ANNALS OF THE NEW YORK ACADEMY OF SCIENCES

VOLUME 93, ART. 5, PAGES 147-206

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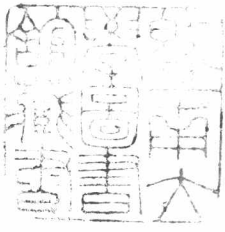

CONTENTS

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Having humbly worked for a number of years in rather widely different branches of mycology, the thought has come to my mind that perhaps it might not be completely uninteresting to the reader if, in this paper, I touched briefly on various mycological subjects, giving my experiences rather than delivering an elaborate dissertation on a single subject.

Persistence and Variability in the Cultural and Biochemical Characters of Certain Fungi of Human Origin Cultured on Artificial Media for 2 to 5 Decades

At the begining of the century, and up to the early 1920s, the majority of mycologists and bacteriologists believed in the "fixity" of mycetes and bacteria: the cultural and physiological characters of these organisms, it was thought, would not significantly vary if they were grown under standard nutritional and environmental conditions. The only change these workers admitted, a biological one, was loss of pathogenicity in old strains. Then the pendulum swung the other way, and a flow of publications commenced that has continued unabated to the present day on the spontaneous changes and variations of fungi cultivated on artificial media.

I propose to make a few remarks on the subject, based chiefly on the study of certain pathogenic fungi isolated by me long ago and kept under almost continuous investigation ever since. These fungi were subcultured on an average of once each month on dextrose agar (4 per cent until 1930, then 2 per cent). I should like to make it clear that I shall merely quote facts and relate observations without any attempt at explaining their causation.

In my experience, fungi of human origin can be separated into three groups: (1) those whose characters do not change, or change only in a minimal way, through the years of subculturing on artificial media; (2) those whose characters may change, even profoundly, but that at long intervals resume their original characteristics; and (3) those whose characters change permanently and irreversibly.

Group 1: Fungi with Permanent Characters

The expression "permanent characters" must be taken *cum grano salis*. Is there anything in nature that is absolutely changeless and immobile? Doubtless changes occur continuously, but they are minimal and, for practical purposes, may be ignored. As examples of this group of fungi I may mention certain species of *Candida* or, more correctly and

exactly, a certain strain of a certain species: *Candida krusei* Castellani (1910) Berkhout, 1923. The original strain, isolated by me from sputum in Ceylon in 1909, is still in my collection. When first isolated, it produced on dextrose agar a growth that was rather dry, with a finely granular or very delicately creased surface. Microscopically, the free yeast like cells were ovaloid or somewhat elongated, and pseudomycelium was formed. Among the six "sugars" at present generally employed for yeast identification, namely dextrose, maltose, galactose, saccharose, lactose and inulin, the strain produces fermentation with gas only in dextrose; among other sugars apart from the standard six it fermented only fructose and mannose. This strain has been reinvestigated by a number of workers, among whom are E.C. Spaar (1926), G. Zepponi (1931), A. Giovannola (1934), J.C.S.Swartzwelder (1937), Biagio Urso (1955), Capocaccia (1956), and others.

No changes have been noted. At present, more than 50 years after isolation, the strain produces a colony on dextrose agar that is somewhat dry, and its surface is finely granular or very delicately crinkled, microscopically, the cells are ovaloid or elongated; of the six standard sugars only dextrose is fermented and, of the other sugars, only fructose and mannose.

In my collection I have also the original strains of *Candida tropicalis* (Castellani 1910) Berkhout 1923, *C. pseudotropicalis* (Castellani, 1911) Bergal 1931, and *C. macedoniensis* (Castellani 1919) Berkhout 1923. Like *C. krusei*, these have remained unchanged culturally and biochemically through the years of cultivation on dextrose agar. An interesting point is that *C. tropicalis*, which was found to be definitely virulent and pathogenic for laboratory animals on first isolation still displays these characteristics after five decades of continuous subculturing, as shown by Biagio Urso and others.

It would appear also that antigenically the original strains of *Candida* isolated by me so long ago have undergone very little, if any, change. In 1934, at the Ross Institute of Tropical Medicine, London, England, Mackenzie-Douglas and I carried out a serological investigation of *Candida* fungi by means of agglutination and complement-fixations tests. We recognized four serological groups: group 1, comprising *C. albicans* and *C. tropicalis;* group 2, comprising *C. macedoniensis* and its varieties; group 3, comprising *C. pseudotropicalis* and its varieties; and group 4, comprising *C. krusei* and its varieties. Groups 1, 2, and 4 were well defined and clear-cut. Group 3 was far less so; in fact, it was badly defined.

A few years ago workers in my laboratory repeated the investigation and came to substantially the same conclusions.

Recent intensive serological studies on the "yeasts" in general, including *Candida*, have been carried out in a number of scientific insti-

tutes in the United States, England, and other countries, including Japan (by Takesshi Tsuchiya and collaborators). An excellent monograph on serological mycology has been published by Hans Seeliger in Germany.

Group 2: Fungi showing Reversible Changes

Several of the fungi I happened to find belong to this group. I mention as examples *Trichophyton balcaneum* Castellani 1916 and *Geotrichum matalense* Castellani 1915; I still have the original strains of both.

Trichophyton balcaneum was isolated by me during World War I, in the Balkans, from cases of a peculiar, diffuse, scaly condition of the scalp resembling a severe form of pityriasis sicca rather than tinea. The fungus grew on dextrose agar, producing a somewhat nodular, crinkled, or slightly convoluted, flattened, glabrous, dirty-whitish or beige colony; it liquefied gelatine rapidly and it clotted milk; microscopically, no macroconidia, no spirals, and no denticulated bodies were seen; only mycelial threads with a few very doubtful microconidia. The fungus continued to show the cultural characters mentioned above for a number of years. Then in 1928, definite changes appeared. The colonies became covered with whitish duvet (aerial mycelium), not very long but quite abundant; when the duvet was scraped off the growth appeared as a smooth, flattish mass, not nodular nor crinkly, nor convoluted in parts. I thought it had become pleomorphic. These new features remained unchanged for about one year, and then the aerial mycelium disappeared and the colonies began to grow again with a glabrous, somewhat knobbly, slightly convoluted aspect. A few years later the colonies once more began to become fluffy, and since then these two totally different appearances of the colonies have alternated at long irregular intervals of years, although the medium has always been the same: 4 per cent dextrose agar until 1930 and 2 per cent later. At present the cultures have the same appearance as on first isolation. The microscopic characters have never varied; macroconidia, denticulated bodies, and other specialized structures have always been absent.

The original strain of *Geotrichum matalense* Castellani, 1915, isolated in 1914, is still in my possession. When first isolated and for years thereafter, the cultures on dextrose agar appeared fluffy and whitish; when this duvet was scraped off, the surface of the colony was smooth.

In 1928, after continuous subculturing on dextrose agar for 13 years (approximately once a month), the duvet disappeared and the growth became deeply rugose and somewhat convoluted in parts, with a smooth, glabrous, somewhat moist-looking surface. Some years later, in 1934, the original characters, with an abundance of duvet, returned. In 1936, the duvet again disappeared, to return a few months later. At present, the cultures show absolutely the same characters as when first isolated, with abundant whitish aerial mycelium present.

Group 3: Fungi showing Irreversible Changes

Every medical mycologist is well acquainted with the irreversible changes shown by certain dermatophytes when they are grown for long periods on artificial media, especially dextrose agar. The fungus loses its original characteristics and becomes fluffy and, microscopically macroconidia, microconidia, spirals, and denticulated bodies are no longer seen; only sterile mycelia are present. The original characters never return; in fact, it may be said that new degenerate races, possibly species, arise with features of their own that remain permanent. This phenomenon was first studied by Sabouraud, who introduced the term "pleomorphism" – not to be confused with "polymorphism" – to indicate it. Once a fungus has become pleomorphic, it remains so indefinitely. The subject of pleomorphism has been treated thoroughly in many books, monographs, and scientific papers, especially by French authors and, in the United States, recently by Reiss and others. I do not propose to discuss it here. I shall merely cite a practical point: Do we have any reliable means to prevent a fungus from becoming pleomorphic? Long ago Sabouraud proclaimed that the use of a poor medium is the best way of preventing pleomorphism, and for this purposed he devised his "maintenance agar," which is prepared with peptone water instead of broth and contains no dextrose or any other sugar. None of the media recommended subsequently, including the so-called natural media and media containing various chemicals and antibiotics, have been completely successful.

In recent years, I have introduced a very simple procedure for the prevention of pleomorphism that thus far seems to be successful: "cultivation" (so to speak) in plain sterile distilled water. This method is based on certain experiments I carried out in the Mycological Department of the London School of Hygiene and Tropical Medicine, London, England, in the years 1938 and 1939, the results of which were published in the *Journal of Tropical Medicine and Hygiene* in 1939.

Long Viability (More Than 12 Months) of Many Pathogenic Fungi in Sterile Water, Suggesting a Simple Method of Maintaining Fungal Strains in Mycological Collections While Apparently Preventing Pleomorphism of Dermatophytes

In the year 1938 I carried out in the mycological laboratories of the London School of Hygiene and Tropical Medicine the following experiment.

On July 5th, 1938, 12 tubes of sterile distilled water were inoculated with the following fungi (each with one fungus): *Candida krusei* Cast.; *C. albicans* Robin var. *pinoyi*; *C. tropicalis* Cast.; *C. pseudotropicalis* Cast.; *C. macedoniensis* Cast.; *Geotrichum rotundatum* Cast.; *Geotrichum matalense* Cast.; *Geotrichum asteroides* Cast.; *Geotrichum rugosum*

Cast.; *Epidermophyton floccosum* Harz; *Cladosporium mansoni* Cast.; and *Aleurisma castellanii* Pinoy (*Acladium castellanii*).

These distilled-water test tubes were inoculated from dextrose agar cultures, and care was taken not to transfer particles of the dextrose medium to the liquid. The tubes were sealed in a flame and kept at the temperature of the room until July 10, 1939. On that day the tubes were opened by breaking the necks after filing and, after shaking them, inoculations were made in dextrose agar tubes. Growth developed in all the dextrose agar tubes within the normal time, and the macroscopic appearance of the cultures was normal.

The *Candida* species were passed through the usual carbohydrates (dextrose, levulose, mannose, maltose, galactose, lactose, inulin). *C. albicans* var. *pinoyi* produced gas fermentation in dextrose, mannose, *C. tropicalis* in dextrose, fructose, mannose, maltose, galactose, and saccharose; *C. macedoniensis* in glucose, fructose, mannose, galactose saccharose, and inulin; and *C. pseudotropicalis* in dextrose, fructose, mannose, galactose, saccharose, and lactose. The microscopic characters appeared to be unchanged. The strain of *Epidermophyton floccossum* inoculated into distilled water was the old laboratory strain that had become partially pleomorphic several years earlier; it was fluffy but still showed a certain amount of characteristic canary-yellow color. The cultures made on dextrose agar, after 12 month's maintenance of the fungus in the distilled water, showed the same partial pleomorphism with some characteristic yellow color present (FIGURE 1).

From the amount of sediment in the inoculated distilled water tubes one had the impression that several of the fungi must have grown slightly. This was certainly the case with regard to *Cladosporium mansoni* and some species of *Candida*.

Since World War II I have repeated the experiment more than once, using the fungi mentioned above and, in addition, the following ones: *Sporotrichum anglicum* Cast., *Glenospora lanuginosa* Cast., *Trichophyton rubrum* Cast., and other species of *Trichophyton* and *Microsporum*; also *Coccidioides immitis* Rixford and Gilchrist strain *metaeuropeus* Cast., *Blastomyces dermatitidis* Gilchrist and Stokes strain *tulanensis* Cast., *Cryptococcus neoformans* Sanfelice, *Cryptococcus neoformans* strain *hondurianus* Cast., *Cryptococcus ater* Cast. (This last species was inoculated in sterile distilled water in May 1959. The results have been the same. After 12 months all the fungi were found alive and grew quite well when inoculated in dextrose agar, producing colonies exactly like the original ones, and the biochemical characters had remained the same.

In recent years I have simplified the technique: I simply use ordinary tubes containing 6, 8, or 10 cc. of sterile distilled water (boiled on 3 consecutive days or autoclaved) and plugged with cotton wool (absorbent

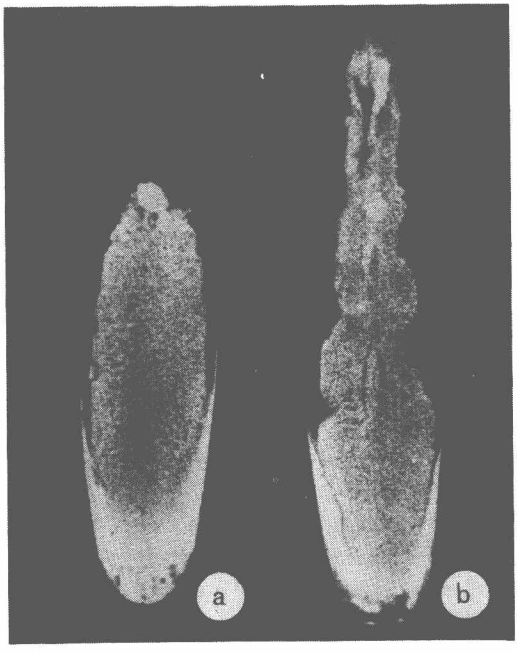


FIGURE 1. (*a*) Four-day-old dextrose agar culture made from water culture of *Candida krusei* 12 months old. (*b*) Four-day-old dextrose agar culture made from stock dextrose agar culture of *C. krusei* (same strain).

cotton) like ordinary tubes of broth or other media. They are inoculated with a "large" inoculum and kept in the laboratory at the temperature of the room (in hot countries it is advisable to use rubber caps to prevent too much evaporation and loss of liquid). When using a large inoculum it is almost impossible to prevent the transfer of some dextrose agar to the tube of distilled water, but the amount of dextrose so added to the water is of such minute quantity that it is not likely to influence sensibly the growth of the fungus or facilitate the development of pleomorphism.

The above experiments have led me to recommend a very simple procedure for maintaining pathogenic fungi, especially dermatophytes, in mycological collections: "cultivation" is done in sterile distilled water, tubes of which are inoculated with the fungi and left alone at room temperature for 12 months. Then transplantations are made from them onto dextrose agar to see whether the fungi have maintained the original characters. Thus far my experience is that they generally have; from these dextrose agar cultures a new series of distilled water tubes are inoculated and left at room temperature (or at 18 to 22 ° C. in the incubator) for one year. Agar dextrose agar cultures are then made and, from these, new series of sterile distilled water tubes are inoculated. This method eliminates the necessity of frequent subculturing and makes un-

necessary the use of lysolitic procedures, which in my experience are much less successful with mycetes than with bacteria. Some mycetes, such as *Cladosporium mansoni*, frequently die in the process. Another practical advantage of the method is that it seems to prevent, to a great extent at least, pleomorphism: none of the dermatophytes experimented with so far has become pleomorphic during its long sojourn in sterile distilled water. This procedure, as I have said, apparently prevents pleomorphism, but of course does not cure it once it has developed; a pleomorphic strain inoculated into sterile distilled water will remain pleomorphic.

Incidentally, I may say that a number of bacteria, especially intestinal bacteria such as *Salmonella typhosa*, *S. schottmuelleri*, and *S. asiatica*, remain viable (and some of them multiply) for one year and longer in sterile distilled water.

Some Little-Known Fungi and Some Little-Known Mycoses

Little-known mycetes and little-known mycoses are legion, but the space at my disposal will allow me to touch upon only a few of them. For convenience, fungal diseases may be separated into two groups: internal mycoses and external mycoses. Among the first group I propose to devote a few words to two little-known bronchomycoses, to tonsillomycoses, and to urethromycoses. Among those of the second group I shall briefly discuss acladiosis, tinea nigra, "cryptococcosis epidermica," tinea capitis decalvans perstans (la-li-tou), tinea tenuis (tinea invisibilis), tinea pedum geotrichica, pruritus ani mycoticus, fissura labialis mediana, chronic ulcerative balanitis with presence of a capsulated yeast, and a polyulcer of the leg with presence of a black pigment-producing capsulated yeast.

Two Little-known Bronchomycoses

The subject of bronchomycoses in general I have discussed in many papers since my Ceylon days, when I first described bronchomoniliasis (bronchocandidiasis) and several other bronchopulmonary conditions due to fungi (see *Ceylon Medical Reports* and *Transactions of the Ceylon Branch British Medical Association*, 1904-1915; Castellani and Chalmer's *Manual of Tropical Medicine*, first edition, 1910; second editions 1913; third editions 1919 and, among more recent publications, *Little-Known Tropical Diseases*, Lisbon, 1954). I shall limit myself to saying a few words on two bronchomycoses that are very little known and are not mentioned in textbooks.

"Tea-taster's cough." When I was in Ceylon, a young assistant in one of the big Colombo firms, a tea taster, came to consult me about a chronic cough that, he said, had not yielded to ordinary treatment and had been suspected by several medical men to be of tuberculosis origin. He

emphatically stated, however, that he did not believe the condition was tuberculous. "I am merely suffering from tea-taster's cough," he said, an expression I had never heard before. The general condition of the patient was good, and physical examination of the chest revealed only a few rales. Microscopic examination of the sputum was negative for tuberculosis: instead I noticed microscopically some mycelial filaments and some yeastlike bodies. I inoculated several dextrose agar tubes and grew a *Candida* fungus, which at the time I believed to be an endomyces.

How did this patient become infected? Tea tasters, in order to judge the various qualities of the tea, not only taste infusions, but also often fill their hands with the tea leaves and bury their noses in them, sniffing them up; in this way a certain amount of tea dust enters the nasal cavities.

On examination of tea dust in Ceylon one finds it contains fungi of the genus *Candida* constantly, of the genera *Aspergillus* and *Penicillium* frequently, and of the genus *Geotrichum* occasionally. (Incidentally, I may say that samples of tea investigated in the temperate zone seldom if ever contain *Candida* fungi.) A peculiar streptococcus is also present. The same organisms are not rarely found in the nasal cavities of tea-tasters and, when bronchial symptoms appear in them, *Candida* fungi are present in the expectoration. It is probable, therefore, that so-called tea-taster's cough is a candidiasis (moniliasis), especially since a guinea pig, into the nostrils of which I insufflated tea dust regularly for months, died with symptoms of chronic bronchopneumonia; at the autopsy a *Candida* was grown from the lungs.

In recent years Biagio Urso and others have shown that animals made to live in an atmosphere artificially charged with *Candida* fungi of the species *tropicalis* and *albicans* become infected and develop pulmonary lesions.

What I have said about tea-taster's cough applies to a great extent to the so-called "tea-factory cough." For many years planters in Ceylon have noted that the coolies doing work in tea factories, where the leaves are dried and there is a large amount of tea dust floating about, after some months become weak, lose flesh, and often have a cough with muco-purulent expectoration. The planters have found by experience that the coolies must be taken away from the factory and sent to work in the fields; then the symptoms slowly disappear. I have examined some of these coolies, and their expectoration almost always contains fungi of the genus *Candida*.

I have little doubt, therefore, that the so-called "tea-factory cough" is a bronchomycosis, probably a bronchocandidiasis (bronchomoniliasis).

Sporotrichum anglicum bronchitis. Of this condition I have observed four cases. They were of medium gravity, hardly any fever, sputum muco-

purulent, general health not much affected, no skin lesions. They all responded to potassium iodide treatment.

Fungi of the genus *Sporotrichum* are *fungi imperfecti* of the order Conidiosporales, characterized by the conidiophores being almost entirely undifferentiated from ordinary hyphae, and by the presence of terminal loose clusters of conidia (the *bouquets* of French authors), as well as of numerous lateral conidia borne on pedicelli. These latter conidia fall out early, but the pedicelli remain and the hypha takes on the aspect of a "rasp" (radula); hence these conidia are referred to by some mycologists as radulospores.

The best known species – according to some authorities the only human species – is *Sporotrichum schenki*, a full description of which may be found in any mycological treatise. It will be sufficient to remind the reader that its cultures are often cerebriform and irregular and that they are at first generally whitish but later very frequently become of a brownish chocolatelike color or completely black, often showing a very dark or black pigmentation; the fungus never produces gas fermentation in glucose or any other sugar. Mycelial threads are about 2μ in diameter; the conidia are oval, 5 to 6μ in length and 3μ in breadth, supported by very short sterigmata. The conidia are extremely numerous and often collect in lateral and terminal clusters, as well as cylindrical longitudinal masses around the hyphae. The fungus, it is well known, causes a skin disease characterized by gummata and other lesions, chiefly situated along certain lymphatics. Cases of primary bronchitis due to it are not found in the literature.

In my cases of sporotrichal bronchitis a totally different species, which I called *Sporotrichum anglicum* Cast. 1939, was found. I give here a short description of it.

In the sputum it appears in the form of yeastlike cells and short mycelial articles, as well as in filaments. It is Gram-positive.

The fungus grows easily on dextrose agar and all the usual laboratory media (FIGURE 2). On dextrose agar the growth is of a white or greyish color, occasionally with a yellowish tone, and shows a slightly rugose or wrinkled surface, at times rather moist, covered often with very short

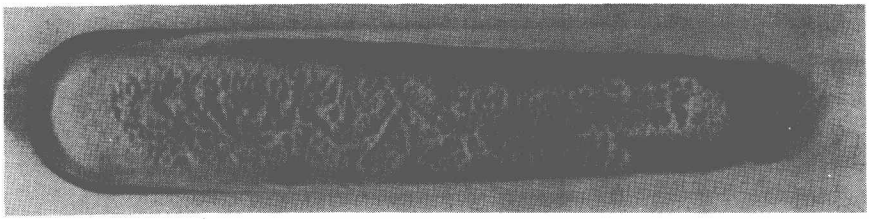


FIGURE 2. Glucose agar culture, 15 days old, of *Sporotrichum anglicum* Castellani.

white duvet. On ordinary nutrient agar the growth is rather scanty. Dextrine agar cultures are very similar in appearance to agar cultures. On soluble starch agar the growth is abundant and very similar to the growth on dextrose agar. On potato the fungus grows well and the colony shows a white, somewhat chalky surface. Carrot cultures are very similar to potato cultures, having a white chalky appearance. On coagulated serum there is abundant growth, whitish, with at times a greenish tinge; there is no liquefaction.

When a dextrose agar plate is inoculated from a sugar peptone water culture, colonies develop that have a tendency to remain separate; their surface often shows spicules.

In hanging-drop cultures (FIGURE 3) the mycelium is abundant and the conidia are numerous, in lateral or terminal clusters. Conidia are

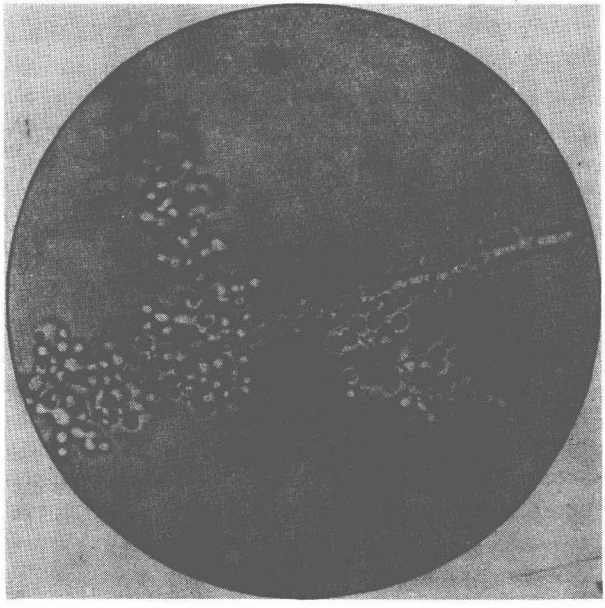


FIGURE 3. A hanging-drop culture of *Sporotrichum anglicum* Castellani.

mostly borne on minute pedicella, and numerous lateral denticles can be seen on some hyphae. The conidia are generally of oval shape, averaging 4 to 6 × 3 to 5 μ, but some conidia may have a maximum longitudinal diameter of 7 μ and others of only 3 μ. The mycelial hyphae are about 3 μ in diameter, but some may be as much as 4 μ and others as little as 2 μ. On slide cultures one notices almost the same features.

The fungus does not liquefy gelatine or serum. It does not coagulate milk but generally renders it alkaline. It produces acidity and gas in dextrose and several other sugars. The three strains in my collection have the same fermentative reactions, producing acid and gas in dex-

trose, fructose, mannose, maltose, and saccharose, but do not ferment with production of gas, mannitol, galactose, rhamnose, inositol, adonitol, arabinose, amygdalin, salicin, sorbitol, dextrine, erythritol, xylose, arbutin and starches.

Although pathogenicity seems to be slight in laboratory animals, the fungus is apparently the cause of the bronchial affection in humans, in the cases I observed. I found that the fungus gradually decreased in amount and finally disappeared from the sputum when the patients were placed on iodine therapy and began improving. All of the patients recovered. In a case in which a *Candida* was also present both fungi disappeared, and it is quite possible that both organisms played a part in the etiology of the condition.

The fungus has been placed in many different genera by various authors, including the genus *Trichospora* by Borelli. I still believe that its correct taxomnomic position is in the genus *Sporotricum* owing to the presence of the typical radulospores.

Tonsillomycoses

A simple classification of the tonsillomycoses (not including actinomycosis) is (1) acute tonsillomycoses: tonsillomycosis follicularis and tonsillomycosis diphtheria-similis vel membranacea; and (2) chronic tonsillomycoses: tonsillomycosis fusca and tonsillomycosis spinulosa.

Follicular tonsillomycosis. In a vast majority of cases the condition is due to yeastlike fungi of the genus *Candida* (tonsillocandidiasis vel moniliasis), the ordinary causative agents of thrush; in reality the condition is a variety of thrush.

On the surface of the tonsils several white or whitish-grey or whitish-yellow spots are seen (FIGURE 4), corresponding to the openings of the follicles. The patient complains of a sore throat and discomfort in swallowing; there may be fever but the general condition seldom becomes serious, and the affection usually heals spontaneously within one to three weeks. Occasionally the mycotic infection spreads to the uvula and soft palate, forming diffuse white patches, and then becomes indistinguishable from the diphtherialike type of tonsillomycosis. In other cases the mycotic infection spreads from the tonsils all over the oral mucosa (thrush).

Long experience has shown me that the best treatment is the local application to the fauces of my old fuchsin paint.* There is no danger if a very small amount of it is swallowed, but the urine may become pinkish.

*Castellani's fuchsin paint is prepared from 10 cc. of a saturated alcoholic solution of basic fuchsin, 10 cc. of 5 per cent aqueous carbolic acid solution, 1 gm. of boric acid, 5 cc. of acetone, and 10 gm. of resorcine.

Tonsillomycosis diphtheria-similis (tonsillomycosis membranacea). The disease is usually caused by yeastlike fungi of the genus *Candida.* The species found are in most cases *C. albicans* and *C. tropicalis.* In a few cases, fungi of the genera *Debaromyces, Willia,* and *Saccharomyces have been described.*

The onset is often sudden, with severe sore throat and difficulty in swallowing; the patient feels very ill and complains of great prostration and, at times, of rheumatoid pains in the joints. Fever is present and may be fairly high (102° to 103° F.). Some of the cervical glands may be swollen and tender. Inspection of the throat will show creamy-white patches on the tonsils, the uvula and, occasionally, the soft palate; the patches often coalesce (FIGURE 5). Removal of these patches may in some cases leave a very slight ulcerative bleeding surface. If the membranelike structure is placed between two slides it often feels like putty, and lacks the elasticity and resiliency of a diphtheria pseudomembrane. It should be kept in mind that in almost every case, in addition to the fungi, streptococci are present and may play a role in the etiology of the condition.

Here are two representative illustrative cases.

Case 1. Pensioner N. (Military Pensioners' Hospital, Orpington, England) developed on August 5, 1921, tonsillitis with a temperature of 102° F., a rapid pulse rate, and prostration. Inspection of the throat showed a white membrane on the tonsils and fauces. It was easily detached but rapidly reformed. Neither in the direct smear nor by culture methods were diphtheria bacilli found. In the direct smear, made at the bedside, a large number of yeastlike cells were present and on Löffler's medium numerous white colonies and *Candida* developed.

Case 2. A Singhalese girl, aged about 11 years, was brought many years ago into the Infectious Diseases Hospital in Colombo, Ceylon, with the diagnosis of diphtheria. There were white patches on her tonsils, uvula, and soft palate. The temperature was rather high (102° F.), and the pulse rate was fast and of low pressure; there was some swelling at the angle of the jaw. The child developed symptoms of bronchopneumonia and died three days after admission. Antidiphtheria serum had been given twice by the physician in charge of the hospital. Microscopic and bacteriological examination of the patches for *Corynebacterium diphtheriae* carried out by the usual techniques of those days (Löffler's serum) remained negative. Rodlike bacteria were not seen in the specimens taken directly from the patches, but numerous mycelial and conidial elements of the fungus were present. The fungus was *Candida tropicalis.*

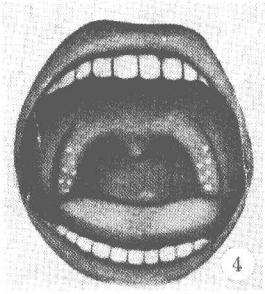
The simplest treatment in each of these cases would have been with the topical application of Castellani's fuchsin paint. Even if it is swallowed there is no danger of poisoning, although the urine may occasionally become pinkish.

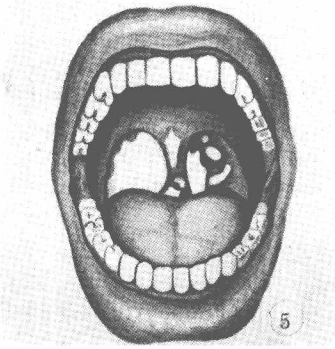
Chronic Tonsillomycoses

Tonsillomycosis spinulosa (tonsillomycosis spiculata, tonsillogeotrichosis spinulosa). On inspection of the tonsils, numerous brownish or greyish-brown or whitish or amber colored erect spicules, sometimes in bundles, several millimeters in length, are seen, usually originating in the crypts (FIGURE 6). The condition, which is not a common one, runs a very chronic course. The patient may complain of slight sore throat but the symptoms are seldom acute or severe, and he can usually live his ordinary life and attend to his work.

Microscopic and cultural examination of the spicules shows that they consist of fungi, usually of the genera *Geotrichum* or *Trichosporon.* In my cases I found *Geotrichum rotundatum* and *Geotrichum asteroides.*

The treatment consists of applying locally diluted tincture of iodine or the fuchsin paint, but to achieve a cure takes a long time.





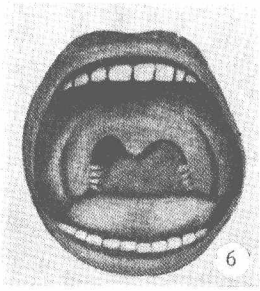


FIGURE 4. Tonsillomycosis follicularis (from a drawing).
FIGURE 5. Tonsillomycosis diphtheria-similis (from a drawing).
FIGURE 6. Tonsillomycosis spinulosa (from a drawing).

Tonsillomycosis fusca. On one of the tonsils and occasionally elsewhere on the oral mucosa, a rather large brownish or dirty greenish patch about one-half centimeter or more in diameter is seen, which cannot be removed easily. When forcibly removed, a superficial ulcerated lesion remains. The patch is composed of an enormous number of mycelial filaments of fungi of the genus *Geotrichum* or *Trichosporon* for example, *G. rotundatum* or *G. rugosum (Hemispora rugosa),* which are identified by many authorities with *Trichosporon cutaneum* de Beumann, Gougerot, and Vaucher, in my humble opinion incorrectly (see my remarks below under *Tinea pedum geotricha*).

The treatment is most difficult and it may take many months to obtain a cure. Tincture of iodine and the fuchsin paint are, on the whole, the best local applications. In a recent case I tried some of the new antifungal antibiotics, but the results were poor.

Urethromycoses

Urethrites of fungal origin may be classified clinically as follows: (1) discharge whitish or yellowish, urethromycosis alba; (2) discharge reddish or pinkish, urethromycosis rubra; and (3) discharge greenish-black or black or dark brownish, urethromycosis nigra.

Mycotic urethritis with whitish or yellowish discharge. This condition is not rare. I have seen several cases in the tropics and a few in the Balkans, southern Europe, and Louisiana. The discharge is generally present in small amounts and is mucoid, but occasionally it may be fairly abundant and may closely resemble gonorrheal urethritis. The fungi found generally belong to the genus *Candida*, usually *C. albicans* and *C. tropicalis*.

Occasionally the fungal infection spreads from the meatus to the whole surface of the glans penis, producing a white pseudomembrane that can be easily detached (thrush of glans penis).

The following cases are illustrative.

During the first World War, a young Serbian officer in Macedonia consulted me for a fairly abundant purulent urethral discharge. He was distressed; he was engaged to be married and believed he was suffering from gonorrhea, although he denied having exposed himself to infection. I examined the secretion: gonococci were not present; instead a large number of yeastlike cells and a few pseudomycelial segments could be seen. Cultural investigation showed the presence of a *Candida*. I prescribed a mixture containing potassium iodide, sodium bicarbonate, glycerine, and syrup of tolu; I also suggested irrigations with a solution of 1:20,000 mercury perchloride. The discharge disappeared completely within 10 days.

Red mycotic urethritis. This condition is rare, but I have seen a few cases in the tropics, the Balkans, and southern Europe. I have also seen a case in New Orleans, La.

The urethral discharge is usually in exceedingly small amounts, mucoid or mucopurulent, reddish or pinkish. The cases of this condition may be divided into the following groups: (1) cases in which the discharge is associated with a red pigment-producing "yeast," usually *Candida pulcherrima* or a *rhodotorula;* (2) cases in which the discharge is associated with a white *Candida* fungus plus a red pigment-producing "yeast"; (3) cases in which the discharge is associated with a white *Candida* plus a red pigment-producing coccus; and (4) cases in which the discharge is associated with a white *Candida* and a red pigment-producing "bacillus."

A case illustrative of this condition is that of a little Singhalese boy, six years old, who was brought to my clinic in Colombo by his parents because they believed he was passing blood from the urethra. The dis-