EFFECT OF CIGARETTE SMOKING ON PLATELET AGGREGATION AND NEUTROPHIL PHAGOCYTOSIS

Thesis

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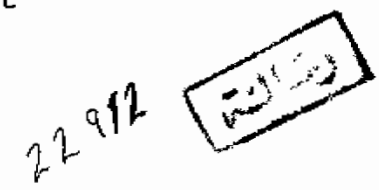

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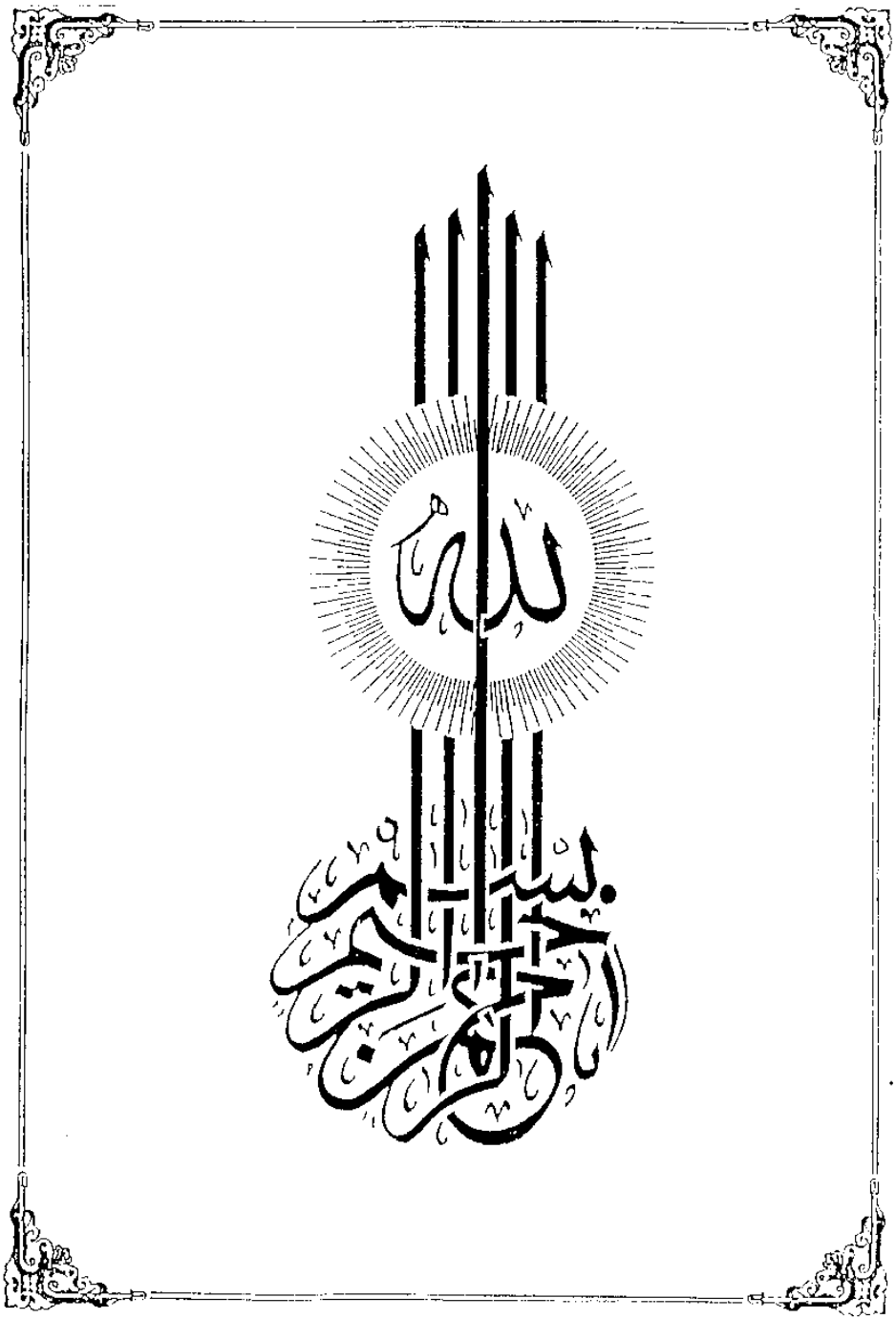

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Introduction

Cigarette smoking is the major preventable cause of increased mortality and premature disability. Smokers have a higher risk of developing chronic obstructive lung disease, lung cancer and coronary heart disease than those who do not smoke (Doll, 1981 and Janoff, 1983).

Many workers have been previously devoted to the study of biological effects of tobacco on blood elements (erythrocytes, leucocytes and platelets) (Heman and Rubenstein, 1975). Some of them indicated that smoking may have an influence on the defense mechanisms of the body (Thomas et al., 1978 and Corberand et al., 1980) which may contribute to the increased susceptibility of smokers to infections (Bridges et al., 1980). Moreover, many conflicting results have also emerged as regards smoking habit and platelet aggregation (Grignani et al., 1977). It was suggested that the association between smoking and coronary heart disease (Breddin et al., 1974 and Seltzer, 1975) might not result from a primary atherogenic effect, but that blood platelets might provide a mechanism. In view of the role played by platelets in thrombosis, it seemed important to examine the effect of cigarette smoking on platelet function (Renaud et al., 1984). Accordingly, the aim of this work is

to study both the phagocytic power of neutrophils and platelet aggregation among heavy and light smokers to find out the effect of smoking on the function of leucocytes and platelets and to clarify its role in susceptibility to infections or thrombosis. A correlation study between the number of cigarettes smoked and the above parameter tests was done.

REVIEW OF LITERATURE

Cigarette Smoking and Health

Prevelance of cigarette smoking

In 1965, in United States, 52% of men and 34% of women over age of 20 were cigarette smokers. By 1980, these percentages had decreased to 38% for men and 30% for women (Doll, 1981). A recent survey in 1984 indicated that the rate of smoking among adults declined to 29% (Mason et al., 1984). Smoking among younger individuals, especially young women remains a major public health concern. Several studies indicated that smoking is now more prevalent among teen age women than men. In spite of the recognized adverse health effects of cigarette smoking, about 15% of adolescents (age 12 through 17) currently smoke cigarettes.

In Egypt a study was done in 1984 by Kalifa et al., on adult and middle aged Egyptian industrial workers. They found that 57% were smokers and 4% were exsmokers.

The overall mortality ratio for adult cigarette smokers versus adult non-smokers is about 1.7 (Mason et al., 1984). The mortality ratio in smokers increases with the amount smoked and is directly proportional to the duration of cigarette smoking. Mortality ratios are also higher for those who start smoking at younger ages.

How cigarettes work

The burning cigarette is a chemical factory that generates thousands of different compounds. The precise chemical composition of smoke depends on the type of cigarette and the way by which it is smoked. Major toxic constituents of cigarette smoke include, but are not limited to, carbon monoxide, nicotine, and particulates that contain most of the carcinogenic aromatic hydrocarbons (Mason et al., 1984).

Adverse effects of smoking

The pathophysiologic mechanisms underlying the health effects of cigarette smoking are complex because of the different smoke components and their many direct and indirect interactions with environmental and genetic factors (Hirayama, 1981). Cigarette smoking is known to be an independent risk factor for chronic obstructive pulmonary disease, lung cancer, and coronary heart disease. Patients with other recognized genetic, metabolic, or occupational risk factors for these diseases must be strongly advised not to smoke (Janoff, 1983). Unfortunately, it is not known why some smokers develop severe chronic obstructive pulmonary disease, lung cancer or coronary heart disease, whereas other individuals are minimally affected. Currently, there is no way of predicting which individuals will develop severe

disease and which individuals will not. Disease can be most effectively prevented by avoiding smoking all together.

Passive smoking

Passive smoking refers to the involuntary exposure of non-smokers, both children and adults, to tobacco combustion products. In enclosed spaces, smoke accumulates and the concentration varies with the number of smokers, with the type of smoking and with the characteristics of the room, especially the ventilation. Attention has only recently been focused on the potential health effects of passive smoking (Correa et al., 1983). There is substantial agreement that passive smoking is annoying and irritates eyes and upper airways. Lower respiratory tract infections are more frequent in infants whose parents smoke cigarettes (Lefcoe et al., 1983).

PHAGOCYTOSIS

Phagocytosis is the major defence mechanism of the body against infections. It serves a protective function by ingestion and degradation of foreign invaders and elimination of altered effect or dead cells of the body (Stossel and Boxer, 1983).

The phagocytes involved in host defence include: neutrophilic polymorphnuclear leucocytes (PMNLs) and mononuclear phagocytes (blood monocytes and tissue macrophages). Both types of phagocytic cells originate in the bone marrow and arise from common pluripotential stem cells. The natural habitat of the neutrophils and monocytes is the blood stream, while various forms of macrophages are found in the tissues. Neutrophils are end cells with a limited life span, whereas tissue macrophages are longer lived and have the capacity to divide and transform into further cell forms. Phagocytosis by neutrophils is composed of 4 interrelated phases: chemotaxis, opsonization, ingestion and killing (Goldstein, 1982).

I- Chemotaxis:

Neutrophils can arrive at an inflammatory site either by increasing their overall random movement (chemokinesis) or by

following a concentration gradient of the inflammatory substances in a directional manner (chemotaxis). The latter represents a change in the direction of leucocytes mobility but not its speed (David, 1978). This directional migration occurs under the influence of chemotactic agents.

Chemotaxis appears to be mediated by 2 means:

1- Chemotaxigens: These are substances not chemotactic by themselves but they generate chemotactic factors after interacting with serum, plasma, components of complement, mast cells or sensitized lymphocytes. Examples are antigen-antibody complexes, endotoxins, certain bacteria, certain enzymes reacting with complement components and lysosomes from neutrophils, macrophages or liver (O'Flaherty and Ward, 1979).

2- Chemotaxins: Most or possibly all chemotaxins are proteins derived from activation of plasma protein pathways such as the complement, fibrinolytic, coagulation and kinin systems (Goetzl, 1978). They act directly to stimulate chemotaxis. Chemotactic factors of complement such as C3a and C5a may be produced following the attachement of specific antibody to the microorganism and fixation of C1 (classic pathway) or directly by the activation of C3 component (alternate pathway). Both neutrophils and mononuclears are influenced by these chemotactic stimuli (Schiffmann et al., 1978).

II- Opsonization:

Opsonization means combination of certain serum proteins with bacteria rendering them more susceptible to ingestion by phagocytes (Winkelstein and Drachman, 1974). Opsonins include specific antibodies (heat stable) of the IgG_1 and IgG_3 subclasses, complement (heat labile), non-complement thermolabile factors and perhaps other factors in the serum such as lysozymes which when adsorbed into particles render them attractive to phagocytic cells (Boxer et al., 1978).

III- Ingestion:

This property is a function of the cell maturity, the presence of specific receptors on the surface of the phagocyte and the energy potential of the cell (ATP). Ingestion requires contact between the surfaces of the phagocyte and the bacteria which results from differences in surface tension between the particle, the suspending medium and the phagocytic cell (Baehner, 1974). Cell pseudopodia fuse on the distal side of the material being ingested and the particle becomes encased within a phagocytic vacuole (phagosome). The phagosome migrates toward the interior of the cell. Neutrophil granules migrate toward , fuse and discharge their contents into the phagocytic vacuole

(Stossel, 1975). There are 2 types of lysozomal granules in the phagocytic cells primary and secondary granules which contain hydrolytic enzymes and bactericidal substances. The primary granules are large, dense, called azurophilic granules and contain acid hydrolases, myeloperoxidase and lysozyme, while the smaller secondary called specific granules contain alkaline phosphatase and lactoferrin. Ingestion is an active energy-dependent process. The neutrophil derive their ATP from anaerobic glycolysis (Bachner, 1974).

Post phagocytic events:

Following ingestion of microorganisms or other particles by neutrophils, a respiratory burst and a discharge of granule contents occur (David, 1978).

1- Respiratory burst:

The metabolic or respiratory burst is a series of enzymatic reactions used by stimulated phagocytes to convert oxygen to various active metabolites important in the bactericidal reactions of the cell. The basic series of reactions in the respiratory burst in neutrophils as stated by Mandell and Densen (1979) results in:

a- Oxygen consumption.

b- Superoxide (O_2) production.