A STUDY OF THE CAUSES OF DELAYED RESOLUTION OF PNEUMONIA

THESIS

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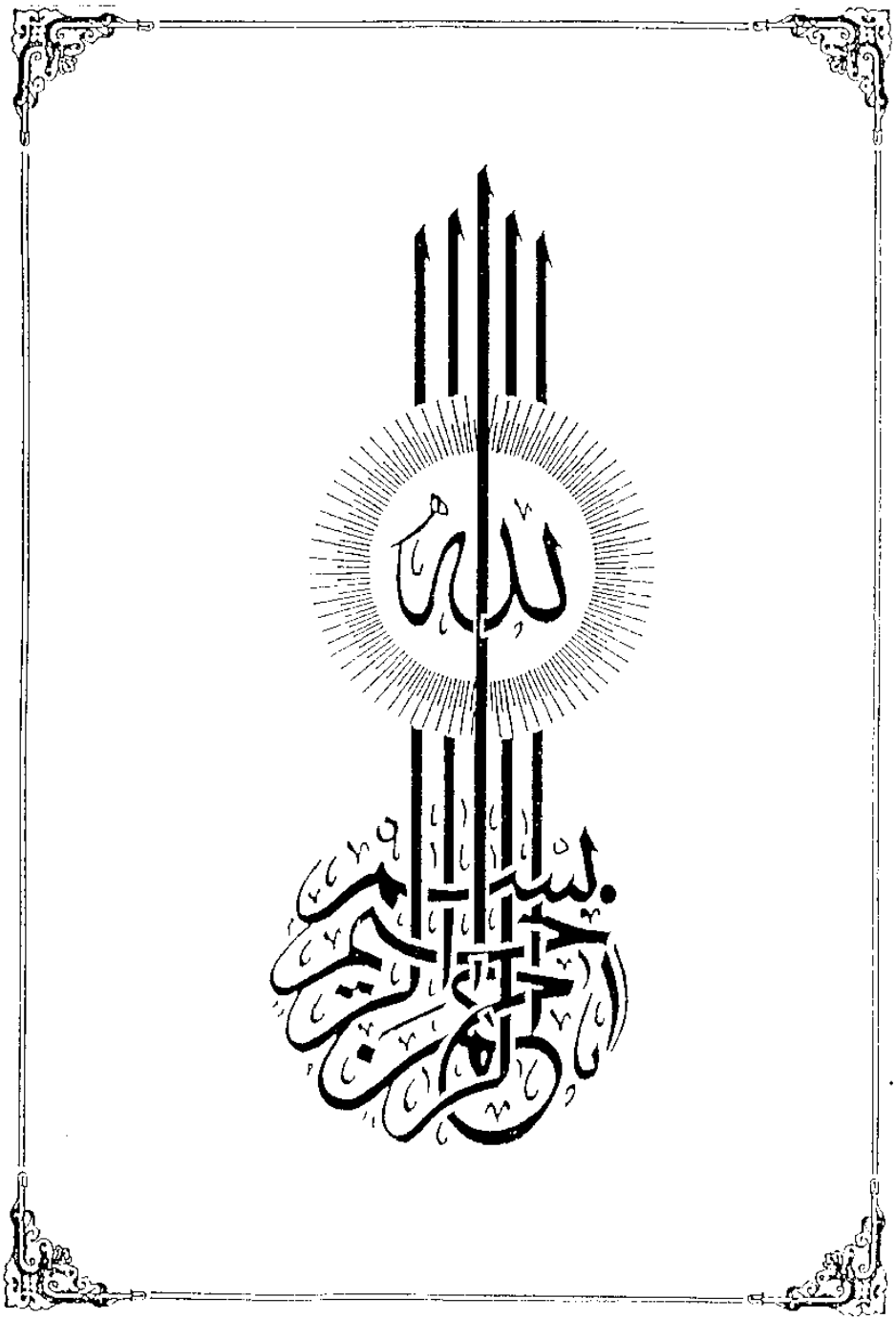

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I N T R O D U C T I O N

Introduction

Pneumonia means inflammation of the lung parenchyma, the most striking feature of which is pulmonary consolidation. (Crofton 1975).

The great majority of pneumonias resolve radiologically completely or almost so within 4 weeks - failure of pneumonia to resolve within this period is termed delayed resolution (Baum 1974). In addition to the persistance of the radidagical opacity, it is associated with continuous low grade fever, râles and moderate dullness to percussion. There has been marked variation in estimates of the frequency of " Delayed Resolution" of pneumonia. This is because of the different diagnostic procedures used. Early in this century the diagnasis was based on persistent abnormal physical signs and exclusion of tuberculosis by sputum bacteriology.

Various previous observers reported this frequency by these methods to be: 0.6% (Chatard 1910), 3.7% (Mc Crae 1910), 4.1 % (Musser, et al. 1907), 7.6% (Lord 1925). (Quoted from Israel, et al. 1956).

In more recent studies in which x - Ray examination have been utilized to measure the rate of resolution, there is still wide variation in the reported frequency of delayed resolution of pneumonia as mentioned by Israel, et al. (1956). They found delayed resolution in 18 cases of 139 patients with pneumonia (13%).

Auerbach, et al (1952) reported this frequency to be 18.3%. (26. 2%) were documented by Gleichman, et al, (1949). Boyd (1975) mentioned that the figure (26.2%) is certainly mislead-ingly high since some of the pneumonias would undoubtely resolve if observation had been continuous beyound the 30 days period.

It is impossible and inflexible rule for the physicians nevere to make a diagnosis of unresolved pneumonia without searching for the cause, otherwise patient with serious or remediable lesions of the lungs may miss the oppertunity of early diagnosis and cure .

Some of the pulmonary lesions as alveolar cell carcinoma, reticuloses, traumatic pulmonary haematoma, etc., may mimic pneumonia with tardy resolution. These will be discussed later.

Factors Affecting Tardy Resolution:

There are several factors responsible for "Delayed" Resolution" of pncumonia. These may be general constitutional, local, and the type of organism causing pneumonia (Boyd 1975).

(1) General and Constitutional Factors:

a- Age: Age itself was the most striking infleunce affecting the occurence of delayed resolution of pneumonia as mentioned by Israel, et al. (1956). They observed that 6 cases of 90 patients (6.6%) under the age of 50 exhibted delayed resolution of pneumonia, while this event was noted in 12 cases among 49 patients (24. 5%) who were 50 years of age or older.

b- Sex , Race:

They do not infleunce appreciably the rate of resolution. The previous authors observed that delayed resolution occured in 12 cases of 103 Negroes patients (11. 6%) and in 6 cases of 36 white patients (16.7 %).

They also mentioned that pneumonia occured in 13.3% of 60 males and in 12.3% of 49 females (Israel, et al 1956).

c- Malnutrition and other constitutional defects in resistance:

Appeared to be of great importance:

(1) Anaemia: has a very little influence in the rate of resolution or pneumonia.

(2) Alchol Consumption:

Delayed resolution of pnewnonia might be related to excess alchol consumption especially alcholic stupors, especially in old patients, because these decreases the resistance of the lungs to bacterial infection through its deprivation of its immunity (Bulmer 1978). Alcholic intoxication inhibits the vascular inflammatory response. The migration of leucocytes at the site of infection is negligible. The bacteria therfore proliferate uninterruptedly as mentioned by Pickrell (1938). In contrast to the previously mentioned statement, Israel, et al, reported that alcholism was not responsible for tardy resolution in his series and the same was noted by Van Metre (1951). Pickrell reporhed also the same effect on the inflammatory

response after ether anaesthesia.

(3) Immunoglobulin Deficiency:

especially (lg A) produced by B- lymphocyes: The immune system can be separated into 4 distinict but, interrelated functional compartements which are:

- B - lymphocytes,
- T - lymphoctes,
- Phagocytes,

and - Complement

(1) B - lymphocyhes:

-B- lymphocytes are responsible for immunoglobulin (antibody) production as mentioned by El- Battawi (Quoted from Gell 1968, Burnet 1969). The antigen at the site of infection is transported to reticulo endothelial cells to lymph nodes of spleen where the antigen is recognised, devision of plasma cells or plasmablasts and maturation (B- lymphocytes) occurs resulting in production of many mature plasma cells. These cells produce speciallized immunoglobulins specific for the antigen,. B- lymphocytes is especia- llized i.e. there are B- lymphocytes for every antigen

known and respond only to this antigen. The infecting antigen itself does not play any further role in production of corresponding antibody beyond stimulation of speciallized B- lymphocytes. Consequently, andtibodies continue to be produced after disappearance of antigenic stimulation. Hence immunoglobulin can be detected in the serum of the patient several years after recovery from the original illness.

There are different varieties of immunoglobulins according to studies on its physiochemical characters of which M, G, A, E and D are known.

Ig M dominates primary andibody response i.e. appears early after antigenic stimulation and does not persist for a long period in the serum. It is produced in response to infectious agents as bacteria and viruses.

Ig G dominates secondary antibody response i.e it persists for prolonged periods, in circulation. It is produced against bacteria, viruses and toxins.

Ig A can pass from the circulation to the mucus surface of respiratory, intestinal and genital system.

It may therefore play an important role in immunity against microbial infections at these sites. The diseases associated with IgA deficiency include recurrent protracted pulmonary infections e.g. delayed resolution of pneumonia and bronchiectasis, autoimmune disease, malabsorption syndrome, allergies and malignant neoplasms.

Ig E participates in hypersensitivity reactions. It has no role in antimicrobial immunity.

Ig D has unknown function. It is found in the serum in trace amounts.

Serum levels of immunoglobulins vary with the age of the patients.

(2) T. lymphocytes:

T- lymphocytes participate in cell mediated immune response, in which the reaction between antigen and sensitized lymphocytes lead to produchion of lymphokines. They are thought to participate in the production of the subsequent inflammatory response. Hence, It is termed "delayed hypersensitivity". lymphokines include the following factors:

The chewotactic factor: which attracts the lymphocytes at the site of the reaction.

The mitogenic factor: which stimulates proliferation of lymphocytes at the site of localization.

The macrophage inhibitory factor which may be resonsible for formation of agreggated macrophages that possibly release lysozomal enzymes which contribute more to the inflammatory response.

The cytotoxic factor: Which may participate in production of necrotic changes.

Both T-, and B- lymphocytes differentiate from the same stem cell during embryonic life. Differentiation of T- cells occur under control of the thymus gland, wherease B- cells differentiate independent of the thymus gland. The normal individual usually has greater than 1500 small lymphocytes / cmm. Values less than 1000 / mm^3 are usually considered abnormal.

(3) Phagocytes:

They are composed of polymorphonuclear leucocyte, and macrophages and are distributed all-over the body. The main function is to engulf foreign particles including bacteria introduced into the body either in

the tissues or Blood, and their destruction or disposal. Another function is that they release enzymes that lead to resolutiou of fibrin exudates which are rich in fibrin and poor in these leucocytes are more apt. to organize. This is a cause in the delayed resolution of pneumonia. The laboratory evaluation of phagocytic function occur by performing a total and differential white Blood cell count.

(4) Complement:

It is a complex group of protein substances that are present in normal serum and tissue fluids except C.S.F. and urine . It has antibacterial action throngh fixation to the serum antibody when it reacts with the antigen. The result of this fixation is immune bacteriolysis if the antigen is bacterial cell, whereasc it is called " immune haemolysis" if the antigen is a red cell. Complement fixation test can be done quantitatively to determine the titre of the complement fixing antibody.

The deficiencies in " humoral immunity" alone render the patient liable to recurrent bacterial infections, whereas this does not happen in cases of viral infections and tuberculosis. Such patients are

susciptible to infection with pneumocystitis carinii.

Patients with defeciency mainly in cellular immunity are particularly susceptible to viruses, candida albicans, infections of mucosa and pseudomonas infection of the urinary tract. Patients with dificiencies in T- lymphocytes fail to develop delayed type of hypersensitivity. Hence the TB. (mantoux testing fails to become +ve after B.C.G. vaccination. The immunological deficiencies may be either congenital or acquired.

- Congenital immunological deficiencies: there is a wide variation of congenitaldeficiency disorders. Fortunately all of them are rare. These can be roughly classified into:

a- deficiency of immunoglobulins.

b- " " cellular immunity.

- Acquired immunological deficiencies: include the following items.

1- Decrease humoral antibodies e.g.

- Primary acquired hypogammaglobulinaemia.
- Chronic lymphatic leukaemia. which may lead to later development of deficieney of immunoglobulins