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PNEUMOMYCOSES

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PNEUMOMYCOSES

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PNEUMOMYCOSES

[Following is a translation of an article Ye. Ryzhkov in Bol'shaya meditsinskaya entsiklopediya (Great Medical Encyclopedia), Vol. 25, 1962, pages 107-120.]

Pneumomycoses (from the Greek pneumon -- lungs, and mykes -- fungus) represent diseases of the lungs caused by fungi. The term "pneumomycosis" was introduced by R. Virchow (which see), who in 1856 described three cases of pneumonia caused by the mold fungus. The agents of the pneumomycoses may be different genera and species of the ray fungi of the class Actinomyces (*Actinomyces Israeli*, *Nocardia*, and others), yeast-like fungi of the genus *Candida* (*C. albicans*, *C. tropicalis*, *C. Krusei*, and others), of the genus *Geotrichum*, of the genus *Blastomyces* (*B. dermatitidis*), mold fungi of the genus *Aspergillus* (*A. fumigatus*, *A. flavus*, and others), of the genus *Penicillium* (*P. glaucum*, *P. crustosum*), of the genus *Mucor* (*M. mucedo*, *M. corimbiformis*, and others), yeast fungi *Cryptococcus neoformans* (a synonym of *Torula histolytica*), *Coccidioides immitis*, *Histoplasma capsulatum*, and others (see special color table, Figures 1-6).

The pneumomycoses have been studied by numerous Russian authors (K. F. Slavyanskiy, 1866; A. Tsioglinskiy, 1899; R. S. Klisich, 1899; V. Kolerov, 1928; M. A. Skvortsov, 1933; I. A. Kusevitskiy, 1934; S. I. Mikhnevich, 1939; R. V. Rubinshteyn, 1949; N. L. Popova, 1952, and others).

The pneumomycoses are divided into exogenous and endogenous. The exogenous pneumomycoses are caused by a fungi introduced into the human organism from the external environment -- the soil (*Coccidioides*, *Histoplasma*, *Blastomyces dermatitidis*), from the air (the mold fungi), especially under occupational conditions, especially in agriculture, milling, the tobacco industry, the fur industry, the silicate industry, etc. Endogenous pneumomycoses are caused by saprophytic fungi which are normal inhabitants of the mucous membranes of the mouth, upper segments of the respiratory tract and the intestine (*Candida*, *Geotrichum*, *Actinomyces*, *Cryptococcus*, *Aspergillus*), which under certain conditions which are favorable for their growth may acquire pathogenic properties and cause disease. Aspergillosis, penicilliosis, mucormycosis, and actinomycosis of the lungs may be of both exogenous and endogenous origin.

Distinction is made in the pneumomycoses between primary infections, which are for the most part exogenous, and which are caused by obligatory pathogens (*Coccidioides*, *Histoplasma*), and less frequently by facultative pathogenic fungi, and secondary pneumomycoses, which develop against a background of already existing disease -- pneumonia, tuberculosis, bronchiectasis, emphysema, pulmonary infarct, cancer, Hodgkin's disease, sarcoidosis, and others. Secondary pneumomycoses are caused, for the most part, by facultative pathogenic saprophytic fungi.

In the pathogenesis of the pneumomycoses, a role is played by severe, chronic, wasting diseases which lead to a loss of the protective and immune forces of the organism, various diseases of the respiratory tracts, diabetes, hypovitaminosis, and different forms of injury to the mucous membranes. In recent years in all countries of the world, there has been an increase in the incidence of endogenous pneumomycoses, which is associated with the wide use of antibiotics. Treatment with antibiotics, especially those with a wide spectrum of antibacterial action, especially when carried on over a long period of time and in large doses, despite the absence of a therapeutic effect, leads to disturbances in the physiologic equilibrium of the microflora of the organism (see the article *Dysbacteriosis*), due to the death of the microorganisms which are sensitive to the antibiotic; on such a background, there is a proliferation of the resistant microorganisms, including the fungi. Of critical importance also is a disturbance in the synthesis of vitamins of the B complex, and others, as well as a decrease in the protective forces of the organism.

The diagnosis of the pneumomycoses is not infrequently attended by considerable difficulties, since the clinical picture is scarcely distinguishable from ordinary pneumonia, pneumonia with abscesses, tuberculosis, and cancer of the lungs. Hence, in all cases of chronic, prolonged, or recurrent pneumonia accompanied by the coughing up of blood which do not yield to the ordinary methods of treatment, as well as in the presence of clinical and X-ray signs of tuberculosis of the lungs, but in the absence of the Koch bacillus in the sputum, it is necessary to keep the possibility of fungus diseases in mind. In connection with this, the diagnosis of the pneumomycoses must be a complex one, based on a comparison of the clinical picture, the course of the disease, and the results of laboratory studies. Most important are results of microscopic studies in native (processed with caustic soda), and also stained preparations of freshly obtained sputum following preliminary careful cleansing of the oral cavity (removal of coagula), as well as bronchial secretions obtained during bronchoscopy or of pleural exudate. Studies for fungi are made of urine, feces, blood, and in a number of cases, bile, biopsies of lymph nodes, sternal punctures, and so forth. However, the discovery in sputum of the mycelia and spores is, in itself, not always sufficient for the diagnosis of pneumomycoses,

especially if there is a question of facultative pathogenic fungi (Candida, Geotrichum, and the mold fungi); moreover, the findings of microscopic studies do not always permit a determination of the genus or the species of the fungus (thus, for example, the mycelial threads may be discovered in pneumomycoses which differ with respect to their etiology). In view of this, considerable importance attaches to the cultures of the fungi after seeding the sputum on nutrient media. But in this, it should be kept in mind that this method of diagnosis requires a longer time and that the growth of the cultures of such fungi as Candida, Aspergillus, Penicillium, and Mucor, may be obtained upon seeding the secretions from the oral cavity of healthy persons. In such cases, for the establishment of the diagnosis, only repeated culturing of numerous colonies of fungi in the majority of the cultured specimens is of importance, especially in the absence of other flora -- microbes. The obtaining of a culture of Coccidioides, Histoplasma, or a pure culture of Cryptococcus, plays a decisive role in the diagnosis of the corresponding pneumomycoses. Of great diagnostic importance is the obtaining of a culture of fungi from the blood of the patient. In diagnosing coccidioidomycosis and histoplasmosis of the lungs, particular importance attaches to the intracutaneous reaction with the fungus antigens, and in the diagnosis of Candida pneumonia, the serologic reaction is of importance. In view of all the difficulties in the differential diagnosis of the pneumomycoses in connection with the presence of common characteristics in the clinical and X-ray picture as well as in the course of the disease, a careful analysis of the peculiarities of the clinical course of the pulmonary process and the concomitant involvement of other internal organs, skin, and mucous membranes, along with the data of laboratory studies, permits, in many cases, not only a diagnosis of the fungous nature of pneumonias but also a determination of the character of the mycosis.

Actinomycosis of the lungs is one of the most frequent and serious of the pneumomycoses, is found in all countries of the world, and occurs in men three to four times more frequently than in women, especially in the age group between 20 and 50 years, but is also seen in children. The primary route of infection is endogenous, as the result of entry into the organism of the saprophytic actinomycetes, which live in the oral cavity. Exogenous infection with actinomycetes, which are saprophytic plants, is encountered rarely. Primary actinomycosis of the lungs, which develops by the aerogenous route as the result of aspiration of fungi from the mouth, is rare. Of considerably higher frequency is secondary actinomycosis of the lungs as the result of the spread of an actinomycotic process from the mediastinum, where the actinomycetes arrive from the oral cavity, the tonsils, the esophagus, or from the peritoneal cavity (through the diaphragm into the lower lobes of the lungs, or along the tissues of the neck) into the mediastinum, or, finally, by the hematogenous route. Actinomycosis of the lungs has

been studied in detail by many Russian scientists (S. A. Lebedev, 1889; N. N. Mari, 1908; A. A. Opokin, 1909; S. I. Spasokukotskiy, 1940; B. L. Osnovat, 1950; G. O. Suteyev, 1951, and others).

The pulmonary process is usually unilateral, and most frequently involves the lower lobes of the left or (even more frequently) the right lung. The clinical picture of actinomycosis of the lungs is diversified, and may resemble that of tuberculosis, chronic pneumonia with abscesses. Initially the process is mild, with a subfebrile temperature, a distressing dry cough with little sputum. Subsequently, the sputum becomes more abundant, and acquires a moldy smell; the production of sputum is accompanied by the coughing up of blood. Individual foci of infection become confluent, forming infiltrates, then abscesses and finally cavities. Upon infiltration of the process into the pleura, symptoms of pleuritis develop (serous, or purulent) with considerable pain. The following are characteristic of actinomycosis of the lungs: a tendency to spread of the process from the center to the periphery of the lung, into the pleura, and finally into the tissues of the thoracic cage -- the intercostal muscles, the ribs, the subcutaneous tissues, and eventually into the skin itself with the production of fistulas; intense pain in the region of the scapula, and the shoulder. In distinction from tuberculosis, there is more frequent involvement of the lower lobes of the lung, and elastic fibers are missing from the sputum. The diagnosis of actinomycosis of the lungs is not difficult when the process appears in the tissues of the thoracic cage; there is a very dense (often wooden) infiltration and swelling of the soft tissues with a bluish discoloration of the skin and the formation of fistulas which do not heal. The general condition of the patient rapidly deteriorates, and cachexia develops. With respect to the X-ray diagnosis, A. Ye. Prozorov (1950) believes that "in the presence of changes in the pulmonary tissues, which bear the traits of chronic inflammatory processes, especially when located in the hilar areas, and with simultaneous changes in the mediastinum and in the paramediastinal pleura, the diagnosis of actinomycosis must be considered." Of diagnostic significance also are pleural changes against a background of an interstitial process in the lung tissues, as well as decalcification of the ribs. Many authors note the darkness and intensity of the shadows and their sharp borders. The diagnosis of actinomycosis of the lungs must be confirmed in the following fashion: (a) the discovery of actinomycetes in the sputum (which is not always possible) or of fine branching threads of mycelia and the recovery of the fungus on culture, (b) a positive skin reaction to the injection of actinolytate. See also the article on Actinomycosis.

Candidomycosis of the lungs (synonyms include moniliasis, candidiasis of the lungs) was rarely seen prior to the introduction of antibiotics, but at the present time it is the most frequent of the pneumomycoses in all countries of the world. Primary candida pneumonia

arises for the most part in patients with any disease during the process of treatment with antibiotics, especially, for example, in the post-operative period in surgical patients, in patients with cancer, leukoses, as well as in elderly patients and in nursing infants. In patients with tuberculosis or with ordinary pneumonias, the pulmonary process is not infrequently complicated by secondary candidomycotic infection (A. M. Ariyevich, 1955; G. P. Kosman, 1957; P. L. Mikhlin, 1957, and others). In the early stages as well as in mild cases, candida pneumonia is characterized by scattered dry rales and a dry hacking cough with scant mucoid or jelly-like sputum, sometimes with a tinge of blood. Later, the sputum becomes mucopurulent, and sometimes has the odor of yeast, is foamy, and proteinaceous grayish-yellow clusters appear in it which contain large numbers of the fungi. The process ordinarily begins with involvement of the smaller bronchi and peribronchial infiltration of the lung tissues. Subsequently, X-rays may show small foci with irregular borders, with fusion of some of the foci, and a tendency to the production of diffuse, nonhomogeneous shadows with processes extending in the direction of the hilus of the lung. The involvement may be reminiscent of catarrhal bronchopneumonia, or of tuberculosis. In severe and prolonged cases, there is a degeneration of the infiltrate with the production of cavities (A. M. Ariyevich, 1956; V. N. Shtern, 1957; W. Weiss, 1956, and others). The process is usually localized in the lower and middle lobes. There is often a lack of correspondence between the physical symptoms and the X-ray picture of this pneumomycosis: abundant moist rales in the absence of significant changes in the X-ray, or merely an increase in the bronchovascular markings, or, on the contrary, marked changes in the X-ray picture -- the presence of large foci of darkening, the appearance of atelectasis, and even abscess formation -- in the presence of negligible physical changes. A characteristic feature is the comparatively rapid change in the X-ray picture: the appearance or disappearance of foci of darkening over the course of a relatively short period of time. In severe cases, there is a variable temperature, heavy perspiration, chills and fever, weakness, inertia, pallor, and not infrequently an expiratory dyspnea. Candida pneumonia is accompanied, as a rule, by a high ESR (40-60 mm per hour), often by a marked lymphopenia in the presence of a normal or slightly elevated number of leukocytes. Recurrences are seen in a number of cases following clinical recovery. Of importance in the diagnosis of candida pneumonia are: deterioration in the pulmonary process under the influence of antibiotic therapy, and the appearance of thrush in the oral cavity. In the sputum (and not infrequently in the urine), microscopic study reveals accumulations of budding yeast cells and mycelial threads; numerous colonies of candida grow out in culture. Immune reactions with the yeast antigens are usually strongly positive; the agglutination reaction reaches titers of 1:160, 1:320, or higher. With improvements in the condition of the patient, the agglutination titer diminishes. See also the article entitled Candidomycosis.

Aspergillosis of the lung is seen in all countries of the world and may be either exogenous or endogenous. Primary exogenous aspergillosis of the lungs is seen primarily as an occupational disease in persons occupied in working with the soil, or who have contact with moldy fruit, grain, grasses, in persons who inhale dust which contains the spores of the fungus in abundance (workers in the silicate industry, workers in the hair, hide, fur, hemp industries, and so forth). In secondary aspergillosis of the lungs, the effects of the mold fungus are "superimposed" on an already existing pathologic process in the lungs (emphysema, bronchiectasis, tuberculosis, cancer, abscess, pulmonary infarct, sarcoidosis, and so forth) and considerably aggravates the course of the underlying disease. In recent years, aspergillosis of the lungs has been described as a complication in treatment with antibiotics. This pneumomycosis has been studied and described by many Russian authors (Ye. I. Martsinovskiy, 1928; R. N. Vol'fovskaya and Ye. A. Vigdorshik, 1939; A. M. Vakhurkina, 1946; T. A. Nikitina, 1955; Ye. V. Ryzhkov, 1956, and others). A distinction is made between the acute bronchopulmonary form and the chronic form of aspergillosis of the lungs. The first involves a high temperature, chills, cough productive of a purulent and often bloody sputum, hemoptysis, crepitant rales usually in the lower lobes of the lungs, and increasing dyspnea in the presence of a serious general condition of the patient. X-rays show foci of infiltration, which rapidly degenerate with the formation of cavities, sometimes with an exudate (odorless), an increase in the hilar lymph nodes. The chronic form of aspergillosis is highly reminiscent of tuberculosis of the lungs, pneumonia with abscess formation (pseudotuberculous aspergillosis) with occasional benign hemorrhages. The X-ray picture is also similar to that of tuberculosis of the lungs. A unique form of aspergillosis of the lungs has been described -- aspergilloma (aspergillous mycetoma) in the form of a round spherical loose-textured dark gray lesion, consisting of a mass of fungi and developing in the walls of the pre-existing cavity of a distended bronchus. In this, the X-rays show, usually in the upper lobes of the lungs, a rounded faint shadow with sharp borders. The mold fungus increases in amount in the form of a grayish coagulum on the walls of the cavities (cavities, abscesses, or distended bronchi); they fill up such a cavity and produce injury to the wall of it with the formation of granulomatous tissue. With maturation in the bronchiectatic cavities of colonies of fungi, the patient experiences periodic attacks of cough, which terminate in the coughing up of a grayish-yellow mass which, under the microscope, appears to consist of a mass of mycelial threads and spores. The prolonged and repeated inhalation of large numbers of the spores of aspergillus may lead, in connection with its sensitizing properties, to the development of a clinical picture of bronchial asthma with a prolonged and intractable course and a high eosinophilia in the blood. For the diagnosis of aspergillosis of the

lungs, importance attaches to the discovery in the sputum of the above-mentioned masses, which represent colonies of aspergillus, and also the repeated detection in fresh sputum of mycelial threads, and especially the characteristic organs of fructification of the fungus (see the article Aspergillosis). The production of cultures of aspergillus upon seeding sputum is of importance in the diagnosis only under conditions in which there is a growth of numerous colonies of a pure culture in the majority of the test tubes seeded.

Penicilliosis and mucormycosis of the lungs, with respect to their clinical and X-ray pictures as well as their course, do not differ from aspergillosis of the lungs, and the etiologic nature of these pneumomycoses can be established only on the basis of recovering corresponding cultures of the appropriate fungi. Both of these pneumomycoses are encountered with extreme rarity and almost exclusively as a secondary phenomena (see the article Mold Mycoses).

Cryptococcosis of the lungs (synonyms: torulosis, European deep blastomycosis, and Busse-Bushke disease) is among the rare pneumomycoses, but nonetheless is encountered in all countries of the world, apparently more frequently than has hitherto been thought. In the USSR, it has been described by A. F. Bilibiniy (1946), N. V. Konovalov (1948), and others. Cohen and Kaufmann (1952) collected and described in the United States 222 cases of this pneumomycosis. It is more common in men in the age group between 40 and 60 years. An endogenous route of infection via the respiratory tract is highly probable; however, cryptococcus is also discovered in the soil, in connection with which an exogenous route of infection cannot be excluded. At the onset of the disease, there is a slight elevation of temperature, a cough with tenacious sputum, sometimes admixed with blood, and negligible physical symptoms. Later, there are foci of intense darkening with sharp borders in different areas of the lungs, as shown by X-ray, which recall the picture of severe tuberculosis, neoplasm, or lung abscess. Sometimes a picture is seen which suggests candidomycosis of the lungs. The mediastinum in cryptococcosis, in distinction from actinomycosis and coccidioidomycosis, is rarely involved, and cavities are formed only in isolated cases. Isolated cryptococcosis of the lungs is rarely encountered, and usually develops secondarily in patients with cryptococcus meningitis, which affords evidence of a hematogenous dissemination of the fungus. The recovery from the sputum of the characteristic round or ovoid budding (with a single bud) cells, surrounded by a gelatinous capsule, is rarely possible; they attract attention only when they are detected in the spinal fluid.

Seeding of the sputum results in the cultivation of yeast colonies which consist only of budding cells.

Coccidioidomycosis of the lungs is endemic in the steppe regions of Latin America and in the southern states of the United States, but is also seen in England, Italy, the Netherlands, and other European

countries. In the USSR, the first cases of this mycosis were recognized in a Kuznets basin by A. N. Araviyskiy (1951), L. I. Shostak (1957), and subsequently in some other areas of the country. Infection of the lungs occurs by the exogenous route upon inhalation of dust contaminated with the spores of the fungus *Coccidioides immitis*, and is seen primarily in agriculturalists, fruit gatherers, miners, and other persons who are in some connection with soil in which this fungus is a saprophyte. The symptoms of primary coccidioidomycosis of the lungs follow after a 2-3 week incubation period; frequently the disease is acute, similar in its clinical picture to influenza, bronchitis, sometimes bronchopneumonia, with slight elevation of temperature, cough with the production of a small amount of mucoid sputum, and not infrequently allergic rash of the type of erythema nodosum over the lower legs. In other cases, coccidioidomycosis of the lungs presents as foci of a pneumonic type accompanied by a high temperature, chills, perspiration, headache, loss of appetite, purulent sputum with an admixture of blood, occasional symptoms of pleuritis with severe pain in the chest; in such a case, physical findings are often negligible. X-rays in cases of moderate severity show small bronchopulmonary infiltrates, which are situated around and radiate out from the hilar region toward the middle and lower lobes of the lungs, and very slowly resolve. Typical are isolated, rarely multiple, foci with a diameter of 2-3 centimeters in the lower or middle lobes of the lungs, which are similar in their X-ray appearance to tuberculosis. After several months, these foci undergo resolution completely or they are converted into a cyst-like cavity with thin walls, which may later either disappear or undergo contraction and be converted into a fibrous, calcified focus; larger cavities may last for years -- in this, the general condition of the patients remains satisfactory. However, if the primary pulmonary focus does not resolve within a month and a half, then it should be kept in mind that the mycosis may have undergone transition to a progressive form with a severe course, high temperature, various lesions of the internal organs, bones, joints, ulcers of the skin, and fistulous tracts.

For the diagnosis of this pneumomycosis, decisive significance inheres in the discovery in the sputum (best in unstained preparations) of the characteristic spherules -- the sporangia of the fungus in the form of thick-walled, double-contoured, round cells which are filled with numerous endospores (see Vol. 8, "Parasitic Fungi," pages 220-221, and the colored table, Figure 8), which may be mixed with "dust cells" or with epithelium which has undergone fatty change. The circulating blood shows a leukocytosis (10,000-12,000), a shift to the left, an eosinophilia, and, in cases of the progressive form of this pneumomycosis, a high ESR. Of great importance in the diagnosis of this pneumomycosis is the skin reaction with coccidioidomycin in a dilution of 1:100 (0.1 ml): a positive reaction takes the form of erythema or an infiltrate of the area with a diameter of 0.5 cm.

Histoplasmosis of the lungs is a common disease in the United States, Africa, the Philippines, and Java; isolated cases have been seen in England, France, and Rumania. This disease has not been described in the USSR. Histoplasmosis affects people of all ages, but most frequently children. In this, the X-rays of the lungs show either individual well-circumscribed foci surrounded by smaller foci, or else multiple foci of approximately the same size. In the center of these foci, there is often degeneration with cavity formation. As the result of hemotogenous spread of the fungus, multiple small foci develop, often with involvement of the pleura. In this disease, the reticuloendothelial system is primarily affected. The characteristic symptoms of histoplasmosis are as follows: a progressive anemia, leukopenia, neutropenia, and a relative or absolute lymphocytosis, especially in children; not infrequently there is an enlargement of the liver and spleen, an enlargement of the lymph nodes, which, along with the lymphocytosis, may lead to the erroneous diagnosis of leukemia. In this disease, there are often ulcers of the skin and mucous membranes of the mouth, pharynx, and nose. Microscopic studies of the sputum, as well as biopsies of the bone marrow, or lymph nodes stained with Gram's stain, or Ziehl-Neelsen, or Giemsa stain, show the elements of the fungus in the form of small, round, budding, yeast cells within the cytoplasm of macrophages; less frequently, they are found lying free. In view of the difficulty of detecting the fungus in the sputum, culture studies are of importance (see the article Parasitic Fungi). Of diagnostic importance also is the skin test with histoplasmin. The prognosis in histoplasmosis of the lungs has hitherto been considered unfavorable, but in recent years cases have been described of recovery with the development of fibrosis and calcification of the foci of the disease in the lungs. See also the article Histoplasmosis.

Geotrichosis of the lungs, with respect to its clinical picture, course, and pathogenesis, is almost indistinguishable from candidomycosis of the lungs and is found rather more frequently than has hitherto been thought. The diagnosis of this disease may be established only on the basis of the recovery from the sputum of the characteristic rectangular or oval elements of the fungus, as seen under the microscope, and cultures of the fungus (see Vol. 8, the article Parasitic Fungi, and the colored table, Figure 13).

Sporotrichosis of the lungs is encountered quite rarely in all countries, especially in the tropics. The fungus *Sporotrichum* causes, as a rule, deep lesions of the skin and subcutaneous tissues. Systemic and visceral forms of this mycosis, with a severe course, frequently terminate in the death of the patient. In the USSR, visceral sporotrichosis with lesions of the lungs has been described by S. G. Gaykuni (1929), T. A. Melikovaya (1935). Infection occurs by the exogenous route. In the diagnosis of this disease, cultures of the fungus must be obtained by seeding pathological material and white rats must be

injected with the material with the production of the disease (see the article Sporotrichosis).

Blastomycosis of the lungs (synonyms: North American blastomycosis, Gilchrist's disease) is rarely seen, since the fungus *Blastomyces dermatitidis* is the agent primarily of deep skin lesions. In the United States and other countries with a tropical climate, generalized systemic forms of this mycosis are seen with lesions in the lungs. The clinical picture and course of this disease are in no way characteristic. X-rays show enlargement of the mediastinal lymph nodes, dense shadows near the hilus of the lungs, forming rays in the lung fields; the picture may simulate bronchogenic carcinoma of the lungs. See also the article Blastomycosis.

The differential diagnosis of the pneumomycoses presents great difficulties, and the diagnosis can be established only by means of laboratory studies, skin tests, and serologic reactions. At the same time, account must be taken of the peculiarities of the clinical picture and the course of each pneumomycosis, the presence of skin lesions, lesions of the mucous membranes, lesions of other internal organs, changes in the blood, and so forth.

The treatment of the pneumomycoses must be a combined treatment, with account being taken of etiologic and pathogenetic factors. The treatment of actinomycosis of the lungs consists in the combined use of penicillin or streptomycin, terramycin, sulfanilimide preparations, and injections of actinolysate; the use of phtivazid has also been recommended. Surgical procedures against the disease are contraindicated. For the treatment of candidomycosis of the lungs, the best approach is nystatin (Mycostatin) in doses of 500,000 units six to eight times a day in repeated courses of 10-14 days each. For the treatment of pneumomycosis due to mold fungus, there is no reliable method of treatment; reports exist in the literature concerning the favorable effect of the antibiotic trichomycin, as well as nystatin; iodide therapy should also be tried, especially in the form of intravenous infusions of 10% sodium iodide (see the article Aspergillosis). In recent years, successful results have been obtained also in the treatment of such severe, supposedly incurable, pneumomycoses as cryptococcosis, blastomycosis, coccidioidomycosis, and histoplasmosis of the lungs, using the antibiotic amphotericin B. In the treatment of blastomycosis of the lungs, good effects have been achieved with a preparation of dihydrostilbamidine; use can also be made of sulfanilimide preparations, and diethylstilbestrol. Sulfanilimide preparations may also be tried in treatment of coccidioidomycosis and histoplasmosis in doses of 4-6 gm per day. Vitamin therapy is also important in treatment of the pneumomycoses, especially vitamins of the B complex. Sulfanilimide therapy and vitamin therapy are carried out in the form of repeated courses. Of importance also are blood transfusions, and injections of gamma globulin. In all pneumomycoses, use should be made

of inhalations with gentian violet or brilliant green (0.1%). Although nystatin is considered specific for the treatment of candidomycosis and geotrichosis, it may also be tried in the treatment of all other pneumomycoses in the form of repeated courses at intervals of 5-7 days.

The pathologic anatomy of the pneumomycoses. In primary pneumomycoses, that is, those which arise in previously unchanged lung tissue, the initial fixation of the fungus occurs, as in the case of other aerogenous infections, in the smaller bronchial radicals (bronchioles); it causes there, initially, catarrhal changes, later leading to necrosis of portions of the bronchial wall. For a long time the process is superficial, and the fungus proliferates rapidly in the lumen of the bronchus, without going beyond the limits of the bronchus, and often forming here, due to the abundant supply of fresh air and oxygen, numerous organs of fructification, which impart to the mass of the fungus a color which is characteristic for each species of fungus (greenish, yellowish-brown, grayish-black, and so forth). From here the infection spreads, on the one hand, by the bronchogenic route, and on the other hand, through the wall of the bronchus into the peribronchial tissues. The latter occurs by means of penetration of the mycelial threads of the fungus through the necrotizing wall of the bronchus into the surrounding alveolar parenchyma, and also, due to the spread of the mycelia along the mucous membrane, they spread into the alveoli by this route.

It is characteristic of the pneumomycoses to produce pneumonic foci (which also are discolored greenish-yellow, brownish-yellow, or grayish-black), some of which are quite dense, others of which show central softening or even the formation of cavities. Microscopic studies demonstrate the presence in such a focus of central necrosis, in which it is not only impossible to distinguish any tissue structures, but also it is often impossible to find the fungus itself (even elastic tissue is preserved, as a rule, only in the form of fragments). Immediately surrounding this necrotic center, the structure of the tissues can still be distinguished, and the changes are primarily necrobiotic; here one can always find abundant masses of mycelia, which are bounded at the periphery by heavy accumulations of leukocytes or (in less rapidly progressive cases) with granulation tissue, which consists primarily of epithelioid elements, often with giant cells. Beyond this band of demarcation there is an area of perifocal pneumonia with a zone of edema surrounding it. The central necrotic focus very frequently undergoes degeneration, being converted into liquid pus; with removal of the pus, a cavity remains which may gradually enlarge as the result of advancement of the process or of fusion of several individual foci.

The mycelial threads occasionally penetrate through the band of demarcation and appear in the pneumonic zone, in which not infrequently there is necrosis of the walls of blood vessels and penetration of them by the fungus, with subsequent thrombosis or disruption of the vessels and hemorrhage. If the process shows a tendency to confinement, then

about the periphery of granulation, a process of scarring may begin, which isolates the focus from the surrounding tissues.

In the secondary pneumomycoses, in which the fungus infects an earlier produced cavity (cavities, bronchiectasis, and so forth), it tends to line the walls of the cavity with mycelia in masses which show their respective coloration. These mycelial masses may grow, enlarging the cavity and causing destruction of the organ or (what occurs more frequently) they may grow primarily in the cavity without involving the surrounding lung tissue. However, in the latter case, hemorrhage is possible as a result of destruction by the fungi of the blood vessels. Whatever might be the origin of the cavity containing the fungus, that is, whether it arose under its influence or whether the fungus grew secondarily in it, an essential sign distinguishing it from the usual gangrenous or bronchiectatic cavity, is the absence of a distinctive odor to the contents, even though these may be present in large amounts in the cavity. The same applies to the sputum which is coughed up by these patients.

In the hematogenous mycoses produced experimentally in animals by the intravenous injection of pure cultures of fungus, tumors are produced in various organs, including the lungs, which are very similar to the tubercles of tuberculosis; they consist of leukocytes and epithelioid cells (sometimes with giant cells) with numerous threads of the fungus in the center. Subsequently, some of these lesions undergo scarring, others become necrotic, soften, and are converted into small cavities, thereby repeating the cycle of growth mentioned earlier. In man, the process may continue for a period of many years, causing the production of granulation nodules, bronchiectasis, cavities, scarring, and so forth, and being very similar in its course and physical symptoms to pulmonary tuberculosis. Death occurs for the most part from the basic disease, which provides the soil for the development of fungus infection (sugar diabetes, tuberculosis, cancer, and so forth). In cases of so-called primary pneumomycosis, the disease very frequently ends in recovery, and only rarely causes death from hemorrhage or marasmus.

Recently, reports have appeared on the outcome of pneumomycosis in fungus sepsis in patients treated with antibiotics. Such complications have been described in children, but they are also to be seen in adults (Ye. V. Ryzhkov).

Cases of pneumomycosis caused by fungi of the genus *Oidium* have rarely been described, and in all cases there has been a secondary fungus infection of the lungs in very debilitated patients, usually children (pneumonia in sugar diabetes, purulent bronchitis, and so forth), in which there has been an accumulation of the fungus on the mucous membrane of the mouth and pharynx (thrush). In the lungs, these fungi have sometimes been found only in the bronchi, but in some cases have penetrated into the lung tissue, where either pneumonic foci with

mycelial threads in the exudate have been found or cavities of a gangrenous type have been seen but without the unpleasant odor and with abundant accumulations of the fungus in the contents. In the literature there is evidence of a marked increase in the number of pneumomycoses caused by candida, which is also related to treatment with antibiotics. In diseases caused by the blastomycetes, a primary aerogenous fungus infection of the lungs has never been described. Only individual cases of blastomycosis of the lungs of metastatic origin, in conjunction with lesions of the skin, have been described. The changes which can be detected in this differ very little from the picture of other fungus lesions of the lungs and are attributable to the appearance in the lung tissue of dense nodules with necrotic centers or of cavities filled with a semiliquid purulent mass. Foci of either type contain large numbers of the yeast cells and are surrounded by a zone of inflammatory infiltrate. In certain forms of experimental blastomycosis in animals, numerous giant cells have been found in the zone of infiltration.

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Summary

The article describes the various forms of pneumomycoses and the clinical course, physical findings, X-ray picture, and outcome to be expected in each. The cultural characteristics of the respective fungi are also described. Distinction is made between primary pneumomycoses and secondary pneumomycoses, and in connection with the latter, a brief discussion is given of the underlying conditions predisposing to them. The article deals for the most part only with the pulmonary lesions of these respective mycoses and reference is made to other articles for a fuller treatment of the clinical conditions as a whole. A brief discussion is given of the microscopic findings in the lesions of the various pneumomycoses and a few remarks are made on the differential diagnosis and treatment of these diseases.

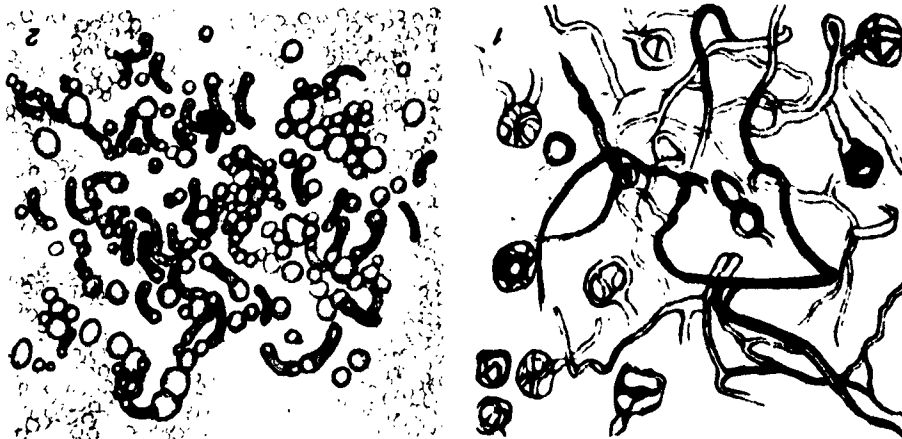


Figure 1. Mycelial threads of the fungus *Micor* in the sputum (native preparation). Figure 2. Mycelial threads of the fungus *Aspergillus* in the sputum.

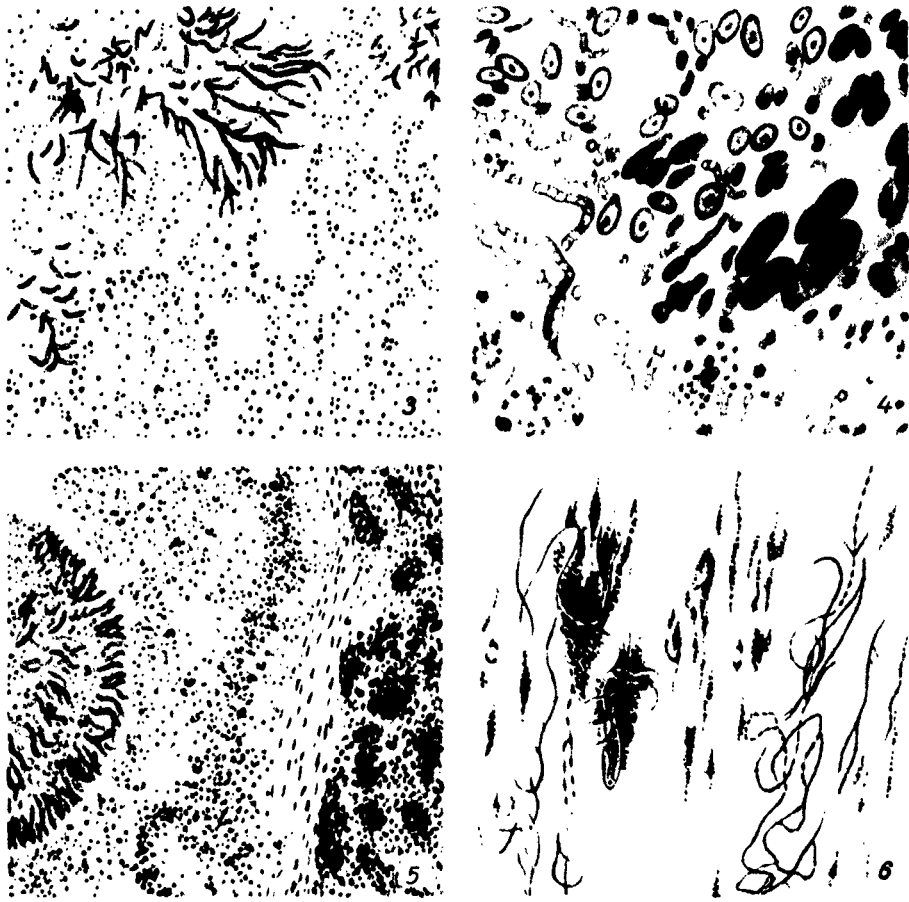


Figure 3. Aspergillous pneumonia. Figure 4. Mycotic granuloma in the lung. Figure 5. Mycelial threads of the fungus *Aspergillus* in the lumen of a cavity. Figure 6. Mycelial threads of the fungus *Scrofungaria* in the sputum.

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