PATHOGENIC POTENTIAL OF ASPERGILLIUS AND PENICILLIUM SPECIES IN EXPERIMENTAL ANIMALS

Thesis

Submitted For Partial Fulfilment Of The

Degree of Master M.S. (Bacteriology)

By

Afaf Shaban Abd El-Rahman

M.B, B. Ch.

Ain Shams University

Under Supervisors :-

- Prof. Dr. ZEINAB MAGID
  Head of Bacteriology Department
  Faculty of Medicine
  Ain Shams University.

- Prof. Dr. MOHAMED KAMAL REFAI
  Veterinary Medicine
  Cairo University.

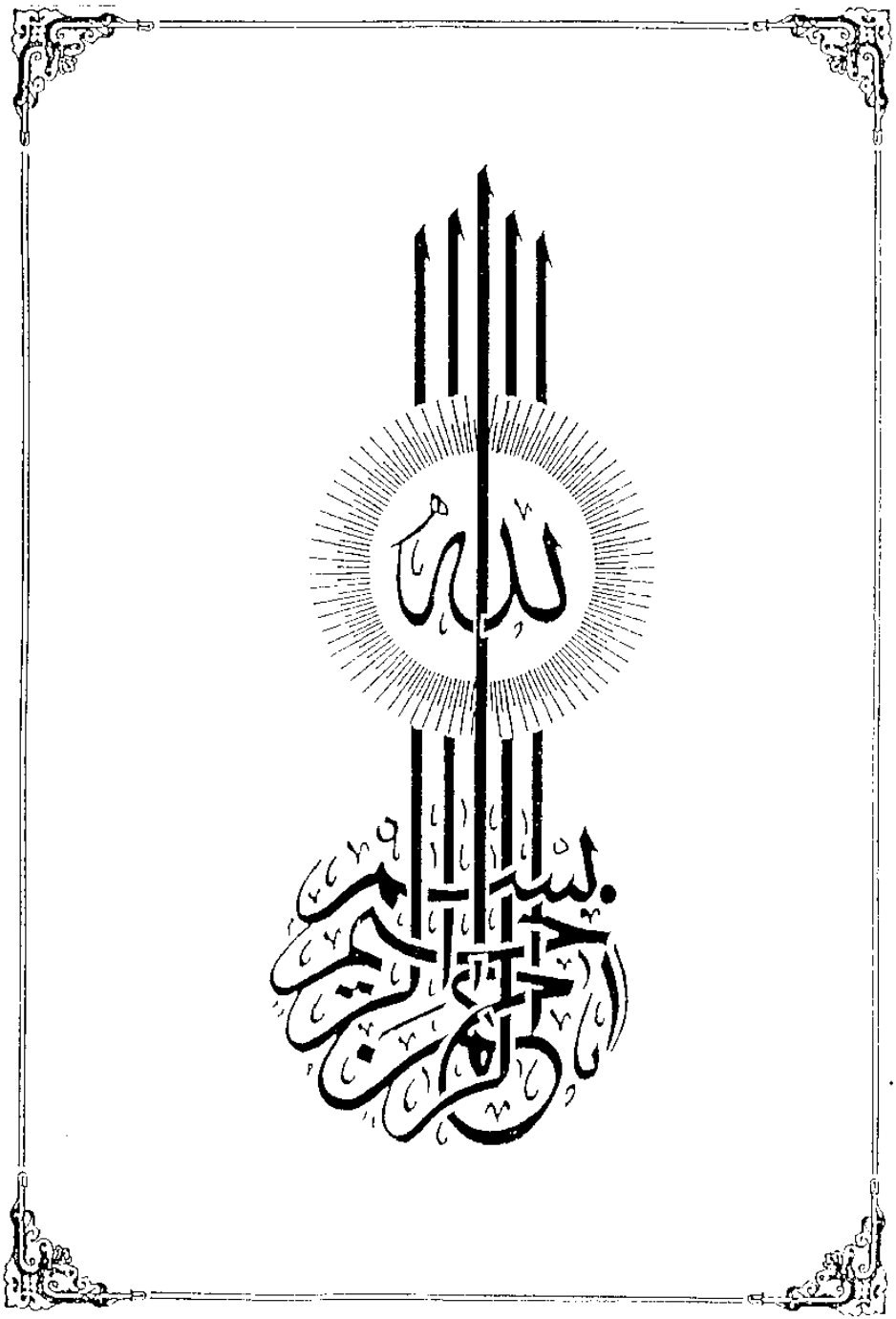
1981

ACKNOWLEDGEMENT

I wish to express my gratitude to Prof. Dr. Zeinab Magid, Head of the Bacteriology Department, Faculty of Medicine, Ain Shams University. Without her continuous support, persistent encouragement and expert advice, this work would have never been completed. I acknowledge her with a deep sense of gratitude.

Many thanks to Prof. Dr. M.F. Hefal Professor of Microbiology, Faculty of Veterinary Medicine, Cairo University, for his continuous support.

Finally, to the technicians at the Department of Bacteriology, Faculty of Medicine, Ain Shams University and Mr. M. Zaghloul, I wish to express my thanks for their effort in preparing the slides and photographs of this study.



CONTENTS

INTRODUCTION & AIM OF WORK

INTRODUCTION AND AIM OF WORK

The causative agents of most systemic and subcountaneous mycoses are saprophytes that are present in abundance in man's environment.

Members of the genus Aspergillus and Penicillium are particularly ubiquitous and survive under variable environmental conditions. Though certain species of Aspergilli as A. niger, A. flavus and A. fumigatus are encountered in human infection yet A. niger is thought to be less pathogenic than the other two species (Bhatia et al, 1969).

Few cases reported about penicillia human infections.

Factors which contribute to the virulence of Aspergillus or penicillium species are still not competely understood.

Ford and Friedman (1967) had compared the relative virulence of several species of Aspergillus for mice. They could find no physiologic or morphologic differences that would explain degrees of virulence.

The present work is an attempt to elucidate some of the factors which contribute to the pathogenicity of different Aspergillus species, and whether the pathogenicity is affected by the relative proportion of spores to mycelia in the injected inoculum. The same studies will also be done on some members of penicillium species.

REVIEW OF LITERATURE

Historical Review

The genus of moulds, Aspergillus, was first described and named by Micheli (1729). The similarity in appearance between its fruiting heads and the brush used for sprinkling holy water (aspergillum) probably suggested the name.

The fungus is very commonly found in soil and decaying organic matter (Thom and Raper 1945). It is present in compost heaps, proprietary hop manures, spoiled grain, hay and straw, and also in rooting wood (Hinson et al., 1952). The Aspergilli are usually found as saprophytic organisms and release spores, particularly through the winter months. The following groups of the fungus are described as pathogenic to man: A . fumigatus, A. niger, A. clavatus, A. flavus, A. versicolor. Of these A. fumigatus is the commonest (Hinson,1952)

Aspergillosis Of Man

Carbone et al.,(1964) had found that the tendency for Aspergillosis to occur in patient with debilatating diseases such as histoplasmosis, tuberculosis, bronchiectasis and with aplastic anemia was noted, and recent reports have implicated corticosteroids, antibiotics, surgery, and cancer chemotherapentic agents that induce leukopenia as factors that allow this saprophyte to produce a serious and, at times, a fatal disease in man.

Aspergillosis can be diagnosed as a clinical cause of disease only if organisms are cultured repeatedly and all other pathothogens are ruled out.

Panke et al.,(1978), stated that the burned patient has long been known to be susceptible to saprophytic fungal growth. Though Candida are the fungi most frequently recovered from burn wounds, Aspergillus species and the Phycomycetes group more commonly invade tissue leading to serious morbidity and mortality. There are several reports of Aspergillus species causing burn-wound infection. Conidiophores of Aspergillus developing in bronchiectatic lungs and lung cevities from diverse causes all have in common exprosure to air. It is anticipated well that

altered tissue such as burn wound with its exposure to the atmosphere will occassionally permit growth of Aspergillus condidiophores.

Stone et al.,(1979), found that during a 15 year period, 18 patients with major burns developed a wound infection due to Aspergillus. Pseudomonas sepsis preceded Aspergillus infection in 16 cases. Thirteen of the episodes occured in three epidemics each apparently related to contaminated air-conditioner ducts & filters. Treatment was based upon wound excision in all 18 patients with recurrence initially in each. Topical and parenteral antifungal agents were never individually successful in controlling the infection. Whenever fungal sepsis involved an extremity alone and thus amputation achieved to help survival of the patient. The overall mortality rate was 78%. Protection of the wound from Aspergillus colonization appeared to be the only reliable method of preventing this often lethal fungus infection.

Wolf,(1969,)observed that an outbreak of pulmonary Aspergillosis and the source of the disorder was traced to be a massive growth of A.fumigatus within the air conditioning system. It could not be determined whether the

cases described represent infection by or allergy to the aspergillus fungus.

El Sheikh Mahgoub, (1971), described a case of mcduromycetoma of the foot in a sudanese patient. The causative organism is Aspergillus nidulans. Diagnosis was made by means of culture, histopathology and demonstration of precipitating antibodies against. A. nidulans in the patient's serum.

Hinson et al.,(1952), described the allergic bronchopulmonary Aspergillosis. Imbeau et al,(1977) reported that the patients with allergic aspergillosis are characterised as having asthma usually allergic, recurrent pulmonary infiltrates with eosinophilia, dual intradermal skin tests with aspergillus antigen (positive skin tests at 15 minutes and 6 hours), precipitating antibodies to Aspergillus antigen, elevated IgE levels, and positive Aspergillus sputum culture. Central saccular bronchiectasis usually develops and extensive pulmonary fibrosis may lead to respiratory insufficiency.

Klein et al.(1980), stated that the fungus Aspergillus can cause a variety of pulmonary disorders. Allergic bronchopulmonary aspergillosis is characterized by eosinophilic pulmonary infiltrates, branchiectasis, and

branchial mucus plugs, and can progress to chronic pulmonary fibrosis. There are four additional varient forms of allergic bronchopulmonary aspergillosis, which may or may not be associated with aspergillus hypersensitivity. They are mucoid impaction of branchi, pulmonary infillrates with eosinophilia, brochocentric granulomatosis, and extrinsic allergic alveolitis. Intra cavitary Aspergilloma (mycetoma, or fungus ball) is a non invasive Aspergillus colonization of virtually any type of pre existing pulmonary cavity or cystic space. Invasive pulmonary aspergillosis is a serious usually fatal infection in patients being treated with immuno suppessants or who have chronic (malignant or non malignant) debilitating disease. Diagnosis of Aspergillus-caused pulmonary disorders-is based on a combination of clinical, laboratory, and radiographic findings, all of which must done.

Golbert et al.,(1970,)found that in pulmonary allergic aspergillosis, the fungus grows in the secretions of the respiratory tract.It's pathogensis results from two types of hypersensitivity to aspeigllus; immediate, due to reaginic antibody, and toxic complex, due to precipitating antibody. Both types were present in the serum of the first case of a patient with pulmonary allergic aspergillosis reporte

in North America. The immediate and toxic complex types of reactivity were transferred to the skin of rhesus monkey recipients. Passive systemic transfer to a rhesus recipient was accomplished by infusion of the patient serum followed by aerosol challenge with asperigllus antigen. The recipient animal developed cutaneous reactivity and pulmonary lesions consistent with the donor's illness. Clinical manifestations of the patient were intermittent fever and cough with peripheral blood and system eosinophilia and fluctuating pulmonary infiltrates. The respiratory secretions contained A. fumigatus, but no evidence of lung tissue invasion was demonstrated by X-ray or biopsy. The disease cleared rapidly with prednisone therapy and had remained absent for 2.5 years after treatment.

Krakowk et al., (1970,) postulated that pleural aspergillosis occurs mostly in established cases of pleural empyema with a bronchopleural fistula. In reported cases, A. fumigatus was related to tuberculosis. In 3 cases with an active, sputum positive tuberculous process, the pleural empyema was a complication of spontaneous pneumothorax in 2, and of lung resection in 1. In 2 cases the empyema occured as a complication of tuberculosis pleuritis, but A. fumigatus infection was noted only after

the sputum had become negative for tubercle bailli. The diagnosis of pleural aspergillosis is made on the basis of microscopical examination and culture of A. fumigatus in the pleural pus. Serum precipitation tests with filtrates of A. fumigatus are further valuable evidence of aspergillus infection. The treatment of pleural arpergillosis by local instillation of Nystatin or Amphotericin B was effective in the reported cases.

Noll et al.,(1972) stated that fungal infections are frequently observed as a complication of a malignant disease, after adminstration of antiblastic, drugs, and after irradiation. The some complication may occur in the course of treatment with corticosteroids and/or antibiotics. Noll presented two cases of fatal massive pneumonia caused by A. fumigatus. These cases occured in patients hospitalized for a non malignent disease who were treated with antibiotics as well as with steroids. Amphotricin B was recommended in these severe cases.

Fischer et al.,(1979) stated that fatal invasive pulmonary aspergillosis may follow viral influenza infections. Two cases with verified influenza A infection were followed by fatal necrotizing pneumonia due to