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History of Medical Mycology

File 2 (1895-1950)

1895

Giuseppe Marconi (1862-1940), born in Naples, Italy, Professor of Veterinary Pathology and Clinic in the Royal University of Pisa, Italy, isolated and cultivated for the first time *Cryptococcus farciminosum*, the agent of epizootic lymphangitis, in the form of sterile mycelium (1895). Piero Redaelli and Raffaele Ciferri transferred (1934) *C. farciminosum* to the genus *Histoplasma*, as *H. farciminosum* (Rivolta and Micellone 1883, Redaelli and Ciferri 1934), mainly because of its dimorphic nature that made it similar to the tissue form of *H. capsulatum* var. *capsulatum* Darling 1906. Robert J. Weeks, Arvind A. Padhye and Libero Ajello, at the Division of Mycotic Diseases, Center for Infectious Diseases, Centers for Disease Control (C.D.C.) Atlanta, Georgia, U.S.A. (1985), observed that this fungus generated macro- and microconidia resembling those of the *capsulatum* and *duboisii* varieties of *H. capsulatum* when incubated at room temperature, thus reducing the fungus to a varietal status as *H. capsulatum* var. *farciminosum* (Rivolta, 1873) Weeks, Padhye & Ajello, 1985. Raffaele Ciferri (1960) reduced *Histoplasma duboisii* (Vanbreuseghem, 1992) to varietal status as *H. capsulatum* var. *duboisii* (Vanbreuseghem, 1992), Ciferri, 1960 [Ajello, 1998; Marcone, 1895; Redaelli and Ciferri, 1934; Weeks et al., 1985].

1896

The American surgeon Emmet Rixford (1865-1938), born in Bedford, Canada, first graduated in engineering and then Doctor in Medicine (1891), and Thomas C. Gilchrist described, at San Francisco's Cooper Medical College, California, U.S.A. (which became Stanford University Medical School in 1908), two fatal cases of fungal infections, "clearly distinct from the doubtfoul, so-called blastomycosis", proven to be related to coccidioidomycosis, a disease described by Roberto Alejandro Posadas and Roberto Joahan Wernicke in Buenos Aires, Argentina (1892). The patients were two men, natives of Portugal, who had lived in the San Joaquin Valley in California, presenting "horribly destructive" cutaneous lesions. They observed the shape of the causative agent in tissues considering it a protozoan and attempted many cultures which were discarded because they were erroneously assumed as contaminated by filamentous fungi. They named the disease protozoan or coccidioidal pseudo-tuberculosis and defined the organism from the first case as *Coccidioides immitis* (Rixford & Gilchrist 1896) and that from the second case as *Coccidioides pyogenes*. They were not sure of the same identity of the two fungi as they had been isolated from patients one with a chronic and the other with an acute disease [Espinel-Ingroff, 1996; Posadas, 1892; Rixford and Gilchrist, 1896; Wernicke, 1892].

The pathologist and dermatologist Benjamin Robinson Schenck (1973-1920), born in Syracuse, New York, U.S.A., as a medical student at the Surgical Clinic of the Johns Hopkins Hospital in Baltimore, Maryland, U.S.A., isolated for the first time, from a 36-year-old male patient with an infection originating from the index finger of the right arm and developing up the radial side along the lymphatic system, "an organism not resembling bacteria" that could reproduce the experimental infection in a dog and mice (1896). The plant pathologist Erwin Fink Smith (1854-1927), born in Gilber Mills, New York, U.S.A., of the Department of Plant Pathology, North Carolina State University, Raleigh, North Carolina, U.S.A., accurately

described the filamentous form of the fungus, then defined *Sporothrix schenckii* (1900) by Ludvig Hektoen (1863-1951), born in Vernon County, Wisconsin, U.S.A., Professor and Head of the Department of Pathology at the University of Chicago, Illinois, U.S.A., and Charles F. Perkins (1866-1935), and placed the organism in the genus *Sporotrichum*, not being able to identify it correctly to a species level on the basis of the scarce descriptions made by Pier Andrea Saccardo of about one hundred species of *Sporotrichum* [Espinel-Ingroff, 1996; Hektoen and Perkins, 1900; Schenck, 1898].

Description of:

Trichophyton mentagrophytes (Robin) Blanchard, 1896

1898

James H. Wright, reported the first clinical case of mycetoma (Madura foot), at the Massachusetts General Hospital, Boston, Massachusetts, U.S.A. (1898). Wright visited a patient, an Italian woman of 26 years, for the evaluation of a mycetoma probably originated from six months. The foot, which had to be amputee, had fistulas containing granules hard, dark, and irregularly shaped that, microscopically, in KOH, turned out to be composed of septate hyphae. The cultivation of grains permitted the development of "tuft of delicate, withish filaments" characterized by the lack of conidia. In culture (potato dextrose agar) the organism, developing dark brown and moist colonies over time, was regarded to be a "hyphomycete" [Espinel-Ingroff, 1996; Wright, 1898].

1900

The Japanese Keizo Dohi (1866-1931), Professor in Dermatology at the University of Tokyo, Japan, founded the Japanese Dermatological Association (1900), and fungal diseases became a relevant topic of interest with particular concern on oral trush, which oftenly took the form

of epidemics. Masao Ota (1885-1945), born in Ito, Shizuoka, Japan, from the Dermatologic Clinic of the University of Tokyo, a disciple of Keizo Dohi, trained in France by Raymond A. Sabouraud and credited as the "founder of Medical Mycology in Japan", published, together with Maurice Langeron, "Nouvelle classification des dermatophytes" (New classification of dermatophytes) (1923) [Homei, 2008; Ota and Langeron, 1923].

The pathologist William Ophüls (1871-1933), born in Brooklyn, New York, U.S.A., Professor of Pathology and Bacteriology at the University of Missouri, Columbia, Missouri, U.S.A., and the American clinician Herbert Charles Moffitt (1867-1950), born in San Francisco, California, U.S.A., Professor of Medicine at the University of California School of Medicine, San Francisco, were the first to describe the phenomenon of dimorphism in fungi (1900). Ophüls and Moffitt observed what was likely considered to be a protozoan in the autopsy specimen (lung) of a farmer admitted to the City and Country Hospital in San Francisco, showing signs of a systemic infection that was reproducible in experimental animals by intravenous inoculation of a mold grown in culture. They stated that the protozoan-like and the fungal form were different phases in the developmental stage of the same organism and proposed the name of *Oidium coccidioides* (Hektoen & Perkins, 1900) [Espinel-Ingroff, 1996].

1901

Description of:

Cryptococcus neoformans (Sanfelice) Vuillemin, 1901/*Filobasidiella neoformans* Kwon-Chung, 1975

1902

After the isolation of *Cryptococcus neoformans* from peach juice and bovine, Francesco Sanfelice consecrated most of his work to his belief that tumors were caused by "*Saccharomycetes*". This idea was supported by the appearance that the inoculation of yeasts, including *C. neoformans*, in various animals produced lesions interpretable as cancers. Joseph D. Weis (1872-1951), of the Harvard Medical School, Boston, Massachusetts, U.S.A., refuted, among others, this hypothesis through controlled experiments. (1902). Weis worked with two *C. neoformans* strains received personally by Sanfelice, one isolated from a human case of adenocarcinoma of the ovary and the other, historically more important, the "first isolated from the surface of ripe peaches and afterwards inoculated into animals with positive results". This finding was corroborated by further isolation of *C. neoformans* from peaches imported from Italy by Friedrich Staib (1972) [Ajello, 1998; Sanfelice, 1895c; Staib et al., 1972; Weis, 1902].

The American surgeon James W. Walker and the American dermatologist Frank. H. Montgomery were the first, at the Rush Medical Center in Chicago, Illinois, U.S.A., to demonstrate the possibility of a disseminated infection in a case of human blastomycosis (1902). Walker and Montgomery initially assumed that the cause of the death of their patient was miliary tuberculosis, but *Mycobacterium tuberculosis* proved to be just a second infectious agent [Espinel-Ingroff, 1996; Walker, 1902].

Description of:

Microsporum canis (Bodin) Bodin, 1902/*Arthroderma otae* (Hasegawa & Usui) McGinnis, Weitzman, A.A. Padhye & Ajello, 1986

Trichophyton verrucosum Bodin, 1902

Trichophyton violaceum Sabouraud, 1902

1903

The Dutch Friedrich August Ferdinand Christian Went (1863-1935), Professor of Botany and Director of the Botanical Garden at the University of Utrecht, The Netherlands, was the person who brought onto the agenda of international scientific organizations the necessity of an international depository for fungal cultures. This matter was discussed during a meeting of the Board of the previous Association Internationale des Botanistes (International Association of Botanists) in Leiden, The Netherlands (1901). The name Centraalbureau voor Schimmelcultures (Central Bureau of Fungal Cultures) (C.B.S.) was created shortly thereafter that Went donated his own official fungus collection created in Utrecht (1904). The first List of Cultures was published (1907) documenting 78 strains including the type of *Rhizopus oryzae*, described (1895) by Went himself together with the Dutch microbiologist and chemist Hendrik Conraad Prinsen Geerligs, born on 1864, Director of the Sugar Experiment Station in Java, Indonesia, which is still viable and available after more than 100 years [Samson et al., 2004].

1905

Description of:

Madurella mycetomatis (Laveran) Brumpt, 1905

1906

The pathologist Samuel Taylor Darling (1872-1925), born in Harrison, New Jersey, U.S.A., one of the world's leading experts in tropical diseases in the early twentieth century, working in the Panama Canal Zone, studying autopsy smears of the lungs of a patient from Martinique who died of suspected miliary tuberculosis, observed tiny unicellular organisms in large numbers, from round to oval in shape, often included in alveolar epithelial cells (1906). Darling wrongly regarded the clear refractive nonstaining rim as a capsule, assimilated the

organism to *Leishmania donovani*, and gave the name *Histoplasma capsulatum* (Darling 1906) (*Ajellomyces capsulatus*, Kwon-Chung, McGinnis & Katz, 1979).

It was the physician, pathologist and infectivologist Henrique da Rocha-Lima (1879-1956), born in Rio de Janeiro, Brazil, one of the founders of the Paulista School of Medicine and of the University of São Paulo, Brazil, to characterize *H. capsulatum* as a fungus (1913) [Darling, 1906; Espinel-Ingroff, 1996; Rocha-Lima, 1913].

1907

The German chemist and zymologist Eduard Buchner (1860-1917), born in Munich, Professor of General Chemistry at the College of Agriculture, Berlin, Germany, and Director of the Institute for the Fermentation Industry in Berlin (1898), Professor at the University of Breslau, Germany (1907-1909), and then at the University of Würzburg, Germany (1911), received the Nobel Prize for Chemistry (1907) in recognition of his achievement that, in the fermentation process, the splitting up of sugar into CO_2 and alcohol is no more the effect of a "vital principle" than the splitting up of cane sugar by invertase. Through the discovery of Buchner, Biology was relieved of another fragment of mysticism [Loeb, 1906].

1908

The Brazilian physician Adolfo Lutz (1855-1940), born in Rio de Janeiro from a family of Swiss origin, studied Medicine in Switzerland, graduating at the University of Bern (1879). After graduation, he went to study experimental medicine techniques in London, U.K., where he studied with Joseph Lister (1827-1912), Leipzig, Germany, Vienna, Austria, Prague, Czech Republic, and Paris, France, where he studied with Louis Pasteur. Lutz, who had also worked at the laboratory of Roberto Joahan Wernicke in Buenos Aires, Argentina, described lesions in the oropharynx due to a multiple budding organism that grew as a mold at room

temperature, highlighting its dimorphic nature but without a designation (1908). Studying the organism, Alfonso Splendore (1871-1953), a mycologist born in Fagnano Castello, in the province of Cosenza, Calabria, Italy, active of São Paulo, Brazil, thought of an ascomycetous yeast, giving the name *Zymonema brasiliense* (1912). The disease was erroneously diagnosed as blastomycosis or coccidioidomycosis until the Brazilian physician Floriano Paulo de Almeida (1898-1977), Professor of Medical Mycology at the Medical Faculty of the University of São Paulo, Brazil, definitively identified the mycosis (1928) whose causative agent was named afterwards *Paracoccidioides brasiliensis* (1930). Paracoccidioidomycosis has emerged as the most important systemic mycosis nowadays reported in Latin America and was called also South American blastomycosis as well as, in their honor, Lutz-Splendore-de-Almeida disease [de Almeida, 1928; Lutz, 1908; San-Blas, 2000; San-Blas and San-Blas, 1997; Splendore, 1912; Wanke and Londero, 1998].

1909

The anatomist and histologist Giulio Tarozzi (1868-1948) born in Turin, Italy, Emeritus of Pathology at the University of Bologna, Italy, and Benedectine Academic of the Institute of the Academy of Sciences, Bologna, while he still was at the Royal University of Cagliari, Italy, described a case of slowly developing mycetoma, lasted for 27 years in the right leg of a 40 years old man who had procured a knife wound at the age of 13 (1909). Tarozzi not only reported the clinical and histological features of the disease, but isolated the etiologic agent in pure culture. In the tissues of the patient's leg and pus draining fistulas, the organism appeared in the form of soft, yellowish granules. From the clinical material seeded in different liquid and solid culture media it produced non acid fast, broad septate mycelium bearing abundant conidia measuring 4-5 µ in diameter. Despite the evidence of mycelial structure, Tarozzi, based on the microbiological belief then in force, not discriminating

between actinomycetes and fungi, considered his isolate as an actinomycete, giving the name *Actinomyces albus.* This error was perpetuated by the mycologist Carrol William Dodge (1895-1988) born in Danby, Vermont, U.S.A., of the Missouri Botanical Garden, St. Louis, Missouri, U.S.A., who proposed the new combination *Actinomyces tarozzi*, reducing *A. albus* to the synonymous state (1935) [Ajello, 1998; Dodge, 1935; Tarozzi, 1909].

1910

The dermatologist Raymond Jacques Adrien Sabouraud (1864-1938), born in Nantes, France, from the Hospital Saint-Louis in Paris, France, published the treatise "Les teignes" (The dermatophytoses) in which he deepened the study of dermatophyte infections (1910). He also developed a cultural method to select fungi with a medium characterized by a low pH and a rather high concentration of sugar. This mycological "universal" medium, has been called "Sabouraud" after him. In addition to being a worldwide known mycologist, Sabouraud, who was son of a painter, was a talented musician with a deep knowledge of the arts and acknowledged as a fine sculptor and painter [Sabouraud, 1910].

1911

It was the merit of two Italians, the Sardinian Francesco Radaeli (1870-1931) and the botanist and mycologist Pier Andrea Saccardo (1845-1920), born in Treviso, author of "*Sylloge Fungorum Omnium Hucusque Cognitorum*" (Proceedings of All Fungi Known So Far) (1882-1913) to correctly classify the organism isolated by Giulio Tarozzi as a fungus in the kingdom Fungi and not as a filamentous bacterium of the kingdom *Prokaryotae*. Saccardo had received by Radaeli (1911) a culture for identification that was isolated from a mycetoma of the foot of a 63-year-old miller. The isolate was thought as a new species by Saccardo who named it *Monosporium apiospermum* owing to pyriform conidia. Saccardo assimilated the

strain isolated from a mycetoma by Tarozzi with the strain of *M. apiospermum* received by Radaeli. Radaeli (1914) rightly refused to consider the grievances of Tarozzi to have been the first to have isolated *M. apiospermum*, since he erroneously considered his isolate to be an aerobic actinomycete [Ajello, 1998; Margulis and Schwartz, 1988; Radaeli, 1911a; Radaeli, 1911b; Radaeli, 1914; Saccardo, 1911; Saccardo, 1913; Tarozzi, 1914].

Increasing the nomenclatural confusion that had arisen around *Monosporium apiospermum*, Pier Andrea Saccardo had informally suggested (1911) that members of that genus could be more properly placed in the genus *Scedosporium*. The reclassification was formally executed (1919) by Albert John Chalmers and Aldo Castellani and, therefore, the valid name for the strains isolated from Giulio Tarozzi and Piero Redaelli was changed in *Scedosporium apiospermum* (Saccardo, 1911) Castellani & Chalmers, 1919. A generation later, the American medical mycologist Chester Wilson Emmons observed that a Canadian strain of *M. apiospermum*, maintained for 6 years in his fungal culture collection, had developed fertile perithecia containing asci with ascospores (1944). The teleomorph of *M. apiospermum* was assimilated by Emmons and the mycologist and plant pathologist Cornelius Lott Shear (1865-1956), born in New York, U.S.A., from the U.S. Department of Agriculture, Bureau of Plant Industry, creator of the American Phytopathological Society, to *Allescheria boydii*, previously reported as an undescribed ascomycete (1922). It should be noted that the teleomorph of *S. apiospermum* was afterwards cited as *Pseudallescheria boydii* (Shear, 1922) McGinnis, Padhye & Ajello, 1982 [Ajello, 1998; Castellani and Chalmers, 1919; Emmons, 1944; McGinnis et al., 1982; Saccardo, 1911; Shear, 1922].

The physician and Professor of Anatomy at the University of Florence, Italy, Guido Banti (1852-1925), born in a typical village of Tuscany, in the lower valley of the Arno River, Montebicchieri, Florence, described a fatal case of cerebral phaeohyphomycosis in a woman that had developed 6 months before her death (1911). In performing the autopsy, Banti

observed, in the brain of the cadaver, numerous nodules of a dark brown color resembling melanotic sarcomas, without apparent pathological abnormalities in other organs. By examination of wet mounts of parts of the nodules, moreover, he noted abundant quantities of phaeoid mycelium. Difficult to explain, Banti stated that he would have described the details of his clinical, histological and cultural studies later, even though nothing followed this intention. Fortunately, however, he had sent the strain for identification in Padua, Italy, to Pier Andrea Saccardo who considered it to be a new species and named it *Torula bantiana* in honor of the discovery of Banti [Ajello, 1998; Banti, 1911a; Banti, 1911b; Saccardo, 1912; Saccardo, 1913].

1912

In the years before and after the World War I, Count Sir Aldo Castellani (1874-1971), a decorated Florentine physician, former student of Professor Guido Banti, awarded Knight Commander of the Order of St. Michael and St. George by the British government and appointed Count of Chisimaio (Somalia) by King Vittorio Emanuele of Italy, for the medical service rendered during the war in Ethiopia (1935-1936), was very involved in the study of pathogenic yeasts. He had been studying tropical diseases at the London School of Hygiene and Tropical Medicine, U.K., under the direction of Sir Patrick Manson, and conducted research in Uganda and Ceylon (Sri Lanka) as a Lieutenant Colonel and later Admiral in the Royal Italian Navy Medical Service. He also became a consultant to the Ministry of Pensions in London, U.K., held staff appointements in London's Ross Institute and, as a Lecturer in Medical Mycology, at the London School of Hygiene and Tropical Medicine. At the same time, he became Professor of Tropical Medicine at Tulane University in New Orleans, Louisiana, U.S.A. Despite all these commitments, he maintained a private practice as a physician in the famous Harley Street in London [Ajello, 1998; Castellani, 1963].

Description of:

Absidia corymbifera (Cohn) Saccardo et Trotter, 1912

Pneumocystis carinii Delanoë & M. Delanoë, 1912

1913

The fungal culture collection of the U.S. Department of Agriculture (U.S.D.A.) was established in Washington D.C., U.S.A. (1913), by Charles Thom (1872-1956), born in Minonk, Illinois, U.S.A., Head of the Division of Soil Microbiology, Bureau of Chemistry and Soils (1927-1934) and Bureau of Plant Industry, U.S.A. (1934-1942), whose work was an important contribution in the field of microbiology of dairy products and soil fungi, together with his associate Margaret B. Church, based on Thom's mold culture collection in Connecticut, U.S.A. [Sleytr and Messner, 2003].

The Brazilian Alexandrino Pedroso, at the Section of Medical Mycology of the Institute of Tropical Medicine, São Paulo, Brazil, described a disease (Blastomycose negra) and isolated a fungal organism (1913), later described by the French parasitologist Emile Josef Alexander Brumpt (1877-1951), born in Paris, as *Hormodendrum pedrosoi* (1922). The Brazilian Paulo de Figureido Parreiras Paulo Horta studied in detail the ascosporic piedra caused by *Piedraia hortae*, a name attributed to the agent of "black piedra" by Olympio da Fonseca Filho (1895-1978) and Antonio Eugenio de Arêa Leão (1895-1971) in his honor (1928). Fonseca himself was subsequently honored by the Argentine Pablo Negroni (1904-1992), founder of the Mycology Centre in the Faculty of Medicine in Buenos Aires, Argentina (then headed by his son Ricardo), who created the genus *Fonsecaea* to place the most common etiologic agent of chromoblastomycosis *Fonsecaea pedrosoi* (Brumpt) Negroni, 1936 [Matsumoto and Ajello, 1998; San-Blas, 2000].

1914

The American Type Culture Collection (A.T.C.C.) took origin as a private resource dedicated to the collection, preservation and distribution of cultures of living microorganisms, including molds and yeasts, as well as, later in time, viruses, DNA probes, plants, and human and animal cells (1914). The collection was later officially established (1925) from representatives of the National Research Council, the Society of American Bacteriologists, the American Phytopathological Society, the American Zoological Society and the McCormick Institute in Chicago, Illinois, U.S.A., and then moving to Georgetown University, School of Medicine, Washington D.C., U.S.A. (1937), to houses in Washington (1947), when it was incorporated as an independent non profit Institution, into a facility in Rockville, Maryland, U.S.A. (1964) and, finally, to Manassas, Virginia, U.S.A. (1968) [Sleytr and Messner, 2003].

1915

The American pathologist Ernest C. Dikson (1881-1939), born in Newmarket, Ontario, Canada, from the Department of Public Health and Preventive Medicine, Stanford University School of Medicine, Stanford, California, U.S.A., reported in the sputum of forty patients who had spent time in the San Joaquin valley, California, the occurrence of an organism and then he found that valley fever was identical with an infection by *Coccidioides* endemic to the area, named coccidioidomycosis (1930) [Homei, 2008].

The first case of infection by *Phialophora verrucosa* has been described in conjunction between dermatologists and pathologists of the Boston City Hospital, Boston, Massachusetts, U.S.A., in a patient aged 19 immigrated from Italy who had a painless lesion on the right buttock (1915). Edgar M. Medlar (1887-1956), from the Department of Pathology, School of Medicine, University of Wisconsin, Madison, Wisconsin, U.S.A., studied histologically and

isolated culturally the fungus requiring the assistance of the taxonomist Roland Thaxter (1858-1932) of the Harvard University, Cambridge, Boston, who, using the classification system of Pier Andrea Saccardo, stated that the strain should be described as a new *taxon* and proposed the name of *Phialophora verrucosa* [Espinel-Ingroff, 1996; Lane, 1915; Medlar, 1915].

Jean V. Cooke, from the Department of Pediatrics, Washington University, Washington D.C., U.S.A., and the St. Louis Children's and Isolation Hospital, St. Louis, Missouri, U.S.A., performed the first serological testing in Medical Mycology (1915). Cooke, using an antigenic extract "precipitinogen" made from dried cultures of *Coccidioides immitis*, detected precipitating, but not complement fixing or agglutinating, antibodies in the serum of a patient with coccidioidomycosis. The serological reaction was somehow specific since the precipitin antibodies did not react with *Blastomyces dermatitidis* antigens thus suggesting to constitute a potential diagnostic tool [Cooke, 1915; Espinel-Ingroff, 1996].

1917

Description of:

Trichophyton interdigitale Priestley, 1917/*Arthroderma vanbreuseghemii* Takashio, 1973

1919

The American radiologist William B. Bowman, at the Los Angeles County Hospital, Los Angeles, California, U.S.A., was the first to claim the X-ray diagnostic potential by studying five patients afflicted with coccidioidomycosis (1919) [Bowman, 1919; Espinel-Ingroff, 1996].

1920

The Imperial Bureau of Mycology (I.B.M.), located in Kew, U.K., was founded modelled on the Imperial Bureau of Entomology (I.B.E.), with Erwin John Butler (1868-1943) as Director (1920). The Imperial Bureau of Mycology become the Imperial Mycological Institute (I.M.I.), which became part of the Imperial Agricultural Bureau (I.A.B.) (1927), then Commonwhealth Agricultural Bureaux (C.A.B.) International, a non profit organization supported by 32 governments [Homei, 2008].

The International Mycology Institut (I.M.I.) Culture Collection took origin in England, as part of an Institute previously founded (1920), being currently part of the Commonwhealth Agricultural Bureaux (C.A.B.) International [Sleytr and Messner, 2003].

1921

Berta Cecelia Fineman, from the Department of Bacteriology and Immunology, University of Minnesota, Minneapolis, Minnesota, U.S.A., adopted the system based on carbohydrate fermentation, already used in bacteriology, to study what she called the "thrush parasite". Previous fungal classification systems had described *Candida albicans* in many different ways since the microorganism was discovered by Charles Philippe Robin (1853). Fineman cultured the yeast on several differential media (e.g., milk, gelatin, carrots), adopted 17 different carbohydrates for testing and used the medium developed in Europe by the French Gabriel Roux (1853-1914), a Microbiology Professor in the University of Lyon, France, and Georges Linossier (1857-1923), Professor of Chemistry in the University of Lyon, for the production of chlamydospores (1890). Fineman demonstrated that strains of *C. albicans* (as *Oidium albicans*) can be successfully identified on the basis of the fermentation of carbohydrates, produce chlamydospores but not ascospores, and tend to be filamentous in liquid media at low oxygen tension and unicellular onto solid media [Espinel-Ingroff, 1996; Fineman, 1921; Roux and Linossier, 1890].

The Brazilian pharmacist, physician and mycologist Paulo de Figuereido Parreiras Horta (1884-1961), Professor of Microbiology and Parasitology, working at the Serviço de Dermatologia e Sifiligrafia (Department of Dermatology and Syphilis) of the Hospital Geral in Rio de Janeiro, Brazil, observed and described the etiologic agent of *Tinea nigra*, *Cladosporium* (now *Hortaea) werneckii*, so named in honor of the Brazilian dermatologist Machado Werneck, Director of the Laboratory where Horta had worked and whom he succeeded (1921) [de Hoog and Guého, 1998; San-Blas, 2000].

Mark F. Boyd e Earl D. Crutchfield, at the University of Texas Medical Branch in Galveston, Texas, U.S.A., observed and reported the first case of mycetoma caused by *Pseudallescheria boydii* (as *Allescheria boydii*), from a lesion of a diseased ankle of a negro infected by injury with a thorn (1921). Cultivating the clinical isolate on cornmeal and glycerine agar, Cornelius Lott Shear observed that the fungus produced conidia, cleistothecia with ascospores and synnemata. Shear named the new patient's isolate *Allescheria boydii* (Shear, 1922) in honor of Boyd. *Pseudallescheria boydii* was the first fungal pathogen recognized to be characterized by sexual reproduction [Boyd and Crutchfield, 1921; Espinel-Ingroff, 1996; Shear, 1922].

1922

Description of:

Trichophyton rubrum (Castellani) Semon, 1922

1923

Description of:

Candida albicans (Robin) Berkhout, 1923

1925

The French J. Margarot and P. Devèze (1925) discovered that hairs infected with *Microsporum*, but not with *Trychphyton* species, showed a brilliant greenish fluorescence under the ultraviolet light obtained from a mercury vapour lamp. This apparatus, described by the American physicist Professor Robert William Wood (1868-1955), of the John Hopkins University, Baltimore, Maryland, U.S.A. (1919), simplified the diagnosis of dermatophyte infections, particularly in dogs and cats, in which the signs are very inconspicuous, by prejudicial selection of samples for microscopic and cultural examination [Margarot and Devèze, 1925].

Description of:

Acremonium kiliense Grütz, 1925

1926

The American dermatologist Joseph Gardner Hopkins (1882-1951) and the American botanist and pioneer researcher on heredity in fungi Bernard Ogilvie Dodge (1872-1960), of the Columbia University, New York, U.S.A., founded the first specialized laboratory of Medical Mycology in the United States at the Columbia-Presbyterian Medical Center, New York [Homei, 2008].

The Italian self-thaught biologist and mycologist Arturo Nannizzi (1877-1961), born in Siena, Director of the Botanical Garden (1934-1950) at the University of Siena, clearly described (1926) how he could, for the first time, induce the complete development of the sexual or ascigerous state of a geophilic dermatophyte now called *Microsporum gypseum* (Bodin) Guiart & Grigorakis, 1928. Nannizzi cultivated a human clinical strain of Swiss origin, then named *Sabouradites gypseus*, on a substrate of sterilized "terriccio di bosco mescolato a piccoli frammenti di vecchio cuoio e di penne di gallinacei" (forest soil mixed

with small pieces of old leather and feathers of gallinaceous birds). Two and half months after inoculation of the baited soil plate and a period of profuse development of echinulate fusiform macroconidia, Nannizzi observed the development of fertile gymnothecia filled with asci containing eight oval ascospores. One of his original drawings clearly represents a section of a gymnothecium with circinate peridial hyphae formed by short dumbell-shaped segments, as well as asci containing ascospores. Thus, Nannizzi stated undoubtedly that the dermatophytes should belong to the ascomycetes, classified in the family *Gymnoascaceae*. Consequently, the perfect state of *Sabouradites gypseus* was named *Gymnoascus gypseus* Nannizzi, 1927, then *Arthroderma gypseum* (Nannizzi) Weitzman, McGinnis, Padhye & Ajello, 1986; *Arthroderma incurvatum* (Stockdale) Weitzman, McGinnis, Padhye & Ajello, 1986) [Ajello, 1998; Nannizzi, 1926; Nannizzi, 1927].

By publishing more than 500 works and editions of "The Manual of Tropical Medicine", written in collaboration with the Director of the Wellcome Research Laboratories, Khartoum, Sudan, Albert J. Chalmers (1870-1920), Sir Aldo Castellani played an important role in teaching and diagnosis of tropical diseases, causing concern for fungi around the world. The publication (1926) of lectures on the mycoses by the Professor of Bacteriology and Hygiene Adolph Gehrmann, born in 1868 in Decatur, Illinois, U.S.A., of the College of Physicians and Surgeons, Chicago, Illinois, submitted to the American Medical Association at the College of Medicine, University of Illinois, Chicago, was essential to promote interest for fungal infections in the international scientific community. During his profitable stay in Ceylon (1903-1915), Sir Aldo Castellani isolated and characterized three important new species of the genus *Candida* of medical interest: *C. guilliermondii* (Castellani, 1912) Langeron & Guerra, 1938 (*Pichia guilliermondii* Wickerham, 1966), *C. krusei* (Castellani, 1910) Berkhout, 1923 (*Issatchenkia orientalis* Kudryavtsev, 1963) and *C. tropicalis* (Castellani, 1910) Berkhout, 1923. He is also credited with the discovery of *Trichophyton rubrum*

(Castellani, 1910) Sabouraud, 1911. Castellani formulated a topical preparation for treatment of skin infections by dermatophytes based on the carbol fuchsin dye known as "Castellani's paint" still in use for the treatment of *Tinea pedis* (athlete's foot) (1928) [Ajello, 1998; Castellani, 1910; Castellani, 1928; Castellani, 1929; Castellani and Chalmers, 1919].

Description of:

Trichosporon cutaneum (de Beurmann,Gougerot & Vaucher) Ota, 1926

1927

Based on the previous studies of Jean V. Cooke, still characterized by some lack of specificity (1915), Edwin F. Hirsch and Harriet Benson, both working at the Henry Baird Favill Laboratory of the St. Luke's Hospital in Chicago, Illinois, U.S.A., successfully developed a specific skin reaction in patients suffering of coccidioidomycosis by using "coccidioidin", an heat-stable (80°C) soluble filtrate antigen extracted from 14-day-old peptone broth cultures of *Coccidioides immitis* (1927). The skin reaction resembled that previously seen with tuberculin and the immediate reaction was similar to the wheal produced by specific pollen extracts in patients with hay fever [Cooke, 1915; Espinel-Ingroff, 1996; Hirsch and Benson, 1927].

Description of:

Mucor ramosissimus Samutsevich, 1927

1928

The biologist and pharmacologist Alexander Fleming (1881-1955), born in Lochfield, Scotland, who had already discoverered the antimicrobial properties of the lysozyme (1922), pupil of Sir Almroth Wright, famous bacteriologist, at the Inoculation (Vaccination) Department of the Saint Mary's Hospital, in Paddington, London, U.K., discovered the crude

filtrate of the first antibiotic, penicillin. The antimicrobial metabolite was produced by *Penicillium notatum* (now *Penicillium chrysogenum* Thom, 1910, as correctly identified by Charles Thom, since it was previously erroneously described as *P. rubrum*), a fortuitous contaminant of a culture of *Staphylococcus aureus* in his laboratory (1928). Penicillin G was subsequently obtained in the purified form by the German-born British biochemist Ernst Boris Chain (1906-1979) and the pathologist and physiologist Howard Walter Florey (1898-1963), born in Adelaide, Australia, of the Sir William Dunn School, Oxford, U.K. (1940). Fleming, Florey and Chain were awarded the Nobel Prize (1945) "for the discovery of penicillin and its curative effect in various infectious diseases" [Bentley, 2005; Chain et al., 1940; Fleming, 1929; Raju, 1999].

On the basis of studies previously performed by Fred D. Weidman and Dorothy Spring, at the Laboratory of Dermatological Research, University of Pennsylvania, Philadelphia, Pennsylvania, U.S.A., Robert S. Hodges, of the University of Alabama, Birmingham, Alabama, U.S.A., described a medium useful for the identification of dermatophytes (1928). As the original ingredients of Raymond A. Sabouraud were no longer easily available, a study was made for other peptones, maltose and dextrose in view of developing a standardized medium composed of procurable and cheap ingredients. The final formulation of the medium was called again "Sabouraud" (broth and agar), and is still the universal medium for growing fungi in the laboratory of Medical Mycology [Espinel-Ingroff, 1996; Hodges, 1928; Weidman and Spring, 1928].

1929

Luz Maria Dalmau, assistant of the medical officer Colonel Bailey K. Ashford (1873-1934), founder of the Institute of Tropical Medicine (later renamed School of Tropical Medicine) in Puerto Rico, prepared a culture methodology (based on corn meal potato dextrose and rice

agar) for studying the microscopic morphology of hyphae and pseudohyphae in yeast colonies now known as “Dalmau’s plate” [Dalmau, 1929; Espinel-Ingroff, 1996].

1930

The seminal discovery of Arturo Nannizzi did not receive due recognition as discredited by Maurice Charles Pierre Langeron (1874-1950), born in Dijon, France, and Sima Milochevitch (1896-1943). These two researchers of the Institute of Parasitology, Faculty of Medicine, Paris, France, unjustly accused Nannizzi of having grown the reference strain on a unsterilized substrate (1930). The objections made by Langeron and Milochevitch were immediately rejected by Nannizzi without success, although he had clearly stated that the soil, feathers and leather used as a substrate had been sterilized in an autoclave. The worthy work of Nannizzi was virtually ignored by Langeron in all subsequent publications including “Précis de Mycologie” (Summary of Mycology) (1945, 1952). An indirect reference to his work, however, is made in a footnote of the first book with the statement that “Personne n’a encore vu de pèrithèce fertile, malgre les affirmations de auteurs italiens” (Nobody has seen perithecium fertile, despite the claims of Italian authors). In the second book (1952) of this text not even this minimalist reference is reported. Unfortunately, the refusal of Langeron and Milochevith’s is still perpetuated as, in present day text books, one can find reiterate the satement that “Nannizzi’s work, however, was discreditaed by other mycologists because the substratum he used was not sterile and thus the fungus was not grown as pure culture” [Ajello, 1998; Langeron, 1945; Langeron and Milochevitch, 1930; Langeron and Vanbreuseghem, 1952; Nannizzi, 1926; Nannizzi, 1930; Pollacci, 1932].

The dermatologist Jorge Lobo, working in Recife, Brazil, described for the first time a new cutaneous disease, which he called “blastomicose queloidiforme” (1930). As a result, numerous cases were identified in Brazil and other Latin American countries, being referred

to as Jorge Lobo's blastomycosis. Different names were assigned to the isolated etiologic agents, such as *Paracoccidioides loboi* (1949) introduced by Floriano Paulo de Almeida and Carlos da Silva Lacaz (1915-2002), Professor Emeritus of the Faculty of Medicine of the São Paulo University, São Paulo, Brazil, and former Director of the Tropical Medicine Institute of São Paulo, *Loboa loboi*, according to Raffaele Ciferri and collaborators (1956) and, more recently, *Lacazia loboi* by Paulo R. Taborda, Valeria A. Taborda, Michael R. McGinnis (1999), to honor not only Jorge Lobo, discoverer of the organism, but also the relevant Brazilian mycologist Carlos da Silva Lacaz [Azevedo et al., 1956; de Almeida and Lacaz, 1948; Lobo, 1930; Pradinaud, 1998; San-Blas, 2000; Taborda et al., 1999].

Description of:

Epidermophyton floccosum (Harz) Langeron & Milochevitch, 1930

1932

The Mycological Society of America (M.S.A.) was founded as a learned Society aimed to serve the mycologists in the United States and Canada (1932). The Society's constitution states that "The purpose of the Society is to promote and advance the science of mycology and to foster and encourage research and education in mycology in all its aspects" through annual meetings and exchanging information about the understanding of fungi and publication of the official journal "Mycologia". Members of the steering committee for the creation of a Medical Mycology Division within the American Society for Microbiology (A.S.M.) met in Phoenix, Arizona, U.S.A., during the second Coccidioidomycosis Symposium to propose the Medical Mycology Society of the Americas (M.M.S.A.) (1965) [Homei, 2008].

The American Robert Alexander Stewart and the bacteriologist, experimental pathologist, virologist, epidemiologist, and ecologist Karl Friedrich Meyer (1884-1974), born in Basel,

Switzerland, from the Departments of Medicine and Dermatology, University of California Hospital, University of California, San Francisco, California, U.S.A., described for the first time the isolation of *Coccidioides immitis* from soil (1932). The ground sample was collected near the dormitories of a ranch close to Delano, Kern Country, California, justifying the infection known as "valley fever" which was still of undetermined origin [Espinel-Ingroff, 1996; Stewart and Meyer, 1932].

The French Emile Rivalier (1892-1979), Raymond A. Sabouraud's successor at the Laboratoire des Teignes (Laboratory for dermatophytoses), Hospital St. Louis, Paris, France, and S. Seydel, described a method for the study of living cultures of filamentous fungi (1932), which proved to be particularly effective for the observation of the modalities of conidiogenesis, known as "slide culture" [Rivalier and Seydel, 1932a; Rivalier and Seydel, 1932b].

Description of:

Candida parapsilosis (Ashford) Langeron & Talice, 1932

1934

Although Arturo Nannizzi was rightly disappointed by the refusal of his findings, he continued his studies by publishing "Repertorio Sistematico dei Miceti dell'Uomo e degli Animali" (Systematic Catalogue of Fungi from Humans and Animals) (1934). This book is a comprehensive directory of all the actinomycetes, fungi and oomycetes isolated from man and animals with clinical signs of infection. Through keys and illustrations, Nannizzi made it possible for readers, regardless of the degree of competence, the microbiological identification of these pathogens. Even today, the volume represents a valuable source of synonyms still considered valid for microbial species [Ajello, 1998; Nannizzi, 1934].

Chester Wilson Emmons (1900-1985), born in What Cheer, Iowa, U.S.A., one of the "fathers of U.S. Medical Mycology", Head of the Medical Mycology Section at the National Institutes of Health (N.I.H.), Bethesda, Maryland, U.S.A., based on the development of conidiophores and conidia (as spores) and using slide cultures as amended by Arthur T. Henrici, proposed to adopt the generic names of *Trichophyton*, *Microsporum and Epidermophyton* for dermatophytes, omitting the names *Achorion* and *Endodermophyton*, more consistent with the clinical classification of Raymod A. Sabouraud [Emmons, 1934; Espinel-Ingroff, 1996].

1938

Researches and publications of the Italian agronomist, botanist and mycologist Raffaele Ciferri (1897-1964), born in Fermo, Ascoli Piceno, graduated in Bologna, Italy (1920), in Agricultural Science, Professor of Botany and Director of the Botanical Institute of Milan, Italy (1942-1964), have contributed greatly to the study of mycobiota and fungal plant diseases in Italy, Africa, Cuba and the Dominican Republic. Ciferri conducted most of his research work in collaboration with Piero Redaelli (1898-1955), born in Milan, receiving his medical degree from the Medical School of Pavia, Italy (1922) and Professor of Pathology at the University of Milan. Redaelli proved to be a valiant fighter as an officer in World War I where he earned the War Cross for his deeds. In World War II, Redaelli actively participated in the Guerilla War (1944-1945) as a commander of a partisan division. The meetings with Sir Aldo Castellani in London. U.K., and Maurice Langeron in Paris, France, persuaded him to focus his interests on mycoses. Redaelli was one of the cofounders of the International Society for Human and Animal Mycology (I.S.H.A.M.) (1954) and he served as the Society's first President until his death. Separately or together, Raffaele Ciferri and Piero Redaelli have published numerous works, often on controversial content on fungi such as *Blastomyces dermatitidis*, species of the genus *Candida*, *Coccidioides immitis*, the *duboisii* and

farciminosum varieties of *Histoplasma capsulatum*, and *Paracoccidioides brasiliensis*. Their articles and their books had a profound impact on the development of Medical Mycology in Italy during the Second World War. Redaelli and Ciferri were the co-founders and Editors (1938) of the international journal "Mycopathologia", later renamed "Mycopathologia et Mycologia Applicata" (1950) to return (1975) to its original name still used by Kluwer Academic Publishers, Dordrecht, The Netherlands, in collaboration with the International Mycological Institute, Egham, Surrey, U.K. [Ainsworth, 1976; Ajello, 1998; Baldacci, 1965; Ciferri, 1956; Ciferri and Redaelli, 1958; Dodge, 1935; Redaelli, 1931; Redaelli and Ciferri, 1934; Redaelli and Ciferri, 1942].

1939

The medical mycologist Rhoda Williams Benham (1894-1957), born in Cedarhurst, New York, U.S.A., pupil of the late Joseph Gardner Hopkins, working at the Laboratory for Medical Mycology of the College of Physicians and Surgeons at the Columbia University, New York, described that *Malassezia furfur* (*Pityrosporum ovale*) required oleic acid to grow *in vitro* (1939). Often working in collaboration with her pupil Lucille K. Georg and the later Director of the Mycology Laboratory at the Columbia-Presbyterian Medical Center, New York, Margarita Silva-Hutner (1916-2002), born in Rio Piedras, Puerto Rico, she then became interested in the study of the nutritional requirements of dermatophytes. In her honor, the Medical Mycological Society of America (M.M.S.A.) established to give a medal, the "Rhoda Benham Award", to those who greatly contributed to the development of Medical Mycology (1969) [Benham, 1939; Espinel-Ingroff, 1996].

The American Doctor in Medicine Arthur Trautwein Henrici (1889-1943), born in Economy, Pennsylvania, of the Department of Bacteriology and Immunology, University of Minnesota, Minneapolis, Minnesota, U.S.A., observed that *Aspergillus fumigatus* produced two

endotoxins, a hemolytic and a pyrogenic one (1939). The relevance of his report was recognized during the epidemic known as "Turkey X disease" that occurred in England in the early '60s. Turkeys, pigs, chickens and cows resulted intoxicated with foodstuffs that contained a metabolite, named "Aflatoxin", produced by *Aspergillus flavus*, introducing to the hera of mycotoxicoses [Espinel-Ingroff, 1996; Henrici, 1939].

Albert Edward Oxford, Harold Raistrick and Paul Simonart, from the Division of Biochemistry, London School of Hygiene and Tropical Medicine, University of London, U.K., developed a metabolite of *Penicillium janczewskii* (*P. griseofulvum*) named "Griseofulvin" (1939). Nineteeen years later (1958), James C. Gentles, of the Medical Mycology Section of the Bacteriology Department, University of Glasgow, Scotland, reported that the antibiotic griseofulvin, markedly shortened the duration of experimental *Trichophyton mentagrophytes* and *Microsporum canis* infections of the skin of guinea pigs. Gentles inspired the botanist E. Glyn V. Evans (1941-2003), born in Cardiff, Wales, to specialise in the area of Medical Mycology until becoming the Head of the National Medical Mycology Reference Laboratory for the Public Health Laboratory Service in Leeds, U.K. [Espinel-Ingroff, 1996; Gentles, 1958; Oxford et al., 1939].

1940

The American mycologist, microbiologist and botanist Kenneth Bryan Raper (1908-1987), born in Welcome, North Carolina, Professor of Bacteriology and Botany at the University of Wisconsin, Madison, Wisconsin, U.S.A., was author of fundamental contributions to the medical and industrial applications of fungi of the genera *Aspergillus* and *Penicillium*. Raper formally established in Peoria, Illinois, U.S.A., The Northern Regional Research Laboratories (N.R.R.L.) (1940), now named National Center for Agricultural Utilization Research

(N.C.A.U.R.), based on Charles Thom and Margareth Church mold collection and Lynfer J. Wickerham yeast collection [Sleytr and Messner, 2003].

1943

The medical Doctor Edward Mellanby (1884-1955), born in West Hartlepool, U.K., Professor of Pharmacology at the University of Sheffield, U.K. (1920), Secretary of the Medical Research Council (M.R.C.), a U.K. organization, (1933-1949), discoverer of vitamin D, organized an informal meeting at the London School of Hygiene and Tropical Medicine (L.S.H.T.M.), U.K., with James T. Duncan, Charles Wilcocks (1896-1977), acting Director of Bureau of Hygiene and Tropical Diseases, Samuel Paul Wiltshire (1891-1967), Director of the Imperial Mycological Institute (I.M.I.), chaired by Ralph St. John-Brooks (1884-1963), Curator of the National Collection of Type Cultures and Micro-organisms at the Linster Institute in Hertfordshire, U.K. The participants "stressed the need for collaboration between medical mycologists and systematic mycologists" and then appointed the Medical Mycology Committee (M.M.C.) for that purpose (1943) [Homei, 2008].

1944

The first observations on the activity of antifungal agents (benzimidazole, propamidine and cycloheximide) are due to Dilworth Wayne Wolley (1914-1966), from the Laboratories of the Rockefeller Institute for Medical Research, New York, U.S.A. (1944), William O. Elson, from the Research Laboratories of Bauer & Black Division of The Kendall Co., Chicago, Illinois, U.S.A. (1945), and Byron Elwood Leach, from the Tulane University, School of Medicine, New Orleans, Louisiana, U.S.A., in collaboration with Jared H. Ford, from the State University of Iowa, Iowa City, Iowa, U.S.A., and Alma J. Whiffen, from the Research Laboratories, The Upjohn Company, Kalamazoo, Michigan, U.S.A. (1947). Although only

propamidine was temporarily used as a therapeutic agent in the treatment of human mycoses, these studies were critical to the search for new antifungal antibiotics in following years [Elson, 1945; Espinel-Ingroff, 1996; Leach et al., 1947; Woolley, 1944].

James T. Duncan, Charles Wilcocks and Samuel Paul Wiltshire started to collect the medical mycological literature in "Annotated Bibliography of Medical Mycology" (1944), a periodical publication that continued until William Arthur Pool (1889-1969), Director of the Commonwealth Bureau of Animal Health (C.B.A.H.), U.K., joined the Medical Mycology Committee (M.M.C.), U.K., and became the Editor of the quarterly "Review of Medical and Veterinary Mycology" in Kew, Surrey, U.K. (1951) [Homei, 2008].

1946

The Communicable Disease Center (C.D.C.), an institution now recognized as synonymous with public health all around the world, was organized in Atlanta, Georgia, on July 1, 1946. The founder, Dr. Joseph W. Mountin (1891-1952), born in Hartford,Wisconsin, U.S.A., established the organization as a descendant of the post-World War II agency Malaria Control in War Areas. The new institution subsequently extended its interests to comprise all infectious diseases, including mycoses. As the scope of C.D.C.'s activities expanded far beyond communicable diseases, its name had to be changed. In 1970 it became the Center for Disease Control, and in 1981, after extensive reorganization, Centers for Disease Control. Finally, in October 1992, Congress changed C.D.C.'s official name to the Centers for Disease Control and Prevention, to recognize C.D.C.'s leadership role in prevention but, by law, the well-known three-letter acronym was retained.

The Public Health Laboratory Service (P.H.L.S.) took over in Britain the already existing Mycological Laboratory at the London School of Hygiene and Tropical Medicine (L.S.H.T.M.), of James Thompson Duncan (1884-1958) and, when the National Collection

of Type Cultures (N.C.T.C.) was reorganized, became a new body specialized in yeasts and molds infecting humans and animals (1948) [Homei, 2008].

The Hungarian histologist George A. Gomori (1904-1957), born in Budapest and emigrated to the United States where he joined the Department of Medicine at the University of Chicago Medical School, Chicago, Illinois, U.S.A. (1938), and Roger D. Baker, Department of Pathology, Louisiana State University, School of Medicine, New Orleans, Louisiana, U.S.A., greatly improved the sensitivity of the histological diagnosis of mycoses (1946). Gomori and Baker described, respectively, a method for specific fungal staining, later amended by Robert G. Grocott (1955), Milton D. Huppert, Dorothy J. Oliver and Sung H. Sun (1978), and tissue reactions in fungal infections with hematoxylin-eosin stain [Baker, 1947; Espinel-Ingroff, 1996; Gomori, 1946; Grocott, 1955; Huppert et al., 1978].

1948

The American yeast taxonomist Lynferd J. Wickerham (1911-1990) and Kermit A. Burton, from the Northern Regional Research Laboratory (N.R.R.L.), Peoria, Illinois, U.S.A., showed that the assimilation test of carbohydrates was a fundamental diagnostic procedure for the taxonomy of yeasts (1948). They pointed out the lack of a well defined, universal and complete basal medium. Such medium was developed by them and was named "yeast nitrogen base". It was used in liquid form and supplied with the carbon source to be tested. Turbidity readings were made to determine the amount of growth. The number of carbon compounds used was then greatly expanded, and the procedure was applied successfully by Wickerham in a study of yeasts belonging to the genus *Hansenula* (1951). The assimilation test was introductory to the development of diagnostic kits commercialized in the '70s [Espinel-Ingroff, 1996; Land et al., 1975; Roberts et al., 1976; Wickerham, 1951; Wickerham and Burton, 1948].

1949

Chester W. Emmons, at the National Institutes of Health (N.I.H.), Bethesda, Maryland, U.S.A., found that *Histoplasma capsulatum* grew saprophytically in soil (1949), leading to the consensus that the infection is acquired by inhalation of the fungal spores. Louis D. Zeidberg, Libero Ajello, Ann Dillon and Laliah C. Runyon, at the Communicable Disease Center (C.D.C.), U. S. Public Health Service, Federal Security Agency, Atlanta, Georgia, U.S.A., noted that the fungus was particularly frequent in case of contamination of soil with the feces of chickens and bats (1952) [Emmons, 1949; Espinel-Ingroff, 1996; Espinel-Ingroff, 2003; Zeidberg et al., 1952].

Kenneth Bryan Raper published "A manual of the *Penicillia*" with Charles Thom (1949) and, then, "The Genus *Aspergillus*" (1965) with the American bacteriologist of the Northern Regional Research Center, Peoria, Illinois, U.S.A., Dorothy I. Fennell (1916-1977), born in Middle Grove, Illinois [Raper and Fennell, 1965; Raper and Thom, 1949].

1950

The U.S. Federal Government established (1950) the Kansas City Field Station, Kansas City, Kansas, U.S.A., and the Mycology Unit at Duke University Medical Center, Durham, North Carolina, U.S.A., as parts of the Communicable Disease Center (C.D.C.), to oversee, prevent and eradicate fungal infections which had developed into something of a public health issue. The designated Director was the plant pathologist Norman F. Conant (1908-1984), trained with the American botanist William Gilson Farlow (1844-1919), at Harvard University, Cambridge, Boston, Massachusetts, U.S.A., and Raymond A. Sabouraud at the Hospital Saint-Louis in Paris, France [Homei, 2008].

The bacteriologist Elizabeth L. Hazen (1885-1975), born in Rich, Coahoma County, Missouri, U.S.A., and the chemist Rachel Fuller Brown (1898-1980), born in Springfield, Massachusetts, U.S.A., reported at the autumn Meeting of the National Academy of Sciences in Schenectady, New York, U.S.A. (1950), the discovery, made at the New York State Department of Health, Albany, New York, of nystatin (as fungicidin), produced by *Streptomyces noursei*. Hazen and Brown showed the activity of the molecule *in vitro* by antifungal susceptibility testing and *in vivo* in animal experimental models. The Food and Drug Administration (F.D.A.), White Oak, Maryland, U.S.A., approving the sale (1954), renamed the fungicide in honor of the Institution in which it was discovered. Hazen shared with Brown the Squibb Award in Chemotherapy (1955) and received a Distinguished Service Award from the New York State Department of Health, Albany, (1968). Hazen and Brown, who donated the royalties (exceeding $ 13,000,000 by 1976) of their patent (expired in 1976) to the Brown-Hazen Foundation Program, a U.S. not-for-profit organization, founded in 1973, dedicated to recognizing, honoring and encouraging invention and creativity through the administration of its programs (1994), were included, after their death, in the National Inventors Hall of Fame, located in Alexandria, Virginia, U.S.A., with satellite offices in the Washington, D.C. area and in Los Angeles, California [Espinel-Ingroff, 1996; Hazen and Brown, 1950].

The first observations concerning the association of a high incidence of severe fungal infections and the use of antibiotics and steroids were reported by Lorenz E. Zimmerman, pathologist at the Armed Forces Institute of Pathology at Walter Reed General Hospital, Washington D.C., U.S.A., then Chairman of the Department of Ophthalmic Pathology of the George Washington University, Washington D.C. Zimmerman described three cases of endocarditis caused by *Candida* spp. and *Aspergillus* spp. which were “apparently

stimulated" by the continuous administration of penicillin (1950) [Espinel-Ingroff, 1996; Homei, 2008; Zimmerman, 1950].

The physician, pathologist and immunologist of the Harvard Medical School, Boston, Massachusetts, U.S.A., Albert Hewitt Coons (1912-1978), born in Gloversville, New York, U.S.A., was the first person to conceptualize and develop immunofluorescent techniques for labeling antibodies in the early 1940s. The veterinarian and mycologist William H. Kaplan (1925-2011), of the Communicable Disease Center (C.D.C.), Atlanta, Georgia, U.S.A., developed a histochemical method for the detection of fungal antigens in infected tissues by using specific antibodies conjugated with fluorescein (1950) [Coons and Kaplan, 1950; Espinel-Ingroff, 1996].

The physician Edouard Drouhet (1919-2000), born in Barlad, Romania, from a family of French descent, described the role of the polysaccharide glucuronoxylomannan as a virulence factor of *Cryptococcus neoformans* (*Torulopsis neoformans*) and identified that as the cause of the immunological paralysis in the course of cryptococcosis. Drouhet also described (1980) a new septicemic ocular and osteo-articular syndrome in young drug-addicts. After contributing to the characterization of fungal antigens for qualitative and quantitative determination of specific serum antibodies in patients with systemic mycoses, he described *Emmonsia pasteuriana* (Drouhet, Guheo & Gori, 1998), a new species named in honor of the beloved Institut Pasteur in Paris, France. Drouhet, together with the agronomist and naturalist Gabriel Segretain (1913-2008), born in Compiègne, Oise, France, first working in plant pathology and then in Medical Mycology until becoming Professor and Chef du Service de Mycologie at the Institut Pasteur in Paris, and the botanist François Mariat (1921-2003), born in Paris, gave rise to the team that played a leading role in the development of Medical Mycology in France and in Europe [Drouhet et al., 1950].