Treatment Outcome of Patients With Advanced Lung Cancer

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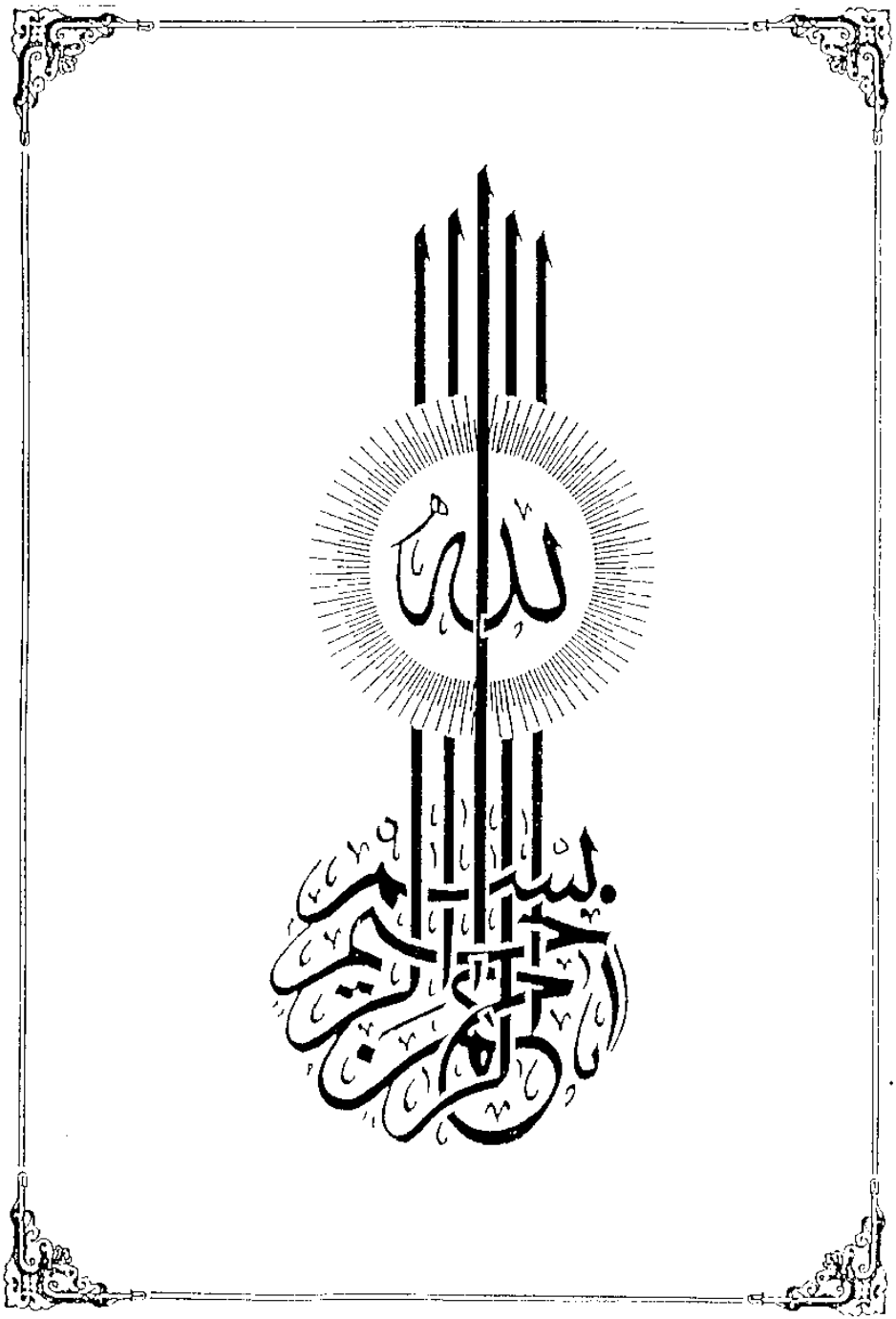

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INTRODUCTION

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The incidence of lung cancer with attendant mortality, remains high in the developed world and is rising rapidly in developing countries throughout the world including Egypt (Mahfouz et al., 1987 and Crofton, 1990).

Lung cancer is the most common cancer in men worldwide and the leading cause of cancer mortality of males. For females, lung cancer is expected to become more common as the percentage of women smokers continues to increase (Parkin et al.,1988 and Silverberg et al., 1990). It is likely that lung cancer will be one of the most common diseases of the early part of the 21st. century (Stanley and Stjernsward, 1989).

It is important to imphasize that lung cancer is virtually preventable, because most of the prediposing and lifestyle factors, are known (Gradishar and Bitran, 1990). However, the health sector is finding it extremely difficult, in practical terms, to bring about the changes in human behavior necessary for its prevention (Stanley and Stjernsward, 1989).

Progress in the treatment of lung cancer has been modest at best, with chemotherapy for small cell disease being virtually the only area with recent significant impovement. However,cure rates are unacceptably low, with a 5-year

survival rate for all stages of the disease at approximately 10-15% (Stanley and Stjernsward, 1989).

Although these observations may suggest an attitude of pessimism, the immediate future holds great promise, because new diagnostic and therapeutic techniques will radically change the current approach to patients with non-small cell lung cancer (NSCLC). Furthermore, the development of new drugs and biologic response modifiers based on specific biologic characteristics of cancer cells may have an impact on the natural history of the disease (Gradishar and Bitran,1990).

The unifying aspect to all the new information and technology is a multidisciplinary team of medical specialists approaching patients with lung cancer in a consistent and rational way. To improve patient survival and quality of life, the specialized skills of pathology, radiology, oncology (surgical, medical, and radiation), and psychiatry are needed (Gradishar and Bitran, 1990).

It is absolutely clear that efforts to counter tobacco consumption are the most effective weapons in this fight. In absence of inexpensive cancer cures, primary prevention provides a cost-effective and possibly the only means to reduce deaths from lung cancer (Cullen et al., 1986).

REVIEW OF LITERATURE

ETIOLOGY OF LUNG CANCER

MAIN ETIOLOGIC FACTORS OF LUNG CANCER (Minna,1989)

1- Smoking.

2- Exposure to other carcinogens .

3- Presence of chronic obstructive airway disease.

4- Role of diet.

5- Familial predisposition.

CARCINOGENS AND LUNG CANCER

Factors that determine the organ specificity of tumor induction by carcinogens include dose, route of adminstration, metabolism, DNA alkylation, and the capacity for the repaire of specific DNA lesions (Saffhill et al., 1985).

Two major steps were individualized in the carcinogenesis (Kouzan and Bignon, 1987):

(1) Initiation: This is an irriversible step (most propably localized to DNA). A single exposition to the initiating molecule is sufficient and the lesion is of very long duration. There is no threshold of action. The initiating doses are widely inferior to the carcinogenic doses. This step is important and obligatory in the carcinogenesis pathway.

(2) Promotion: The promoting substance is not carcinogenic in itself but to which repetitive exposure will allow cellular transformation to the form of tumor. It is a reversible and reparable process, at least initially. It is cumulative process and should follow initiation. The interval between initiation and promotion might be long.

A single substance might have the double action i.e. initiation and promotion.

The most important phenomena induced by the promotors are as follows (after Kouzan and Bignon, 1987):

* Biochemical effects:

1- Polyamine synthesis and augmentation of the *ornithine* decarboxylase activity.

2- Augmentation of DNA and RNA synthesis.

3- Augmentation of metabolism of phospholipids.

4- Augmetation of plasminogen activator synthesis.

5- Augmentation of protaglandin synthesis.

6- Augmentation of picking up of ions, sugars, and thymidine.

7- Alteration of membrane glycoproteins.

* Biologic effects:

1- Inhibition of cellular differentiation.

2- Modification of cellular morphology.

3- Augmentation of mutation expression.

4- Induction of inflammation and hyperplasia.

5- Alteration of cellular adherence.

SMOKING AND LUNG CANCER

The major cause of lung cancer is smoking, particularly of cigarettes (Parkin, 1989). In addition, there is a significantly increased risk of lung cancer for pipe and cigar smokers whether or not they also smoke cigarettes (Benhamou et al., 1986; and Damber and Larsson, 1986). At least 80% of all cases of lung cancer are caused by tobacco (Stanley and Hansen, 1985), especially small cell lung cancer (SCLC) and squamous cell carcinoma (Bergh, 1990).

A clear-cut dose-response relationship has been observed between cigarette smoking and lung cancer, and the risk has been found to be greater among those who started smoking at a young age (Kouzan and Bignon, 1987; and Parkin, 1989). The risk of lung cancer in nonsmokers is increased by 25%-35% due to passive (enforced) smoking (Stanley, 1986). The majority of lung cancers in nonsmoking women are probably related to passive smoking (Garfinkel et al.,1985; Kuller et al.,1986; and Pershagen et al., 1987).

Benzopyrene is ,however, one of the chemicals identified in cigarette smoke. More of these chemicals are carcinogenic in animals, and several are N-nitroso compounds, a highly potent group of carcinogens producing tumors at diverse sites in animals (O'Connor, 1989). Many of the nitroso compounds require metabolism to form chemically active intermediates and those which transfer small alkyl(e.g. methyl and ethyl)

groups to DNA show affinities for respiratory tissue (Hecht and Hoffmann, 1988).

It has been shown that the particulate phase of smoking contains radioactive isotopes (polonium 210 and plomb 210), which adsorb the radon which is present in the domicile environment and inhibiting its soil deposition and permiting its longtime air suspension and hence favor its inhalation (Marmostein, 1986; and Svensson et al., 1987).

Besides its initiation effect, the predominant action of tobacco smoking is promotion hence reversible and this is evident from the fact that stoppage of tobacco smoking leads to progressive diminution of the risk of lung cancer till it reaches, within nearly 15 years, the risk of non-smokers (Kouzan and Bignon, 1987).

OTHER CARCINOGENIC AGENTS

Exposure to Asbestos

Mineral fibers, particularly asbestos, represent the greatest cause after cigarette smoking of respiratory cancer attributable to air pollutants (Hughes and Weill, 1986). All studies show a strong dose-response effect with asbestos exposure (Seidman et al., 1986). Of great importance, the combination of occupational asbestos exposure and smoking further increases lung cancer risk; this association is strongest with SCLC and weakest with adenocarcinoma (Kjuus et al., 1986). All common commercial types of asbestos