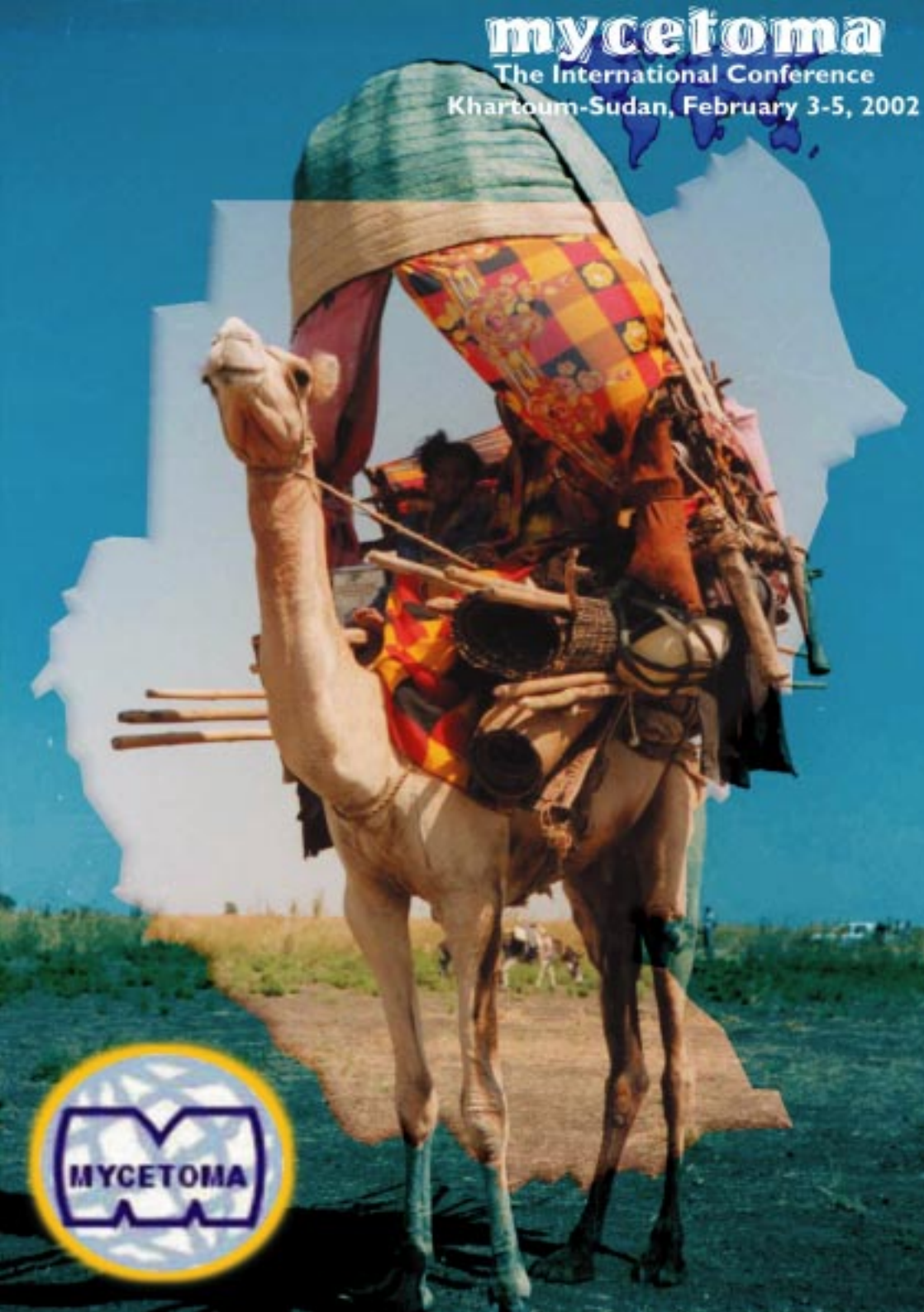
mycetoma

The International Conference

Khartoum-Sudan, February 3-5, 2002




An Invitation
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The International Conference
Khartoum-Sudan, February 3-5, 2002
The Organizing Committee
of the Mycetoma International Conference
is pleased to invite you to its Opening Ceremony
at the Friendship Hall
on Saturday February 2, 2002 at 7:00 PM
The Opening Ceremony will be honoured by
His Excellency the Vice President of the Republic of the Sudan
The Organizing Committee Would Also Like To Invite You
To Its Scientific Sessions Which Will Take Place
During The Period February 3-5, 2002 Daily At 9:00 AM
At the Grand Holiday Villa, Khartoum
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Abstracts

Amikacine-Trimethoprim-Sulfamethoxazole in the Treatment of Actinomycetoma

Oliverio Welsh Lozano
Department of Dermatology, University Hospital, U.A.N.L. Monterrey, Mexico.

Actinomycetomas are infectious diseases caused by actinomycetic aerobic bacteria that affect the skin and the underlying tissues. It is characterized by a firm increased volumen of the affected area, and the presence of nodules and abscesses, that contain granules of the causative agent. In Mexico, the largest percentage of the cases is caused by N. brasiliensis. The purpose of this study is to present the therapeutic results of this disease treatment with Amikacine-Trimethoprim-Sulfamethoxazole (TS).

Fifty-one adult patients with actinomycetoma were included in the study; all of them had a poor response to traditional treatments or risk to dissemination to an organ or joint. The patients with auditive, renal or hepatic pathologies as well as pregnant women, patients with allergy to any of the antimicrobiens were excluded from the study. In 44 patients the primary cause of the disease was the N. brasiliensis, A. madurae in 4, N. sp in 2 and in 1 N. asteroides. The treatment was given in cycles of five weeks in each cycle amikacine 15 mg/kg/day was administrated during 3 weeks and trimethoprim-sulfamethoxazole 8 and 40 mg/kg/day during the 5 weeks.

Of the 51 patients studied, 19 received one cycle, 15 received 2 cycles, 15 received 3 cycles and two patients received 4 cycles. One of the patients that received 3 cycles had a recurrence of the disease. The therapeutic outcome with these

antimicrobials was superior at those historically reported using other combinations and antimicrobials. The complications were observed in 20% of the cases and were characterized by a minimal decrease of high tones audition only detected by audiometry.

Amikacin T-S treatment has been the most efficient therapeutic for this disease with a cure rate above 90%.

This treatment is indicated for cases unresponsive to traditional therapy. The patients treated must have periodic creatinine clearance and audiometries before each cycle of treatment.

An Experimental Model of Madurella Mycetomatis Infection (Eumycetoma) In Mice

Abdalla Ahmed[1,2], Irma Bakker[1], Alex van Belkum[1], Ahmed Fahal[2] and Henri Verbrugh[1]

1. Department of Medical Microbiology and Infectious Diseases, Erasmus University Medical Center Rotterdam 2. Mycetoma Research Group, Institute of Endemic Diseases, University of Khartoum, Sudan

Few investigators were successful in developing Madurella mycetomatis infection in laboratory animals with characteristic black grains, but a reproducible animal model for this infection has not been reported. We infected Balb/c mice with various inocula of M. mycetomatis mycelia, ranging from 0.8 to 120 mg wet weight, suspended in sterilized soil (4 mg/mL) as a natural adjuvant. Mice differed with respect to their immune status, being immuno-competent (adult or young) or immuno-compromised after treatment with corticosteroids or cyclophosphamide. Various routes of inoculation (s.c., i.p. or i.v.) were used. To monitor the course of infection, mice were sacrificed at various intervals (day 17-51) after inoculation, and checked for the presence of black grains. Several organs were cultured for viable M. mycetomatis and/or bacteria. From infected organs histopathological studies were performed. In addition, survival of mice was monitored.

It was found those immuno-competent female mice, either young (6 wks old) or adult (12 wks old), developed M. mycetomatis infection with the characteristic black grains, in an inoculum-dependent way. Abdominal mycetomas with many mature black grains were seen at day 17 after i.p. inoculation of at least 40 mg. Increasing the inoculum up to 120 mg resulted in an increase in infection rate up to 75%. Immuno-competent male mice seemed to be most susceptible to the infection, but showed higher mortality rates. After subcutaneous inoculation of female mice in few cases typical mycetoma lesions were seen only in corticosteroids-treated mice.

Future studies using this model will focus on the pathogenesis, as well as prevention and treatment of the infection.

Contributions to the Study of Mycetoma from Sudan over a Century

ES Mahgoub

Gill in 1942, in his dispensary report from Madura district in Southern India, drew the attention to a disease of the foot which produced swelling, deformity and fungoid excrescencies discharging an offensive ichorous fluid. This was the first recorded case of Mycetoma.

About 60 years later we have the first published record of Mycetoma from Sudan, by Balfour in 1904. From then onwards, Sudanese studies started to gain

momentum and access to international literature. This is basically due to the endemicity of the disease, the keenness of researchers and the quality of studies. Studies by British scientists cover the period from the beginning of the 20th.Century up to 1964, and those by Sudanese scientists from 1964 to date.

Contributions from Sudan covered all aspects of the disease in an attempt to understand the biological nature of mycetoma namely: the clinical, pathological, mycological, immunological and epidemiological aspects, as well as diagnostic procedures and treatment.

Such rich information has been documented in Books, numerous papers in local and international Journals, Theses in Sudanese and British Universities, International Lectures and Conferences and of late as Electronic Publications and the first Web Site.

This paper highlights the work of past and present scientists whose aim in the first place was and still is to understand the disease and consequently provide the best of care to those who suffer from Mycetoma, not only in Sudan but to sufferers in the world at large.

Cranio-Spinal Mycetoma; The Surgical Option?

Mohamed A.R. Arbab, M.D, Ph.D.
Department of Surgery, University of Khartoum. National Centre of Neurological Sciences. P.O Box 102 Khartoum. E-mail: mohamedarbab@hotmail.com

Objective: Although mycetoma of the nervous system is uncommon, more patients continue to present with varying neurological deficits. This study aims to analyze retrospectively the clinical criteria that necessitated surgical intervention in twenty patients with mycetoma of the cranium and spine whom underwent surgery.

Methods: Twenty- six patients with mycetoma of the head and spine were seen at the Neurosurgical department, National Centre of Neurological Sciences between 1990-2000. All patients had full clinical examination with special emphasis on the neurological status. The diagnosis of mycetoma was made through serological tests, countercurrent immunoelectrophoresis (CIE), and culture of aspirates and histopathological identification of the organism. The clinical criteria that indicated the surgical intervention were reviewed.

Results: Patients were aged 14-45 years (mean 34 years). Serological tests were positive in 10 patients (38%). Twenty patients (16 cranial and 4 spinal) underwent surgical intervention either to establish the diagnosis (4 patients) or to resect the pathology (16 patients). Sixteen patients with cranial mycetoma were subjected to surgery because of increasing focal neurological deficit and/or alarming symptoms and signs of increase intracranial pressure (12 patients); the remaining four patients were operated upon for diagnostic biopsy. The four spinal patients all underwent excision surgery. Six patients with multiple neurological deficits were treated medically. The causative organism was found to be Streptomyces somaliensis in 21 patients, Madurella mycetomatis in 3 patients, Actinomadura and Actinomyces pelletierii in one patient each.

Conclusion: Serological tests alone can miss patients with CNS mycetoma. Results of treatment of CNS mycetoma by multiagent chemotherapy has its beneficial effect, however, advancement of neurological deficits makes the surgical option a necessity, while widespread pathology limits that option.

Epidemiology of Mycetoma in India

H C. Gugnani
Department of Medical Mycology, Vallabhbhai Patel Chest Institute, University of Delhi Delhi-110007, India

The earliest descriptions and documented reports of mycetoma were from India during the period 1842-1874. Etiological studies of mycetoma have been undertaken during the past five decades. Both actinomycetoma and eumycetoma have been reported from several parts of the country with widely variable geographic conditions. Actinomycetoma is more common in southern part than in the northern part. The States of Tamil Nadu and Andhra Pradesh in the south, West Bengal in the east, and Rajasthan in northwest represent highly endemic areas. The pattern of etiological agents varies with the geographic areas. White-grained mycetoma due to Pseudallescheria boydii, Acremonium kiliense, A. receife and A. falciforme is known from parts of eastern, western and southern India. Black-grained mycetoma due to Madurella mycetomatis has been reported from many parts of India, wherever the disease has been looked for. Mycetoma due to M. griesa has been reported in a few cases from Tamil Nadu, Rajasthan, and Chandigarh. A few cases due to Leptosphaeria senegalensis and L. tompkinsii are known from Tamil Nadu. Exophiala jeanselmei has also been known to cause mycetoma in a few cases originating from several parts if India. A few cases caused by Curvularia lunata and Cylindrocarpon sp have also been reported. Yellow-grained mycetoma due to Actinomadura madurae and red-grained mycetoma due to Actinomadura pelletieri have been frequently reported from several areas in southern, western (including the semi-arid northwestern part, viz. Rajasthan), and central India. Streptomyces somaliensis induced mycetoma is very common in semi-arid areas of Rajasthan. Cases of mycetoma due to Nocardia brasiliensis have been frequently reported from several parts of India. Mycetoma due to N. asteroides and N. otitidiscaviarum is rare; however, a large series of cases caused by N. asteroides has been recorded in the eastern State of West Bengal. Mycetoma is scarcely reported from several North Indian States, viz. Delhi, Uttar Pradesh, Himachal Pradesh, Jammu & Kashmir and Bihar. The single predominant etiological agent may also vary with geographic locale. Madurella mycetomatis appears to be the principal agent of mycetoma in northwest region, N. brasiliensis and A. pelletieri in southern part while Madurella mycetomatis and Nocardia species (mainly N. brasiliensis) appear to be equally common in the northern part of the country. In the State of Rajasthan, a very large are of high endemicity, the ratio of eumycetoma to acinomycetoma is 3.2:1 in north-west region with annual rainfall of less than 350 mm, 1.5:2 in central region with annual rainfall of 350-550 mm and 1:2 in south-east part with annual rainfall of more than 650 mm. Foot is the predominant site of infection in mycetoma but a good proportion (10-38 per cent) of cases involve other sites, viz. upper extremities, axilla, trunk, shoulder, face, forehead, jaw, scalp, neck, groin, hips and perineum, and middle ear cleft. Bone involvement occurs in about 25% of the cases with soft tissue invasion, being more frequent in mycetoma caused M. mycetomatis than in that caused by

actinomycetes. Primary osseous lesions occur in about 3% of the patients. Most cases of mycetoma are aged 20-40 years, males being more frequently affected than the females. The disease occurs more commonly in farmers, field labourers or herds' men who come in contact with soil in endemic areas where fungi and actinomycetes causing mycetoma are present. In the highly endemic semi-arid and arid areas of Rajasthan, thorny trees like Acacia are abundant. The role of prick injury with Acacia followed by contact with soil in the causation of mycetoma has been emphasized. In one study, Madurella sp. was recovered from soil in an area of high endemicity of mycetoma; P. boydii and E. jeanselmei have also been recovered from soil in some parts of India. Isolation of Nocardia asteroides, N. brasiliensis and N. otitidiscaviarum from soil has been reported from several pars of the country. The role of fine needle aspiration and development of serological methods in early diagnosis of mycetoma is emphasized.

Epidemiology of Mycetoma in West Africa with Special Reference to Nigeria

H. C. Gugnani
Dept. of Medical Mycology, V. P. Chest Institute University of Delhi, Delhi-110007, India

Mycetoma is common in tropical and subtropical regions of Asia, America and Africa. In Africa, a high endemicity of the disease has been noted in the Sahelian belt stretching from Senegal and Mauritania in the west to Somalia and the Republic of Djibouti in the east where there are long dry seasons and short rainy seasons. In West Africa, the number of cases reported from Anglophone countries is relatively much smaller than that from Francophone countries. Despite the fact that deep mycoses are frequently reported from several parts of Nigeria, mycetoma is only scantly recorded. Actinomycetoma is much more prevalent than eumyctoma in West Africa, the pattern of etiological agents varying with the climate. In southern Nigeria, where the rainfall is heavy, actinomycetoma (manly caused by N. brasiliensis) is much more prevalent than eumycetoma (manly caused by Madurella mycetomatis) while in the arid or semi-arid northern Nigeria, both types of mycetoma are more or less equally common. Streptomyces somaliensis is exclusively recorded in the drier areas of northern Nigeria; other etiological agents of actinomycetoma include Actinomadura pelletieri and N. brasiliensis. Also in Mali, actinomycetoma appears to be more common with Actinomadura pelletieri, A. madurae and Streptomyces somaliensis as the etiological agents in order of frequency; eumycetoma is caused generally by M. mycetomatis and rarely by Leptosphaeria senegalensis. In Niger, S. somaliensis and A. pelletieri are the commonest agents of actinomycetoma in northern and southern zones respectively, eumycetoma due to M. myctematis being recorded from both areas. Actinomadura pelletieri is again the predominant agent of mycetoma in the very humid southern part of Senegal while in the northern part M. mycetomatis and L. senegalensis are predominant. Foot is the commonest site of infection but leg, thigh, hand, arm, and buttocks are frequently involved. Some unusual localization of mycetoma due to M.

mycetomatis, viz. skull, neck, occipit, orbit, and paranasal sinuses have been recorded in some West African countries, viz. Nigeria, Niger, Mali and Mauritania. Most of the cases occur in farmers and herdsmen who live in rural areas and frequently sustain minor penetrating wounds by thorns or splinters. Nocardia transvalensis recorded as a rare etiological agent of mycetoma in South Africa has been found to cause mycetoma of the thumb in one case in Nigeria. In experimental studies, N. transvalensis was able to cause mycetoma of the skin and footpad of laboratory mice. Similar lesions in mice were also experimentally produced by Streptomyces griseus. Cases of mycetoma due to Pseudallescheria boydii, a universally recognized agent of have also been reported from many countries in West Africa. It is presumed that the etiological agents of mycetoma are associated with soil and woody plants. A comprehensive investigation on the natural occurrence of etiological agents of mycetoma in Nigeria has shown that Nocardia species, viz. N. brasiliensis, N. asteroides and N. otitidiscaviarum occur naturally in soils in gardens, cultivated fields, poultry habitats, cattle sheds, and in compost and other related substrata. Nocardiopsis dassonvillei known to be a cause of mycetoma in USA and some other countries but not yet in Africa was also recovered from several naturals sources. The need for extensive studies on the prevalence of mycetoma in population groups at risk and development of simple mycological and serological diagnosis of early cases of this disabling affection is emphasized. Health campaigns are also advocated for prevention and early treatment of mycetoma.

Epidemiology of Mycetoma in West-Africa

M Develoux
Laboratoire de parasitologie-mycologie, Hôpital Tenon, 4 rue de la chine 75020 Paris, France

The north of West-Africa including Mauritania, Senegal, Mali and Niger is endemic for mycetoma. It is important to remind that the first case of african mycetoma was described by aristide Le Dantec in Senegal in 1894. Some of important mycetoma agents were first described in West-Africa: Madurella mycetomatis, Leptosphaeria senegalensis, Actinomadura pelletieri. Remarquable works were achieved by mycologists, pathologists, radiologists and surgeons from Dakar forty years ago on different aspects of the disease. Medical thesis of Michel Rey: "Mycetoma in West Africa" presented in 1961 was the most important contribution on mycetoma in this part of Africa. Rey described three endemic zones for mycetoma in the Mauritania-Senegal area. In each zone annual average rain was different and main mycetoma agents were different. In the northern zone situated in Mauritania, Streptomyces somaliensis was the main agent. In the intermediate zone, on the bank of the river Senegal natural frontier between Mauritania and Senegal, black grain mycetoma was predominant. The southern zone, in Senegal, was endemic for red grain mycetoma. An ecological investigation was carried out between 1966 and 1972 by Segretain and Mariat in Senegal. They isolated M mycetomi from soil and termitaria, L senegalensis from acacia thorns. Nocardia asteroïdes and Nocardia brasiliensis were also isolated from soil.

After these studies, during twenty years,

little attention was given to mycetoma in West Africa. Last decade a new interest was taken in the disease. The main reason is that mycetoma is always an important problem in this part of the world. Two series of patients were published, one from Mauritania and the other from Senegal. It is interesting to compare the results with the ones of 1961.

For the first time data were obtained from Niger and Mali with the publication of etiologic results from mycetoma patients. Actinomycetoma were predominent in these two countries. With little differences the three zones described by Rey in Senegal-Mauritania where founded in Niger and Mali.

In the other countries of West Africa, more humid, mycetoma is sporadic. Results concerning Ivory Coast, never published, were presented in 1987 at the second mycetoma symposium in Taxco (Mexico). Ivory Coast is divided in two bioclimatic zones: a savanna zone in the north and a forest zone in the south. In the first one M mycetomi was the predominant agent, in the second Nocardia spp. In the forest zone some white grain eumycetoma were also diagnosed.

There are few data concerning Nigeria, in this country most of mycetoma are caused by Nocardia spp

Foot Swellings in Khartoum

MA Obeid*, AH Fahal, H EL Shiek#, IA EL Hag##**

Department of Surgery, Mycetoma Research Centre**, Departments of Radiology# and Pathology##, Faculty of Medicine, University of Khartoum*

In this prospective study of 181 patients, mycetoma, lipoma, chronic non-specific granuloma and corn were the commonest causes of foot swellings and their incidences were 50.3%, 11.1%, 8.8% and 8.3% respectively. Most of the patients were from the Khartoum State followed by patients from the Middle and Western States. This may be due to the availability of medical facilities, transport and reasonable health education in these areas.

Foot swellings were observed more frequently in males, middle age groups and students who represent the most active members of the community; and this may explain the predominance of mycetoma in this study.

The incidence of recurrence after previous surgical excision was found to be low (14.4%) and it was significantly related to the use of local anaesthesia. The latter should be avoided in patients with foot swellings as most of these swellings proved to be mycetoma.

Most of the patients had no plane radiological bone changes at presentation. In these patients only soft tissue shadows were detected. The plane radiological findings were neither sensitive nor specific for the diagnosis of foot swellings and should be selectively used in such patients.

Ultrasound was found to be sensitive, specific and useful in the diagnosis of most common foot swellings. This is important in planning the surgical incision and procedures to be offered to patients. The technique provides information that is alone difficult to obtain on clinical and plane radiological examination. It is a simple, sensitive, non-invasive and cost-effective method of investigation. In this study, surgical excision of foot swellings under general anaesthesia with tourniquet was proved to be easy, safe and without morbid complications. Local anaesthesia proved to be an important cause of recur-

rence after previous surgical excision. Ultrasound may help in planning the type of anaesthesia used during surgical intervention.

Further epidemiological surveys on the problem of foot swellings should be established to estimate their incidence in the Sudan at large.

Herbal Treatment of Eumycetoma Caused by *Madurella mycetomatis*

AG Elfadil[1], SA Gumaa[2], HA Musa[3], HE Khalid[4], AA Sirro[5]

1. University of Juba, 2. University of Khartoum, 3. National Ribat University, 4. Medicinal & Aromatic Plant Research Institute, and 5. Ministry of Health

This is a preliminary study on the effect of using plant (x) in the treatment of patients with black grain eumycetoma due to *Madurella mycetomatis.*

The use of herbal treatment in Sudanese patients has been well known over the country since a long time ago. Due to the mutilating surgical and prolonged medical treatment by drugs which are very expensive and have side effects, people started looking back on native treatment.

Stimulated by my own experience with plant (x) in the treatment of eumycetoma due to M. mycetomatis by which my own sister was treated several years ago, I decided to carry out a preliminary study on the same plant (x) for the treatment of similar cases.

The trial started since 1997, when 186 patients presenting with black grain eumycetoma whose diagnosis was confirmed by clinical and serological examination, were included in this study, after obtaining the patient's consent and ethical clearance from the Ministry of Health for using the herb for treatment.

The duration of treatment ranged between 1-12 months, depending on the extent of the lesion and the response to treatment.

Out of the 186 patients, 74 (39%) did not continue the treatment and failed to come for follow up.

112 patients (61%) had the treatment and were followed up clinically and serologically until complete cure was obtained and for a 3-years period after complete cure.

2-4 weeks after applying the paste to the lesions, more sinuses opened up discharging the grains. This was followed by closure of the sinuses, decrease in the size of the granuloma, and the skin going gradually back to normal. The duration depended on the extent of the lesion.

The crude plant and its extract were used in vitro sensitivity testing against *M. mycetomatis*. The work was carried out in the Mycology Laboratory, University of Khartoum.

Different concentrations of the crude plant were prepared and incorporated in the media (Sabouroud's Agar) after sterilization. The concentrations were 100 mg, 50 mg and 25 mg per 100 ml medium. A control was included with each test. The test and control were inoculated with equal inocula of *M. mycetomatis.*

After two weeks, when good growth in the control tubes was obtained, the test was read and it was found that the organism was inhibited by all the different con-

centrations of the crude plant.

The etanolic extract of the plant was tested in the same way using the following concentrations: 35 mg, 25 mg, and 15 mg per 100 ml medium. All the concentrations inhibited the growth of *M. mycetomatis*.

Host Tissue Reaction Matched to the Type of Grain in Mycetoma

JM Dangou*; MH SY; R Monteil*; V Mendes**

**Laboratoire d'Anatomie et de Cytologie Pathologiques, Faculté de Médecine, Université C.A.D. de Dakar. **Service d'Orthopédie et de Traumatologie, Hôpital A. Le Dantec, Dakar*

Mycetoma is a chronic inflammatory tumor-like lesion characterized in most cases by discharging of grains of two causative organisms; fungal or actinomycotic. These two groups must be distinguished as their treatments are different. Each group is composed of numerous types of grains and host tissue reaction varies according to the grain's nature. This article described a six year retrospective study conducted in Dakar on 98 histologically confirmed cases of mycetoma. In our series, the causative agents were fungal grains (Madurella mycetomatis) in 40% and about 50% of all cases had a padal localization. Their identification was easy by histologic examination and around these grains a polymorphic inflammatory process developed. Peripheral fibrosis of the inflammatory granuloma was the fact of all actinomycetomas and only of certain species of eumycetomas. Giant cells were absent in actinomycosis. Eosinophilic polymorphonuclear and presence of epithelioid cells are other elements which contribute in the orientation of tissue reaction. This study revealed an association between host tissue reaction and the species of the etiologic agents of mycetomas. Appreciation of these elements can help pathologists in the determination of the type of grain and the course of the disease.

How Many Species of Streptomyces Cause Actinomycetoma?

Quintana, E.T.[1], Elzein, S.[2], Hamid, M.E.[2], Maldonado, L.A.[3], Fahal, A.H.[2], Ward A.C.[3] and Goodfellow, M.[3]

1.Department of Preventive Medicine and Public Health and 2.Institute of Endemic Diseases, University of Khartoum; 3.Department of Agricultural and Environmental Science, University of Newcastle, Newcastle upon Tyne, UK.

The genus Streptomyces encompasses more than 500 validly described species. The only streptomycetes that have been unambiguously shown to be pathogenic have been assigned to the taxon Streptomyces somaliensis. In the present investigation, fifteen isolates from patients in the Sudan suffering from actinomycetoma were provisionally assigned to the genus Streptomyces using a combination of chemotaxonomic and morphological criteria. The assignment of the tree isolates and marker strains of Streptomyces somaliensis to the genus Streptomyces was confirmed by 16S rDNA sequence data which also showed that the tested strains formed 4 multimembered and 3 single membered clades in the streptomycete tree. It is evident that streptomycetes which cause actinomycetoma belongs to several novel species, an observation that has profound implications

for the treatment of actinomycetoma in the Sudan.

Interest of the Molecular Methods for the Identification and the Characterisation of Nocardia Agents Responsible For Actinomycetomas

Patrick Boiron
Faculté de Pharmacie, Lyon, France. E-mail: boiron@univ-lyon1.fr

Mycetomas are still frequent in their principal endemic areas. They represent a problem for public health in the semi-arid tropical regions. The principal problem is the delay for the diagnosis.

Molecular biology techniques find more particularly their place in the study of the micro-organisms whose culture is slow or whose identification is difficult. The bacteria belonging to the Nocardia genus, frequently responsible for actinomycetomas, have this double characteristic.

Recently several methods were developed allowing the rapid and simple identification of genus and, generally, species, of Nocardia based on PCR and on analysis of the restriction profiles of amplification products (RFLP). The combination of PCR-RFLP techniques constitutes an important progress in the diagnosis of the infections due to Nocardia. It should allow the best dealt with the infected patients and the setting up of an early adapted treatment.

In addition, the molecular application of typing techniques to the infra-specific analysis of the strains of Nocardia gave promising results. A simple, fast and inexpensive molecular typing method was recently described. This RAPD typing methods should in the future allow a more precise study of the methods of transmission and ecological niches of Nocardia, to better understand the pathogenesis and the development of the infections which they cause.

Management of Mycetoma: Medical V Surgical Treatment and the Ethical Issue

ES Mahgoub, Sudan

In spite of successes in treatment of mycetoma, still many practicing physicians and surgeons or even patients believe that only surgical excision can provide radical treatment of mycetoma. Such a misconception is based on unfounded beliefs that no drug is yet available to provide complete cure, no facilities are available to isolate and test causative organisms, the type of patient can not be trusted with long term treatment etc. etc.

A compelling question of an ethical nature always arises; Who decides on the amputation of a limb or ablative surgery? Do we get consent by coercion, persuasion or true informed consent? Do we offer satisfactory artificial limbs to maintain function of the amputated part? Above all do we guarantee absence of recurrence beyond doubt?

In such dilemma, what is the best approach: Surgical or Medical or Combined?

Molecular Diagnostics and Epidemiology of Fungal Infections

Alex van Belkum, Erasmus MC
Department of Medical Microbiology & Infectious Diseases, Dr. Molewaterplein 40, 3015 GD Rotterdam, The Netherlands (e-mail: vanbelkum@bacl.azr.nl).

Molecular techniques have conquered the mycology laboratory over the past

decade. DNA and RNA sequences have become available for a wide range of genes and intergenic regions for a multitude of fungal species. These known sequences can be translated, in principle, into successful nucleic acid mediated fungal detection and identification assays. In addition, several nucleic acid tests have been developed that are instrumental in the characterisation of previously unidentified DNA molecules or regions thereof. These latter techniques have proven to be very useful in investigation of fungal taxonomy and epidemiology.

Among the most frequently used DNA sequences in this respect are those of the ribosomal genes. Species-specific DNA probes can be identified and the ribosomal gene sequences can be translated into species-or genus-specific oligonucleotide primers to be used in various nucleic acid amplification tests such as the PCR and NASBA. In combination with adequate nucleic acid extraction protocols efficient identification tests for species such as Candida albicans and Aspergillus fumigatus have been developed in our laboratory. These assays have been used as important tools in various clinical studies, either in patients or animal models. Recently, in collaborations with Sudanese researchers we successfully developed ribosomal sequence-based detection tests for Madurella mycetomatis, the prime agent of mycetoma in Sudan.

Fungal typing for taxonomic or epidemiological purposes can be performed by techniques as diverse as karyotyping through pulsed field gel electrophoresis (PFGE), random amplification of polymorphic DNA (RAPD) analysis or size variation assessment among tandemly repeated DNA loci (VNTR analysis). These techniques have been used for identification of strains from a broad range of fungal species, some of these techniques are currently under development of M. mycetomatis as well.

The presentation will cover technological and applied aspects of the methods used for detection and identification of fungi in clinical specimens. General discussions will focus on C. albicans and A. fumigatus. More specifc applications will be presented for M. mycetomatis, a species for which we have been trying to establish taxonomic, diagnostic and typing frameworks in close relationship with the environmental and clinical situation encountered in Sudan.

Mycetoma Due To Actinomadura pelletieri in Senegal

Michel Develoux*, Mame Tierno Dieng, Hassane Kane**, Bassirou N'Diaye****

** Laboratoire de parasitologie-mycologie, Hôpital Tenon, 4 rue de la chine, 75020 Paris, France ** Clinique dermatologique, Hôpital Le Dantec, BP 3001, Dakar, Sénégal*

Mycetoma is endemic in Senegal (west-Africa). During a 15 years period, 197 histologically proven cases of mycetoma were observed at the dermatological clinic of Dakar, 63.5% were actinomycetoma and 36.5% eumycetoma. The commonest etiological agent identified was Actinomadura pelletieri (red grain mycetoma): 47.2% of all mycetoma and 74.4% of all actinomycetoma. Several aspects of red grain mycetoma are original. They affect extrapedal sites more frequently (43/93: 46.2%) than mycetoma due to others organims (32/104: 30.7%).

Red grain mycetoma are aggressive, involvement of bones occurs early and lym-

phatic disseminations are not rare. In spite of the severity of clinical pictures, favorable results were obtained with trimethoprim-sulfamethoxazole combination.

Senegal is the only endemic country for mycetoma where the most common etiologic agent is Actinomadura pelletieri.

Mycetoma in Animals

M.E Hamid[1], E.T. Quintana[2], S. El Zein[1], L. Maldonado[2], M. Goodfellow[2]
(1) Department of Preventive Medicine and Public Health, Faculty of Veterinary Medicine, University of Khartoum (2) Department of Agricultural and Environmental Science, University of Newcastle

Between 1999 and 2001, domestic animals were surveyed for the presence of mycetoma-like lesions in some localities at Khartoum, Gezira and Gedarif states. Such lesions were found to be not a problem among domestic animals. However, chronic mycetoma-like granulomatous lesions with sinuses among donkeys, the so-called fistulous withers (FW), were encountered at a low incidence. FW was reported to be an old persistent problem with serious consequences.

Samples from 10 donkeys out of 15 with FW were subjected to bacteriological examination. Aspirated purulent materials were inoculated onto Tryptic Soya agar medium, incubated aerobically at 37ºC for up to 3 weeks. Six strains were recovered from the 10 samples using the above culture condition. These isolates were identified tentatively as members of the genus Streptomyces on the basis of cultural and morphological properties. The strains were found to be Gram positive, with stable branching filaments and extensive aerial hyphae on colony surface.

The assignment of these isolates to the genus Streptomyces was confirmed by using 16S rDNA sequence analysis. The report represents an unquestionable evidence to incriminate streptomyces in the aetiology of actinomycetoma in animals, thus correlates between mycetoma in man and animals. Research is underway to elucidate these agents and the disease.

Mycetoma in México: A Non Resolved Problem

López-Martínez R*, Méndez-Tovar LJ, Welsh-Lozano O, Arenas R, Bonifaz A, Lavalle P, Saul A.
** Department of Microbiology and Parasitology, Faculty of Medicine. National Autonomous, University of Mexico.*

Mycetoma is a true health problem in countries localizated in the intertropical zone of the world, as Mexico, Sudan, India, and Brazil. A survey was carried out in Mexico to determine some epidemiological characteristics of mycetoma. Data from a total of 2105 cases of mycetoma throughout a 30 years period, with an average incidence of 70 new cases per year were obtained. Results showed a sex distribution of male 76% and females 24%. The age distribution indicated a 58% from 16 to 40 years old. Most cases occurred in land-workers (60.2%) and in housewives with rural residence (21.3%). Lesions occurred most frequently in lower limbs (64.1%), trunk (17.4%) and upper limbs (13.6%). The geographical distribution within Mexico revealed that zones with the highest incidence were located at the south of Tropic of Cancer. The predominant etiologic agents corresponded to actinomycetes (97.8%), which Nocardia brasiliensis (86.6%) and

Actinomadura madurae (10.2%) showed the higher frequency. Eumycetoma had a low frequency (2.2%) and was principally due to Madurella grisea and M. mycetomatis.

Mycetoma in Sudan: Epidemiology, Clinical Presentation and Radiological Manifestations in Man and Animals

Samia A. Gumaa
Department of Microbiology, Faculty of Medicine, University of Khartoum

Mycetoma presents a serious mycological problem in Africa in general, and in Sudan in particular where it is endemic. It is found in the central belt lying between latitudes 12-18 and has been reported from different areas in Sudan extending eastward, westward, and northward. The highest prevalence is in the Blue Nile Province where it has a high morbidity and affects mainly peasants and herdsmen. Only few cases have been reported from the South. The predominant organisms, in descending order of frequency, are Madurella mycetomatis, Streptomyces somaliensis, Actinomadura madurae, Actinomadura pelletierii, Nocardia brasiliensis, Aspergillus nidulans, and Curvularia lunata. Rare cases have been reported due to Aspergillus flavus and Actinomyces israeli. The disease is not contagious and although it affects males more than females between age groups 15-45 years, no age or occupation is immune and mycetoma patients usually have partial deficiency in their cell mediated immunity (CMI).

Clinical Presentation: Knowledge about the incubation period is still deficient. Although the disease is predominantly seen in the foot, mycetoma has been seen in all different sites of the body including the head and neck which is the most serious type. Primary bone infection has been encountered in the superficial bones like the tibia and calcaneum where the conditions were diagnosed radiologically or during surgical exploration

Radiological Manifestations: The granuloma is presented by multiple dense opacities. In the small bones like the metacarpal and metatarsal bones, the first sign of bone involvement is periosteal erosions. In long bones, there is usually osteoporosis and cavity formation. The latter are few, big and well-defined in eumycetoma, whereas in actinomycetoma, they are small, numerous with ill-defined margins. These are filled with grains giving support in place of the destroyed bone, thus explaining the rarity of pathological fractures. In flat bones, like the skull, no cavities are formed but there are sclerotic changes with dense bone formation increasing the bone thickness. At the same time that there is bone destruction, new bone formation is laid on the periosteum.

Mycetoma in Animals: Natural mycetoma infection in animals has been reported in 3 goats and a donkey. Two goats had actinomycetoma due to A. madurae and one was caused by A. pelletierii. The donkey had a black-grain eumycetoma due to M. mycetomatis.

Experimental infection was carried out in immunosuppressed goats using A. pelletierii. The incubation period ranged between 5-9 months. The lesions in both naturally and experimentally infected goats differed clinically from human lesions in that they were localized due to the presence of a capsule. The grains were very similar to those from man both histologically and electron-microscopically.

The fate of mycetoma in goats differed from that in man, where in the latter, self-healing has never been reported whereas in goats, spontaneous cure occurred.

Mycetoma in Venezuela: A Social Disease. Epidemiological and Basic Sciences Approach

Jose A. Serrano M.D.
Department of Pathology, School of Medicine, University of Los Andes, Merida Venezuela. E. Mail:jacielo@cantv.net

Venezuela is a northern South American country embedded within, the intertropical zone, in the so-called lower latitudes. Its astronomical location lies between 0o 45' and 12° 11' 45" (north latitude) and between 59o 48' and 73o 11' 49" (west longitude).

Venezuela has tropical and subtropical climates. Most mycetoma cases reported in the Venezuelan literature (about 51.1 %) have been found in the State of Lara. In addition, several other cases have reported in the states of Bolivar" Falcon, Portuguesa, Zulia and Yaracuy" Lara State is conformed by tropical and subtropical green semiarid and xerophytic valleys and hills (ranging altitudes from 300 to 2,500 meters). This region forms a transitional zone between the coastal mountain chain and the Andes. It comprises about 3% of Venezuela's total area. The Venezuelan central western State of Lara has two major types of forest: (a) a semiarid (xerophytic) forest with a rain index of 200-500 nm/yr at altitudes up to 400 meters, and (b) a deciduous forest with a rain index of about 1,000 to 2,000 mm/yr at altitudes from 1,200 to 2,400 meters above sea level.

Most mycetoma cases (about 63.8%) have been reported from the xerophytic forest. This type of forest is dry, with trees and bushes such as Acacia tortuosa (cuji negro), Acacia flexuosa (cuji), Prosopis fuliflora (cuji jaque), Amarantus espinosus (pira brava), Cereus SP (cardon), as well as different types of cactus plants, such as Opuntia caribea and Opuntia wentiana. Since these trees and cactus plants have many thorns, it is not unusual that individuals (local habitants) easily puncture their skin while walking or working. If thorns are contaminated with eu-or actinomycetes, primary infections may start. Thereafter the initial lesion may also develop into a mycetoma.

Etiologic agents most common reported in Venezuela for actinomycetoma and eumycetoma are Actinomadura madurae (39.7%), Nocardia brasiliensis (27.6%), Nocardia spa (15.5%), Streptomyces somaliensis (8.8%), N. asteroides (5.2%), N. otitidiscaviarum (1.7%), A.pelletieri (1.7%). Eumycetomas are associated to Pyrenochaeta mackinnonni (32.0%), P.romeroi (23.7%), and Madurella grisea (24 (32.0%).

A summary of Venezuelan previously reported clinical cases, or series of cases, suggests (1) Predominance in males (75.5%) for actinomycetoma and (76.0%) for eumycetoma infections. (2) Highly frequent among 30-59 years old group (about 72% for actino-and eumycetoma), (3) Most common among field workers, 76.6% for actinomycetoma and 48.0% for eumycetoma. (4) Most frequently seen in feet (63.8%), legs (12.8%), and knees (12.8%).

In the present talk, we will show results of our studies on ecological aspects of actinomycetes, as well as our results on cytochemistry and molecular biology, for rapid diagnostic of Nocardia and S.

somaliensis as etiologic agents of actinomycetoma. Also we will show aspects of our epidemiological model based in a multidisciplinary family-case comparison epidemiological study.

Mycetoma is commonly underreported. In addition local and national morbidity is incomplete since communication to health authorities is not required. Only usually resistant-to-treatment advanced dermatologist or some general practitioners diagnose cases. Antibacterial and antimycotic therapy-resistance may be explained either by the difficulty to establish an early diagnosis, or as a consequence of immunological or nutritional deficiencies, or by means of natural drug-resistance itself. Usually mycetomas (mainly the eumycetomas) become a lifetime lasting disease.

Mycetoma is a social disease and must be prevent using strong and active educational programs address to health care people as well to the general population, particularly to those inhabitants of endemic areas.

Mycetoma of the Head

Oliverio Welsh
Department of Dermatology, University Hospital, UANL, Monterrey, Mexico

A 19-year-old female seen in 1971 at the University Hospital in Monterrey, Mexico with is a chronic ulceration and granulomatous tissue of six months evolution located in the frontal region of the head. The patient mentioned a traumatism with a window on that site 7 years earlier. Streptomyces somaliensis was identified both in a surgical biopsy from the lesion and in the culture. A skull X-ray and tomography revealed involvement of the frontal and parietal bones. The patient was treated with streptomycin and trimethoprim-sulfamethoxazole (T-S) as well as the surgical removal of the frontal bone of the skull and an acrylic prosthesis was inserted; however an ulcer developed and it was removed weeks after. The patient was lost for follow up and 5 years later; she was seen with involvement of the parietal bones and an extension of her disease to the frontal brain lobe. The patient was restarted on T-S and both parietal bones were removed surgically. The patient developed seizures (Grand Mal), which were controlled with anticonvulsant drugs. The medical treatment for actinomycetoma included minocycline 200mg/day, T-S. and streptomycin. After 2 years of medical treatment with the skin and brain lesions cured. The skull was repaired with the patient's own ribs and since then she has remained asymptomatic in spite of two pregnancies. This patient was treated before we begun our therapeutic study with amikacin, T-S.

Mycetoma: Clinical Experience from the Sudan

AH Fahal
Mycetoma Research Centre, University of Khartoum, Khartoum, Sudan

Mycetoma is a major mycological health problem in the Sudan. For various understandable reasons its true prevalence in the Sudan remains unknown. Male predominance is a constant finding in mycetoma. This is commonly attributed to the greater risk of exposure to organisms in the soil during outdoor activities. However, in areas where mycetoma is prevalent in the Sudan, both sexes go barefooted and in Western Sudan women take

a more active part in the field and yet the incidence of the disease is the same as that observed in other parts of the country. It may be that women are inherently less susceptible to infection with mycetoma. It is interesting to note that, during pregnancy mycetoma lesions become more active and aggressive.

Mycetoma occurred more frequently in the second and third decades of life but no age was exempt. Males and females had the same mean age at presentation and age distribution pattern. All patients below the age of 10 years were from Khartoum, Middle and North States. This study did not confirm the previous observation that mycetoma is a disease of peasant herdsmen and farmers as most of our patients were students. Workers were the next commonest affected group.

The Middle State seems to be the homeland of mycetoma in the Sudan. The disease is uncommon in the South, East and North of the Sudan. Climatic factors and/or the soil nature may be the causes of this geographic variation in the prevalence of mycetoma.

In the various age groups, in both sexes and in the different States M. mycetomatis was the commonest causative organism. The mean age of eumycetoma patients at presentation is significantly lower than those with actinomycetoma and the majority of patients (84%) who were less than 10 years old had eumycetoma, this tendency of eumycetoma to affect young patients is unclear. Streptomyces somaliensis was the commonest organisms causing actinomycetoma. In our patients, the duration of the disease prior to presentation is rather long and this is due to understandable reasons. The majority of patients had no definite history of trauma at the mycetoma site. This raises the question of the role of trauma in the pathogenesis of mycetoma, suggested by previous reports.

Inspite of the chronicity of mycetoma, there was no significant association between mycetoma and other illnesses including amyloid disease, which is known to be associated with chronic illness. The familial tendency for mycetoma observed in this study may be a genuine inherent genetic link or it may be due to the fact that, all members of the family share the same epidemiological risks for infection.

The clinical course of the disease was typical in the majority of patients; however in three patients the disease course was stormy and aggressive.

The foot was the commonest site for mycetoma. The left foot was more affected than the right one. Eumycetoma commonly affected the foot in contrast to actinomycetoma, which affected unusual sites as the abdominal wall, chest, head and neck; the explanation of this is obscure. The right hand ranks as the second commonest site of mycetoma; this may imply a traumatic basis of the infection in this site. Double infection, in this study is more than that reported elsewhere. So far there is no staging system reported for mycetoma and the lesions are categorized in vague terms as early small, moderately

advanced and advanced lesions. Massive lesions were observed in male patients with actinomycetoma. None of the patients had clinical evidence of local trophic or neurological disturbance not even those with long standing disease the, explanation of this is enigmatic.

The incidence of enlarged nodes was higher than that reported elsewhere. Unilateral venous varicosity is not an uncommon feature of mycetoma. The pathogenesis of this varicosity is unclear; it is unlikely to be due to proximal obstruction by the enlarged lymph nodes as only 9.6% of these patients had enlarged nodes. We noticed an increase in the temperature locally over the mycetoma lesions even in the absence of sinuses compared with other parts of the body. Local hyperhydrosis was noted in 66.4% of the tested patients. No association was found between the blood types and the various types of mycetoma ($P>0.1$). Patients with mycetoma proved to have normal thyroid function. The chronicity of the disease, effects of inactivity and economic loss that lowers the patients' activity may render them not unlike hypothyroid patients in their activity.

None of our patients was HIV seropositive. The incidence of hepatitis B surface antigens in this study was higher than that reported in the general population; the repeated surgical treatment, the use of injections for medical treatment and local native treatment may be the explanation of this.

Most of our patients at presentation had radiological changes this may be due to the fact that the duration of their illness was rather lengthy. These radiological changes were commonly seen in patients with actinomycetoma. The majority of patients (63.6%) with A. pelletieri mycetoma had bone changes at presentation and this aggressive behavior may be partly explained by the absence of the cement substance.

Bony changes were seen more in males than in females, in massive mycetoma lesions, in patients with multiple recurrences and with a long duration of illness. No significant correlation was found between the presence of sinuses and bone changes.

We used real-time ultrasound in the clinical management of mycetoma patients; it is a simple, rapid, sensitive and non-invasive method to document the presence of mycetoma and its classification into eumycetoma and actinomycetoma. It can be used in the routine diagnosis of mycetoma and epidemiological surveys.

Mycetoma can be accurately diagnosed by Fine Needle Aspiration (FNA) cytology. The mycetoma lesion has a distinct appearance in a cytology smear. FNA allows morphological identification of mycetoma and its classification into eumycetoma and actinomycetoma. The technique is simple, cheap, rapid, and sensitive and can be tolerated by patients. Due to the simplicity of the technique it can be used in epidemiological survey of mycetoma and for detection of early cases.

Mycology of Mycetoma Agents in Sudan

ES Mahgoub, Sudan

There is a tendency to assume that all black–grain mycetomas in Sudan are eumycotic and that the causative agent is Madurella mycetomatis, while the pale coloured ones are actinomycotic, either Streptomyces somaliensis or Actinomadura madurae. This assumption is not completely true. Only cultural identification will determine the ultimate definition of the causative organism and consequent planning of antibiotic or antifungal susceptibility testing before treatment.

This paper will discuss similarities and differences between fungi isolated from Sudanese patients infected with mycetoma, namely: Corynespora cassiicola, Aspergillus nidulans, A.flavus, Curvularia lunata, and Madurella grisea.

Phylogeny and Typification of Madurella mycetomatis

G.S. de Hoog[1]*, D. Adelmann[1], A. Ahmed[2], A. van Belkum[3], A.H. Fahal[2]

*1. Centraalbureau voor Schimmelcultures, Utrecht, The Netherlands; 2. Institute for Endemic Diseases, University of Khartoum, Khartoum, Sudan; 3. Department of Microbiology, Erasmus University Medical Center, Rotterdam, The Netherlands. *Correspondence: Centraalbureau voor Schimmelcultures, P.O. Box 85167, NL-3508 AD Utrecht, The Netherlands. E-mail: de.hoog@cbs.knaw.nl.*

In 1902, Laveran described the first case of eumycetoma from Djibouti. The fungus was named Streptothrix mycetomi Laveran, and is now known as Madurella mycetomatis (Laveran) Brumpt. No type material is known to be preserved. The original description matches well with that of a common agent of eumycetoma in northeastern Africa, which consistently was proven to be a single species. Strains of that species in vitro exude a brownish pigment into the medium and remain sterile; phialoconidia may be present and sclerotium-like bodies are occasionally produced on casein-agar. We indicate one of the Sudanese strains as neotype strain of Madurella mycetomatis. The SSU rDNA domain of this strain was sequenced and compared with over 1050 similar sequences available at CBS. The species was shown to be a member of the ascomycete order Sordariales, and was found to cluster close to members of the genus Chaetomium. This was an unexpected finding, since Chaetomium species are rarely involved in human mycoses. In contrast, another currently accepted species of Madurella, M. grisea, clustered in the Pleosporales, close to the genus Leptosphaeria and some known pycnidial potential agents of subcutaneous mycoses. It is concluded that the genus Madurella is a heterogeneous assemblage. It will be re-defined, with M. mycetomatis as type species, as a phialidic genus of Sordariales, because sterility per se is an ambiguous diagnostic criterion. Madurella grisea then cannot be maintained in Madurella. Current research focuses on revealing teleomorph or synanamorphic connections by rDNA ITS similarity among relatives of the nearest neighbours of the two species.

Search and Discovery for a New Compound from Thermophilic Actinomycetes for the Therapy Of Actinomycetoma

Amira Mahmoud AL-Tai and Ron Byrom
Micro-Ecology Development Ltd., Central Chambers,London Road, Alderley Edge,Cheshire,SK9 7DZ,U.K.

Pathogenic actinomycetes are aerobic filamentous bacteria that cause several chronic diseases: tuberculosis, mycetoma and other infectious illness. Mycetoma is dominant in the tropical regions and affects the skin, subcutaneous tissue, bones and other organs causing enormous functional disability. The treatments of these diseases are becoming more difficult especially with the development of resistant strains to known antibiotics.

The antimycetoma activity of 23 strains of thermophilic actinomyctes isolated from "Catalyst MED" was tested against 3 clinical isolates of Streptomyces somaliensis(A1, A9 and A11) isolated from mycetoma-patients from Sudan and 21 strains of the actinomycetes tested against Gordona bronchalis NCTC 10677. The results obtained showed that 68% and 38% of the thermophilic actinomyctes produced secondary metabolite that inhibited the growth of S. somaliensis and G. bronchalis respectively.

The aim of this study is to discover a new drug from a novel group of thermophilic actinmycetes isolated from "Catalyst MED" which could play an important role in medical field.

Serological Diagnosis of Nocardia brasiliensis' Actinomycetoma Using Specific Antigens

Salinas Carmona, M.C., Welsh, O. and Perez Rivera, L.I.

Facultative intracellular microorganisms like Mycobacterium tuberculosis; Listeria monocytogenes, Nocardia brasiliensis, etc. produce human chronic infections in normal and immunocompromized individuals. Nocardia brasiliensis is the major etiologic agent of actinomycetoma in Mexico. The diagnosis is made on clinical findings like chronic, painless tumefaction usually located to extremities. The lesions are ulcers and sinuses discharging microcolonies called granules. The diagnosis is confirmed by microbiological culture of the filamentous N. brasiliensis colonies, but this usually takes about three weeks. The slow growing rate of this microorganism in many circumstances is clinically unacceptable and justifies a rapid serological test. The serodiagnosis of Nocardia brasiliensis infections had been attempted in the past with little success, in part due to the low sensitivity of the used tests. The use of non-purified antigens was also responsible for both crossreactivity and low specificity. We used a proteic N. brasiliensis extract to identify the immunodominant antigens in a Western blot assay. Three main antigens were recognized in sera from Nocardia brasiliensis actively infected patients. The P61, P26 and P24 immunodominant antigens were not recognized by circulating antibodies from leprosy or tuberculosis patients (Zbl. Bakt. 276:390. 1992). Using the P24 antigens we then set up an ELISA test (J. Clin. Microbiol. 31:2901. 1993) to quantitate anti-P24 antibodies. Anti-N. brasiliensis antibody

titer was compared in active and cured actinomycetoma patients using the ELISA test. The results showed a high anti-P24 antibody titer above 0.3 OD Absorbance units (cut off level). Patients that were under medical treatment and diagnosed as cured, gave anti-P24 antibody titer below the cut off level of 0.3. Three patients presented a reactivation of the mycetoma lesions and the antibody titer anti-P24 was increased again. Thus showing the clinical benefit of this test: the rapid and specific diagnosis of active infection and the assessment of the patients' outcome after medical treatment.

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Systematics of the Causal Agents of Actinomycetoma

Michael Goodfellow
Department of Agricultural and Environmental Science, University of Newcastle, Newcastle upon Tyne, NE2 7RU, UK.

The importance of modern taxonomic methods, both individually and collectively, in shaping the classification of actinomycetes will be considered with particular reference to the causal agents of actinomycetoma. This disease is endemic in certain geographical areas in tropical and subtropical regions of the world where it can have a devastating effect on patients as it often leads to deformities and amputation of the affected organs. It is important to isolate, characterise and identify the causal agents of actinomycetoma if patients are to receive correct treatment. The main causal agents are usually considered to be Actinomadura madurae; Actinomadura pelletieri, Nocardia brasiliensis and Streptomyces somaliensis though particular species seem to predominate in different geographical areas. The importance of the improved classification of aerobic, clinically significant actinomycetes in the recognition, characterisation and identification of novel causal agents of actinomycetoma will be highlighted.

The Efficacy of Itraconazole in the Treatment of Patients with Eumycetoma Due to Madurella mycetomatis

A.H. Fahal*, I. A. Rahman,* A. M. El-Hassan, **E. E. Zijlstr **
The Mycetoma Research Center, Institute of Endemic diseases ** University of Khartoum. Khartoum-Sudan*

This was a prospective study to evaluate the efficacy of Itraconazole in the treatment mycetoma due to M. mycetomatis. It included 15 patients with confirmed eumycetoma due to Madurella mycetomatis treated with oral Itraconazole. They showed good clinical response to 400 mg itraconazole daily but when the dose was reduced to 200 mg daily, the clinical response was less. Surgical exploration showed that, in all patients the lesions were well localized, encapsulated with thick capsule and they were easily removed surgically. Histopathological examination of the post-treatment remaining mycetoma lesion showed evidence of healing. Patients followed up post-treatment for variable periods (range between 24-36 months) only one patient had recurrence. High dose of Itraconazole in combination with surgery is recommended for eumycetoma patients to avoid unnecessary mutilating surgery.

The Immunopathology Of the Actinomycetoma Lesions Caused By Streptomyces somaliensis

A.M. EL Hassan, A.H. Fahal, A.G. Ahmed, A. Ismail and B. Veress.
Mycetoma Research Group Institute of Endemic Diseases, University of Khartoum.

The immune responses in actynomycetoma lesions caused by Streptomyses somaliensis were characterized by immuno-histochemistry. In sections stained with haematoxylin and eosin, the inflammatory reaction around the grain was of 2 types. In Type I there were three zones; a neutrophils zone immediately surrounding the grain, an intermediate zone containing mainly macrophages and a peripheral zone consisting of lymphocytes and plasma cells. Zone 1 stained positively for CD15 (neutrophils), zone 2 for CD68 (macrophages) and CD3 (T lymphocytes) and zone 3 for CD20 (B lymphocytes). In type II reaction, there was no neutrophils zone, the grains being surrounded by macrophages and giant cells. IgG and IgM and complement were demonstrated on the surface of the grain and on filaments inside the grain. Neutrophils and macrophages were recruited into the lesion by complement and were involved in the fragmentation of the grain. The cytokine response was of a dominant Th2 pattern (IL-4 and IL-10).

The Pathology of Mycetoma in the Sudan

A.M. EL Hassan
Department Of Immunology And Clinical Pathology, Institute Of Endemic Diseases University Of Khartoum.

This presentation discusses the morphology of the more common agents of Mycetoma in the Sudan and the associated tissue reaction under light and electronmicroscopy. The most common cause of eumycetoma is Madurella mycetomatis. Two types of grains are identified: the filamentous and the vesicular of which the former is more common. Ultrastructurally the septate hyphae are embedded in cement substance. Three types of tissue reaction are found. Type I reaction is characterized by a neutrophils zone around the grains. These adhere to the surface of the grain causing its disintegration. Type II reactions follows on Type I reaction and consists of macrophages and giant cells surrounding the grain. In type III reaction, there are epithelioid granulomas that appear to form as a reaction to residual local antigen after hyphae are destroyed.

Of the actynomycetoma, the commonest organisms are Streptomyces somaliensis, Actinomadura madurae and Actinomadura pellitieri. The light microscopic and ultrastructural morphology of those organisms will be described. Type I and II reactions are seen but Type III reaction apparently does not occur. Vascular changes and bone lesions in eu-and actinomycetoma will be discussed.

Usefulness Of The rpoB Gene To Identify Members Of The Genera Actinomadura And Nocardia

Maldonado, L.A., Quintana, E.T., Ward, A.C. and Goodfellow M.
Department of Agricultural and Environmental Science, University of Newcastle, Newcastle upon Tyne, UK.

Members of the genera Actinomadura and Nocardia have had a long and tortuous taxonomic history mainly due to the overemphasis placed on morphological criteria. The clarification of each of these taxa has been greatly improved by the application of polyphasic procedures though better methods are needed for the rapid and reliable assignment of unknown clinically significant strains to validly described species. The aim of the present investigation was to determine whether comparative analyses of the rpoB gene provided data of value for the classification and identification of clinically significant actinomadurae and nocardiae. The sequence data underpinned the taxonomic status of A. latina, A. madurae and A. pelletieri and one strain isolated from a patient in the Sudan, all of which are causal agents of actinomycetoma. Similarly, rpoB data allowed the separation of nocardiae, including, N. brasiliensis, that encompasses clinically significant strains.

Venous Varicosity in Mycetoma

AH Fahal, S El Sheik, AM El Hassan
Mycetoma Research Centre - University of Khartoum. Khartoum - Sudan.

Introduction: Unilateral varicose veins are noticeable phenomena in mycetoma patients, however its pathogenesis was not studied previously.

Patients and Methods: In this prospective study, which included 60 patients with histological and ultrasonic confirmed mycetoma, the venous system of the affected limb was studied using sonographic, venographic and histologic techniques.

Results: Varicose veins were more evident in patients with long standing mycetoma, with massive lesions and with radiological bone changes. Certain venous abnormalities were demonstrated. In histological sections, veins and venules showed marked muscular hypertrophy, intimal and advential thickening, oedema and lumen narrowing but no venous occlusion or arterio-venous shunts were observed. These changes were confirmed ultrastructurally. Venography showed a brisk venous circulation in the vicinity of mycetoma lesion, which was more evident in eumycetoma. However at the site of mycetoma lesion there was displacement and distortion of the venous circulation and evidence of early venous varicosity above the lesions. The vascular doppler study showed increased both arterial and venous blood flow in the affected limb.

Conclusions: These venous changes could be compensatory mechanism to the increased venous return secondary to increase in the arterial blood flow at the mycetoma lesion and could be treated conservative.

Memos

Memos

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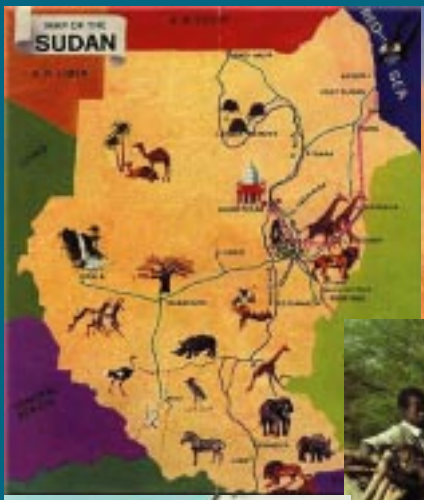

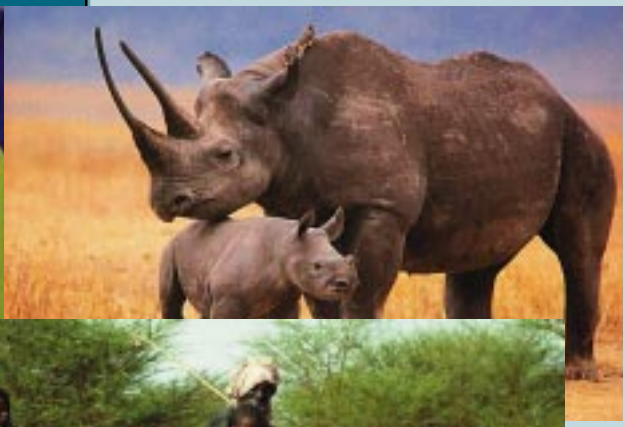

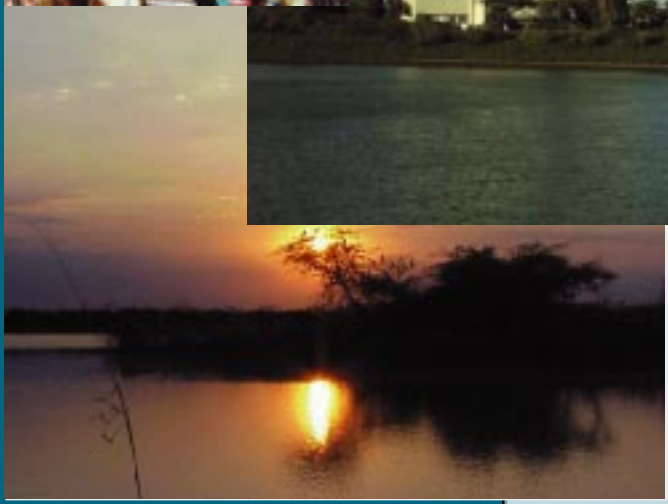

Sudan

a land of peace, variety & wonders

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