CLINDAMYCIN IN TREATMENT OF PLEURO PULMONARY INFECTIONS

THESIS

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BY

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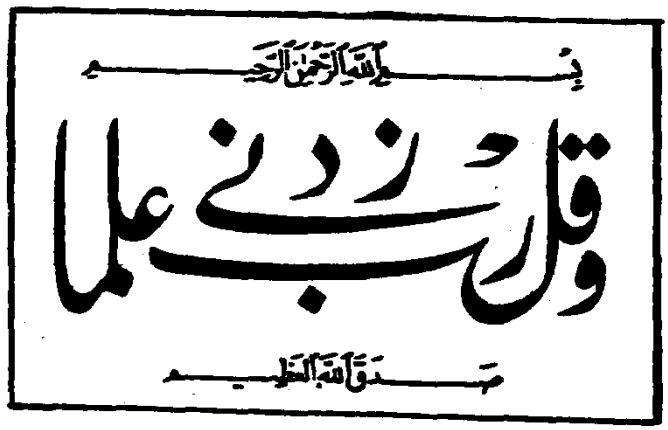

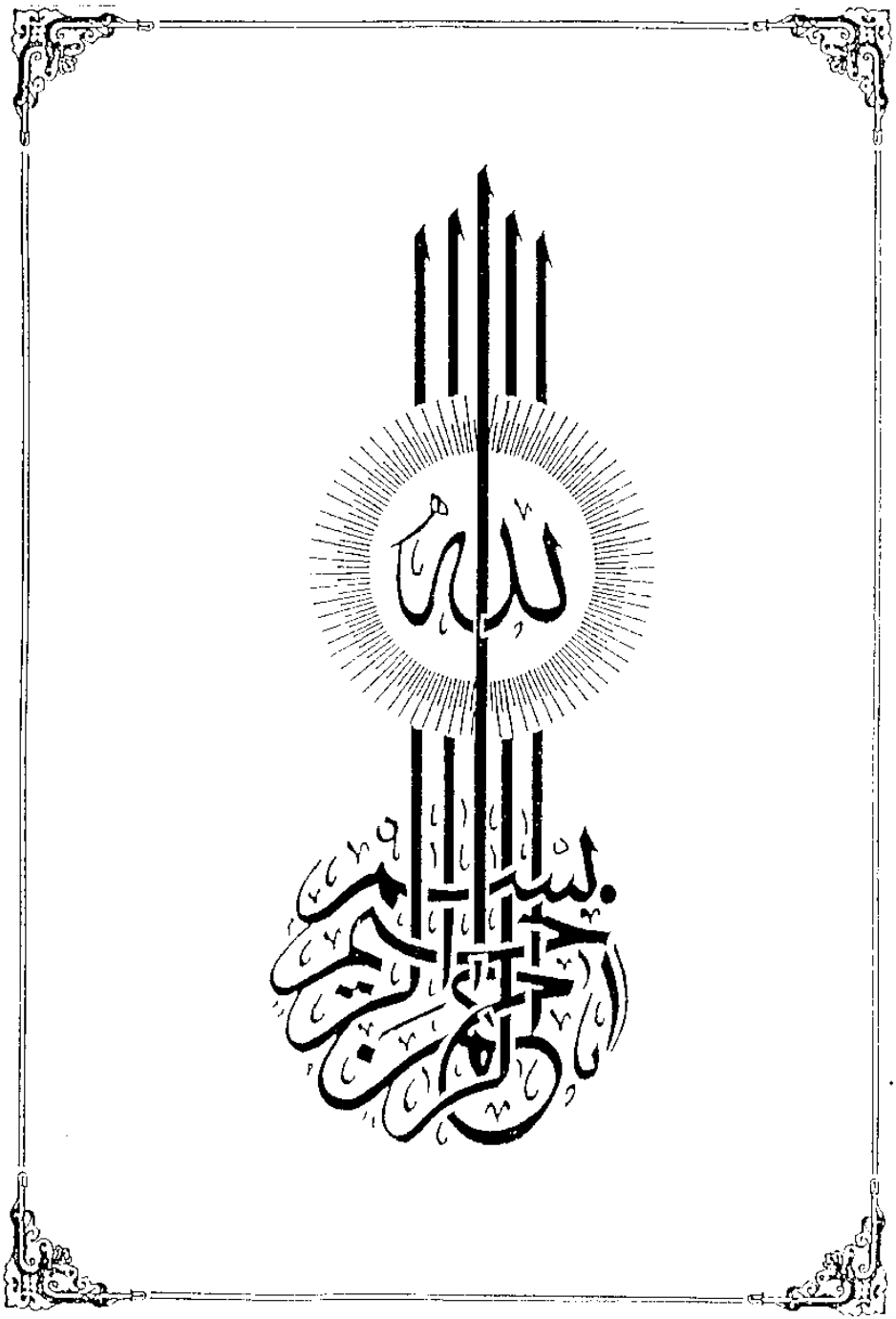

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CONTENTS

AIM OF THE WORK

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Is to search for microorganisms, especially anaerobic ones, in specimens obtained from tracheobronchial tree or pleura in different pleuropulmonary infections, and to use clindamycin as a trial testing both its efficacy as well as safety in treatment of such cases.

We also used transtracheal aspiration as a new technique for getting specimens from the tracheobronchial tree for bacteriological cultures, testing its values and limitations.

INTRODUCTION

&

REVIEW OF LITERATURE

The Role of Anaerobic Organisms in Pleuropulmonary Infections

Introduction:

Anaerobic bacteria are undoubtedly the most overlooked bacterial pathogens of the lower respiratory tract. Experience has shown these infections to be rather common. This is not a new observation, because extensive studies of anaerobic pleuropulmonary diseases have been reported in the past. The first major report was published by Guillmot and associates in 1904. These authors noted that the pleural fluid in 13 cases of empyema showed multiple bacterial forms on direct smear, but that the ordinary aerobic cultures were either sterile or yielded unlikely pathogens in small numbers. They were able to recover multiple anaerobic species in every case. Because the isolates resembled those previously identified as normal flora, the authors hypothesized that aspiration and pneumonitis preceded empyema

During the ensuing 40 years, numerous investigators extended those observations, and anaerobes were incriminated as major pathogens in lung abscess, necrotizing pneumonia aspiration pneumonia, and bronchiectasis, as well as in empyema Kline, and Berger, 1935; Cohen 1932. These reports were unique by present-day standerds because the natural course of the untreated disease could be followed and surgical or autopsy specimens were often available for bacteriologic studies. The role of anaerobes was documented by tissue sections showing the characteristic forms of these organisms and by the recovery of oxygen-sensitive bacteria from resected abscess cavities

(Varney 1920). Moreover, the anaerobes isolated from typical lesions predictably reproduced the pathologic conditions when inoculated into the trachea of experimental animals. (Bartlett and Finegold 1974).

Since the introduction of antimicrobial drugs there have been relatively few reports of bacteriologically confirmed pleuropulmonary diseases. A review of the literature since 1945 suggests that aspiration pneumonia, lung abscess, necrotizing pneumonia; and empyema have become diseases caused primarily by various aerobic bacteria. Recent studies have emphasized the emergence of unusual pulmonary pathogens such as staphylococci, Enterobacteriaceae, and Pseudomonas aerogenosa. It appeared that the antibiotic era produced a bacteriologic shift and that the anaerobic infections, studied so elegantly in the past have become diseases of merely historic interest. Several years ago, a number of cases of anaerobic pleuropulmonary infections were noted that were clinically and bacteriologically similar to those described in the older studies. In seeking an explanation for those findings, it was concluded that the failure to obtain appropriate specimens and to utilize optimal techniques for their transport and cultivation accounted for a common failure to identify cases involving anaerobes (Bartlett and Finegold 1972).

Before discussing the organisms causing pleuropulmonary infections, we have at first to discuss the bacteriology of the respiratory tract.

Bacteriology of the respiratory tract

In normal individuals, the infralaryngeal respiratory tract is sterile (Huxley et al., 1973), however, the supralaryngeal mucous linings are teeming with bacteria. Approximately 200 different species of bacteria have been identified in the oropharynx (Rosebury T. 1966). The oral microbial flora is subdivided into several ecologic systems, and although the species and concentration of bacteria vary at different anatomic sites, the majority are anaerobic at any one site. Saliva contains 10^8 to 10^9 bacteria per milliliter. Anaerobic bacteria are 10 times more common than aerobic and facultative anaerobic bacteria especially in presence of oropharyngeal or periodontal disease, anaerobes become even more dominant e.g. a dental plaque may contain 10^{11} bacteria per gram. (Kumar and Kuzmowych 1981, Richardson, Jones 1958).

Common anaerobic organisms isolated from anaerobic pleuropulmonary infections:

Anaerobic pleuropulmonary infections tend to be polymicrobical (Gorbach and Bartlett 1974).

(1) Gram negative bacilli:

- Bacteroides melaninogenicus.
- Bacteroides fragilis.
- Fusobacterium nucleatum.
- Fusobacterium necrophorus.

(2) Gram positive cocci:

- Peptococcus species.
- Peptostreptococcus species.
- Microaerophilic streptococci.

(3) Gram positive bacilli:

- Eubacterium species.
- Bifidobacterium species.
- Propionibacterium species.
- Clostridium species.

All of these except Bacteroides fragilis and possibly clostridia are common inhabitants of human oropharynx. A study was made by Bartlett and Finegold-1974-which included 143 cases with pleuro-pulmonary infections involving anaerobic bacteria. All the cases were observed by one or both authors, all becteriologic studies were accomplished in one of the anaerobic research laboratories of respective hospitals. Criteria for inclusion of patients were (1) the recovery of anaerobic bacteria from a reliable specimen source and (2) clinical findings indicating that these organisms were responsible for a pulmonary parenchymal or pleural space infection. Bronchiectasis and thoracic actinomycosis were not studied. In some cases, a combination of aerobic and anaerobic pathogens were recovered. In this situation the role of anaerobes may be difficult to assess.

The relative numbers of different organisms and the presence of putrid discharge or other characteristic clinical findings indicates

that the anaerobes were contributing significantly to the pathologic process, but sometimes this was an arbitrary decision. The significance of these aerobic organisms in anaerobic pleuropulmonary is unknown at present, although symbiosis and even complex synergistic relationships between aerobic and anaerobic organisms have been postulated. (Kumar and Kuzmowych 1981).

Pleuropulmonary Diseases Due to Anaerobic Infections:

In the bove mentioned study, done by Bartlett and Finegold 1974, clinical charts, roentgenograms, and bacteriologic findings in acceptable cases were reviewed. A computer program was used to facillitate data analysis. Cases were divided according to roentgenographic findings and pleural fluid analysis into:

1.	Lung abscess without empyema	30 cases.
2.	Lung abscess with empyema	15 cases.
3.	Necrotizing pneumonia without empyema	18 cases.
4.	Necrotizing pneumonia with empyema	10 cases.
5.	Pneumonitis without empyema	44 cases.
6.	Pneumonitis with empyema	25 cases.
7.	Empyema without evidence of parenchymal infection	1 case .
		143 cases.

The incidence with which a pure anaerobic flora was obtained varied from 37% in patients with empyema to 66% in patients with necrotizing pneumonia, in most of the remaining patients mixed anaerobic and aerobic bacteria were isolated.

Predisposing Factors to Anaerobic Pleuropulmonary Infections:

In all the cases the underlying conditions could be:

1. Periodontitis
2. Suspected aspiration. Aspiration is considered to be the first cause of anaerobic pulmonary infections . In normal individuals, aspiration of oropharyngeal secretions is a common occurance during deep sleep, however, the most of these remain "silent" and the infralaryngeal respiratory tract remains sterile.

   This is the result of an incredibly efficient mucociliary clearing mechanism, and an effective phagocytic system composed of pulmonary alveolar macrophages and polymorphonuclear leukocytes. Thus for an anaerobic infection to establish itself in the lung, several important and interrelated factors come into play. These include the character of the aspirate, the inoculum size, the virulence of aspirated organisms, synergism among aspirated organisms, any preceding pulmonary pathology (such as bronchiectasis or after common forms of obstructive disease) which would favour growth of anaerobes, conditions which would compromise normal host defense mechanisms, including cough, and conditions that predispose to aspiration as:

   a) Depression of level of consciousness as alcohol, seizure disorder, cerebrovascular accident, sedative or narcotic use, general anaesthesia, and old age.