THE INCIDENCE OF FUNGI IN VARIOUS DISEASED CONDITIONS.[1, 2]

By

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Medical mycology is gradually assuming its proper place in the field of medicine. Its neglect is due to the facts that the fungi are of comparatively little importance in the acute epidemic diseases; exhibit slight pathogenicity; and have an obscure and slow development, and a complicated morphology.

Fungous spores abound in the air, and even if found in the tissues are not necessarily significant. We have been interested in collecting some data on the percentage incidence of fungi cultured aseptically from diseased tissues, and in presenting records of our limited survey in the past year, as well as some statistical data from the recent literature. A serious consideration of fungous etiology, primary and secondary, may do its part to reduce the large quantum of undiagnosed disease.

Survey of literature.

This material has been arranged according to specific types of fungi where possible. The references have been randomly selected and the survey is not intended to be exhaustive.

Dermatomycosis.

The dermatophytes (including especially the Trichophytoneae and to a lesser extent the yeast-like fungi) are responsible for the most prevalent mycotic infections; of world-wide distribution; and contagious and chronic.

Incidence reports of ringworm infections of the hands and feet are enlightening. At the University of California (Legge, Bonar, and Templeton, 1929) the percentage of infections increased in 9 months from 53.3 per cent of the men and 15.3 per cent of the women to 78 per cent of the men and 17 per cent of the women. Gilman

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(1933) reported the disease in 60 per cent of the men and 57 per cent of the women at the University of Pennsylvania. Differential studies of these latter showed 50 per cent of the cases to be ringworm of the toes. Of the total number 15 per cent showed involvement of the groin. Of the 72 per cent which revealed fungi in the scales upon microscopic examination, only 5 per cent yielded positive cultures.

Besides the dermatophytoses where members of the Trichophytoneae are isolated, there are clinically similar lesions in which *Monilia* or other yeast-like organisms are found (Hopkins, 1929). In addition to dysidrosiform eruptions there are numerous cutaneous lesions, frequently of an eczematous nature, from which strains of *Monilia* have also been cultured (Jacobson, 1932). Benham and Hopkins (1933) were unable to isolate a single strain of *Monilia* from the nails or skin in a series of 100 persons with apparently healthy skins, but they did find Cryptococci in the skin of 72 per cent of these. Although most of the latter organisms are probably common saprophytes of the skin, Greenbaum and Klauder (1922) found four pathogenic strains occurring on 35 of 150 normal skins. In all experimental studies it has been shown that abrasions in the skin are essential for infection to occur. In diabetes there are characteristic associated cutaneous lesions in genito-anal and mammary regions, in which *Monilia* is believed to be etiological (Bloch, 1930).

Moniliasis.

Skin. This is discussed in the preceding section.

Lungs. *Monilia* are commonly found in sputa, often associated with debilitating diseases such as tuberculosis, syphilis or carcinoma. Tanner, Lampert and Lampert (1927) found that approximately 10 per cent of "normal" throats harbor monilial organisms as demonstrated by culture. Norris (1936) grew *Monilia* from 15 per cent of the tuberculous patients he examined from two large sanitoria in Georgia; moreover, in a large number of these no tuberculosis organisms were demonstrated. One of us in 1934 ran cultures on 50 tuberculous patients in the Douglas County Hospital and found *Monilia* from the sputa of 35.

The significance of pulmonary moniliasis is problematical. It is possible that the invaders are mainly secondary and of a saprophytic nature. Ikeda (1936) has adequately described 5 cases thought by him to represent primary moniliasis of the lungs. Animal experimentation with certain strains has demonstrated the unquestionable virulence of some of these organisms (Stovall and co-workers, 1934).

Alimentary tract. Thrush presents a fairly typical clinical picture recognized even during the time of Hippocrates, when it was called "stomata aphthoda" (Dodge, 1935). Although less common now than in the past, it is still a frequent mycosis, particularly of infants and senile individuals.

Monilia and other yeast-like fungi have been isolated from the feces in many intestinal disturbances and also reported from "normal" individuals. Anderson (1917) found yeast-like fungi in a large survey of healthy individuals, but none were referable to *Monilia psilosis.* Due to the works of Ashford, the latter organism has been indicated as an etiological agent in sprue. In 1929 he concluded that this clinical entity represented primarily an exhaustive process in which *Monilia* as a secondary invader might complicate the situation. His clinical-laboratory data from Puerto Rican residents is nevertheless interesting. From the stools of 280 cases of clinical sprue, *M. psilosis* was isolated in 52.7 per cent; from those of 178 healthy boys, in 5.6 per cent.

Genito-urinary system. Castellani (1928) and others have isolated *Monilia* from numerous cases of purulent vaginitis. Dodge (1935) reports it in the bladder of diabetics. It has been our experience that cutaneous disturbances in the form of eczema, urticaria and the like, may be associated with a vaginal discharge in which *Monilia* is found and suspected in etiolation. We have also found the organism in several urines (non-diabetic) where the patients likewise had allergic manifestations. In one case an eczema was shown to be an associated condition, which was healed by desensitization with an autogenous vaccine.

Actinomycosis.

Anaerobic types. Sanford and Voelker (1925) recorded from the literature 678 cases of the sulphur-granule type of actinomycosis in the United States. Sanford and Magath (1922) listed 96 cases as seen at the Mayo Clinic since 1909. The geographical regions of greatest frequency, proportionally speaking, include Illinois, Wisconsin, Iowa, Minnesota and North Dakota (Henrici, 1930). Regarding regional location of the infection in the body, Lord (1933) says that about 50 per cent of human cases involve the head and neck, 30 per cent the abdominal region, and 20 per cent the lungs. Skin manifestations are rare and localized.

The situation with animals is interesting for comparison. The

Federal Meat Inspection Report for 1920 states that of 9,709,819 cattle to be killed, 176,456 were retained because of actinomycotic infection. The disease seems to be more prevalent in range (grass-fed) cattle than in corn-fed ones. Comparative reports from various large stock yards indicated that 4 per cent of all the cattle to be killed at St. Paul had actinomycosis, 2 per cent at Omaha and at Chicago, 0.3 per cent at Los Angeles, and 0.1 per cent at New York.

"Streptothrix" group. Henrici (1930) says that there have been recorded in the literature 26 cases greatly resembling tuberculosis where acid-fast actinomycetes were isolated. Thompson (1929) noted the presence of streptothrix in the sputa of those suffering with asthma, bronchitis, bronchiectasis and tuberculosis in 65 per cent of a series of 1,000 cases. Woytek (1936) gives a most complete review of streptotrichosis. In German clinics 8 or more cases are seen annually. Lung localization is the commonest type, and of 15 cases studied by him, 9 were fatal. The cerebral type is very serious, whereas the prognosis for the cutaneous localization is good.

In the 24 cases of madura foot recorded from the United States, 18 were due to species of *Actinomyces* (Gammel, 1929).

Sporotrichosis.

Foerster (1926) said 148 cases had been reported in the United States, of which 130 were confined to the Mississippi basin. With better laboratory methods, doubtless this number has increased greatly. Henrici (1930) lists the infection as "perhaps the most common of the serious fungous diseases." Meyer (1915) had found 400 cases described in the international literature. He was interested in the infection in the horse and was successful in converging "epizootic lymphangitis" in the United States with true sporotrichosis. In Pennsylvania, where there have been as many as 150 cases of equine infection annually, there was never any evidence of direct contagion. Only three recorded human cases are known from that region.

Aspergillosis.

Siebenmann (1883) stated that 1 per cent of all the otomycoses in Germany could be attributed to *Aspergillus* or near relatives. Henrici assumed that the incidence in this country is less, whereas it is considerably higher in India. Pulmonary infections of human beings have been rather common in France and to a lesser extent in Germany. The disease was related to the practice of insufflation of grains to feed

birds. Apparently the infection is very rare here and most likely to be confused with tuberculosis. Lapham (1926) found acid-fast filaments of *Aspergillus* in tissues.

Mucoriasis.

According to Henrici 4 per cent of otomycoses can be attributed to species of *Mucor*. Lung infections are very rare, and more prevalent in Europe than in the United States. Ernst (1918) reported a primary lung infection in the United States due to *M. corymbifer*.

Torulosis.

The disease is probably naturally rare, and apparently even more so because infrequently searched for. Freeman (1931) reported only 44 cases described in the literature.

Coccidioidal granuloma.

Moore (1932) stated that 286 cases had been reported, of which 254 were localized in California. Eighty per cent of all cases are estimated by Jacobson (1932) to have been restricted to the San Joaquin Valley. This endemism is thought to be associated with a peculiar saprophytic substratum (plant, perhaps) upon which the organism ordinarily exists.

Blastomycosis due to Endomyces dermatitidis.

The term blastomycosis, in the clinical sense, has included various etiological agents. The organism isolated by Gilchrist in 1896 is the commonest cause of the infection in this country, but at present we know of no reliable figures as to its percentage incidence. Moore (1933) gives a good discussion of the disease.

Miscellaneous fungous diseases.

In the tropics, especially, a number of the Fungi Imperfecti have been reported as parasites in various infections, particularly of the madura foot type. Species of *Aspergillus, Madurella, Penicillium,* and *Actinomyces* are indicated. Gammel (1927) has reviewed the subject reporting 43 cases in North America. Of late years "Chromoblastomycosis" (caused by members of the *Hormodendron complex*) has been attracting attention. Three cases have been identified in the

United States (Martin, Baker, and Conant, 1936), 21 from South America and several from other countries.

Various investigators are finding miscellaneous fungi on culture from asthmatic individuals and are able to induce positive skin reactions with controlled extracts. Storm Van Leeuwen (1925) reported that 50 per cent of his asthmatic patients were sensitive to mould allergens. The fungi occurring here most commonly are species of *Aspergillus, Mucor, Penicillium, Alternaria* and other Imperfects. Brown (1936) said that 6 of 30 individuals seen by him, allergic to moulds, reacted to an *Alternaria* extract. The organism is commonly found on the skin and has been suggested as an etiological factor in asthma and eczema (Hopkins, Benham and Kesten, 1930). The former stated that *Saccharomyces cerevesiae* (the beer yeast) was the most common offender, 60 per cent of fungous-sensitive patients reacting to it. Grain rusts (Cadham, 1924) and smuts (Wittich and Stakman, 1937) are also suspected as asthmatic allergens.

Original data.

We have cultured 200 miscellaneous cases during the period from November 1935 to September 1936, in Omaha, Nebraska. The patients were frequently allergic and in most instances fungi were previously suspected (i.e., they were not just randomly selected, hence the incidence of fungi may be higher than it would be in the latter case).

Table 1 distributes the organisms according to the type of disease. These cases have been further segregated according to locations in the host from which cultures were made, and again subdivided as to the organisms concerned (table 2). Finally, the organs as attacked by specific fungi are listed (table 3).

These data represent compilations of our observations in selected conditions only, where we were searching for fungi. We have made no attempt to secure similar organisms from normal controls, or from saprophytic substrata or from plants. Whereas only a few of these are known to be definitely pathogenic (i.e., *Sporotrichum Schenckii, Actinomyces Israeli,*[3] *Monilia albicans,* and a few others), the large incidence of such as *Alternaria, Aspergillus,* etc., bear consideration at least from an allergic standpoint.

[3] After Dodge, 1935.

TABLE 1.

Fungi classified as to type of disease.

	No. of cases
1. Eczema	*23*
No fungi	9
Aspergillus	10
Monilia	5
Geotrichum	3
Alternaria	3
Yeast	2
Mucor	2
Cephalosporium	2
Acremonium	1
Basidiomycete	1
Penicillium	1
2. Urticaria	*11*
No fungi	4
Monilia	7
Aspergillus	1
3. Asthma	*46*
No fungi	11
Monilia	13
Mucor	10
Actinomyces	10
Aspergillus	9
Penicillium	5
Yeast	3
Acremonium	2
Geotrichum	1
Endomyces	1
Hormodendron	1
4. Colitis	*4*
No fungi	1
Yeast	1
Monilia	2
Penicillium	1
Alternaria	1
Aspergillus	1
5. Rhinitis and hayfever	*13*
No fungi	7
Alternaria	4
Penicillium	3
Aspergillus	1
6. Otomycoses	*10*
No fungi	1
Yeast	1
Mucor	1
Aspergillus	4
Scopulariopsis	2
Penicillium	1
7. Dermatophytoses	*12*
No fungi	2
Trichophyton	4
Monilia	2
Alternaria	2
Hormodendron	1
Geotrichum	1
8. Skin abscesses	*9*
No fungi	2
Sporotrichum	3
Actinomyces	2
Pullularia	1
Yeast	1

TABLE 2.

Fungi classified as to organic source.

	No. of cases
Lungs (including sputa, pus and pleural fluid)	*82*
No fungi	15
Monilia *	18
Aspergillus	10
Mucors	10
Penicillium	5
Actinomyces †	13
(*Actinomyces Israeli* ‡ .....4)	
Alternaria	2
Acremonium	2
Cephalosporium	2
Yeast	2
Endomyces	1
Hormodendron	1
Geotrichum	1
Nose and throat	*26*
No fungi	6
Monilia	2
Yeast	2
Penicillium	4
Alternaria	4
Actinomyces	3
(*Actinomyces Israeli* .....2)	
Geotrichum	1
Aspergillus	1
Fungi Imperfecti	2
Mucor	1
Stools (including ulcer at anus)	*43*
No fungi	8
Monilia	13
Aspergillus	9
Geotrichum	7
Yeast	2
Alternaria	1
Penicillium	1
Mucor	1
Cephalosporium	1
Skin (including nails)	*60*
No fungi	17
Monilia	3
Alternaria	6
Aspergillus	5
Trichophyton	4
Sporotrichum Schenskii	3
Yeast	6
Penicillium	2
Mucor	2
White Imperfects	2
Actinomyces	3
(*Actinomyces Israeli* .....2)	
Acremonium	1
Ustilago	1
Pullularia	1
Basidiomycete	1
Hormodendron	1
Cephalosporium	1
Geotrichum	1
Cervix (including vagina, uterus and tubes)	*12*
No fungi	4
Monilia	7§
Actinomyces Israeli	1
Ear	*10*
No fungi	1
Aspergillus	4
Yeast	1
Mucor	1
Penicillium	1
Scopulariopsis brevicaulis hominis	2
Eye	*8*
No fungi	6
Geotrichum	1
Hormodendron	1

* A paper on types of Monilia is in preparation.

† We have used Actinomyces to encompass Streptothrix also.

‡ Work is being done of a morphological nature which will no doubt reveal a number of varieties of what is here lumped as *A. Israeli.*

§ Organisms seen in smears but cultured only 4 times.

TABLE 2—*Continued.*

	No. of cases
Miscellaneous	
1. Abscesses	*5*
Head	
No fungi	1
Shoulder (axillary lymph glands)	
Actinomyces Israeli	1
Neck	
Actinomyces Israeli	3
2. Abdomen	*3*
No fungi	2
Yeast	1
3. Urine	*7*
No fungi	5
Monilia	2
4. Gall bladder	*2*
Monilia	1
Actinomyces Israeli	1
5. Spinal fluid	*1*
Monilia	1

TABLE 3.

Organisms and sources.

	No. of cases
1. *Monilia*	*47*
Lungs	18
Nose and throat	2
Stools	13
Skin	3
Cervix	7
Urine	2
Gall bladder	1
Spinal fluid	1
2. *Actinomycetes*	*23*
Lungs	13
Nose and throat	2
Skin	6
Cervix	1
Gall bladder	1
3. *Aspergillus*	*29*
Lungs	10
Nose and throat	1
Stools	9
Skin	5
Ears	4
4. *Penicillium*	*11*
Lungs	5
Nose and throat	4
Stools	11
Ears	1
5. *Alternaria*	*13*
Lungs	2
Nose and throat	4
Stools	1
Skin	6
6. *Mucor*	*15*
Lungs	10
Nose and throat	1
Stools	1
Skin	2
Ears	1
7. *Geotrichum*	*11*
Lungs	1
Nose and throat	1
Stools	7
Skin	1
Eyelids	1
8. *Sporotrichum*	*3*
Skin	3
9. *Cephalosporium*	*4*
Lungs	2
Stools	1
Skin	1
10. Yeasts	*13*
Lungs	2
Nose and throat	2
Stools	2
Skin	6
Ears	1
11. *Trichophyton*	*4*
Skin	4

Conclusions.

The writers are not attempting to draw any conclusions from the data presented. We wish to point out the fact that when fungi are sought for, they can be found to occur in a great many and varied pathological conditions. The frequency with which they occur in our series of cases would stress the importance of further work to determine whether or not their presence is important in determining the etiology of various diseased conditions studied.

We would like to point out, particularly, the incidence of *Monilia, Actinomycetes* and *Aspergillus* in the cases studied.

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