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History of Medical Mycology

File 3 (1951-1982)

1951

Lucille Katharine Georg, dead on 1980, former President of the Medical Mycological Society of the Americas (M.M.S.A.), Libero Ajello and Morris A. Gordon, at the Communicable Disease Center (C.D.C.) in Atlanta, Georgia, U.S.A., included cycloheximide in a mycological medium, named "mycobiotic agar" or "Mycosel", for the selective isolation of *Coccidioides immitis* (1951). The medium, integrated with the antibiotic at low concentrations, inhibiting the growth of saprophytic fungi but also of some pathogens (such as *Cryptococcus neoformans*), had a great impact in the mycological culture studies [Espinel-Ingroff, 1996; Georg et al., 1951].

Morris A. Gordon, of the Laboratories for Mycology and Mycobacteriology, Infectious Disease Institute, Centers for Laboratories and Research, New York State Department, Albany, New York, U.S.A., then at the Communicable Disease Center (C.D.C.), reported that he had succeeded to cultivate "spherical forms" of *Malassezia furfur* (*Pityrosporum orbiculare*) by including olive oil or saturated fatty acids in Sabouraud dextrose agar [Espinel-Ingroff, 1996; Gordon, 1951].

Edward E. Evans and John F. Kessel, from the Department of Medical Microbiology, School of Medicine, University of Southern California, Los Angeles, California, U.S.A., described,

on the basis of previous studies by Evans himself, that *Cryptococcus neoformans* may be distinguished into three serological types, A, B and C, according to the antigenic differences detectable by agglutination reactions (1951). Soluble capsular polysaccharide of types A, B, and C gave similar results by precipitin reactions. Further experiments demonstrated that the capsular materials of type B is composed by two carbohydrate fractions (SB1 and SB2). Subsequently, Ralph A.Vogel, from the Medical Research Division, Veterans Administration Hospital, Atlanta, identified the fourth serotype, D (as R) (1968) [Espinel-Ingroff, 1996; Evans, 1949; Evans and Kessel, 1951; Vogel, 1966].

James M. Neill, John Y. Sugg and D. W. McCauley, from the Department of Bacteriology and Immunology, Cornell University, Medical College, Ithaca, New York, U.S.A., showed the occurrence of cryptococcal antigen (as serologically active substances) in the body fluids of a patient suffering of cryptococcosis (1951). This finding led Norman Bloomfield, Morris A. Gordon and DuMont Frelinghuysen Elmendorf, an American physician specialized in pulmonary diseases, at the Division of Laboratories and Research, New York State Department of Health, Albany, to the development of the latex agglutination test for the diagnosis of systemic cryptococcosis, still commercially available today (1963) [Bloomfield et al., 1963; Espinel-Ingroff, 1996; Neill et al., 1951].

1952

The physician Raymond Vanbreuseghem (1909-1993), born in Monceau sur Sambre, Charleroi, Belgium, specialized in Tropical Medicine, Professor at the University of Brussels, Belgium, and founder of the Service of Medical Mycology at the Prince Leopold Institute in Antwerp, Belgium, based on the observation (1946) of John S. Karling, Purdue Lafayette, Indiana, U.S.A., introduced massively the technique of baiting the soil with hair for the specific purpose of isolating dermatophytes (1952) [Karling, 1946; Vanbreuseghem, 1952].

1953

The prefoundation of the International Society for Human and Animal Mycology (I.S.H.A.M.) originated in Italy, in the restaurant "Giardino dei poeti" (Garden of Poets), located in Trastevere, a picturesque district of Rome close to the river Tevere (1953). A small group of mycologists, mostly European, including Raymond Vanbreuseghem (Antwerp, Belgium), Geoffrey Ainsworth (London, U.K.), Gabriel Segretain, Edouard Drouhet and François Mariat (Paris, France), Jacomina Lodder (Delft, The Netherlands), Heiti Paldrolck (Stockholm, Sweden), Heinz Seeliger (Würzburg, Germany), and Juan Mackinnon (Montevideo, Uruguay), were invited by Piero Redaelli and Raffaele Ciferri (Milan and Pavia, Italy) to an informal dinner. After enjoying delicious pasta and fungi (as illustrated in the hand drawings of a talented guest together with the names of the diners on the menu), the proposal for a New Society, dedicated to the study and development of Human and Animal Mycology, was enthusiastically approved [Drouhet, 1997].

M. F. Gridley modified the staining technique with periodic acid-Schiff (PAS) (1953), in which the acid was deputed to release the aldehydes of the fungal cell wall enabling the reaction with Schiff's reagent. Gridley replaced the periodic acid with chromic acid, allowing to view hyphae and yeast cells colored in pink still maintaining an effective yellowish contrast [Espinel-Ingroff, 1996; Gridley, 1953; Kligman et al., 1951].

Walter J. Nickerson, in collaboration with Zbigniew Mankowski, at the Arnold Biological Laboratories, Brown University, Providence, Rhode Island, U.S.A., began fundamental studies on the mechanism of cell division and morphogenesis of *Candida albicans* (1953). Nickerson found that the replacement of glucose with soluble starch, glycogen or dextrin decreased the filamentation of the yeast and the growth of budding cells was dependent on glucose as a carbon source. Nickerson was then able to identify a mechanism of cellular

oxidation essential for cellular budding, but not for growth, at the locus of flavoproteins, by the development of a filamentous mutant of *C. albicans*. Later, in collaboration with Gian Kessler, of the Department of Biochemistry, University of California, Berkeley, California, U.S.A., Nickerson isolated "clean cell walls" of three *C. albicans* strains and determined that they contained a glucan-protein and two different glucomannan-proteins (1959) [Espinel-Ingroff, 1996; Kessler and Nickerson, 1959; Nickerson, 1953; Nickerson, 1954; Nickerson and Mankowski, 1953].

Description of:

Saksenaea vasiformis Saksena, 1953

1954

The International Society for Human and Animal Mycology (I.S.H.A.M.) was officially founded in Paris, France, at the Institut Pasteur, during the 8th International Congress of Botany (1954). On the I.S.H.A.M. foundation document can be recognized the signatures of some of the prefounders who took part at the first meeting in Rome, Italy, and became official members as Piero Redaelli (Italy), President, Raymond Vanbreuseghem (Belgium), General Secretary, Geoffrey Ainsworth (U.K.), Gabriel Segretain (France), Chester W. Emmons (U.S.A.) and Pablo Negroni (Argentina), Vice Presidents, as well as other charter members as Raffaele Ciferri (Italy), Pedro Lavalle (Mexico) and Gerard A. De Vries (The Netherlands). The I.S.H.A.M.'s journal was initially called "Sabouraudia", later "Journal of Medical and Veterinary Mycology", to become nowadays "Medical Mycology" [Drouhet, 1997].

The genetist Guido Pontecorvo (1907-1999), called by his friends with the nickname "Ponte", born into a distinguished Jewish family in Pisa, Italy, was the older brother of the particle physicist Bruno and the filmmaker Gillo. Pontecorvo discovered the parasexual cycle in

fungi. In this process, haploid nuclei containing half the normal amount of genetic material in vegetative cells fuse to become diploid. The results are similar to those occurring in sexual reproduction, crossing over and recombination of genes (1954) [Pontecorvo, 1954].

The mycologist Alfonso Trejos (1921-1988) born in San Josè, Costa Rica, at the Laboratorio Bacteriológico (Laboratory of Bacteriology), Hospital San Juan de Dios, San José, described the second most common etiologic agent of chromoblastomycosis, *Cladosporium* (now *Cladophialophora*) *carrionii*, a species named in honor of his Puerto Rican colleague Arturo L. Carrión, from the School of Tropical Medicine, San Juan, Puerto Rico (1954) [Matsumoto and Ajello, 1998; San-Blas, 2000; Trejos, 1954].

The biochemist Leo Pine (1992-1994), at the National Institutes of Health (N.I.H.), Bethesda, Maryland, U.S.A., studied the conversion of the mycelial form of *Histoplasma capsulatum* and developed a three-amino-acid medium for yeast conversion (1954). Pine, together with Carl L. Peacock, of the same Institute (1958), confirmed earliest findings of Samuel B. Salvin, National Microbiological Institute, Rocky Mountain Laboratory, Hamilton, Montana, U.S.A., that were the sulfhydryl groups influenced by temperature to determine the form of growth of *H. capsulatum* (1949) [Espinel-Ingroff, 1996; Pine, 1954; Pine and Peacock, 1958; Salvin, 1949].

1955

William Gold, Helen A. Stout, Joseph F. Pagano and Richard Donovick, at the Squibb Institute for Medical Research, New Brumswick, New Jersey, U.S.A., isolated two antifungal compounds, Amphotericin A and Amphotericin B, from the culture broth of a *Streptomyces* sp. (1955). They showed that Amphotericin B was more potent against yeasts and filamentous fungi *in vitro* and *in vivo* but less soluble than Amphotericin A. Both Amphotericins A and B exerted antifungal therapeutic activity *in vivo* when administered

subcutaneously to experimentally infected animals. Richard E. Harrell and Arthur C. Curtis, from the Department of Dermatology, University of Michigan, Detroit, Michigan, U.S.A., successfully treated with intravenous Amphotericin B four cases of male patients affected by disseminated blastomycosis resistant to stilbamidine (1957) [Espinel-Ingroff, 1996; Gold et al., 1956; Harrell and Curtis, 1957].

John L. Converse, from the U.S. Army Biological Laboratories, Fort Detrick, Frederick, Maryland, U.S.A., was able to grow *in vitro* the spherules of *Coccidioides immitis* in a medium composed of glucose, inorganic salts and ammonium acetate, noting that the addition of an anionic surface-active agent allowed to keep the shape of the tissue form through serial transfers (1955) [Converse, 1955; Espinel-Ingroff, 1996].

Heinz Bauer, Elizabeth Adams and Useda Domingo Hernandez, of the Department of Pathology, Emory University, School of Medicine, Atlanta, Georgia, U.S.A., and Libero Ajello, of the Division of Mycotic Disesaes of the Communicable Disease Center (C.D.C.), Atlanta, were the first to isolate *Rhizopus arrhizus* (*R. oryzae*) (Fischer 1892) as a causative agent of rhinocerebral zygomycosis [Bauer et al., 1955; Espinel-Ingroff, 1996].

Chester W. Emmons, at the National Institute of Health (N.I.H.), Bethesda, Maryland, reported that *Cryptococcus neoformans* was often present in the pigeon stool, and that their feces represented a good substrate for the growth of the fungus. Emmons did not fully appreciate the significance of his observations due to the low incidence of cryptococcosis at the time [Emmons, 1955; Espinel-Ingroff, 1996].

1956

Edouard Drouhet, Gabriel Segretain and François Mariat, of the Institut Pasteur in Paris, France, founded the Société Française de Mycologie Médicale (S.F.M.M.) (1956) then

adopting the “Journal de Mycologie Médicale”, which replaced the “Bulletin de la Société Française de Mycologie Médicale”, as official journal (1990) [Viviani, 1999].

The Japanese Society for Medical Mycology (J.S.M.M.) was formed (1956) as successor to the Research Team on Candidiasis set up with Grant-in-Aid for Scientific Research from the Japanese Ministry of Education (1955). The aim of the Society was the development of Mycology in the medical field, but encompassing researchers in biology, immunology, pharmacy, agriculture, fishery, veterinary medicine, and food microbiology. A meeting was established to be held every year whose results will be then published in the Japanese Journal of Medical Mycology, the official organ of the Society (1960) [Homei, 2008].

Rolland P. Reynolds and Abraham I. Braude (1956), from the Departments of Medicine and Pathology, the University of Pittsburgh School of Medicine, the Presbyterian Hospital of Pittsburgh, Woman’s Hospital of Pittsburgh and Eye and Ear Hospital of Pittsburgh, Pittsburgh, Pennsylvania, U.S.A., described “the filament-inducing property of blood for *Candida albicans*”, which was comparable with the method of the American medical mycologist Claire L. Taschdjian (1914-1998) of the New York University, Maimonides Medical Center in Brooklyn, New York, U.S.A. The Doctoral thesis of the Scottish Donald W. R. Mackenzie, later Head of the Mycological Reference Laboratory, London School of Hygiene and Tropical Medicine, London, U.K., also explicitly included photomicrographs and described germ tube formation by *C. albicans* (1958) [Mackenzie, 1958; Reynolds and Braude, 1956].

1957

Lucille K. Georg and LaVerne B. Camp, of the Communicable Disease Center (C.D.C.), Public Health Service, U. S. Department of Health, Education and Welfare, Atlanta, Georgia, U.S.A., developed the procedures for the study of the nutritional requirements of

dermatophytes that were behind the production of commercial products (*Trichophyton* agars) for their identification in the clinical laboratory (1957) [Espinel-Ingroff, 1996; Georg and Camp, 1957].

Libero Ajello and Lucille K. Georg, at the Division of Mycotic Disesaes of the Communicable Disease Center (C.D.C.), based on the observation previously reported by the dermatologist Andrew McConnell Davidson (1885-1972), born in Edinburgh, Scotland, Lecturer of Dermatology at the University of Manitoba, Winnipeg, Manitoba, Canada, and the pioneer aerobiologist and mycologist Philips Herries Gregory (1907-1986), born in Exmouth, Devon, U.K., of the University of Manitoba Medical College, Winnipeg, (1934), on the ability of *Trichophyton mentagrophytes* to produce wedge shaped perforations in human and animal hair *in vitro*, developed a method of support for its distinction from *T. rubrum* [Ajello and Georg, 1957; Davidson and Gregory, 1934; Espinel-Ingroff, 1996].

1958

Douglas C. Heiner, of the Department of Pediatrics, University of Arkansas Medical Center (U.A.M.S.), Little Rock, Arkansas, U.S.A., improved (1958) the methodology (1949) of the Swedish physician Örjan Outcherlony (1914-2004), Professor of Bacteriology at Gothenburg University, Gothenburg, Sweden (1952-1980), member of the Royal Swedish Academy of Sciences (1968), for the serological diagnosis of histoplasmosis (detection of M and/or H band), obviating the poor specificity of the complement deviation reaction and the inadequacy of anti-complementary sera [Espinel-Ingroff, 1996; Heiner, 1958; Ouchterlony, 1949].

1959

Gabriel Segretain, at the Institut Pasteur in Paris, France, after accidental puncture of his finger, observed and described *Penicillium marneffei*, a dimorphic fungus having its natural reservoir in Vietnamese bamboo rats and representing the cause of an important (endemic and imported) opportunistic mycosis in human immunodeficency virus (H.I.V.)-infected patients (1959) [Segretain, 1959].

Edmund L. Keeney, Scripps Clinic and Research Foundation, La Jolla, California, U.S.A., and Milton Huppert, Mycology Research Laboratory, Veterans Administration Hospital, San Fernando, California, performed the first study on active immunization against superficial fungal infections (*Trichophyton mentagrophytes*) in experimental animals and human volunteer subjects, thus introducing the concept of antifungal vaccinology (1959) [Huppert and Keeney, 1959; Keeney and Huppert, 1959].

1960

The discovery of *Torula bantiana* by Guido Banti and Pier Andrea Saccardo (1911) would have remained neglected if it was not for Dante Borelli (1920-1998), medical mycologist born in Parma, Italy, of the Instituto de Medicina Tropical of the Universidad Central de Venezuela in Caracas, Venezuela, who imposed their publications to the attention of the mycological society. Borelli expressed the conviction (1960) that *Cladosporium trichoides*, a new species and agent of cerebral phaeohyphomycosis described by Chester W. Emmons, was identical to *T. bantiana*. He based his belief on the careful observation of unpublished microphotographs made by Saccardo of the conidiophores and conidial chains of *T. bantiana*, furnished by the Director of the Botanical Garden of Padua, Italy, Carlo Cappelletti, Saccardo' successor, and their comparison with the structures described in the Emmons' type culture of *C. trichoides*. Borelli stated that *T. bantiana* was a species belonging to the genus *Cladosporium* and proposed the new name of *Cladosporium bantianum* thus reducing *C.*

trichoides to the rank of a synonym of *C. bantianum* [Ajello, 1998; Banti, 1911a; Banti, 1911b; Saccardo, 1912; Saccardo, 1913].

Arturo Nannizzi was repaid by the rediscovery of *Gymnoascus gypseus* by the Australian Donald M. Griffin, of the School of Agriculture, University of Sidney, South Wales, Australia (1960). In recognition of the findings of Nannizzi (1961), Phyllis Stockdale (1927-1989), of the Commonwealth Mycological Institute, U.K., proposed the new genus *Nannizzia* to classify the teleomorphs of the *Microsporum* species, renaming *Gymnoascus gypseus* as *Nannizzia gypsea* (Nannizzi) Stockdale, 1964. Pino Pinetti (1924-1979), born in Molfetta, in province of Bari, Italy, graduated in Medicine at the University of Pavia, Italy, who succeeded his father-in-law as Director of the Dermato-Syphilitic Clinic of the University of Cagliari, Sardinia, Italy, where he founded the "Centro di Studi Micologici" (Center for Mycological Studies), summarized the unpleasant dispute on the discovery of *M. gypseum* teleomorph in his tribute to the memory of Arturo Nannizzi with the following words "The fundamental observations carried out by Nannizzi long ago in 1927 have thus found a precise and definitive confirmation. Regretfully, Arturo Nannizzi was unable to learn of this authoritative confirmation and he closed his eyes forever poor and forgotten without the confort of at long last seeing his most original scientific achievement finally confirmed after so many years of bitterness ans delusions" (1962) [Ajello, 1998; Griffin, 1960; Pinetti, 1962a; Stockdale, 1961; Stockdale, 1964].

1961

Following the studies of Dante Borelli, Raffaele Stigliani, Director of the Istituto di Anatomia e Patologia (Institut of Anatomy and Pathology) of the University of Modena, Italy, published a detailed study of the historical case of Guido Banti that had never been described before (1961). The study contained the original drawings of the dematiaceous hyphae of

Torula that Banti observed in the victim's brain and relative elicited tissue reactions. Photomicrographs of histological preparations of the patient's brain and brain of rabbits experimentally infected with *T. bantiana* by Banti himself were also reported. The study of Stigliani unequivocally proved that the strain was correctly identified as a *Cladosporium* species, earning the name *Cladosporium bantianum* (Saccardo, 1912) Borelli, 1960 [Ajello, 1998; Stigliani, 1961].

Herbert F. Hasenclever and William O. Mitchell, of the Department of Health, Education and Welfare, Public Health Service, Department od Allergy and Infectious Diseases, National Institutes of Health (N.I.H.), Bethesda, Maryland, U.S.A., studying the structure of mannans in the cell-wall, identified two serotypes, A e B, in *Candida albicans* [Espinel-Ingroff, 1996; Hasenclever and Mitchell, 1961].

1963

Dante Borelli's thesis was rejected by Chester W. Emmons, Chapman H. Binford, John P. Utz and Kyung J. Kwon-Chung in the first (1963) and then subsequent editions (1970, 1977) of the textbook "Medical Mycology". Their refusal was based primarily on the description of Pier Andrea Saccardo of "a fungus with unbranched conidiophores, bearing short, unbranched chains of only five to ten spores, the spores being nearly twice the size of spores of *Cladosporium trichoides*, indicating that the two fungi were quite different and, indeed, definitely excludes *Torula bantiana* from the genus *Cladosporium*" [Ajello, 1998; Emmons et al., 1963; Emmons et al., 1970; Emmons et al., 1977].

1964

Donald B. Louria and Robert G. Brayton, from the Infectious Disease Laboratory, Second (Cornell) Medical Division, Bellevue Hospital, New York, U.S.A., observed that *Candida*

albicans hyphae penetrated viable neutrophils *in vitro* and *C. albicans* cells survived when phagocytosed within the leukocytes after their intravenous administration in mice (1964). These results were preliminary to the studies of Robert I. Lehrer and Martin J. Cline, from the Cancer Research Institute and the Department of Medicine, University of California Medical Center, San Francisco, California, U.S.A., designed to quantitatively assess the candidacidal activity of human leukocytes and serum from healthy individuals and patients with fungal infections (1969). Their studies demonstrated the fundamental role exerted by leukocytes in the immunity against candidiasis and that the lysosomal enzyme myeloperoxidase and its oxidant substrate, hydrogen peroxide, were important in the lethal activity of neutrophils against *C. albicans* [Espinel-Ingroff, 1996; Lehrer and Cline, 1969; Louria and Brayton, 1964].

The oral antifungal agent 5-Flucytosine was developed in the Laboratories of Hoffmann-La Roche in Basel, Switzerland, by Daniel Tassel, from the Departments of Medicine, Choate Memorial Hospital, Woburn, Massachusetts, U.S.A., and Morton A. Madoff, from Tufts University School of Medicine, Medford/Somerville, near Boston, Massachusetts, and the Medical Services of the Lemuel Shattuck Hospital, Massachusetts, Department of Public Health (1964). They observed that 5-Flucytosine was effective in the treatment of candidiasis and cryptococcosis in two patients and experimentally infected mice (1964). Edward R. Block, Anne E. Jennings and John E. Bennett, from the Laboratory of Clinical Investigation, National Institute of Allergy and Infectious Diseases, and the Department of Clinical Pathology, Clinical Center, National Institutes of Health (N.I.H.), Bethesda, Maryland, U.S.A., reported the first case of induction of resistance to 5-Flucytosine in a patient treated for cryptococcosis (1973). Smith Shadomy, from the Department of Medicine, Medical College of Virginia, Virginia Commonwealth University, Richmond, Virginia, U.S.A., conducted the first systematic study on the synergistic activity of 5-Flucytosine with

amphotericin B against *C. neoformans* (1969) [Block et al., 1973; Espinel-Ingroff, 1996; Shadomy, 1969; Tassel and Madoff, 1968].

1965

The German physician and veterinarian Friedrich Staib (1925-2011), born in Uhingen, Württemberg, Germany, Head of the Mycological Laboratory at the University of Würzburg's Institute for Hygiene and Microbiology, Würzburg, Germany, reported on the production of proteinases in *Candida albicans* (1965) which were later characterized by Reinhard Ruchel, from the Department of Medical Microbiology, Institute of Hygiene, University of Gottingen, Gottingen, Germany, as different strain-dependent enzymes (1981). Kyung J. Kwon-Chung, at the National Institute of Allergy and Infectious Diseases, Bethesda, Maryland, U.S.A., in collaboration with Donna Lehman, Carol Good and Paul T. Magee, of the Department of Microbiology and Public Health, Michigan State University, East Lansing, Michigan, U.S.A. (1985), definitely characterized them as specific virulence factors in experiments conducted in a mouse model with a proteinase deficient mutant, its parent, and one proteinase producing revertant (1985) [Espinel-Ingroff, 1996; Kwon-Chung et al., 1985; Ruchel, 1981; Staib, 1965].

1966

The American Roger Storck, from the Department of Microbiology, The University of Texas, Austin, Texas, U.S.A. (1966) and, later (1968), Axel Stenderup and Leth A. Bak, from the Institute of Medical Microbiology, University of Aarhus, Aarhus, Denmark, investigated the nucleotide composition of DNA from filamentous fungi and 18 species of the genus *Candida*, including *C. albicans* and *C. tropicalis*. Storck and Stenderup found that the mean base composition, most frequently expressed as the percent guanine plus cytosine content, was

variable among the species studied and that this kind of analysis could have taxonomic and phylogenetic value, thus introducing to the field of molecular mycology (1968) [Espinel-Ingroff, 1996; Stenderup and Leth Bak, 1968; Storck, 1966].

1967

Glenn S. Bulmer, Professor Emeritus of Microbiology and Immunology, Mary Delaine Sans and C. M. Gunn, from the Department of Microbiology, University of Oklahoma School of Medicine, Oklahoma City, Oklahoma, U.S.A., studied the capsular mutants of *Cryptococcus neoformans* with regard to virulence (1967). They found that non-encapsulated mutants were initially avirulent for mice, but after several months of subculturing were able to revert to the encapsulated state regaining various degrees of virulence. They also found that phagocytosis was approximately three times more effective when nonencapsulated mutants were used, which indicated that the polysaccharide capsule inhibited the phagocytosis of *C. neoformans* [Bulmer and Sans, 1967; Bulmer et al., 1967; Espinel-Ingroff, 1996].

1968

W. Marcus Newberry, John W. Chandler, Tom D. Y. Chin and Charles H. Kirkpatrick, from the National Communicable Disease Center, Bureau of Disease Prevention and Environmental Control, Public Health Service, Department of Health, Education and Welfare, Atlanta, Georgia, U.S.A., and the Department of Medicine, University of Kansas, School of Medicine, Kansas City, Kansas, U.S.A., investigated the stimulation or the transformation by histoplasmin of peripheral blood lymphocytes from both histoplasmin-negative and -positive individuals and in patients either with acute or chronic histoplasmosis (1968). Using the uptake of a radioactive DNA precursor as a more “sensitive indicator” of lymphocyte transformation, they observed that lymphocyte transformation was depressed in

chronically ill patients. These findings gave evidence that cellular immunity was an important factor in chronic histoplasmosis [Espinel-Ingroff, 1996; Newberry et al., 1968].

1969

John W. Rippon, Professor Emeritus at the University of Chicago, Chicago, Illinois, U.S.A., and Edward D. Garber, from the Department of Medicine, Section of Dermatology and the Department of Biology, The University of Chicago, undertook pioneer enzymologic studies in dermatophytes, associated the yield of elastase and collagenase with the more virulent forms of dermatophytoses and established that the production of enzymes also correlated with mating types (1969) [Espinel-Ingroff, 1996; Rippon and Garber, 1969].

The plant ecologist Robert Harding Whittaker (1920-1980), born in Wichita, Kansas, U.S.A., held teaching and research positions at Washington State College in Hanford, Washington, U.S.A., the Hanford National Laboratories, Washington, (where he pioneered use of radioactive tracers in ecosystem studies), Brooklyn College, New York, U.S.A., University of California-Irvine, California, U.S.A., and, finally, Cornell University, Ithaca, New York. Based on peculiar physiological characteristics (biosynthesis of lysine by L-α-aminoadipic acid, occurrence of chitin in the cell-wall), Whittaker was the first to propose the five-kingdom taxonomic classification of the world's *biota* into the *Animalia*, *Plantae*, *Fungi*, *Protista* and *Monera* which represented a crucial boost in the development of mycology as a distinct science (1969) [Espinel-Ingroff, 1996; Whittaker, 1969].

1970

Martha D. Berliner and Maria E. Reca, from the Department of Microbiology, Harvard School of Public Health, Boston, Massachusetts, U.S.A., succeeded in the production of living protoplasts from albino and brown types of *Histoplasma capsulatum* as tools to study

the cell wall composition, physiology, cytology and genetics of fungi and preceeding the studies of Alvin Sarachek, Douglas D. Rhoads, Robert H Schwarzhoff, from the Department of Biological Sciences, Wichita State University, Wichita, Kansas, U.S.A., in *Candida albicans* (1981) [Berliner and Reca, 1970; Espinel-Ingroff, 1996; Sarachek et al., 1981].

H. Jean Shadomy, from the Department of Microbiology, Medical College of Virginia, Virginia Commonwealth University, Richmond, Virginia, U.S.A., as a result of her studies on *Cryptococcus neoformans* regarding the production of hyphae and the occurrence of "clamp connections", included the yeast in the *Basidiomycetes* (1970). Kyung J. Kwon-Chung, at the National Institutes of Health (N.I.H.), Bethesda, Maryland, U.S.A., using a selective medium (40% sucrose and growth factors), observed a basidiomycetous state in four pairs of *C. neoformans* that she named *Filobasidiella* (1975), now distinguished into the varieties *neoformans*, anamorph *C. neoformans* var. *neoformans*, and *bacillispora*, anamorph *C. neoformans* var. *gattii*, then *Cryptococcus gattii* (Vanbreuseghem & Takashio) Kwon-Chung & Boekhout, 2002 [Espinel-Ingroff, 1996; Kwon-Chung, 1975a; Shadomy, 1970].

1971

Description of:

Kluyveromyces marxianus (Hansen) van der Walt, 1971/*Candida kefyr* (Beijerinck) van Uden & Buckley, 1983

1972

Kyung J. Kwon-Chung, at the National Institutes of Health (N.I.H.), Bethesda, Maryland, U.S.A., identified two mating types (1 and 2) among natural and clinical isolates of *Histoplasma capsulatum* and named the teleomorph *Emmonsiella capsulata*, in honor of her mentor Chester W. Emmons. Kwon-Chung also reported (1975) that the sexual state of *H.*

duboisii was identical *to E. capsulata* “because the cleistothecia and ascospores produced by mating *H. capsulatum* and *H. duboisii* were identical to those of *E. capsulata*”. *Histoplasma duboisii*, therefore, should be regarded as a variety of *H. capsulatum* rather than a separate species. Michael R. McGinnis and B. Katz, transferred *E. capsulata* to the genus *Ajellomyces*, so named in honor of Libero Ajello (1979) [Espinel-Ingroff, 1996; Kwon-Chung, 1972; Kwon-Chung, 1975b; McGinnis and Katz, 1979].

1974

Libero Ajello, and Lucille K. Georg, from the Center for Disease Control (C.D.C.), Atlanta, Georgia, U.S.A., the Professor of Medicine, Pathology, Microbiology and Pharmacology Roy T. Steigbigel, from Stanford University, Division of Infectious Diseases, Stanford, California, U.S.A., and the Professor Emeritus of Botany and Mycology Chun Juan K. Wang, State University of New York, College of Environmental Sciences and Forestry, Department of Forest Botany and Pathology, Syracuse, New York, U.S.A., described the new species *Phialophora parasitica* (now *Phaeoacremonium parasiticum*) using a strain isolated, for the first time, from a subcutaneous infection in a patient undergoing a kidney transplant [Ajello et al., 1974; Espinel-Ingroff, 1996].

Juneann W. Murphy, Jay A. Gregory and Howard W. Larsh, from the Department of Botany and Microbiology, University of Oklahoma, Norman, Oklahoma, U.S.A., developed animal models (guinea pigs, mice) to investigate the mechanism of pathogenicity in cryptococcosis (1974). T-lymphocyte-mediated mechanisms appeared to be the primary defense of host immunity in this disease as well as in other mycoses, such as histoplasmosis (1977, 1979), coccidioidomycosis (1977, 1978), aspergillosis (1978), mucormycosis (1978) and candidiasis (1978) [Artz and Bullock, 1979; Beaman et al., 1977; Diamond and Krzesicki, 1978;

Diamond et al., 1978; Espinel-Ingroff, 1996; Galgiani et al., 1978; Howard and Otto, 1977; Murphy et al., 1974].

1976

Dante Borelli described *Pyrenochaeta mackinnonii*, named in honor of his former Uruguayan mentor Juan Mackinnon (1905-1987), Professor of Medical and Parasitology Natural History at the Faculty of Medicine of the University of Montevideo, Uruguay [Marcano, 1997; San-Blas, 2000].

Paul G. Standard and Leo Kaufman, at the Division of Mycotic Diseases of the Center for Diseases Control (C.D.C.), Atlanta, Georgia, U.S.A., developed the exoantigen test for the serological identification of mycelial cultures of *Histoplasma capsulatum* (1976). This technique was then adapted for the diagnosis of many other fungal cultures, leading to the production of commercial exoantigen kits available since the 1980s [Espinel-Ingroff, 1996; Standard and Kaufman, 1976].

Description of:

Pneumocystis jirovecii Frenkel, 1976

1977

The American medical mycologist Libero Ajello (1916-2004), born in New York City, U.S.A., formed under the tutelage of Rhoda Benham, working for 43 years at the Center for Disease Control (C.D.C.), Atlanta, Georgia, U.S.A., where he became the Director of the Division of Mycotic Diseases, was the first to adopt the concept of "milestones" to report fundamental contributions to our knowledge of the mycoses (1977) [Ajello, 1977].

The Asociaciòn Espanola de Micologia (Spanish Association of Mycology) was founded (1977) and the "Revista Iberoamericana de Micología" (Iberoamerican Journal of Mycology)

was adopted as official journal together with the Asociaciòn Venezolana de Micologia (Venezuelan Association of Mycology) and the Asociaciòn Argentina de Micologia (Argentinian Association of Mycology) (1990).

Pino Pinetti's mycological studies on dermatophytes were summarized in his book "Le Dermatofizie" (The dermatophytoses) (1977), published two years before his death (1979). Ferdinando Serri (1916-1995), Director of the Istituto di Dermatologia (Institute of Dermatology) of the Faculty of Medicine of the Catholic University in Rome, Italy, in his memorial, acknowledged that "Pinetti'death left a great emptiness in the field of dermatology as a whole" (1979) [Ajello, 1998; Pinetti, 1959; Pinetti, 1961; Pinetti, 1962b; Pinetti, 1964; Pinetti, 1977; Riva, 1979; Serri, 1979].

Michael R. McGinnis, from the Departments of Pathology, Microbiology and Immunology, University of Texas Medical Branch at Galveston, Texas, U.S.A., revised the clinical nomenclature and clarified the taxonomy of nine human pathogenic species of *Exophiala*, *Phialophora*, and *Wangiella*. The original classification of Pier Andrea Saccardo was based on an artificial system of classification neglecting natural relationships and causing confusion because of the pleomorphic nature of many of the black fungi (1977) [Espinel-Ingroff, 1996; McGinnis, 1977].

Bruno Maresca, then at the International Institute of Genetics and Biophysics, Naples, Italy, Gerald Medoff, Division of Infectious Diseases, Washington University School of Medicine, Washington, U.S.A., David Schlessinger, Chief, Laboratory of Genetics, National Institute on Aging, National Institutes of Health (N.I.H.), Bethesda Maryland, U.S.A., George S. Kobayashi (1927-2005), a chemist and mycologist born in San Francisco, U.S.A., Professor of Medicine and Molecular Microbiology at the Washington University in Saint Louis, Missouri, U.S.A., and Judith Medoff, Department of Biology, St. Louis University, St. Louis, Missouri, investigated the role played by sulfhydryl groups in defining the phases of

Histoplasma capsulatum growth. They found that the temperature of 37° C caused a series of biochemical reactions resulting in variations of the intracellular level of cyclic AMP that was proven to be fivefold higher in the mycelial than in the yeast form. This alteration was considered determinant for the morphological shape and the pathogenic potential of the dimorphic fungus (1977). Maresca and coworkers also stated that cysteine stimulated oxygen consumption in the yeast but not in the mycelial form and suggested a model to describe the peculiar biochemical events that occur during the temperature-induced form transitions of *H. capsulatum* [Espinel-Ingroff, 1996; Maresca et al., 1977].

Description of:

Exophiala jeanselmei (Langeron) McGinnis & Padhye, 1977

1978

Description of:

Candida glabrata (Anderson) S.A. Meyer & Yarrow, 1978

1979

Ayodele F. Olaiya and Stephen J. Sogin, from the Department of Biology, University of Houston, Houston, Texas, U.S.A., microfluorometrically studied the DNA content of haploid, diploid, triploid, and tetraploid strains of *Saccharomyces cerevisiae* in comparison to that of *Candida albicans*. They determined that *C. albicans* was characterized by a diploid amount of DNA. This finding was contrary to the consolidated belief that *C. albicans*, as other species in the genus, was a haploid yeast and introduced to important achievements on the fungal genetics (1979). These remarks were supported by the studies of William L. Whelan, of the Department of Biochemistry, University of Cambridge, Cambridge, U.K., Roger M. Partridge and Paul T. Magee, of the Department of Microbiology and Public Health,

Michigan State University, East Lansing, Michigan, U.S.A., on the induction of mitotic recombination in auxothrophic strains obtained by U.V. irradiation (1980) [Espinel-Ingroff, 1996; Olaiya and Sogin, 1979; Whelan et al., 1980].

Errol Reiss and Paul F. Lehmann, at the Immunology Branch, Division of Mycotic Diseases, Center for Disease Control (C.D.C.), Public Health Service, U.S. Department of Health and Human Services, Atlanta, Georgia, U.S.A., studied the occurrence of specific antigens in the serum of animals undergoing experimental infections with *Aspergillus fumigatus* (1978). They characterized galactomannan as the circulating factor in case of invasive aspergillosis (1979), leading to the formulation of commercial kits currently available as potential diagnostic marker [Lehmann and Reiss, 1978; Reiss and Lehmann, 1979].

Timothy E. Kiehn, Edward M. Bernard, Jonathan W. M. Gold and Donald Armstrong, of the Infectious Disease Service, Department of Medicine, Memorial Sloan-Kettering Cancer Center, New York, U.S.A., during their studies on the detection of mannose, found, by liquid gas chromatography, arabinitol occurring in the serum of patients affected by disseminated candidiasis (1979). Brian Wong and Karen L. Brauer, of the Department of Internal Medicine, University of Cincinnati College of Medicine, Cincinnati, Ohio, U.S.A., then credited arabinitol as a possible diagnostic marker, reporting that infected patients had elevated serum levels of D-arabinitol and normal levels of L-arabinitol (1988) [Espinel-Ingroff, 1996; Kiehn et al., 1979; Wong and Brauer, 1988].

1981

Michael R. McGinnis in collaboration with Dante Borelli (1981) and, successively, with Borelli himself, Libero Ajello and Arvind A. Padhye (1986), of the Division of Mycotic Diseases of the Centers for Disease Control (C.D.C.), Atlanta, Georgia, U.S.A., accurately revised the type material for *Cladosporium bantianum* and the type culture of *C. trichoides*.

They compared them to many other cultures identified as *C. bantianum* or *C. trichoides*, isolated from different sources (cat, dog, human, sawdust, soil, tree). Differently from the findings of Chester W. Emmons, Chapman H, Binford and John P. Utz (1963), they observed that Guido Banti's isolate was characterized by long branching chains made up of more than 5-10 conidia, the size of which was included in the range of variation referable to the cultures of *C. bantianum* that they investigated [Ajello, 1998; Emmons et al., 1963; McGinnis and Borelli, 1981; McGinnis et al., 1986].

1982

John N. Galgiani, Professor of Medicine, Director of the Valley Fever Center for Excellence, Program Director for Infectious Diseases, University of Arizona, Tucson, Arizona, U.S.A., was deputed (1982) by the National Committe for Clinical Laboratory Standard (N.C.C.L.S.), then renamed (2005) Clinical Laboratory Standard Institute (C.L.S.I.), a volunteer driven, membership supported, nonprofit, standards organization with headquarters located in Philadelphia, Pennsylvania, U.S.A., promoting the development and use of voluntary laboratory consensus standards and guidelines within the health care community, to constitute a sub-committe with the aim to define the guidelines for the *in vitro* drug susceptibility testing of antifungal drugs against yeasts (1992) and moulds (1995) [Espinel-Ingroff, 1996].

Eric S. Jacobson and Herschell S. Emery, from the Department of Microbiology and Immunology, Virginia Commonwhealth University, Richmond, Virginia, U.S.A., investigated the phenotypic and genetic characteristics of capsular mutants in *Cryptococcus neoformans*. They reported that chromosomal genes, not linked to auxotrophic markers, were responsible for the synthesis of the capsule (1982). Afterwards, Jacobson and Emery demonstrated genetically a correlation between melanization, resistance to oxygen toxicity and virulence in *C. neoformans* and stated that melanin protected the yeast against the

oxidants of the leukocytes (1991) [Espinel-Ingroff, 1996; Jacobson et al., 1982; Jacobson and Emery, 1991].