THE

British Medical Journal.

THE JOURNAL OF THE BRITISH MEDICAL ASSOCIATION.

LONDON: SATURDAY, JULY 1st, 1911.

Remarks

ON

A CASE OF SPOROTRICHOSIS.

BY

NORMAN WALKER, M.D.,

PHYSICIAN FOR DISEASES OF THE SKIN, THE ROYAL INFIRMARY,
EDINBURGH;

AND

JAMES RITCHIE, M.D.,

SUPERINTENDENT OF THE LABORATORY OF THE ROYAL COLLEGE OF
PHYSICIANS, EDINBURGH.

(With Special Coloured Plate.)

CLINICAL, BY DR. NORMAN WALKER.

IN December, 1910, Dr. McKerrow, of Workington, wrote asking me to admit to my ward a patient suffering from peculiar ulcerative growths on the arm, who was steadily getting worse in spite of assiduous treatment. The patient was admitted on January 14th, and the cast, which is reproduced in the coloured plate, was taken two days later by my secretary, Miss Rae. With the exception of an unbroken lesion just above the elbow, the cast shows the whole extent of the disease.

Robert B., aged 46, a strong, healthy man, married, seven healthy children, is a native of the Isle of Man, and his father and mother are both hale and hearty at the age of "about" 80.

He works eight hours a day in the open air, and his work consists in mixing iron ore with lime and coke, filling the mixture into barrows, and wheeling these to a lift which raises them and tips the contents into the furnaces.

On August 3rd last, when working on night duty, instead of shovelling the ore as usual, he was packing his barrow, by hand, with large pieces of ore, and accidentally bruised the knuckle of his right forefinger with a piece of limestone. He took no notice of the trifling bruise until three or four days later, when it commenced to fester. He applied domestic remedies, including soap and sugar, but no improvement resulted, and about a fortnight later a number of little pimples appeared on his forearm. These did not interfere with his working capacity, and it was only their persistence and steady increase in size which sent him, ten weeks after the injury, to consult Dr. McKerrow. Dr. McKerrow painted the spots with iodine and ordered him to stop work. The spots seemed to "go back," and he resumed work a week later. But with the resumption of work the spots again began to enlarge, and poultices were ordered. Several of the lesions were incised and dressed with lint; to others ointment was applied. But no treatment seemed to do any good. The lesions simply stood still; they got neither better nor worse. During the three weeks prior to his admission to hospital the lesions did, if anything, somewhat diminish.

Although I had never seen a case—this is, indeed, the first reported in this country—the appearances so closely resembled those shown in a photograph in Stellwagon's latest edition, that I at once suspected that we had to do with a case of sporotrichosis. One of the lesions—the only one not shown in the plate—had not broken down, and from it cultures and inoculations were made, which are described later by Dr. Ritchie. It suffices here to state that they confirmed the suspicion.

The credit of first recognizing this disease belongs to Dr. Schenk, who published in the *Johns Hopkins Bulletin* of December, 1898, a paper on "Refractory Subcutaneous Abscesses caused by a Fungus probably related to the *Sporotricha*."

The case was that of a male who, on November 30th, 1896, presented himself at the Surgical Clinic of the Johns

Hopkins Hospital with an infection of an unusual nature of the right hand and arm. The disease first showed on the index finger, extended up the radial side of the arm, and gave rise to several circumscribed indurations. Three months previously the patient had scratched his finger with a nail while reaching into a red lead keg. The lesions were treated with antiseptic solutions, but were very refractory to treatment. On examination there was evidence of extensive tuberculosis of the lungs and there were bacilli in the sputum. The fungus was cultivated from the pus.

Another case was published by Hektoen and Perkins in the *Journal of Experimental Medicine*, 1900 (page 77).²

A boy of 5 suffered from a sore on the left index finger, where he had struck himself with a hammer. The injury did not heal up, and, as in Schenk's case, a chain of nodules developed up the line of the lymphatics. The pus from the lesions was of a mahogany colour, thick and tenacious.

These authors refer to a case, described by Brayton in the *Indianapolis Medical Journal*, 1899,³ and comment upon the similarity of the lesions developing after comparatively trifling injuries—a scratch with a nail, a blow with a hammer, and a puncture by a wire.

The disease was next recognized in France, where a case was described by de Beurmann and Ramond in 1903 under the title, "Multiple subcutaneous abscesses of mycotic origin."⁴ This report was rapidly followed by reports of other cases, and the disease was found to be widespread in France, for in 1909 no fewer than six columns of the *Bibliographical Annexe* to the "Annales de Dermatologie" are occupied with references to it.

In 1907 cases were reported in Brazil, and since then it has been observed in Germany, Switzerland, Austria, Belgium, and Madagascar.

The case now described is, I believe, the first definite case recognized in this country, though Dr. v. Ofenheim published in the *Lancet* of March 11th, 1911,⁵ a case in which a fungus resembling in many respects a sporothrix was found. He notes that it grew better at room temperature than in the incubator. The principal lesion was over the tibia, and when opened the cavity contained semi-gelatinous material.

Various clinical types are recorded. The earliest cases seem to have very closely resembled that now described, there being a history of a minor injury on the hand and a spread from this of lesions up the line of the lymphatics. Later, other types have been noted, especially in France, where multiple wide-spreading abscesses, both hypodermic and dermic, have been observed. These are described as syphilitic or tuberculous in type, and it seems more than likely that some of us have overlooked earlier cases and classed them with one or other of the diseases suggested by these names.

The lesions are characterized by multiplicity of form, indolence, firm feeling, suggestive of new growth, crateriform surface, and the presence of viscid yellow-grey pus. It is exceptional to find any enlargement of the glands, and the general health is as a rule unaffected. But the disease is not confined to the skin and subcutaneous tissue; cases have been recorded where it has appeared on the mucous membranes, in the joints, in the epididymis, and in the periosteum. In the affections of the mucous membrane, for example, larynx, etc., the ulcerated lesions do not produce destruction of tissue, as do those of tubercle and syphilis. Some observers have noted the similarity of the lesions to those produced by other fungus diseases, such as ringworm in the kerion form, actinomycosis, blastomycosis, etc.

Diagnosis.

The diagnosis as a rule is easy, provided one is familiar with the existence of this disease, and the main object of this paper is to make the practitioners of this country familiar with a disease which will probably before long be appearing widely among us.

In the first type of case the diagnosis should really present no difficulty. The history of a slight injury to the hand, followed by the appearance of a chain of gummatoid lesions up the arm, should suggest the possibility, and fortunately the investigation is in such instances an easy one. In the more widespread cases the diagnosis is more difficult. But, although the lesions resemble those of tubercle and syphilis, there is usually a something about them which leads one to hesitate before arriving at an absolute diagnosis. Once that doubt is recognized, and the possibility of this disease considered, investigation will lead to its detection.

In various discussions which have taken place in the Parisian Dermatological Society—and it is important to note, as evidence of the increased prevalence of the disease in France, that the number of cases shown to the Dermatological Society is becoming less—attention has been drawn to various points in connexion with the diagnosis. These nearly always centre around that to which I have already alluded—the more or less close resemblance of the lesions to those of tubercle and syphilis. In some cases the crateriform character suggestive of the syphilitic gumma is dwelt upon; in others the violet coloration with which one is familiar in the slow-growing tuberculous gumma. Other cases have resembled warty lupus. Again and again the speakers draw attention to the importance of not confusing the disease with either of these, and more especially with syphilis. If that disease is diagnosed and iodides are administered, the benefit produced confirms the physician in his wrong diagnosis to the great detriment, moral and physical, of the patient.

Attempts have been made to devise a sort of von Pirquet reaction, but up to now these have not been attended with much success. Pautrier,⁶ in 1909, injected a killed culture and produced a general reaction with a rise of temperature and local congestion. Vidal and Abrami⁷ obtained an agglutination by the use of serum from an affected patient; unfortunately, only less marked than with the serum from other individuals. There is some reason to hope that the Wassermann type of reaction may prove more useful. De Beurmann, Gougerot, and Vaucher⁸ have suggested another diagnostic test: the injection of a culture intraperitoneally in the rat sets up an orchitis, just as does the injection of the bacillus of glanders in the guinea-pig.

Reactions of the Pirquet type are not easily attained with fungi. Dr. Low has been for some years endeavouring in vain to get definite results in cases of ringworm and favus.

Prognosis.

The prognosis is good, unless the patient's health is bad, and it is reported that diabetes is a specially unfavourable complication. There is no tendency to spontaneous cure.

Treatment.

Schenk's earliest case was treated surgically, and not very much stress is laid by him upon its results; his paper is rather devoted to the scientific aspect of the disease.

The remedy which is generally admitted to be almost specific in its action is the iodide of potassium. Its use was first suggested in 1903 by M. Sabouraud—always ready and resourceful—on account of its good effects in actinomycosis. It is very important that iodide should not be commenced until a definite diagnosis is arrived at, for its administration has an almost immediate effect upon the vitality of the fungus and makes it exceedingly difficult to cultivate. Once the diagnosis is made it should be

administered freely, internally and externally. The dose should be liberal and, if necessary, run up to as much as a drachm three times a day, and it should be continued for some time after all clinical evidence of the disease has disappeared.

According to de Beurmann the drug has no direct effect upon the fungus, which may indeed be grown in a medium which contains iodine; it therefore only acts indirectly by stimulating absorption. Locally, iodine in the form of Gram's solution has a useful effect, and there is no objection to surgical measures, such as scraping, although they are not really necessary.

The treatment above indicated was pursued in the case of my patient. As Dr. Ritchie will describe, the fungus was found without any difficulty and we were able to commence treatment early. Under doses of iodide, running up to 80 grains per diem, the lesions rapidly involuted and the patient was able to return home on February 28th, with directions to continue the medicine at home until all the lesions had disappeared.

Etiology.

I leave the discussion of the fungus and its relations to Dr. Ritchie, but it is an important practical point to know that it may apparently exist as a saprophyte on vegetables and parasitically upon caterpillars and flies.

Careful inquiry was made in the hope of throwing some light on a possible source of infection. The patient, whose political views were not inquired into, was inclined to blame "foreign" ore, which is largely mixed with the native article, but he was quite certain that the original injury was with a piece of "home-grown" limestone. He lives a little out of the town of Workington in a four-roomed house with a garden, and he keeps a few hens, but he has nothing to do with any animals. It may be that the abraded knuckle was infected by something in the food of the hens on which the fungus was growing.

It will be noticed in the plate that the nails of the second and fourth fingers are not healthy. Their appearance suggested the fungus affection of the nails of which we have lately had so many cases, and the

examination of scrapings showed abundance of fungus, indistinguishable by the microscope from that of ringworm. This condition had lasted to the patient's knowledge for fifteen years.

This discovery of a fungus in the nails at first interested us greatly, for it seemed possible that it might throw light upon the disease as a whole. My colleague, Dr. Cranston Low, recently published⁹ a remarkable series of cases of fungus affections of the nails which have occurred in my clinic during the last three years, and it seemed just possible that these might prove the forerunners of an outburst of sporotrichosis. But that possibility has been exploded by the careful investigations which Dr. Low made on the fungus from the nails of this patient, which proved to be one of the less familiar forms of ringworm (*Trichophyton rosaceum*), and in cultivation had no resemblance to the fungus which was causing the disease of the skin.

It is, however, interesting to note that de Beurmann and Gougerot produced experimentally lesions resembling those of sporotrichosis, by the inoculation of *Trichophyton gypsum*; and Thibierge and Weissenbach, Gaucher and Fouquet observed cases where the lesions were exceedingly suggestive of kerion.

PATHOLOGICAL, BY DR. JAMES RITCHIE.

Morbid Anatomy.

A small piece of tissue was excised from one of the lesions on the forearm and fixed in formalin. On microscopic examination, it was found to consist of a granuloma in which there was a central area with a rather sharply differentiated margin; in this area a diffuse necrotic process was going on (see Plate, Fig. B). The neigh-

DESCRIPTION OF COLOURED PLATE.

Fig. A.—Cast of arm on admission to hospital. Note primary lesion at base of index finger and other lesions secondary to that distributed along the lines of lymphatics. Note also ringworm of nail of middle finger.

Fig. B.—Low power view (×40) of section from back of hand showing granuloma with giant cells and plasma cells. Here and there are also collections of polymorphonuclear leucocytes = commenting abscess formation. Stained with haematoxylin and eosin.

Fig. C.—Oil-immersion view (×1000) of granuloma from mouse which had been inoculated six weeks previously with culture from patient. Stained with pyronin and methyl green. Note masses of grouped spores. Cells with red protoplasm are plasma cells.

Fig. D.—Growth on maltose peptone agar (Sabouraud's proof medium) inoculated direct from lesion—twelve days old.

Fig. E.—Growth on potato inoculated direct from lesion—ten days old.

TO ILLUSTRATE DR. NORMAN WALKER'S PAPER ON SPIROTRICHOSIS.

bouring epithelium was normal or slightly thickened, but over the central necrotic mass it was thinned out and on the point of rupturing. In the tissues bordering on the central area the vessels were congested and the tissue packed with young connective tissue elements and many plasma cells staining well with Pappenheim's stain, but there was here very little leucocytic exudation. In the central area the tissue was more open, fibroblasts and cells being embedded in a fibrinous-like exudate (*fibrilles collagènes* of Beurmann). Many of the cells were undergoing degeneration and necrosis, and there was a very pronounced leucocytic exudation, consisting chiefly of polymorphs, spreading along the capillaries coming from the deep layers of the skin, there being here and there microscopic abscesses. Some of these seemed to be forming in the capillaries, as many of the latter could be seen plugged with leucocytes. There was a considerable number of giant cells scattered irregularly throughout the granuloma. Generally speaking, the lesions bore a resemblance to what is found in actinomycosis of the chronic variety, such as develops, for instance, in the jaw of the ox. Though many different staining methods were employed, no mycelium could be demonstrated, but there were scattered—singly or in groups throughout the newly-formed tissue—bodies corresponding in size and appearance with sporotrichon spores. A probable explanation of the absence of mycelium will be given later. The recognition of the presence of spores is rendered very difficult by the frequency of karyorrhexis in the tissue cells. The fragmentation of nuclei thus occasioned originates appearances closely resembling those of phagocytosed spores (Plate, Fig. C). A careful examination of sections has, however, convinced us that cells containing spores do exist in the lesions: One such cell taken from the edge of an experimental lesion in a mouse is seen in Text Fig. 1.

Cultural Characters of the Sporotrichon.

On January 21st, 1911, the skin over one of the lesions which had not yet ulcerated was carefully purified and the granuloma incised. From the breaking-down material expressed, potato and plain agar tubes were inoculated and incubated at 22° C. No growth was visible until the fourth day, when, on the potato, small, white, woolly colonies appeared. During the next few days the whole potato became covered with a growth gradually developing a brown pigment (Plate, Fig. E) and becoming tortuously heaped up so as to resemble cerebral convolutions, as has been described by other authors. On microscopic examination the growth was found to consist of a felted mycelium bearing numerous spores. A similar growth appeared on the agar tubes (compare Text Fig. 2). No other organism was present.

The organisms grew readily on all the ordinary media. On potatoes the characters were those just described, but a striking feature was the variability in the amount of pigmentation. Sometimes the growths remained quite white. In others they

preserved a light brown appearance, whilst in others again they were almost black. These variations cannot at present be completely accounted for, but one factor appears to be the amount of moisture present in the air surrounding the growth, the lighter appearances being associated with a deficiency or excess of water vapour, and the darker with an intermediate and optimum moisture. In old potato cultures a pigmented growth may lose its colour and become white; this appearance may wholly or in part be due to the occurrence of pleomorphism. On ordinary agar (+ 10 on Eyre's scale and free from sugar) the

growth appears at first as a finely grained, matt-surfaced, grey film, easily scraped off, and this appearance may persist; but here and there, on an agar slope, especially where the surface has been wounded, heaped-up, dense growth occurs, with a black centre, and this cannot be easily removed without detaching some of the medium along with it. Under a hand lens the whitish growth is seen to consist of groups of colonies, each of which presents a coarsely stellate radiation from a centre. The pigmented parts have a similar appearance, but the radiation is finer, and has a spiky appearance. Old agar cultures tend to present a dirty greyish colour. On glucose agar the growth was more abundant, soon presenting a heaped-up appearance, and becoming markedly pigmented. On maltose agar (Sabouraud's proof medium) growth readily took place (Plate, Fig. D), with the heaped-up appearance, and formation of pigment. On a gelatine stab, at room temperature, an abundant growth appeared of an inverted fir-tree order, and no liquefaction was observed even after two months.

In peptone solution containing various sugars free growths occurred. Acid formation was specially noticeable with inulin, and was also observed with glucose, maltose, galactose, raffinose, saccharose and mannite, but with lactose, dulcitol, inositol, adonitol, sorbitol, and salicin, the medium remained alkaline. In no case was there any gas formation. In other ordinary solid media no characteristics other than those described were disclosed. No indol formation was observed. The organism was definitely aerobic. No growth occurred on agar in a tube from which the oxygen had been removed, and in fluid cultures, the growth was most abundant on the surface of the medium.

Relation of Growth to Temperature.

During the period of observation growth was much more luxuriant at a temperature of 22° C.—this being true of the primary as well as of the secondary cultures—than at 37° C. For four months after isolation a scanty growth at the latter temperature was observed, taking several days to be visible and never advancing beyond the stage of forming a thin film on the surface of the medium. On transferring the cultures to 22° C., or growing subcultures at this temperature, vegetative activity was regained.

Pleomorphism.

On cultures on potato, ordinary agar and maltose agar, after several months, white centres appeared on the pigmented growth. On subculture from these, a white growth of a very vigorous character and showing much less tendency to pigmentation was obtained. The microscopic characters were, however, unchanged, except that possibly

there was a greater tendency to the formation of the large round bodies described below.

Microscopic Appearances in Cultures.

The microscopic appearances were best studied in hanging-drop agar cultures. (Text Fig. 2.) Free mycelium formation is here observed, the filaments passing out from the centre of growth in long strands usually not quite straight. They measure about 1 μ in thickness, are irregularly septate, and often contain fine granules. Lateral branches are given off sometimes at regular intervals, sometimes irregularly. Even in the youngest filaments

Fig. 1.—Edge of granuloma from mouse killed six weeks after inoculation. Near centre is seen a cell containing a group of spores. $\times 650$.

Fig. 2.—Edge of living colony on agar hanging-drop, five days at 22° C. $\times 200$.

spore formation is much in evidence. The spores are oval with a pointed free extremity, and measure from 3μ to 4μ long by 1.6μ to 3μ broad. They are often set singly on stalks about half their long diameter in length on the lateral aspects of the filaments. Spore formation also takes place in whorls round a main filament at the end of a short branch. In the latter case the filament is often continued from the centre of the whorl, and after growing for a short distance may produce a new whorl at the extremity. In the older filaments the spores are set so thickly together as to give the appearance of ropes of these bodies.

In older cultures, especially in sugar solutions and in cultures on solid media showing pleomorphism, appearances were seen which suggested another form of spore formation. In one part of a mycelial thread, there might be seen a chain of usually short segments of twice or three times the ordinary breadth. In the middle of these there frequently occurred, sometimes singly, often in pairs, large circular elements, $5-6\mu$ in diameter and resembling the zygosporidia seen in Mucedineae. In the interior of these a large oval body was frequently seen, and when two of the containing cells were present on a thread, these contained bodies were frequently situated at the point of contact of the cells. In a preparation presenting such appearances, single circular bodies containing groups of spore-like bodies could be seen. Whether this represents a sexual stage in the life-history of the fungus cannot as yet be determined.

When fresh agar was inoculated with a mixture of filaments and spores, there was evidence that the former soon degenerated, and fresh growth apparently only took place from the spores. At 22°C ., these during the first twenty-four hours assumed a circular form and increased in size, and at the end of that time could be seen throwing out a filamentous sprout, the first segment being often shaped like an Indian club attached at its broad end to the parent spore by a short stalk. During the next twenty-four hours these increased in size; usually a second, and sometimes a third, sprout appeared from the parent spore, and, from these, filaments as described above were continued. Frequently by the time the filament had attained a length of $20-25\mu$, the lateral spore formation was commencing.

At 37°C ., direct division of the spores could be seen to occur, in certain cases short, sausage-like elements being formed. This suggested an attempt at mycelium formation, but no filaments such as occurred at 22°C ., were observed. Instead the spores usually developed into round bodies which attained a size of about 5μ . After a day or two fresh spores began to sprout off from those round bodies to which they were attached by short stalks, a complete circle of spores being sometimes seen round the larger bodies (Text Fig. 3). The larger bodies seemed to represent the filaments seen in a growth at 22°C ., as after the spores had sprouted from them they could be observed degenerating like the filaments in old cultures. It is obvious that these observations may be important from the point of view of the absence of mycelium in the granulomata. Probably, at the body temperature, mycelium formation was in abeyance, and this was borne out by the fact that short mycelial threads were occasionally seen in the superficial parts of ulcerated areas in mice—that is, where the temperature was probably below that of the body.

The organism possesses considerable vitality, and was successfully subcultured from dried cultures on potatoes three months old. It stained by all the ordinary dyes, and retained the stain in Gram's method. It was not acid-fast.

Inoculation Experiments.

The material used was a brown culture on potato. Six mice were inoculated subcutaneously, one intraperitoneally, three rats subcutaneously, one intraperitoneally, one rabbit intravenously, and one guinea-pig subcutaneously.

During a period of three months' observation, no lesions occurred except in the mice subcutaneously inoculated. In all of these in about ten days a subcutaneous nodule developed which tended to break down and ulcerate through the skin. The mice were killed at various intervals up to six weeks, at the end of which time emaciation was beginning to be pronounced. In all except one case (in which ulceration and septic infection had occurred), the sporotrichon was isolated from the granuloma. The characters of the latter were in every case identical with those already described in the human lesion. Again the absence of mycelium formation was noteworthy, but in one case a few short threads were seen in the purulent floor of an ulcer of some duration. If the inability to form a mycelium at body temperature is the cause of its absence in the

granuloma, the thermal condition of parts exposed to the air may explain a commencing mycelial formation in the ulcer.

The organism described above corresponds closely with those isolated by Schenk,¹ Hektoen, and Perkins,² and later by de Beurmann,⁴ from various human lesions. Though the general morphological and cultural characters of the various strains isolated by different authors generally correspond, individual differences have been observed. In our case, the most important character is that it has always grown better at 22°C . than at 37°C ., thus differing from that of Hektoen and Perkins; further, it differs from de Beurmann's strains in growing very readily on ordinary sugar-free agar. An important point of variation in different strains is the behaviour on gelatine. Those of Schenk and Hektoen and Perkins had liquefying capacity, although Foulerton,¹⁰ working with a subculture supplied by Hektoen, found this quality wanting. Page, Frothingham, and Paige¹¹ note that a strain isolated by them sometimes liquefied gelatine and sometimes did not, so that the liquefying quality may be variable. In this respect our organism corresponds with the description given by de Beurmann. If, as is probable, this group of sporotricha has a widespread distribution on decaying vegetable matter, it is possible that a number of allied species exist, and this may explain the variations observed. Meantime, pending further knowledge, it is convenient to adopt the convention of denominating the organism, *Sporotrichon beurmanni*. Its botanical relationships are as yet unknown, as its full life-cycle has not been worked out, and it is to be placed in the indefinite group of the Fungi imperfecti.

The evidence for the pathogenicity of the *Sporotrichon beurmanni* rests on its invariable presence in certain pathological lesions, on its isolation from these in pure culture, on its reproducing lesions of the same order in animals, and on its being recoverable from the experimental lesions.

The organism was originally isolated by Schenk¹ in 1898 from refractory subcutaneous abscesses in man; and from 1903 onwards great attention has been paid to the subject, especially by de Beurmann and his co-workers, on

account of the relationship of the fungus to a somewhat heteromorphic group of skin granulomata. Gougerot,¹² reviewing the subject, gives cases of infection of other parts of the body also—the mucous membrane of the pharynx and larynx, muscle, bone, and synovial membrane, and in animals, both under natural and experimental conditions, generalized granulomatous infections of the serous cavities and solid organs have been observed. The animals most susceptible to experimental infection are the rat and the mouse, and in them a generalized infection may occur; local lesions have also been originated in the cat and the monkey. In connexion with generalized infections it may be mentioned that in one case of disseminated skin granulomata the organism was isolated from the blood (Landonzy¹³).

The lesions, both natural and artificial, are granulomata which tend to break down to form abscesses, at first of microscopic size, but later assuming a size clinically recognizable. Some observers have attempted to claim for the sporotrich granuloma special histological features. In our opinion this is not justified by facts, and the recognition of the presence of sporotrichosis must rest on the isolation of the organism. The granuloma shares with many other similar lesions the character of a diffuse connective tissue proliferation, not characterized by being formed by the confluence of smaller foci, as is the case with many tuberculous lesions. The presence of caseation is not a marked feature, and the necrosis which occurs is not massive, but is essentially a matter concerning individual cells, living and dead cells being freely intermingled. The softening of the necrobiotic areas is related to the microscopic abscesses described.

Fig. 3.—Film from agar culture grown at 37°C . for ten days. Gram's stain. $\times 1,025$. Note large circular bodies with spores sprouting off; also a few sausage-shaped elements.

The presence of spores in the granulomata with an absence of mycelial development has been noted by all observers. Whether the explanation put forward to account for this phenomenon in our case is generally applicable we cannot say. It has been recorded, as stated above, that certain strains grow best at 37° C., but, so far as the published accounts go, little attention appears to have been paid to the relationship of the temperature factor to the microscopic characters of the fungus.

Serum Reactions.—In sporotrichosis, as in other diseases, the properties of the serum have been studied—in this case by Vidal,¹⁸ who recommends that a portion of an agar culture, four to six weeks old, should be emulsified and filtered through filter paper, so as to give a concentration of from 130 to 150 spores per field of a microscopic magnification of about 400 diameters. With such an emulsion a reaction has been observed with serum in a dilution of from 1 in 200 to 1 in 400, or even higher. Complement deviation has also been observed, the antigen being the above emulsion of spores, used in a proportion of 1 part of emulsion to 2 parts of serum. In the case of both the agglutination and complement deviation tests, however, the position is complicated by the fact that the serum of patients suffering from other mycotic infections—for example, thrush, actinomycosis—reacts to *Sporotrichon beurmanni*.

The *Sporotrichon beurmanni* has been found living on decaying vegetable material (de Beurmann and Gougerot),¹⁸ and recently considerable attention has been paid to the part which it plays in animal disease. Gougerot and Caravan¹⁴ have described three cases of sporotrichosis in the dog, in two of which there were ulcerating granulomata in the neck, and in the third an affection of the peritoneum, the liver, and lungs. Spontaneous epidemics have also been observed in the rat. The most important observations, however, relate to the discovery of a sporotrichon as a causal agent in epizootic lymphangitis in the horse—a condition characterized by superficial granulomata bearing a resemblance to glanders, but of a benign nature. Whether all cases of the disease which go under this denomination are due to the same cause seems as yet undetermined. The condition is often associated with the presence in pus from the lesions of a large body said to be capsulated, usually referred to as the "cryptococcus of Rivolta." The botanical relationships of this organism have not been worked out, but it has been grouped amongst the blastomycetes, as, for instance, by Tokishige.¹⁶ In America (Page, Frothingham, and Paige¹¹) certain cases of epizootic lymphangitis have, however, been traced to a sporotrix apparently identical or closely related to that of de Beurmann, and similar results have been obtained in Madagascar by Carougeau.¹⁶

Hyde and Davis¹⁷ have considered the possibility of such observations being important from the standpoint of human pathology, as in one case of sporotrichosis in man there was a strong suspicion that infection had arisen from a horse; and they note that during the last seven or eight years twelve human cases have occurred in the southern part of North Dakota, a district in which sporotrichosis in the horse has probably been fairly common.

Pathological Diagnosis.—It is stated that if the pus of a sporotrichon lesion be examined without staining, the spores can be recognized as highly refractile double-contoured objects. It is further stated—by Landouzy¹⁹—that if, after inoculating a sloped agar tube, a droplet of the pus be smeared on the naked glass opposite the medium, sprouting of mycelium from the contained spores can be observed with a low power of the microscope.

The diagnosis, however, essentially rests on the isolation of the organism. For this purpose tubes of potato or of glycerinated carrot, of plain sloped agar and glucose agar, should be inoculated, preferably from a non-ulcerating lesion. One set of tubes should be incubated at 37° C., and another at 22° C., and kept under observation for at least a week.

It is evident that cases of sporotrichosis can easily be overlooked. To ensure that the primary cultures shall be pure, material from unbroken lesions must be obtained and the difficulty of microscopically demonstrating the fungus in the lesions, the necessity in many cases for the use of media containing sugar, the special thermal relationships of the organism, the non-appearance of visible growth till several days after inoculation, the peculiar microscopic appearances which often suggest the presence of yeasts, the relative insusceptibility of the guinea-pig to inoculation, all open up paths for the organism being missed. Further, the marked therapeutic effect of potassium iodide may suggest a diagnosis of syphilis and obscure the recognition

of the true condition present. It is obvious, however, that in all granulomata, especially of the skin, which cannot be clearly attributed to the ordinary causes of such lesions, the possibility of sporotrichosis should be kept in view. Usually, if such precautions as those we have detailed be observed, little difficulty will be experienced in the fungus being isolated, if it be present.

We must acknowledge our great indebtedness to Dr. R. Cranston Low for the drawings of which reproductions appear in the coloured plate. We also owe our thanks to the Carnegie Trust for a grant from which the expenses of the inoculation experiments were defrayed.

REFERENCES.

- ¹ Schenk: *Johns Hopkins Hospital Bull.*, 1898, vol. ix, p. 286.
- ² Hektoen and Perkins: *Journ. Exper. Med.*, 1900, vol. v, p. 77.
- ³ Brayton: *Indianapolis Med. Journ.*, 1899, vol. xviii, p. 272.
- ⁴ De Beurmann and Ramond: *Annal. de Derm.*, 1906, pp. 837, 914, 993.
- ⁵ Ofenheim: *Lancet*, 1911, vol. i, p. 659.
- ⁶ Pautrier and Lubentacher, *Bull. de la Soc. Franc. de Dermatologie*, 1909, p. 254.
- ⁷ Vidal and Abrami: *Bull. de la Soc. de Méd. des Hôp. de Paris*, June 5th, 1908.
- ⁸ De Beurmann, Gougerot, and Gaucher: *Bull. de la Soc. de Méd. des Hôp.*, 1908, No. 20, p. 837.
- ⁹ Low: *Edin. Med. Journ.*, February, 1911, p. 121.
- ¹⁰ Foulerton, *Trans. Path. Soc. Lond.*, 1901, vol. lii, p. 259.
- ¹¹ Page, Frothingham, and Paige, *Journal of Medical Research*, 1910, vol. xxviii, p. 157.
- ¹² Gougerot, *Gaz. des Hôp.*, 1909, pp. 537, 581.
- ¹³ De Beurmann and Gougerot, *Bull. Soc. de Méd. des Hôp.*, 1908, vol. xxvi, p. 753.
- ¹⁴ Gougerot and Caravan, *Presse médicale*, 1908, p. 337.
- ¹⁵ Tokishige, *Centralbl. f. Bakteriöl.*, 1896, Abth. I, vol. xix, p. 105.
- ¹⁶ Carougeau, Reference in *Centralbl. f. Bakteriöl.*, 1910, Abth. I, vol. xlv, p. 610.
- ¹⁷ Hyde and Davis, *Journ. Cutan. Diseases*, New York, 1910, vol. xxviii, p. 321.
- ¹⁸ Vidal, *Ann. de l'Inst. Pasteur*, 1910, vol. xxiv, p. 1.
- ¹⁹ Landouzy, *Presse médicale*, 1909, p. 785.

CARCINOMA OF THE LARYNX

EXTIRPATION OF PRIMARY AND
SECONDARY GROWTHS: GLANDULAR RECURRENCE:
TREATMENT WITH THYROID EXTRACT:
DISAPPEARANCE OF GROWTHS.*

BY ROBERT H. WOODS, M.B., F.R.C.S.I.,

PRESIDENT OF THE ROYAL COLLEGE OF SURGEONS IN IRELAND;
SURGEON FOR THE THROAT, NOSE, AND EAR TO
SIR PATRICK DUN'S HOSPITAL.

MR. CHAIRMAN AND GENTLEMEN,—I should not trouble you with a paper on so well-worn a subject as extirpation of the larynx, were it not that the following case has points of quite exceptional interest.

The patient, M. W. L., aged 51, was sent to me by Dr. William Hamilton, of Boyle, in November, 1909. He complained of pain and difficulty in swallowing for about two months, the pain latterly increasing in severity and shooting towards the right ear, while the dysphagia was so great that only fluid and so-called semi-fluid foods could be taken.

The patient had a very intolerant throat, and examination could only be conducted after cocaine had been applied. The right side of the larynx was seen to be occupied by a large growth having an ulcerated surface presenting backwards and outwards towards the sinus pyriformis and the opening of the gullet. A gland or two over the carotid sheath at the level of the upper border of the thyroid cartilage were palpably but not greatly enlarged. There was no history of syphilis or any other important complaint. A diagnosis of malignant disease was made, and a portion of the growth removed for microscopic examination. Dr. Earl, to whom it was submitted, reported it to be a flat-celled carcinoma. Sir Charles Ball saw the patient in consultation with Dr. Hamilton and me, and agreed that total extirpation of the larynx offered the only hope of saving the patient's life. This course was agreed to by the patient.

With a view to lessening the severity of the sepsis which necessarily follows such an operation, it was decided to

* A paper read before the Surgical Section of the Royal Academy of Medicine in Ireland, May, 1911.