacilli and nonpathogenic staphylococci were grown from swabs of the surface of the ulcer. Further material for culture was then obtained by needle aspiration through intact skin just outside the margin of the ulcer: *Sporothrix schenckii* was isolated from this specimen.

Treatment with large doses of potassium iodide by mouth resulted in healing of the lesion within four weeks. As a precaution against relapse the treatment was continued for six weeks after the ulcer had become completely covered by epithelium. When last seen, four years later, the patient had had no further symptoms and his only complaint was of the unsightliness of the rather puckered and heavily pigmented scar.

*Comment.* Clinically this was a typical example of a solitary sporotrichotic lesion. In such cases the correct diagnosis is likely to be made only if the clinician thinks of the possibility of sporotrichosis, or if – as in this patient's case – a lucky chance leads to detection of the fungus in the course of laboratory investigations.

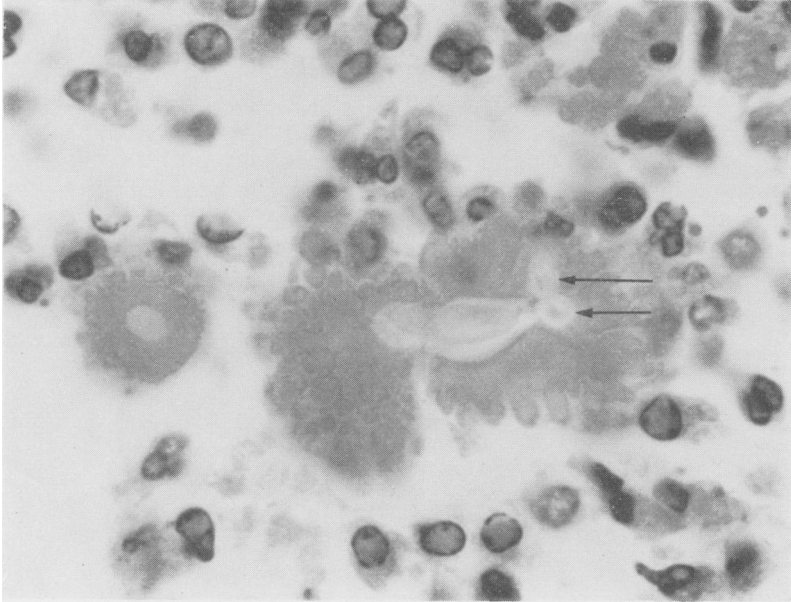


FIG. 3. *Candida* asteroids for comparison with the sporothrix asteroid in Fig. 2. The smaller asteroid is indistinguishable from a sporothrix asteroid. The larger one shows the development of the elongated and segmented pseudohypha from the arrowed candida spores. The radially patterned mass of hyaline coagulum formed from the inflammatory exudate is readily seen. (From an unpublished case of chronic *Candida albicans* septicaemia.) Haematoxylin-eosin.  $\times 1,000$ .

In general, biopsy is to be avoided in cases of sporotrichosis. Biopsy wounds are liable to heal slowly, particularly if treatment is delayed, and this may increase the unsightliness of the inevitable scarring that accompanies recovery from the infection. Also, unlike other deep-seated fungal infections, sporotrichosis is characterized by the difficulty of demonstrating the causative fungus in tissue sections (or, for that matter, in stained films of exudate), even with the help of the special staining methods that are in general use for showing the presence of fungi<sup>(15)</sup>. In exceptional cases the sporothrix is found in the form of the so-called asteroid: this consists of a hyaline, eosinophile complex of fibrin and globulin derived from the

(15) It is now possible to demonstrate and specifically identify certain fungi, including *Sporothrix schenckii*, in tissues by treating histological sections with the appropriate specific antiserum in which the antibodies to the fungus have been labelled with the fluorescent dye, uranin (fluorescein). The labelled antibody becomes attached to the fungal elements in the infected tissue and these can be recognized by their fluorescence when the section is examined microscopically in ultraviolet light (Kaplan and Ivens, 1960). The method is not available outside specialist laboratories.

inflammatory exudate in the host's tissues and deposited with a more or less well marked radial orientation on the surface of the fungal cell (Fig. 2). These asteroids are easily seen in haematoxylin-eosin preparations. A comparable reaction takes place in some other conditions, e.g., in the formation of the 'clubs' at the surface of the colonial grains of *Actinomyces israelii* and *Streptomyces madurae*, round the hyphae of the fungi responsible for subcutaneous phycomycesetosis, and round some metazoan ova in the tissues. However, none of these structures is likely to be confused with the sporothrix asteroid: in contrast, the asteroid of certain cases of coccidioidomycosis and of exceptional cases of septicaemic candidosis may be sufficiently like the sporothrix asteroid to be mistaken for it – of these candidosis is obviously the one that might cause confusion in practice in the British Isles (coccidioidomycosis does not occur here naturally [Symmers, 1967a]). In candida asteroids the fungi are present both in yeast-like form and as pseudohyphae (Berge and Kaplan, 1966–67): the latter (Fig. 3) do not occur in sporotrichosis, a point that should be valuable in distinguishing between sporothrix and candida asteroids. These fungal asteroids are, of course, quite distinct from the finely radiating structures in the multinucleate giant cells of some cases of sarcoidosis and other tuberculoid granulomas that have also been referred to as asteroids (Symmers, 1966a): the fungal asteroid always has a demonstrable fungal cell at its centre, and nothing likely to be confused with this is present in the asteroid of tuberculoid giant cells.

In view of the circumstances in which this patient acquired his infection it is worth noting that there is no evidence that birds play any part in the ecology of the sporothrix or in the aetiology of sporotrichosis, as they unquestionably may do in relation to histoplasmosis (Ajello, 1967) and cryptococcosis (Symmers, 1967b). In the case under discussion it is probable that the hooks used to catch birds were contaminated by the fungus through contact with the shrubs in which the lines were laid.

#### Case 4<sup>(16)</sup>

A 12-year-old boy, while at school in Belfast in 1929, was hit in the right eye by a pellet of sago or the like projected from a 'pluffer'<sup>(17)</sup>. The point of impact was on the sclera, a few millimetres lateral to the limbus. The injury caused a small haemorrhage into the conjunctiva. Generalized conjunctivitis developed during the next week, with very marked hyperaemia and considerable oedema. This reaction was greatest over the injured area, and a small superficial ulcer appeared at the site of impact. The ulcer had a yellow base and was surrounded by a ring of particularly intense hyperaemia. There was some mucopurulent exudate in the conjunctival sac. The family doctor advised frequent bathing with a boric acid lotion and

(16) This report has been compiled from contemporary notes of observations by Mr. James Craig, Sir Thomas Houston and my father.

(17) The 'pluffer' was standard pocket armament among otherwise reasonably responsible children in some schools in Belfast, and doubtless elsewhere, possibly under other names, at the end of the 1920s. For all I know, it still may be so. It was a straight piece of laboratory glass tubing, five to ten centimetres long and of a bore little larger than the average grain of sago, barley or rice, which was the usual ammunition. The propellant was air, forcibly expelled from the mouth into the loaded end of the tube, which was held in the lips and aimed in the general direction of blackboard, windows, lamps or school-fellows.

instillation of silver nitrate solution. Two weeks after the injury much of the generalized conjunctival reaction had subsided. In contrast, the ulcer had enlarged to about five millimetres in diameter and there was well-marked circumcorneal vasodilatation. The child complained increasingly of pain in the eye and blurring of vision.

Four weeks after the injury the patient was admitted to hospital and was seen for the first time by an oculist (Mr. James Craig <sup>(18)</sup>), who found that the inflammation had extended into the bulb of the eye: there was severe, generalized iridocyclitis, a hypopyon and clouding of the cornea. The disease progressed: two weeks after admission to hospital the eye was excised because its disorganization had advanced so far that clearly there was no possibility of its sight being recovered, and because of the risk of sympathetic ophthalmia.

The eye was examined in the fresh state in the laboratory by Sir Thomas Houston<sup>(19)</sup> and my father. Cultures gave a pure growth of *Sporothrix schenckii*; the identification of the fungus was confirmed by Henri Gougerot, then *professeur de clinique des maladies cutanées et syphilitiques* in the Faculty of Medicine of Paris, to whom subcultures were sent<sup>(20)</sup>. No micro-organisms were found in histological sections of the eye; the sections showed much of the normal structure to have been replaced by chronic suppurative and tuberculoid granulomatous tissue.

The post-operative course was uneventful. There was no evidence of residual infection of the orbit, and the disease did not recur.

*Comment.* The source of the infection in this child's case is uncertain. The missile that struck the eye may have carried the fungus, or the latter may have been a subsequent invader of the injured tissue. Sir Thomas investigated the fungal flora of several samples of sago, rice and barley that had been carried by schoolboys as ammunition for their pluffers: he found several varieties of moulds, including two strains of *Sporotrichum*. Neither of these sporotricha had the characteristics of *Sporothrix schenckii* or was pathogenic to guinea-pigs or rabbits, and both were therefore classed as examples of commonplace saprophytic species.

The patient was a town boy, living in a gardenless part of the city and with none of the pursuits that might have carried a particular risk of exposure to infection by fungi in soil or on plants or other vegetable matter. He seldom went into the country, and he did not often take part in outdoor games.

Ocular sporotrichosis occurs frequently enough to need particular notice among the fungal infections that involve the eyes. Nevertheless, it is rare, and appreciably rarer than, for instance, mycotic keratitis due to various species of *Aspergillus* (Gingrich, 1962). The most recent review of ocular sporotrichosis dates from 1947, when Gordon analysed 48 published cases that had been so diagnosed: in about a third of these cases the ocular infection was secondary to sporotrichosis elsewhere in the body. Only six of the 48 patients in the series reviewed by Gordon suffered involvement of the interior of the eye.

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(18) James Andrew Craig (1872-1958), ophthalmic surgeon, Royal Victoria Hospital, Belfast.

(19) Sir Thomas Houston (1868-1949), clinical pathologist, Royal Victoria Hospital, Belfast.

(20) Gougerot, whose collaboration with de Beurmann in the early days of the history of this disease has already been mentioned (page 87), remained interested in sporotrichosis throughout his life. In 1947, at the first conference on medical mycology to be held in the United States of America, he summarized over forty years' personal experience of the disease (Gougerot, 1950). He died in 1955, aged 73.



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