CARCINOEMBRYONIC ANTIGEN AS A RELIABLE TUMOR MARKER IN BRONCHOGENIC CARCINOMA IN COMPARISON WITH CHRONIC OBSTRUCTIVE AIRWAY DISEASE

THESIS

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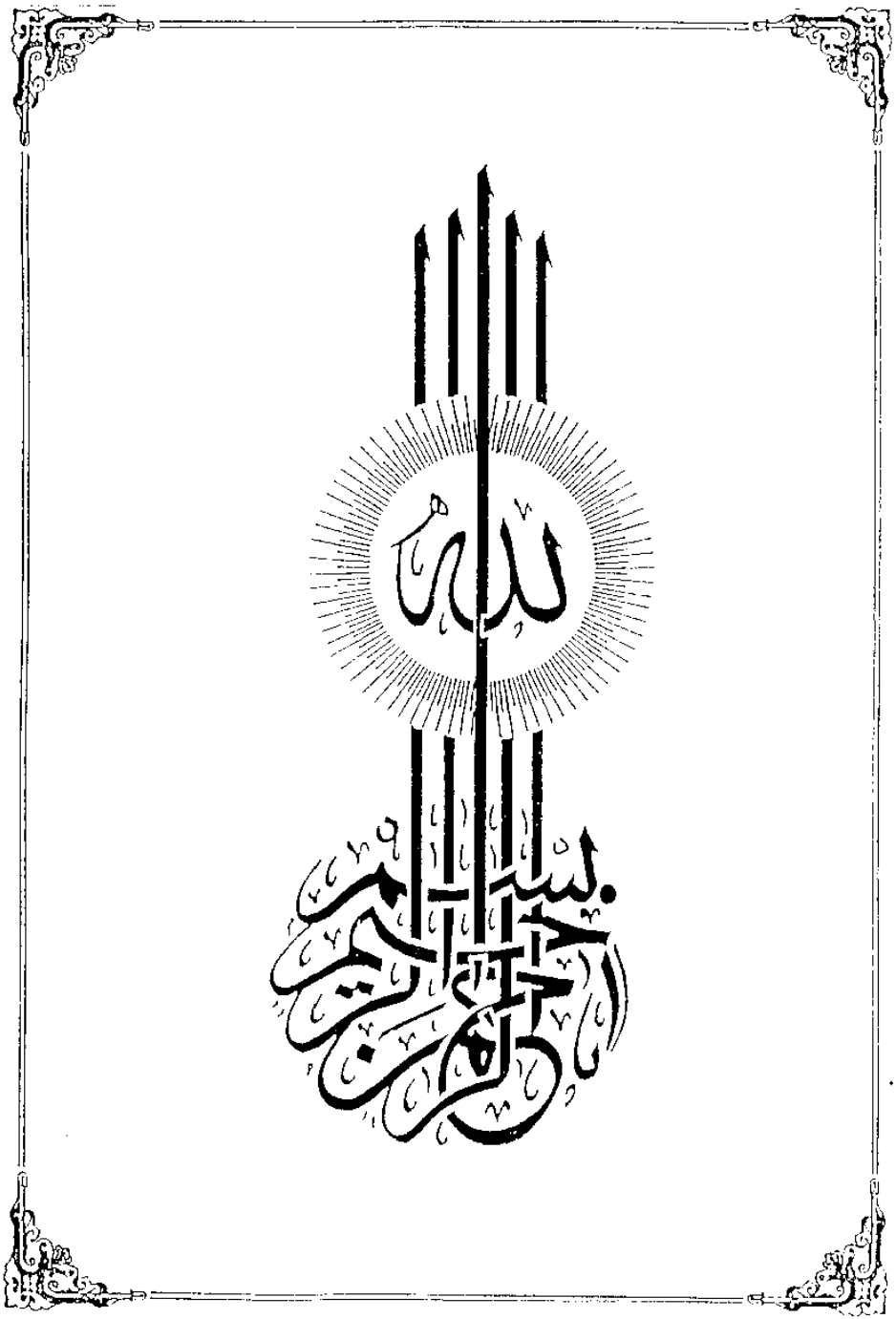

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INTRODUCTION

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Cancer is responsible for about 17 % of all deaths (next to the heart disease) and; is the second leading cause of death. In any given year, nearly one million Americans under medical care for neoplastic disease and meanwhile over 600,000 new cases are diagnosed. About 150,000 new cases of lung cancer were expected in the U.S.A. in 1986. Furthermore, it was reported that lung cancer accounts for 35 % of cancer deaths in men and 18 % of cancer deaths in women, and its incidence in man is rising rapidly. About 50 % of patients who develop malignant tumors can be cured with the various therapeutic strategies now in use, including surgery, radiation and drugs. Of the other 50 %, the majority die because of metastases (Khalifa, 1987).

The increasing incidence of lung cancer with its relatively poor response to present means of therapy presents the clinician with a formidable problem. A means of detecting the presence of the lung tumor at an early clinical stage or the means od assessing the completeness of a surgical resection or the effectiveness of radiation or chemotherapy may be of infinitive value. A carcino-embryonic antigen (CEA) thought to be specific for adenocarcinoma of the colon was described by Gold and Freedman in 1965; subsequent studies have demonstrated that CEA concentrations appear to be elevated in presence of malignant tumors other than those of gastrointestinal

origin including lung cancer (Vincent, et al., 1975).

Recent experience in the management of some tumors, in particular choriocarcinoma and gonadal tumors, has demonstrated the value of biochemical markers, with the advent of more effective chemotherapy and radiotherapy in bronchogenic carcinoma it has become apparent that such biochemical tests of disease activity would be of immense benefit in this disease also, they would be of assistance not only in mass screening but also in the differential diagnosis of pulmonary tumors, in addition to diagnosis a "tumor index substance" could serve as an adjunct to staging and to early prediction of recurrence of tumor postoperatively, it is likely that chemotherapy is more effective when the tumor load is small and sequential monitoring would enable chemotherapy to be given much earlier in the evolution of metastatic disease, with the advent of more sensitive biological and immunological methods of detecting circulating and stored components of human tumors, many materials have been found in abnormal concentrations in malignant tissue in patients with bronchogenic carcinoma, the prime example of this is the carcinoembryonic antigen (CEA) of Gold and Freedman, (1965); but evaluation of this product (CEA) in bronchogenic carcinoma is complicated by the fact that many patients with non-neoplastic lung diseases (e.g. pulmonary T.B.; chronic bronchitis, emphysema and cor-

pulmonale) have high levels, further, heavy smokers have elevated plasma levels (Coombes, R.C., et al., 1978).

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AIM OF THE WORK

This study will deal with the estimation of carcinoembryonic antigen (CEA) in sera of patients with lung cancer as well as in patients with chronic obstructive airway disease (COAD). Results will be correlated in order to declare the usefulness of "CEA" as a reliable marker in lung cancer.

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REVIEW OF LITERATURE

TUMOR MARKERS

In man, tumors of every cell type can be accompanied by biochemical abnormalities in the peripheral blood or urine. Most of these abnormalities are specific neither for tumors nor for diseases of the particular organ, but there are a few quantitative and qualitative abnormalities that are more frequently demonstrable in patients with particular forms of cancer. Most often those have been detected because of the effects they produce (Coombes, et al., 1978).

Tumors of endocrine glands and their secretions are the prime examples. With the advent of more sensitive biological and immunological methods of detecting circulating and stored components of human tumors, many materials have been found in abnormal conditions in plasma of patients with cancer and often no clear function for these materials has been defined, either in the tumor or in the host. The prime example of this is the carcinoembryonic antigen (CEA) of Gold and Freedman, (1965) (Coombes, et al., 1978).

Actually the investigations concerned with tumor markers started since the isolation of carcinoembryonic antigen from tumors of human colon in (1965), followed by the demonstration that many human cancer produce a variety of substances such as "oncofetal antigen" and "ectopic hormones" (Deranaley and Coombes, 1981).

Hansen and Pedersen, (1986); reported that neoplastic cells produce and release several substances corresponding to their normal counterparts.

In some cases the occurrence of such substances have not been documented in the normal cells, leading to the term "ectopic production". In addition, peptides similar but not necessarily identical to the genuine hormonal counterpart may be released. When the substances are characteristic of the fetal development, they are referred to as "oncofetal antigens". (Hansen and Pedersen, 1986)

Within the past 15 years some tumors were found to produce substances with such consistency that they become of importance in the management of these tumors, i.e.; HCG in choriocarcinoma and some testicular cancers, calcitonin in medullary carcinoma of the thyroid; and æ-fetoprotein in hepatomas and some testicular cancers, as well as some gastrointestinal (GI) peptide hormones in islet-cell tumors (Hansen and Pedersen, 1986)

DEFINITION

Khalifa, (1985) stated that ideal tumor marker would :

[1]-be a substance that is not normally present in blood.

[2]-give a uniformly positive test results in all patients.

[3]-be present with its specific tumor, in a concentration proportional to the size or activity of the tumor.

By these criteria no ideal tumor markers have been found, i.e.; current tumor markers are neither highly sensitive, nor tumor specific. Therefore, the principal value of these markers is in estimating prognosis or in monitoring response to therapy, not in screening for occult disease. So, it is better now to define a tumor marker as any substance that can be related to the presence or progress of a tumor.

CLASSIFICATION OF TUMOR MARKERS

Coombes, et al., (1978); classify the biochemical markers in malignancy into THREE groups; the **"products"** supposedly originate from the tumor cells, **associated changes"** that derive from functional or structural alterations to surrounding structures; included in this latter group are the changes in plasma proteins that occur in response to the presence of tumor cells, the third group includes the **"tumor-specific"** bronchogenic carcinoma antigens.

Khalifa, (1985); reported that as a result of the extensive investigations carried out in recent years, **THREE groups of markers have emerged :**

[1]-**Tumor specific markers**, i.e.; produced only by the malignant cells.

[2]-**Tumor associated markers** which comprise substances secreted by normal or benign epithelial cells which, when produced by invasive carcinomatous tissue, are

released in the circulatory system in excessive quantity.

[3]-**Altered body proteins markers**; which are normal body proteins that undergo changes in blood level as a result of the presence of the carcinoma.

CLINICAL APPLICATIONS OF TUMOR MARKERS

McKenzie et al., (1977); reported that the practical importance of any circulating tumor marker depends on 3 main factors. Firstly; the frequency with which the marker is found in any population of tumor patients, secondly; a good correlation between the marker level and the mass of tumor, and thirdly; the availability of an effective treatment for the malignancy in question. The importance of marker frequency depends on the way in which it is intended to use the information obtained. If it is intended to use the marker as a screening or diagnostic test, then it must be present in virtually 100% of cases, in this context, Concanon, et al., (1974); concluded that CEA is of no value in bronchial carcinoma. Similarly, if the marker is to be applied as to a test for disseminated disease, and thus exclude patients who are unsuitable for surgery, it must correlate very closely with the presence of metastases. The correlation between the level of tumor marker and the mass of tumor depends on a number of factors. However, the plasma level at any one time reflects a balance between production and degradation.

Class Of Marker	Examples	Tumor Sources
1.Hormones.	-ACTH.	-Carcinoma of lung, colon, prostate and ovary. -Chromophobe adenoma of pituitary.
	-ADH.	-Carcinoma of lung.
	-Calcitonin.	-Medullary carcinoma of thyroid. Carcinoma of lung, pancreas prostate and breast.
	-HCG.	-Hydatiform mole, choriocarcinoma. -Carcinoma of liver, lung.
	-Prolactin.	-Carcinoma of lung.
	-Parathyroid hormone.	-Parathyroid tumors. Carcinoma of lung, kidney, liver and breast.
2.Tumor Antigens.	-AFP.	-Hepatoma, Teratoma.
	-CEA.	Carcinoma of colon and other gastrointestinal sites breast cancer.
	-CA15-3.	Breast cancer.
	-CA-125.	-Ovarian cancer.
	-CA-19.9.	-Cancer rectum. -Cancer stomach. -Cancer pancreas.
3.Enzymes.	-Acid phosphatase.	-Prostatic carcinoma.
	Alkaline phosphatase.	-Carcinoma of gastro intestinal tract, liver.

Table [1]

A guide table for tumor markers.

(Khalifa, 1985)

ACTH = Adreno-corticotrophic hormone.
ADH = Anti-diuretic hormone.
HCG = Human Chorionic Gonadotrophins.
AFP = Alpha Feto-protein.
CEA = Carcino-embryonic antigen.