DEEP FUNGAL INFECTIONS DIAGNOSED IN JOHANNESBURG IN THE PERIOD 1987 - 1996

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A research report submitted to the Faculty of Health Sciences,University of the Witwatersrand,in partial fulfillment of the requirements for the degree of Master of Medicine in Dermatology.

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I, David Wayne Klevansky, declare that this research report is my own work. It is being submitted for the degree of Master of Medicine in Dermatology to the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at this or any other University.

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D.W. KLEVANSKY

25th day of March 1998

This research report is dedicated to my parents Hymie and Leonie Klevansky, to my wife Lauren and to my daughter Rachel.

ABSTRACT

The aim of this study was to update the knowledge concerning the types and relative prevalence of the various deep fungal infections of the skin encountered in the Johannesburg region. Two previous studies have been published concerning deep fungal infections in this area, first by Lurie in 1955 (1) and the last by Martin and Berson in 1973 (2).

Over a ten year period from 1987 to 1996, 120 cases of deep fungal infection of the skin were recorded. This included patients with sporotrichosis (the commonest disease), mycetoma, nocardial infections, chromoblastomycosis, actinomycosis and blastomycosis. The present data were compared with the two previous studies and it was found that the relative incidence of sporotrichosis, chromoblastomycosis and actinomycosis has declined, while that of blastomycosis appears to have increased in recent years.

The relevant South African literature regarding deep fungal infections is reviewed. In this study, three species are reported to cause deep fungal infections in South Africa for the first time, viz. *Nocardia dassonvillei, Actinomyces meyeri and Nocardia caviae*..

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PREFACE

The main purpose of this study is to update knowledge regarding the deep fungal infections which occur in the Johannesburg area. A subsiduary aim is to facilitate similar studies for future investigators.Because deep fungal infections are uncommon in South Africa, many clinicians and pathologists are unfamiliar with their clinico-pathological features. For non-mycologists, even the definition and the classification of the causative organisms are confusing. For these reasons, the classification, epidemiology, clinico-pathological features and diagnosis of those deep fungal infections which occur in South Africa are briefly reviewed.

Reports concerning the ocurrence of deep fungal infections in South Africa are few in number and many are not readily accessible. It is hoped that the rather detailed review of the South African literature will be of use and of interest to other workers in the field.

INTRODUCTION

1. The definition of deep fungal infections of the skin

Fungal diseases of the skin are divided into four main groups - superficial, cutaneous, subcutaneous and systemic. ***Superficial*** fungal infections, such as tinea versicolor, are due to invasion of the keratinous structures of the epidermis, with little or no reaction in deeper tissues. In ***cutaneous*** fungal infections, for example dermatophyte infections, the organisms are also confined to the non-living stratum corneum, but they give rise to an inflammatory response within the deeper layers of the skin (3). The causative organisms of superficial and cutaneous fungal infections in man may be anthropophilic, zoophilic or saprophytic. The ***subcutaneous*** mycoses are caused by organisms which are saprophytic in nature and are traumatically implanted into the dermis or subcutaneous tissues. The infection may remain localized or spread to adjacent tissues, contiguously or via the lymphatics. ***Systemic*** mycoses are almost always primary infections of the lung, caused by inhalation of fungal spores. Many internal organs as well as the skin may be involved, due to direct or haematogenous spread (3).

The so-called ***deep*** fungal infections consist of subcutaneous and systemic infections which involve the skin. They are caused by a wide variety of organisms that are saprophytic in nature but may be pathogenic in man. Their natural habitat is plants, soil and water. These organisms are classified into two main groups. The first consists of filamentous bacteria and the second of true fungi.They cause a similar clinical picture in

the skin characterized by granulomatous or warty plaques, or discharging sinusses. Deep seated infections which result in swelling and discharging sinusses involving the skin, subcutaneous tissues and sometimes the bone, are known as mycetomas. The term ***mycetoma*** is defined by Rippon as the triad of tumefaction, draining sinusses and grains (4).

This study deals with those organisms traditionally regarded as causing deep fungal infections. Not included are infections due to *Candida*, and saprophytic fungi such as *Aspergillus*. These cause superficial infections of the epidermis in normal persons,but may give rise to subcutaneous and systemic infections in immunocompromised hosts. Also excluded from this report is rhinosporidiosis, caused by *Rhinosporidium seeberi*. This fungus is classified as a subcutaneous mycosis (5). It cannot be cultured and is diagnosed on smears. Rhinosporidiosis was reported in the records of the South African Institute for Medical Research (SAIMR) in Johannesburg in the late 1930s (6); subsequent reports were from Natal, the last being in 1987 (7). I omitted discussing histoplasmosis and cryptococcosis because, on analysing the available laboratory records,no patients with cutaneous histoplasmosis and only one patient with cutaneous cryptococcosis were recorded.

2. Classification of organisms causing deep fungal infections in South Africa

Diseases caused by filamentous bacteria have traditionally been included in the deep fungal infections and studied by mycologists (4). These organisms give rise to three disease

entities - actinomycosis, nocardiosis and actinomycotic mycetoma (actinomycetoma). All of these filamentous bacteria belong to the order *Actinomycetales.* Those causing disease in humans belong to the 4 genera *Actinomyces, Nocardia, Actinomadura* and *Streptomyces.*

Members of the genus *Actinomyces* may be anaerobic or aerobic. Anaerobic actinomycetes, which are commensals in the oral cavity, cause actinomycosis (4). Aerobic actinomycetes are the commonest cause of actinomycotic mycetoma.

In South Africa the following species of filamentous bacteria and true fungi have previously been recorded as causing human disease:

I. FILAMENTOUS BACTERIA

ACTINOMYCOSIS

Actinomyces israelii (1)

NOCARDIOSIS

Nocardia asteroides (1)

Nocardia gypsoides (1)

Nocardia madurae (1)

ACTINOMYCETOMA

Actinomadura madurae (8)

Actinomadura pelletieri (8)

Streptomyces somaliensis (10)

II. TRUE FUNGI

SPOROTRICHOSIS

Sporothrix schenkii

S..s. var. schenkiii (11)

CHROMOBLASTOMYCOSIS

Fonsecaea pedrosoi (1)

Cladosporium carrionii (12)

EUMYCOTIC MYCETOMA

Madurella grisea (2)

Madurella mycetomatis (2)

Petriellidium (Pseudoallescheria) boydii (2)

Phialophora gougeroti (2)

BLASTOMYCOSIS

Blastomyces dermatitidis (13)

3. Epidemiology, clinico-pathological features and diagnosis of deep fungal infections occuring in South Africa

SPOROTRICHOSIS

Sporotrichosis has a worldwide distribution which is uninfluenced by climate (14). It is most frequently observed in Japan, China, India, Australia , Mexico and Brazil and is found mainly in rural areas (4). Age, sex and race play no role in the epidemiology of the disease,which depends on occupational or recreational exposure to the fungus. The natural habitat of the fungus is soil and plant matter such as straw, flowers and mine timbers. The fungus may infect animals such as cats, dogs, horses and rats (15).Transmission is usually by cutaneous inocculation which occurs especially in farmers, gardeners, florists, miners, healthcare workers and animal handlers (15).

Sporotrichosis is caused by a single species of fungus, *Sporothrix schenckii* (16). It most commonly presents either as a fixed cutaneous form or as a lymphocutaneous form. A cutaneous disseminated form may rarely follow either of these commoner presentations. Systemic sporotrichosis develops subsequent to an asymptomatic pulmonary infection and may be unifocal or multifocal. The unifocal form may affect the lungs, a single or symmetric joints, the genitourinary tract, or rarely the brain. The multifocal form tends to involve the skin, several joints and the lungs (17).

Histological examination of skin lesions shows pseudoepitheliomatous hyperplasia of the epidermis, with a granulomatous infiltrate and polymorphonuclear abscesses in the dermis. If found, the asteroid body which represents eosinophilic material surrounding yeast forms of the fungus, supports the diagnosis, but its absence does not exclude sporotrichosis (3). Cigar bodies are oval yeast forms of Sporothrix schenckii. They are not easily found in biopsy specimens of patients with sporotrichosis (18).The diagnosis of sporotrichosis may easily be confirmed by culture on Sabouraud's medium.

CHROMOBLASTOMYCOSIS

Chromoblastomycosis is a chronic fungal infection of the skin and subcutaneous tissue which is caused by *Cladosporium carrionii, Fonsecaea compacta, Fonsecaea pedrosoi, Phialophora verrucosa or Rhinocladiella aquaspersa* (4).The natural habitat of these fungi is wood and soil and infection follows traumatic implantation of the fungus into the skin. The disease has a worldwide distribution, but most cases are found in tropical and subtropical regions, such as Central and South America and Africa. It affects all age groups especially young adults. Children are least affected. Ninety percent of cases occur in men, especially barefoot rural and agricultural workers (15).

Clinically chromoblastomycosis presents as plaques, nodules or tumours which are often warty or hyperkeratotic. They may become eroded, crusted or ulcerated. Satellite lesions are common. The disease is chronic and slowly progressive. Scarring can occur and

squamous cell carcinoma is a rare complication. Lymphatic spread is common and may give rise to lymphoedema. Haematogenous spread is rare but may result in brain abscesses even without obvious skin disease (16).

The diagnosis of chromoblastomycosis may be made on skin biopsies where the characteristic dark brown, thick walled spores are seen within the dermis. They are ovoid or spherical, lying singly, in chains or clusters, either free or within giant cells. Cross walls may be seen in some spores (17).The definitive diagnosis is confirmed on fungal culture on Sabouraud's glucose agar where black colonies containing aerial hyphae appear. The type of spore formation and the spore structure differentiate the five main causative fungi(19).

ACTINOMYCOSIS

This is a chronic suppurative and granulomatous disease caused most commonly by *Actinomyces israelii*, and occasionally by other species such as *A.naeslundii, A. viscosus, A. odontolyticus,* and *A. meyeri* (4). These are commensals in the mouth. The disease is characterised by the formation of multiple draining sinus tracts through which the characteristic sulphur granules are discharged. Five main clinical types are recognised: cervicofacial, thoracic, abdominal, primary cutaneous and pelvic (16). The infection may spread to other organs of the body including the skin, bones and central nervous system, by direct extension, haemotogenous or lymphatic spread (3).

Granules may be seen on histological examination of biopsies. They are large,and are

bordered by eosinophilic club-like projections known as Splendore-Hoeppli material. This is thought to be a glycoprotein resulting from an antigen -antibody reaction on the surface of the granule (3). This material is surrounded by a dense neutrophillic infiltrate. The diagnosis is confirmed by taking pus swabs from the sinus tracks and plating them anaerobically on blood or brain heart infusion agar. The colonies formed are hard, grey-white in colour, and glistening (13).

NOCARDIOSIS

This is an exogenous subacute or chronic granulomatous disease caused by members of the genus *Nocardia* which are saprophytes in nature. The species most frequently implicated are *N. asteroides, N. brasiliensis and N.caviae.* The disease may be systemic, usually with a primary infection in the lung, it may present as single or multiple subcutaneous lesions, or as a mycetoma. Direct spread from the lungs may result in subcutaneous abscesses and sinus tracts in the overlying skin. Subcutaneous nocardiosis may result from systemic disease or may occur as a result of direct inoculation of the fungus into the skin (3). Primary cutaneous disease may present as pustules, cellulitis, a lymphocutaneous form resembling sporotrichosis and subcutaneous abscesses (4).

N. brasiliensis is more virulent than *N. asteroides* or *N. caviae*, and is a common cause of mycetoma. It can however also cause systemic nocardiosis. *N. asteroides* commonly causes lung and systemic nocardiosis, and is the causative organism in approximately half of the cases of primary skin infection. Its role in causing mycetoma is questionable (4)

On histological examination, abscesses composed of neutrophils contain the organisms which are gram-positive, filamentous bacteria. These have a tendency to break up into short bacillary segments rather that aggregating into "sulphur granules" like *A.israelii.* A modified acid-fast stain is used to demonstrate the organism, while Sabouraud's agar is the medium used to culture these actinomycetes.

MYCETOMA

Mycetoma is a localised chronic infection which involves the skin, subcutaneous tissue and bones of the feet, hands or other parts of the body. Tissue swelling, draining sinuses and grains should be present in order to make a diagnosis of mycetoma (4). The causative organisms are either true fungi giving rise to eumycotic mycetomas, or filamentous bacteria giving rise to actinomycotic mycetomas (4). They are found as saprophytes in soil or on vegetable matter and infection usually follows a penetrating injury. The same species may cause mycetoma as well as non mycetoma infections. For instance, *Nocardia braziliensis* is the most frequent cause of actinomycotic mycetoma in South America but *Nocardia* in general more commonly gives rise to primary infection in the lungs with a tendency to distant spread; the disease is then called nocardiosis and is not classified as a mycetoma (4).Although *A. israelii* infection may present clinically as mycetoma, actinomycosis is excluded from the mycetomas because of its systemic nature involving internal organs, and the endogenous source of the infection.

Botryomycosis must be differentiated from the mycetomas as it may give rise to a similar clinical picture. It is caused by true bacteria, usually *Staph. aureus*, or Gram negative bacilli such as *Pseudomonas* and *E. coli.* It is distinguished by the presence of Gram positive cocci and Gram negative rods, and the absence of branching filaments in the grains (4).

Mycetomas prevail in tropical and subtropical countries and are highly endemic in Mexico, Central America and Venezuela (13). In Africa they are commonly found in Senegal, Sudan and Somalia, and in Asia in India and Thailand.Climate has a definite influence on the distribution of mycetomas; most of the countries with high endemicity are relatively dry areas with a short rainy season followed by a long dry season.

Mycetoma occurs more frequently in men than women and affects predominantly the age groups between 16 - 45 years. All races are affected. In Africa, eumycetes more frequently give rise to mycetoma than do actinomycetes. *M. mycetomatis* and, in West Africa *Leptosphaeria senegalensis,* are especially common. Actinomycetes are also important causes of mycetomas in Africa. *Streptomyces somaliensis* is particularly common in East Africa (Somalia and Sudan) and *A. pelletieri* in the West (Senegal and Nigeria). *A. madurae* is also common in Africa. *N. brasiliensis and N. asteroides* are seldom found in Africa except in the less arid regions of Uganda and Zaire (13).

Clinically mycetoma is characterized by relatively painless swelling of the tissues and by

sinuses through which a purulent exudate containing grains is discharged. In order to identify the causative organism, the grains should be examined fresh to determine their size, colour, texture and staining affinities. The size alone does not help to differentiate between true fungal and actinomycotic grains (3), but the colour of the grains may well be a clue to the aetiological agent. Brown to black grains are produced only by true fungi such as Madurella species, while only *A. pelletieri* produces bright red grains (20). The grains are then crushed and stained with potassium hydroxide, Gram stain and a modified acid fast stain (21).Actinomycetes have thin branching filaments, while eumycetes have thick branching hyphae. Biopsy specimens are stained with haematoxylin and eosin, PAS, Gram, a silver stain and an acid fast stain. In most cases these tests are sufficient to determine the species or at least the genera of the etiological organisms. However cultures are the most accurate method of identifying the organism.

For the culture of eumycetoma grains, Sabouraud's dextrose agar containing 0,5% yeast extract and antibiotics is used. For actinomycetoma grains, cultures are made on brain heart infusion agar incubated aerobically and anaerobically at 37 C without antibiotics in the culture media (22).

BLASTOMYCOSIS

This disease, also known as North American blastomycosis, is caused by *Blastomyces dermatitidis.* It is found in regions other than North America and has been described in Africa, India, South America and other countries (13).

Blastomycosis affects primarily the lungs but may disseminate to the skin, bones, central nervous system and other organs. Although infection is usually acquired by the inhalation of spores, it occasionally occurs as a result of inoculation in laboratory accidents. Such cases usually do not become systemic (4). The fungus has been recovered from domestic animals such as dogs , and from the soil (23), but its true habitat has not yet been discovered (3).

The skin lesions of blastomycosis may be solitary or numerous. They present as verrucous plaques, ulcers or subcutaneous abscesses. The verrucous lesions have central scarring and a raised warty border containing numerous pustules. The subcutaneous abscesses usually develop as an extension of bone lesions (17).

Histological examination in verrucous lesions shows epidermal hyperplasia, which may be pseudoepitheliomatous, intraepidermal abscesses, dermal microabscesses and multinucleated giant cells. The yeasts of *B. dermatitidis* have a thick wall giving them a double-contoured appearance. They may be seen lying free in the tissue, especially in abscesses, but are more commonly found within the giant cells, appearing as small round holes within their cytoplasm (17). Occasionally, a single broad-based bud is seen which is distinctive for this fungus (3).

The diagnosis may be confirmed by culture on Sabouraud's, or more enriched agar (24).

4. Review of the South African literature

The first comprehensive review of fungal diseases published in Southern Africa was by Lurie, from the Hillbrow branch of the South African Institute for Medical Research (SAIMR) in Johannesburg. He reviewed the findings based on the results of positive cultures over the years 1947 to 1954 (1). In 1973 Martin and Berson reviewed cases seen over a 21 year period from 1950 to 1970 at the Hillbrow SAIMR and the National Research Institute for Occupational Diseases in Johannesburg (2). Prior and subsequent to these large surveys, isolated reports concerning deep fungal infections involving the skin have appeared in the South African literature.

In Lurie's report of fungal diseases diagnosed at the SAIMR in Hillbrow between 1947 and 1954, the following number of cases were documented:

Actinomycosis and nocardiosis	-	96
Chromoblastomycosis	-	41
Sporotrichosis	-	34
Maduramycosis	-	22

Martin and Berson recorded the following number of cases for a 21 year period (1950 - 1970) in the same area:

Sporotrichosis	-	688
Actinomycosis	-	119
Maduramycosis	-	70

Chromoblastomycosis	-	64
Nocardiosis	-	32
Blastomycosis (1 with skin lesions)	-	3

Other reports of deep fungal infections involving the skin are reviewed according to the specific diseases.

SPOROTRICHOSIS

In 1927 Pijper and Pullinger recorded an outbreak of sporotrichosis in South Africa (25). It occurred at the Modder East Mine, and affected 14 black gold miners, all of whom presented with the lymphocutaneous type. In 5 cases culture of the fungus was successful while the other 9 cases were diagnosed on clinical grounds.

The first case of sporotrichosis reported in a white person was in 1931 by Goldberg and Pijper (26). The patient was a 42 year old German man who had been living in Bechuanaland (Botswana) for 7 months. He presented with multiple abscesses on the face and trunk as well as variously located deep seated abscesses.

In 1941 Dangerfield and Gear reported an outbreak of 74 cases of sporotrichosis in two of the Witwatersrand Gold Mines (27). The infection occurred in miners in contact with both timber and rocks, and they postulated that infected water may have contaminated rock, timber, machine handles or open wounds. Attempts to trace the source of infection were

unsuccessful.

In 1942 Dr CJ du Toit reported to the Transvaal Mine Medical Officers Association, an outbreak of sporotrichosis at the Venterspost Gold Mining Company, where 650 cases had occurred (28).

In a report from the Transvaal Chamber of Mines in 1947, it was stated that 1406 positive cultures of sporotrichosis had been recorded at the SAIMR Johannesburg, but the time period involved was not stated. The disease had been contracted from 17 different mines in the Witwatersrand (18).

Helm and Berman investigated 2441 cases of sporotrichosis at Venterspost Gold Mine between March 1941 and July 1943, and 384 cases at Consolidated Main Reef Mine between August 1942 and October 1944 (29). They found that only 83 patients were white, while the remaining 2742 were black mine workers. They believed that the skin had to be traumatised for the fungus to be implanted, in spite of the fact that the majority of patients had no history of a preceding wound. The hands and arms were most commonly affected, and pustules and ulcers were the most common lesions. Many cases of the lymphocutaneous type were seen, but no patients with metastatic disease.

Brown and her collegues at the Transvaal Chamber of Mines Timber Research Laboratory found that untreated timber was the source of the fungus but, as the timber decayed, it became progressively more difficult to find spores, because the pathogen was destroyed by

other wood-attacking fungi (28). Once the presence of the fungus on underground timber was confirmed, both by visual examination, and by culture methods, spraying with "Yard Mixture" or "Dowicide" was begun. Furthermore, all the new timber was treated before being sent underground, and thus the epidemics of the early 1940's started to decline. The origin of the fungus in the mines has not been elucidated. The germination of spores was found to be poor in mine water, on mud and on wet rock. Experimentally where well seasoned timbers were used, it was found that *S. schenckii* would not establish itself on the wood unless the relative humidity was between 95 - 100%. From experimental research, water and insects were thought to play an important role in the distribution of the spores but air was not considered to be an important transport vehicle. The fungus may have been introduced by an infected patient, or by infected timber from plantations or from storage yards. A search for *S. schenckii* in the forests of Zululand by Weintroub and Wilton yielded negative results (28) but the fungus was isolated from the feet of miners with what appeared to be athletes foot by Brandt and van Niekerk (30) .These strains however had different cultural characteristics to classical *S. schenckii* and did not cause clinical disease in experimental animals.

James, cited by Findlay (30), thought that the origin of the fungus was probably the timber plantations, but, the findings of Brandt and Van Niekerk suggest that the wood could be contaminated by the soil in the vicinity of the mines (30).

Most cases of sporotrichosis in South Africa are of the localized or lymphocutaneous type and are commonly seen by dermatologists in private practice and not reported. Patients

with widely disseminated sporotrichosis are however rare. Cases with involvement of muscles, bones and viscera, were reported by Lurie in 1963 (32) and by Schamroth, Grieve and Kellen in 1988 (33). Two patients with disseminated sporotrichosis involving bone have also been seen, one in Pretoria in the 1970s and the other in Johannesburg in 1996. [Schulz EJ Personal Communication].

Gluckman in 1965 described 3 cases of sporotrichosis in children and stated that the clinical appearance of the lesions in children may differ from the classical lymphocutaneous form found in adults, and present rather as a chronic non- healing granulomatous ulcer on a limb (34). Cases of sporotrichosis in white children are regularly seen by dermatologists in private practice. These patients normally contract the disease, which includes the lympho-cutaneous type, while playing in the garden.

CHROMOBLASTOMYCOSIS

The first six cases of chromoblastomycosis in what was then the Union of South Africa were documented by Simson and co-workers in 1943 (35). Three patients were diagnosed at the King Edward VIII Hospital in Durban, while the other three were from Umtata, Uitenhage and the Consolidated Main Reef Mine Native Hospital respectively. Four patients were black and two were Indian. Five were males and one female. All had involvement of the lower limb. The causative fungus was isolated from two cases, one of which had the characteristics of *Fonsecaea pedrosoi* while the other was not classifiable.

In 1949 Friedlander and Moss described a case in a Natal Indian in which the diagnosis was made microscopically without culture (36).

In 1955 Lurie documented a further 41 cases diagnosed in the Johannesburg area over an 8 year period i.e. about 5 cases per year (1). Most of the patients were black, and the diagnosis was established histologically. In six cases where tissue was submitted for culture *Fonsecaea pedrosoi* was isolated. In 1957 Findlay reported a case of chromoblastomycosis in a 51 year old white male from Thabazimbi who had involvement of the left forearm and was found to have a *Hormodendrum* species on culture (37).

In 1962 Harwood-Nash described a 50 year old coloured male from Caledon with involvement of a foot, ear and side of the head. *Phialophora verrucosa* was isolated (38). Five years later,in 1967 Whiting described 4 cases of chromoblastomycosis seen in Pretoria (39). They were all due to *F. pedrosoi.*

In 1971 Bayles reported that while conducting a trial of thiabendazole therapy in patients with chromoblastomycosis, she had recruited 19 patients over a 3 year period from different areas of Natal (12). The majority of the patients were female, apparently because women in Zululand carry out the agricultural duties. *F.pedrosoi* was isolated from six patients , and *C. carrionii* from one.

In 1973 Martin and Berson reported 64 cases of chromoblastomycosis diagnosed in the Transvaal over the 21 year period from 1950 - 1970, i.e. an incidence of approximately 3 cases per year (2). Culture of material occasionally yielded *F. pedrosoi.*

In 1985 Heyl described 2 patients with chromoblastomycosis due to *C carrionii* who were treated with itraconazole (40).

ACTINOMYCOSIS

The first South African case of actinomycosis was recorded in 1907 by Willoughby Smith who described a man from Middelburg, Transvaal with the cervicofacial form of actinomycosis (41). In 1912 Ricono described two Basuto women from East Griqualand, each presenting with the cervicofacial from of actinomycosis (42).

In 1927, reporting from the Transvaal, Pijper and Pullinger stated that they had seen only one case of actinomycosis in several years (43). The patient was a white boy with abscess formation in the neck and yellowish grains in the exudate. Anaerobic cultures yielded what was called at that time *Cohnistreptothrix israeli*.

In 1931 Forman described a 27 year old white man with pulmonary actinomycosis in whom the diagnosis was made by demonstrating the sulphur granules in pus drained from a swelling over a rib (44).

In 1955 Lurie recorded 96 cases of actinomycosis and nocardiosis which he grouped together (1). Of the 27 cases in which cultures were positive, 14 were due to *A israelii*. The commonest sites involved by these actinomycetes were the skin and subcutaneous tissue (79%), followed by the lung (14%).

In 1973 Martin and Berson documented 119 cases of actinomycosis in the Transvaal seen over a 21 year period - i.e about 6 cases per year (2). Two of these , both black males, had

generalised superficial actinomycosis.

NOCARDIOSIS AND MYCETOMA

Nocardia species are a common cause of mycetoma. Reports concerning nocardiosis and mycetoma often overlap and they are therefore dealt with together under one heading.

The earliest record of mycetoma in South Africa was the report by Blaine in 1894 who described the disease in two black patients, one from Kimberley and the other from the Transkei (45). In 1905 Bays documented Madura foot in a black patient from Port Elizabeth (46). The causative organisms were not cultured in these earlier reports.

In 1914 McMurtrie described a case of black grain mycetoma in a 62 year old black woman seen at his hospital in the Transkei (47). She presented with swelling and sinus formation on the left foot, and black grains were seen on surgical exploration.

In 1921 Krige reported a case of Madura foot which had been misdiagnosed as leprosy at the Pretoria Leper Asylum (48). Also in 1921 Welchman and Pirie reported a case of mycetoma of the right foot in a 66 year old black male from Middelburg in the Transvaal (49). On culture *Nocardia indica* was isolated. At the medical meeting where this patient was presented only two of 40 members present had seen similar cases in South Africa. Dr. A Pijper had seen one in the Lydenburg (Transvaal) district where the causative organism had not been determined, and Dr. JG Becker had seen specimens from two patients, an

Indian and a white man from South West Africa. In both specimens the fungus isolated was a black species. Subsequently Dr. Brebner and Dr. Girdwood reported on similar cases in the Transkei and from what is now Mozambique.

Pijper and Pullinger in 1927 reviewed their cases of nocardiosis which included 11 patients with mycetoma, in five of whom the feet were involved (43). Three cases of actinomycotic mycetoma were reported as being due to new varieties of *Nocardia*, but at least one of these was later found to be *S. pelletieri.*

In 1928 des Ligneris reported 10 cases of mycetoma, all involving the foot, which he had seen at Elim hospital in the Northern Transvaal over a period of 15 years (50). The first case, seen in 1913, had pale granules but of the subsequent cases, 7 had black granules and 2 had red granules. The patients were all middle-aged Pedi and Venda males.

In 1948 Buchanan and co-workers reviewed the available records of actinomycotic infection in South Africa and described a further 8 patients who were infected with aerobic *Actinomyces*, and presented with either empyema, subcutaneous abscesses, a combination thereof, or otomycosis (51).

In 1971 Findlay and Roux described two cases of mycetoma due to *S. pelletieri* (9). The first case was that of a 59 year old white farmer who used water from the Limpopo river to irrigate his land. He developed a mycetoma pedis without a history of previous trauma. The second case was a 45 year old black farm worker with an infection of the feet. In both

patients characteristic red grains were found. Also in 1971 Lawson and Davey reported that they had isolated *S. pelletieri* from river water in the area where these two patients had worked (52). However this fungus differed in growth requirements from that isolated by Findlay and Roux, and its pathogenicity was considered doubtful.

In 1974 Vismer and Morrison described the first case of confirmed *Actinomadura madurae* mycetoma in South Africa (8). Their patient was a 28 year old black man from the Pietersburg district who had a mycetoma of the left foot with multiple sinuses containing yellow white granules which on culture proved to be *A. madurae.* This organism is easily recovered from soil, and a strain resembling existing pathogenic strains was isolated by botanists from a tributary of the Jukskei river near Johannesburg (52).

Findlay and Vismer analyzed the black grains formed by *M. mycetomi* in tissues. They found that the melanoprotein in the grain cement was extremely hard and inpenetrable, making it resistant to treatment with drugs (53).

In 1975 Freed and co-workers reported the first case of actinomycotic mycetoma due to *S. somaliensis* (10). The patient was a 40 year old white male miner who developed a mycetoma of his left foot.

In 1977 Dogliotti and Young from Johannesburg reported an additional case of *S. pelletieri* induced mycetoma in a 41 year old black farmer (54).

BLASTOMYCOSIS

The first case of blastomycosis in South Africa was recorded by Emmons and co-workers in 1964 (55). The patient was a 29 year old black mine worker seen at the Ernest Oppenheimer Hospital in Welkom in 1961. He presented with backache and was found to have osteolytic lesions of the twelfth rib and lumbar spine with an associated abscess and sinus tract. Culture of the abscess wall revealed *B. dermatitidis.*

Osmond, Schweitzer, Dunbar and Villet in 1971 reported a 39 year old Zulu patient with paraplegia due to blastomycosis of the spine (56). The diagnosis was established histologically. The fungus was however never cultured.

In 1973 Martin and Berson documented three cases of blastomycosis (2). The first patient was a 50 year old black female, seen at the Edenvale Hospital in 1959. She presented with abdominal symptoms, and biopsy of the mesenteric lymph glands showed giant cell granulomata and yeast cells consistent with *B. dermatitidis.* Culture was not done. The second patient was a 27 year old black male seen at Baragwanath Hospital in 1967. He presented with multiple bony abscesses from which *B dermatitidis* was cultured. The third patient was a 36 year old white male from Natal who presented with destructive lesions of the vertebrae and a rib. Pus from a paravertebral abscess revealed yeast cells consistent with *B dermatitidis,* but culture proved negative.

Fragoyannis, van Wyk and de Beer in 1977 described a 46 year old black mine worker

from the North Eastern Transvaal who presented at Ga-Rankuwa hospital with a single large ulcer on a leg, without evidence of systemic disease (57). The diagnosis was made on direct smears as well as biopsy of the edge of the ulcer, but culture results were not stated. In the same year Young reported a case of blastomycosis involving the knee of a black man where the diagnosis was confirmed by fluorescent antibody studies in the absence of culture (58).

Simon, Berson and Young in 1977 reported a 63 year old white male with a chronic ulcerative tumour on the tongue which histologically showed the presence of yeasts and giant cell granulomas (59). Culture confirmed the diagnosis of *B. dermatitidis* infection. At post mortem examination, lesions due to *B. dermatitidis* were also present in the lungs.

Hurwitz and co-workers in 1986 described a 47 year old white male seen at the Johannesburg Hospital, with a diffuse pulmonary infiltrate, right cervical adenopathy and enlarged tonsils (60). A biopsy of the right tonsil revealed organisms with a broad-based bud consistent with blastomycosis. In the same year, de Villiers, Smith and Vismer reported a 45 year old black male farm labourer from the eastern Transvaal, who presented with weight loss, pulmonary symptoms, granulomatous ulcers and subcutaneous abscesses with underlying bone destruction (61). *B. dermatitidis* was found in skin biopsies and on culture.

In 1987 Berkowitz and Diamond described a 24 year old black male seen at Baragwanath Hospital with a diffuse alveolar infiltrate and subcutaneous abscesses (62). *B. dermatitidis*

was isolated on culture of pus, sputum and urine (61).

Cooper, Lalloo and Naran in 1988 described two patients from Natal with cerebral blastomycosis, the diagnosis being made post mortem in each case (63). The first patient was a 44 year old black male who presented with a verrucous ulcer on the right nostril, left sided bronchopneumonia and lytic bone lesions. *B. dermatitidis* was cultured from a biopsy of the ulcer and was also seen histologically at post mortem in a cerebellar abscess. The second patient was a 50 year old black man who presented in a confused state and soon died. At autopsy involvement of the basal ganglia in the right cerebral hemisphere by yeasts consistent with *B. dermatitidis* was confirmed by histological examination.

In 1989 Frean and co-workers reviewed *B. dermatitidis* infections in South Africa (64). Until 1988, only 20 cases of blastomycosis had been confirmed. The patients were from all four provinces, the majority coming from the Transvaal. Only two of the patients were female. and four were white. It is of interest that between 1952 and 1989, 81 cases were reported from Africa, including 28 in Zimbabwe.

In 1993 Frean, Blumberg and Woolf described two black male patients from the northern and north-western Transvaal, who presented with disseminated blastomycosis, initially misdiagnosed as tuberculosis (65).

PRESENT STUDY

1. Materials and Methods

Data were obtained from the records of the Departments of Mycology and of Anatomical Pathology of the SAIMR at Baragwanath Hospital and at the Central Institute of the SAIMR in Hillbrow, Johannesburg. The latter drains seven regional hospitals as well as outlying areas.

The cases included in this study were those in which a positive diagnosis of deep fungal infection had been made, either by biopsy or by culture, from specimens obtained from the skin. Thus only deep fungal infections with cutaneous manifestations were included. The site of the lesions from which the specimens were taken was determined from the laboratory records where recorded.

Records of the results of fungal culture from 1987 to 1996 were obtained from both mycology laboratories.

Results of histological examination of skin biopsies from 1987 to 1996 were available from the Department of Anatomical Pathology at Baragwanath Hospital, where they had been filed according to diagnosis. At the SAIMR in Hillbrow this information was only available for the period 1990 to 1996.

From the laboratory record books, the patients' hospital numb , were obtained and the bedletters traced where available. The age, sex and place of residence of the patients were determined as far as possible from the hospital files. In many cases these files were no longer accessible, as they had been destroyed or mislaid. Where the specimens had been submitted by private dermatologists, these particulars were obtained from the doctors' records.

2. Results

GENERAL

A total number of 120 cases of deep fungal infections were diagnosed at the Hillbrow and Johannesburg branches of the SAIMR during the years of the survey. This includes diagnosis by both histological means as well as culture. The breakdown according to disease is shown in the following table:

Table 1 Deep fungal infections diagnosed at the SAIMR, Hillbrow and Baragwanath, Johannesburg 1987-1996

DISEASE	HILLBROW	BARAGWANATH	TOTAL
Sporotrichosis	34	23	57
Chromoblasto-mycosis	7	9	16
Mycetoma Actinomycetoma Eumycetoma	 Unknown 7	 Unknown 0	 ? 7
Actinomycosis	9	2	11
Blastomycosis	3	2	5

The diagnosis of deep fungal infection was made on histological grounds in 24 cases, in some of which it was confirmed by positive culture. The breakdown according to method of identification and branch of the SAIMR where the diagnosis was made is shown in Table 2 .

Table 2 Histological diagnoses of deep fungal infections at the SAIMR Johannesburg 1987-1996

	SAIMR Baragwanath		SAIMR Hillbrow/ Johannesburg	
Disease	Number of cases	Positive cultures	No.cases	positive. cultures
Sporotrichosis	8	2	0	0
Chromoblastomycosis	6	2	5	not done
Actinomycetoma	3	not done	0	0
Blastomycosis	1	not done	1	"done"
Total	18	4	6	

The positive cultures obtained at the two branches of the SAIMR are shown in the following tables:

Table 3. Positive cultures of deep fungal infections in the Johannesburg area 1987-1996

Organism	**Baragwanath**	**Hillbrow**	**Total**
S schenckii	15	34	49
N asteroides	6	14	20
N dassonvillei	0	2	2
N caviae	0	2	2
N brasiliensis	0	1	1
S somaliensis	0	1	1
C carrionii	1	0	1
F pedrosoi	2	2	4
P boydii	0	6	6
A israelii	0	9	9
A meyeri	2	0	2
M mycetomatis	0	1	1
B dermatitidis	1	3	4
Total	27	74	101

Table 4. Positive fungal cultures in deep mycoses at the SAIMR Baragwanath Hospital 1987 - 1996

DISEASE	NUMBER OF CASES	ORGANISM
Sporotrichosis	15	S. schenckii
Chromoblastomycosis	3	F. pedrosoi 2 C. carrionii 1
Mycetoma Actinomycetoma Eumycetoma	 ? 0	 N. asteroides 6
Actinomycosis	2	A. meyeri
Blastomycosis	1	B. dermatitidis

Table 5. Positive fungal cultures in deep mycoses at the SAIMR Hillbrow 1987 - 1996

DISEASE	NUMBER OF CASES	ORGANISM
Sporotrichosis	34	S. schenckii
Chromoblastomycosis	2	F. pedrosoi
Mycetoma Actinomycetoma Eumycetoma	 ? 7	 N. asteroides 14 N. dassonvillei 2 N. caviae 2 N. brasiliensis 1 S.somaliensis 1 P. boydii 6 M. mycetomatis 1
Actinomycosis	9	A. israelii
Blastomycosis	3	B. dermatitidis

?:Uncertain whether they were true cases of actinomycetoma or not-see text!

Table 6. Species of fungus implicated according to disease

DISEASE	FUNGUS
Sporotrichosis	S. schenckii
Chromomycosis	F. pedrosoi C. carrionii
Mycetoma	?N. asteroides ?N. dassonvillei ?N. caviae ?N. brasiliensis S. somaliensis P. boydii M. mycetomatis
Actinomycosis	A. israelii A. meyeri
Blastomycosis	B. dermatitidis

?:Uncertain whether true cases of mycetoma or not-see text.

SPOROTRICHOSIS

There were 57 cases of sporotrichosis recorded: 34 at the SAIMR Hillbrow, and 23 at the SAIMR at Baragwanath Hospital. The breakdown according to method of diagnosis is as follows:

Table 7. Cases of sporotrichosis in the Johannesburg area 1987 - 1996

Method of diagnosis	SAIMR Hillbrow	SAIMR Baragwanath	Total
Positive culture	34	15	49
Histology	0	8	8
TOTAL	34	23	57

All cases were of the fixed cutaneous or lymphocutaneous forms.

The majority of patients (40) were black while 15 were white and two Indian. Patients lived in both urban and rural areas, and some worked on the mines as is shown in the following table.

Table 8. Domicile or workplace of patients with sporotrichosis

Place		No. cases
Johannesburg	-	9
Durban Deep Mine	-	2
Leratong	-	4
Vereeniging	-	1
Springs	-	1
Goldfieldswest	-	1
Krugersdorp	-	1
Edenvale	-	1
Westvaal	-	2
Middelburg	-	2
Sasolburg	-	1
Soweto	-	1
Unknown	-	31
Total		57

CHROMOBLASTOMYCOSIS

There were 16 cases of chromoblastomycosis recorded: 7 from the SAIMR Hillbrow and 9 from the Baragwanath laboratory - see tables 9 and 10.

Table 9. Cases of chromoblastomycosis in the Johannesburg area 1987 - 1996

Diagnostic method	SAIMR Hillbrow	SAIMR Baragwanath
Culture (+)	2	3
Histology (+)	5	6
TOTAL	7	9

Table 10. Species isolated in cases of chromoblastomycosis

Species	Number of cases
F. pedrosoi	4
C. carrionii	1

The known domicile or workplace of the cases of chromoblastomycosis is as follows:

Table 11. Domicile or workplace of patients with chromoblastomycosis

Place		Number
Soweto	-	2
Johannesburg	-	2
Boksburg	-	1
Mocambique	-	2
Springs	-	1
West Vaal mine	-	1
Unknown	-	7
Total		16

ACTINOMYCOSIS

In the 9 year period of the study, 11 cases of actinomycosis were documented. Nine patients were recorded with this disease at the SAIMR Hillbrow where the causative organism was *A. israelii*. Of these, one was a black male from Heidelburg who had thoracic actinomycosis, while a patient from Masinga in Natal presented with a parotid

abscess. Clinical details of the rest of the cases are unknown. At the Baragwanath mycology laboratory, two cases were recorded, both due to *A. meyeri* (see Table 12).

Table 12. Cases of actinomycosis recorded in the Johannesburg area 1987 - 1996

Species cultured	SAIMR Hillbrow	SAIMR Baragwanath	TOTAL
A. israelii	9	0	9
A. meyeri	0	2	2
Total	9	2	11

The recorded place of domicile or work for patients with actinomycosis are shown in the following table:

Table 13. Domicile or workplace of patients with actinomycosis

Place		Number
Hillbrow	-	3
Natalspruit	-	1
Coronation	-	1
Unknown	-	6
Total	-	11

MYCETOMA

The cases of mycetoma recorded in this study are classified as actinomycetoma or eumycetoma. Under the heading actinomycetoma are included all the recorded cases of Nocardia infections involving the skin. The laboratory source of positive diagnoses of

mycetoma are shown in table 14.

Table 14. Cases of mycetoma diagnosed in the Johannesburg area 1987-1996

	SAIMR /	Hillbrow	SAIMR /	Baragwanath
	Culture (+)	Histology (+)	Culture (+)	Histology (+)
Actinomycetoma	?	0	?	3
Eumycetoma	7	0	0	0

Actinomycotic mycetoma

There were 20 cases of *N. asteroides* infection documented, an average of 2 cases per year. Two cases of *N. dassonvilleii* and *N.caviae* infection, and one case each of *N. brasiliensis* and *S. somaliensis* infection were recorded. One patient with *N. dassonvillei* infection was a coloured diabetic from Ennerdale with blisters from which the fungus was isolated; the other was a white male from Ermelo but no clinical details were availabie. One patient with *N. caviae* infection was a black female from Port Elizabeth. The culture specimen was sent to the mycology laboratory at the SAIMR in Hillbrow for fungal identification without any clinical details. The second patient was an HIV positive black male miner from Kinross who had a crushed hand amputated following a rockfall. The stump became infected and N. caviae was cultured.

The species isolated in cases of actinomycetoma are shown in table 15.

Table 15. Species isolated in possible cases of actinomycetoma

Species isolated	Number of cases
N. asteroides	20
N. dassonvillei	2
N. caviae	2
N.brasiliensis	1
S. somaliensis	1

Two cases of actinomycotic mycetoma of the foot were diagnosed histologically at the South African Institute for Medical Research at Baragwanath Hospital but none at the South African Institute for Medical Research in Hillbrow.

Seven cases of **eumycetoma** were recorded, all at the SAIMR in Hillbrow and none at the Baragwanath laboratory. Six were due to *P. boydii* and one to *M. mycetomatis.* The majority of patients were males. The species isolated are shown in table 16.

Table 16. Species isolated in cases of eumycetoma

Species	Number of cases
P. boydii	6
M. mycetomatis	1

The residence of patients with mycetomas is listed in table 17. Four of the patients with *P. boydii* infection were from Krugersdorp.

Table 17. Domicile or workplace of patients with mycetoma

Place	Number
ACTINOMYCETOMA	
Coronationville (*N. dassonvillei)*	1
State Health Johannesburg	1
Rand Mutual Mine Hospital	1
Hillbrow	2
Witbank	1
Springs	1
EUMYCETOMA	
Leratong Hospital	4
Randfontein	1
Rand Mutual Mine Hospital	1
Unknown	20
Total	33

BLASTOMYCOSIS

Five cases of blastomycosis involving the skin were recorded over a 10 year period from 1987 to 1996, 3 at the SAIMR Hillbrow and 2 at the SAIMR Baragwanath Hospital. The diagnosis was confirmed by culture in most cases.Two of the patients documented by fungal culture at SAIMR Hillbrow were inpatients at Rietfontein hospital. The first patient was a 40 year old black male from Pietersburg. He presented with chest disease, a paravertebral abscess at T4/T5 with overlying sinus formation, and was misdiagnosed as having tuberculosis. Anti-TB treatment was initiated but he died before the fungal culture result was known.

The second patient was a 31 year old miner from Thabazimbi. He also presented with chest disease, a spinal lesion at T12 and extensive abscesses on his face, forehead ears and

anterior chest as well as dry scaly lesions. He did not respond to anti-TB treatment and later when treatment was changed to Amphotericin B he improved steadily. These two cases were published as " Disseminated blastomycosis masquerading as tuberculosis" by Frean and co-workers in 1993 (65).

The third patient was a 30 year old HIV positive white male who was seen at the Johannesburg Hospital with pyrexia, meningitis and an extensive, erythematous, papular rash on his face trunk and limbs. Large plaques resembling erythema multiforme were present on his trunk. A skin biopsy revealed numerous yeasts within macrophages in the dermis. Fungal culture was interpreted as histoplasmosis, but DNA fingerprinting done at the Center for Disease Control in Atlanta established the diagnosis of blastomycosis. The patient initially responded to treatment with amphotericin B and fluconazole but later died.

I was unable to recover the hospital files of the patients with blastomycosis seen at Baragwanath Hospital. The one patient was a 44 year old black male with an abscess of the right cheek. A biopsy showed the presence of fungal elements consistent with blastomycosis within the dermis. Culture was not performed. The second patient was a black male with an abscess on the chest from which *B. dermatitidis* was cultured.

DISCUSSION

The records used for this study do not include cases from the private sector, and the numbers thus do not reflect the true prevalence and incidence but only the relative frequency of the deep fungal infections encountered in the Johannesburg area. Clinical information was not always available at the relevant hospitals and this was restrictive in certain aspects of this report. By comparing these results with two similar studies it is however possible to draw conclusions about whether the diseases are increasing or decreasing. To facilitate comparison the results of the three surveys are summarised in Table 18 on page 40.

SPOROTRICHOSIS

This study confirms previous observations that sporotrichosis is the commonest deep fungal infection in the Johannesburg area (1,2). My figures do not reflect the total number of cases as many, if not most, are diagnosed in the private sector, and presumably this was also the case in earlier reports.

Sporotrichosis was the commonest deep fungal infection documented at both Baragwanath SAIMR and the central institute at Hillbrow with 23 and 34 cases respectively (see Table 1). At Baragwanath 15 of the cases were diagnosed on culture, and 8 on histological grounds. Only 2 of the 8 patients had both histology and fungal cultures performed which implies that the diagnosis was not obvious clinically in the other 6 patients. At Hillbrow all

Table 18. Comparison of surveys of deep fungal infections in the Johannesburg area

Diseases Number of cases Organism	Lurie 1955 8 years 1947- 1954	Martin&Berson 1973 21 years 1950-1970	Klevansky 1997 10 years 1987-1996
Sporotrichosis	34 *S. schenkii*	688 *S. schenkii*	57 *S. schenkii*
Chromoblasto-mycosis	41 *F. pedrosoi* 6 rest not cultured	64 *F. pedrosoi* on occasion, otherwise not stated	16 *F. pedrosoi 4* *C. carrionii 1* *rest not cultured*
Actinomycosis	96 *Nocardiosis* and actinomycosis	119	11 *A. israelii* 9 *A. meyeri* 2
Mycetoma	22 *Madurella spp* 3 *Monosporium apiospermum* 1 rest not cultured	70 *M. mycetomi* commonest *A. madurae* *A. pelletieri* *S. somaliensis* *P. boydii* *M. grisea* *P. gougeroti*	29 *N. asteroides* 20 *N. dassonvilleii* 2 N.caviae 2 N.brasiliensis 1 S.somaliensis 1 *P. boydii* 6 *M. mycetomatis* 1
Blastomycosis	0	3	5

the cases were diagnosed on culture.

In this study the incidence of sporotrichosis was found to be almost 6 cases per year - slightly greater than the approximately 4 cases per year recorded by Lurie during the 1950s (1), but far less than the approximately 33 cases per year documented by Martin and Berson during the epidemics in the mines in the 1970s (2). This dramatic decrease in the incidence of sporotrichosis in the Johannesburg area since 1970 is certainly due to the effective treatment of timber used in the mines which prevented the outbreak of further epidemics.

In this study some patients had a history of trauma to the skin while others did not. Many were unsure where and how they had contracted the disease. In many cases of sporotrichosis diagnosed at the Hillbrow SAIMR the specimens had been submitted by private practitioners. Most of the patients seen in private practice in the Johannesburg area contract the infection in their gardens.

No cases of disseminated sporotrichosis were recorded in this study and I know of only two cases seen in the vicinity in recent years. The one was a white male, seen at Pretoria Hospital in the 1970s and the other, a black male, was diagnosed at Baragwanath Hospital in 1996. Both had bony involvement (Schulz E.J. Personal communication).

CHROMOBLASTOMYCOSIS

According to the finding in this study of 1,6 cases per year, the number of patients with chromoblastomycosis recorded in the Johannesburg area has declined since documented by Lurie (approximately 5 cases per year), and Martin and Berson (approximately 3 cases per year). The reason for this may be that the black population has become more affluent in recent years and can afford protective shoes and clothes. The increasing urbanization of the black population may be an additional factor for this decline as most infections result from trauma occurring in the rural areas. The lower incidence of chromoblastomycosis in the Transvaal as compared to Natal, where in the 1960's it was reported by Margaret Bayles as approximately 6,3 cases per year (12), is most likely attributable to the tropical climate found in the latter province. In Natal the majority of the patients with chromoblastomycosis were female, which was ascribed to the fact that (at that time) in Zululand, women carried out the agricultural duties (12). In this study 7 of the patients were male and 6 female. All the patients were black except for one elderly white female who had a subcutaneous cyst on a finger. The patients resided in both urban and rural areas (see table 11), however it was impossible to ascertain exactly where they had contracted the infection.

The two species documented as aetiological agents in this series were similar to those previously recorded in the South African literature. Two of the Hillbrow cases were diagnosed on culture (both *F. pedrosoi*), and five on histology. Of the Baragwanath cases 3 were diagnosed on culture (*F. pedrosoi* - 2, *C. carrionii* -1), and the remainder histologically. None of the Hillbrow patients, and only two of the Baragwanath patients

were diagnosed on both histology and culture.

ACTINOMYCOSIS

Of the 11 cases of actinomycosis recorded in this study, 9 were due to *A. israelii* and 2 were due to *A. meyeri,* the latter were both cultured at the SAIMR at Baragwanath Hospital. As far as I can establish this is the first time that *A. meyeri* has been documented in South Africa as a cause of actinomycosis. No clinical details of the patients were available. *A.meyeri* is also an uncommon cause of actinomycosis in other parts of the world; it has been reported to cause disseminated infection (66).

In this study an average of just over one case of actinomycosis per year was noted. It is not possible from Lurie's article of 1955 to establish the total number of cases of actinomycosis documented, but in 15 patients *A. israelii* was cultured - about 2 cases per year. The number of cases in the present study is appreciably lower than the 6 cases per year of Martin and Berson (2). The apparent decline in the incidence of actinomycosis may be due to improved dental hygiene.

MYCETOMA

Because of the lack of clinical data, it is difficult to compare the findings of the incidence of actinomycetomas in this study to those of Lurie (1) and of Martin and Berson (2). In the older reports it was not stated whether the patients were suffering from mycetomas or from other forms of deep fungal infection involving the skin. Lurie grouped actinomycosis and nocardiosis together, and noted 96 cases over the eight year period - an average of 12 cases

per year. The combined total of cases of actinomycosis plus nocardiosis in Martin and Berson's report is 151, i.e.7,2 cases per year, and for the present study is 36, i.e 3,6 cases per year.

Martin and Berson recorded 32 cases of nocardiosis, an incidence of 1, 5 cases per year. The incidence of nocardial infections in this study was 2,5 cases per year.

Lurie noted that 22 cases of maduramycoses had been confirmed over an 8 year period, an average of almost 3 cases per year. Martin and Berson documented 70 cases of "Maduramycosis" over a 21 year period, just over 3 cases per year, while the incidence of eumycetomas in this study was less than one case per year.

In Lurie's series *Madurella* species and *Monosporium apiospermum* were isolated in cases of maduramycosis (1). In Martin and Berson's series the actinomycetes isolated included *Streptomyces (Actinomadura) madurae, S. pelletieri* and *S. somaliensis,* while the true fungi included *P. boydii, Madurella grisea, Madurella mycetomatis* (the commonest) and *Phialophora gougeroti* (2). Martin and Berson, as well as Findlay and Roux (9) identified cases of mycetoma due to *S.pelletieri*, contrary to the report by Mariat in 1963 which stated that with the exception of Madagascar no cases occurred south of the equator (67).

In the present investigation S. somaliensis was the only streptomyces species recorded as causing actinomycetoma. *P. boydii* was by far the commonest cause of eumycetomas .

In this study, two organisms are reported as possibly causing mycetoma in South Africa for the first time , *N.dassonvillei* and *N. caviae*. *Nocardia (Nocardiopsis) dassonvillei* was previously thought to be a rare cause of mycetoma, but is now known to be quite widespread in the United States (68) where the first case was reported in 1985 (69).

N. caviae is an infrequent cause of mycetoma.Cases have been reported from Israel, Japan, Tunisia, India and Indonesia (5). It is thought that many cases of mycetoma reported as being due to *N.asteroides* in other parts of the world were actually caused by *N.caviae* (5). The few cases recorded resembled *N. brasiliensis* infection (4). *N. caviae* may also cause skin abscesses, osteomyelitis, lung infection, keratitis and disseminated disease (4). *N.caviae and N.dassonvillei* have not previously been described as causing nocardiosis or mycetoma in South Africa and it will be interesting to see if further cases will be recorded in the future.

BLASTOMYCOSIS

Blastomycosis, although very rare seems to have an increasing incidence in South Africa. Lurie documented no cases in his 1955 review (1). Martin & Berson reported 3 cases in 21 years (3), whereas in my series 5 cases were diagnosed in 10 years. It is interesting to note that all the cases in my series were males and that one was HIV positive. It is possible that the disease is more common in males because of greater exposure to the fungus as a result of their outdoor occupations. HIV infected patients with blastomycosis have been recorded in the medical literature, but *B. dermatitidis* is not generally regarded as an

opportunistic pathogen (70). It is also noteworthy that often the disease mimicked tuberculosis and that the patients were misdiagnosed and treated as such.

Carman reviewed the cases of blastomycosis described on the African continent (14). Between 1951 and 1987 a total of 81 cases were recorded; this included 13 previously unreported cases from Mozambique, Namibia, South Africa and Zimbabwe. They compared the clinical features of the African patients to their North American counterparts. The lungs, bone and skin were organs most likely to be affected in African patients. Their skin presentation also differed. African patients more often had ulcers or subcutaneous abscesses, rather than the verrucous plaques seen in American patients. This was confirmed in the patients recorded in my series. Kaufman and co-workers suggested that there are differences between strains of *B dermatitidis* isolated in Africa compared with the North American strain in terms of morphology, mycelial yeast conversion and antigenic structure - antigen A being common in North America isolates but rare in the African ones (71).

CONCLUSIONS

With the exception of sporotrichosis, deep fungal infections of the skin are so uncommon in the Johannesburg area that even dermatologists have little practical experience of them. Chromoblastomycosis,never common here as in Natal, is seen only occasionally, as are cases of mycetoma,actinomycosis and blastomycosis.Sporotrichosis is probably the only condition locally acquired due to its ubiquitous presence in plants and soil with the disease often being contracted in gardens.Fortunately the epidemics on the mines have resolved.The small number of cases of chromoblastomycosis and mycetoma can probably be ascribed to the following: the organisms are sparse in nature and more confined to rural areas; an increasing urbanization of the population; and the wearing of protective clothing, especially shoes.The number of cases may increase in the future due to the influx of infected individuals from countries beyond the borders of South Africa.Further research needs to be done to establish the role of *N.caviae* and *N.dassonvillei* in cases of mycetoma.

Actinomycosis is far less common than documented in the past possibly because of improved dental hygiene.Additional cases due to *A.meyeri* may be recorded in the future. Blastomycosis remains a very rare disease.It is speculative whether the increase in the number of cases is actually a true increase, or whether as a result of the AIDS epidemic increased specimens are being sent for fungal culture with a higher pickup rate.
Since the advent of the AIDS epidemic, atypical disseminated forms of cutaneous histoplasmosis and cryptococcosis are being seen locally and worldwide, and the number of

cases is likely to increase.

Additional studies are necessary to compare the findings of this report with statistics of deep fungal infections from other provinces in South Africa.

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