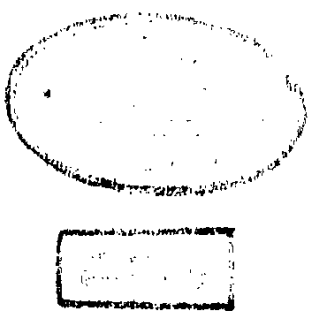
TUMOURS OF THE URINARY BLADDER

THESIS

Submitted For Partial Fulfulment Of a Master Degree Of Urology



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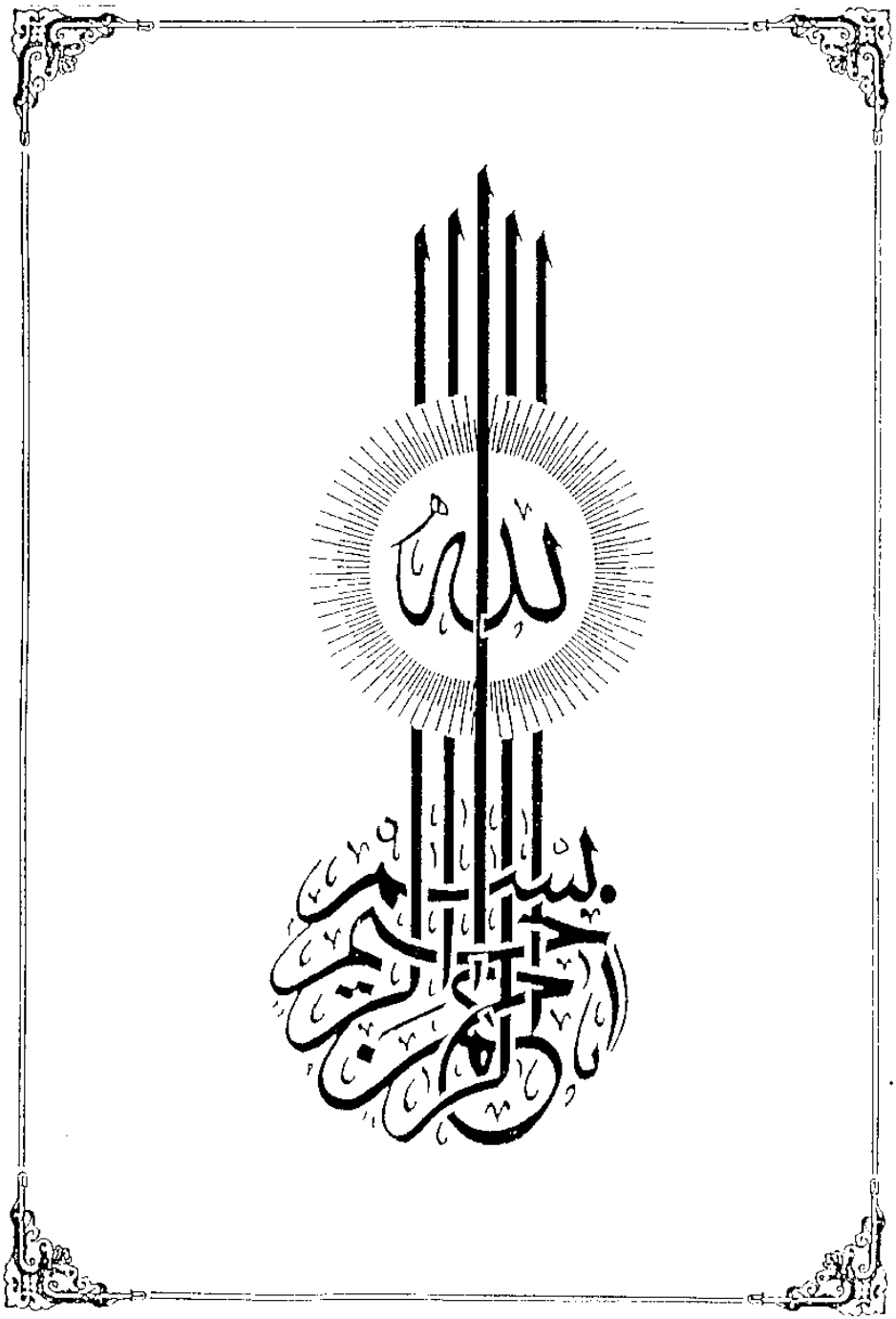

C O N T E N T S

LYMPH DRAINAGE OF THE BLADDER

Lymph drainage of the bladder takes origin from three plexuses within the bladder wall : sub-mucosa, intramuscular and adventitia.

(a) Lymphatics from the superior surface converge on the postero-lateral angle and go upwards and laterally across the lateral umbilical ligament to reach the external iliac, internal iliac and common iliac lymph nodes.

(b) Lymphatics from the infero-lateral surface run upwards with those from the superior surface.

(c) Lymphatics from the region of the trigone emerge on the base of the bladder and run upwards and laterally to reach the presacral, internal iliac and common iliac and

Types of tumours of the bladder

(A) Primary (1) Epithelial tumours : Caroinoma.
- (a) Bilharzial carcinoma
- (b) Non-Bilh Carcinoma.

(2) Mesothelial tumours :
- (a) Benign : fibroma, neurofibroma, haemangioma, leiomyoma .
- (b) Malignant : sarcoma, Myxosarcoma.

(B) Secondary tumours : from prostate, G I T, female genitalia and urethra.

INCIDENCE OF CANCER BLADDER

Tumours of the bladder are the second most common of all genitourinary neoplasms.

Only prostatic tumours occur more frequently. 75% are found in men.

Cancer bladder forms 98% of all bladder tumours.

Cancer bladder forms about 3% of all malignant diseases.

20-30% of all cases of malignancy delt with surgically in Egypt are cancer bladder.

In industrial countries, cancer bladder is 32 times more commoner than the non-industrial countries.

(Farouk M. Fahmy, 1979)

Six : In non-Bilh cancer, males are 3 times more affected than females.

In Bilh. cancer, males are 5 times more affected than females due to the more frequent exposure of males to bilharzial infection during working in the fields.

Age : 1- Non-Bilh. Cancer bladder : over 50 years old and the maximum incidence is in the sixth and seventh decades in both sixes.

2- Bilh. Cancer bladder : 75% of both males and females are before the age of 50 years.

The maximum incidence in males is between 20-40 years, while in females it is between 20-40 years.

AETIOLOGY OF CANCER BLADDER

(1) Occupational and Enviromental exposure :

Exposure to industrial amines for long time e.g 2-naphthylamine, benzidine and 4-aminodiphenol. They are called exogenous carcingens and act as a co-carcinogens. The sources of the industrial amines : dyes, rubbers, aniline dyes, gas, tars, textile, leather (Wyander and Gold Smith 1969 - 1974).

Workers subjected to the known industrial carcinogens have up to 10 times greater chance of developing bladder cancer (Glashan and Carturite, 1981).

(Richard G. et al, 1975) found an increased rate of developing transitional cell carcinoma among benzidine workers.

(2) Endogenous carcinogens : (Boyland, et al. 1963), suggested that cancer of the bladder in general may be due to increased excretion of tryptophan metabolites : 3 hydroxy kenurinine, 3-hydroxyanthranilic acid, 2-amino -3- hydroxyacetophenone.

Boyland has suggested that increased excretion of the above mentioned orthophenols may be due to abnormality of tryptophan metabolism.

The industrial aromatic amines and trytophan metabolites are metabolized by the liver into orthophenols.

The ortho-aminophenols are conjugated with sulphate or glucouronicacid and excreted through the kidneys.

In urine they are hydrolyzed by sulphatase and B-glucuronidas liberating orthophenols.

(Farouk M. Fahmy, 1979)

(Kallet & Lapco 1967) claim that glucuronidase enzyme is elaborated by urologic epithelium that have been damaged, so an increase of its level in urine is of no diagnostic Value.

There is evidence that the activity of urinary beta-glucuronidase is increased by forcing fluids, vesical infection and schistosomiasis.

B-glucuronidases are found in increased amounts in prostatic carcinoma, B. E. P. , renal cyst, urolithiasis, renal infection.

The activity of B-glucuronidase is depressed by saccaro 1-4 lactone.

(3) Smoking : Higher risk of bladder cancer of smokers, twice more than in non-smokers (Lelienfeld 1964 , Morgan and Jain 1974, Schwartze et al. 1961)

(Kerr et al. , 1965) have observed a rise of tryptophan metabolites in smokers and so they suggested that smoking may cause cancer bladder by inhibiting the metabolism of tryptophan.

Smokers have 50% increase in tryptophan metabolites excreted in urine.

Urinery chemi-luminescenc show highest levels in smokers th an non-smokers (Rose & Wallace 1973). They found that ascorbic acid decrease this activity in smokers and non-smokers.(Hammond and Horn 1956) & (Weir and Junn 1970) have proved higher incidence of cancer bladder in tobacco users.

(Wyander et al. 1963) have found 2-naphtylamine in cigarettes in very small quantities.

(Anthony and Thomos 1970) suggested that heavy smokers have aworse prognosis and higher risk of recurrences.

(4) Coffee : (Cole 1971 Simon et al. 1975) have shown relative risk of cancer bladder in woman drinking more than one cup of coffee as high as 2.6 to 1.Coffee drinking, independant of smoking is related to cancer bladder (Wynder and Gold Smith 1969 - 1974).

(5) Phenacetine abuse : (Rathert, Melchior and Lutzeyer 1975) incriminate phenacetine abuse as a cause of vesical neoplasms. (Bengtsson et al 1968) suggested that phenacetine causes transitional cell carcinoma in the renal pelvis rather than in the urinary bladder.

(Johansson et al. 1974) reported tumours of renal pelvis and bladder in patients suffering from nephropathy.

(6) Artificial sweetners : Saccharine and cyclimate studies have shown no increased risk for cancer bladder, (Armstrong and Doll 1974), but Hicks and chowaniec, 1977) have proven that saccharine is a very potent co-carcinogen.

(7) Schistosomiasis : There is evidence of an association between S. haematobium and cancer bladder (Gelfand et al, 1967).

It is responsible for the high incidence of squamous cell carcinoma in Egypt. It is commoner in farmers. Bilharzial carcinoma occurs in younger age than in non-Bilharzial variety.

Males are more affected than females.

Pathogenesis of carcinoma in Bilh. Cancer :

(1) The alkaline sepsis irritation theory :

(Dolby and Moore 1924) suggested that alkaline sepsis due to inflammed bilharzial bladder was responsible for cancer.

It is true that cancer bilharzial colon is less common because the acidity of the medium.

Againist this theory, alkaline sepsis occurs in severe chronic proteos cystitis without producing cancer.

(2) The mechanical irritation theory :

The trauma of ova or the mechanical irritation by the calcified ova is followed by attempts of healing, so

that the process of epithelial repair changes into hyperlasia then into malignancy.
Against this theory, rubbing of the bladder mucosa by spiky stones for years without malignancy.

(3)- The meracidial toxins :

Fibrosis and calcification of the bladder prevent ova to be discharged and excreted in urine.
The incarcerated ova die, liberating their toxins, which are believed to be carcinogenic.
Against this theory that calcification occurs in lower ureters and seminal vesicles without producing cancer.

(4)- The role of urinary carcinogenic factors:

(Abdel-Tawab et al, 1966) suggested that Bilh. cancer bladder is related to excretion of tryptophan metabolites and beta-glucuronidases in the urine.

(Fripp, 1965)believed that S.haematobium infestation may cause cancer bladder by increasing B-glucuronidase which could hydrolize any inactivated carcinogenic glucuronide in urine.

(Brooks et al ,1972, Hicks et al, 1978 & 1982) supposed that the presence of nitrosamines in bouts of bacteruria may be an initiator of bilharzial cancer bladder.
Bilharzial cancer bladder may be due to all the above mentione factors acting together as a dual machanisms

(A) Local vesical factors :

Increased suseptibility of the mucosa to malignant transformation. These are ischaemia of the mucosa, stasis, chronic irritation, and repeated attempts at healing.

(B) Systemic factors :

Due to increased excretion of tryptophane metabolites serotinine and B-glucuronidase as a result of nutritional defects and hepatic dysfunction.

(8) Chronic irritation and infection :

Chronic indwelling Folly catheters and stones in genesis of squamous cell carcinoma were supposed by (Koufman et al. 1977).
Also, chemical dystitis associated with cyclophosphamide drug may cause squamous cell carcinoma.
(Wall and Clausen, 1975) reported five patients had squamous cell carcinoma with cytoxan therapy.

(9) Oncogenic RNA viruses :

Most uroepithelial tumours do contain traces of viral genomes (Fraley et al. 1976)
They found that viruses from transitional cell carcinoma produces cytopathic changes in cultured cells.

The affected cells contain virus-like particles resembling those in the original tumour and in cultured tumor cells.

Also, sera from patients with transitional cell carcinoma prevent the cytopathic changes in the cell culture.

(Elloit et al. 1973) have isolated a single RNA virus from four TCC. They demonstrated the virus by electron microscopy in the original tumour and culture.

10- Local vesical factors :

a- Extrophied bladder soon after birth develops areas of squamous and glandul-ar metaplasia.
(Smith and Hardy, 1971).

b- A diverticalum of the bladder: It predisposes to tumour formation. (Peterson et al, 1973) found that tumours were recorded in 3.6% of 2053 cases.

c- Leukoplakia : (Morgan & Cameron, 1980) have reported the development of invasive tumours in 25-28 % of their cases.

d- Von-Brunn's nest , cystitis cystica and cystitis glandularis : They are regarded as indications of unstable mucosa.

Immunological Considerations of Cancer bladder

It is the study of the relation between cancer bladder and immunological mechanism in the human body. The hypothesis was proposed by (Burnet and Thomas 1960). They said that the immune system can recognise the mutant patterns in the body and try to eliminate them.

Tumour-Associated Antigens (TAAs) were demonstrated in bladder papilloma, carcinoma and in a variety of tumours including sarcoma, leuckaemia, lymphoma, neuroblastoma, melanoma.

By experimental studies on animals bladder carcinoma is chemically induced, but nephroblastoma is of viral etiology as proved by crossreactivity of the TAAs.

Bladder tumours caused by benzidine in workers are more prevalent in workers who have reduced levels of complement component properdin. (J. Vivian Wells et al, 1981).

Immune response to TAAs :-

TAAs appear mainly on the membranes of the affected cells, so it cannot be isolated in pure forms, because of the presence of normal membranous components.
Detection of TAAs depends on their eliciting of immune responses in the tumour bearing host.

1- Humoral immunity :-

By circulating anti-bodies, or immuno-globulins secreted by plasma cells; that develop from B- cells (Bursa or bone marrow derived lymphocytes).
These circulati-ng antibodies may inhance tumour growth.

2- Cellular immunity:-

It is mediated by T cells (Thymus derived) and soluble lymphocyte products (lymphokines) liberated when these lymphocytes react with their specific target antigens .
Patients with tumours which are heavily infilterated with plasma cells; lymphocytes; eosinophils survive longer than the average, regardless of their clinical stages. The relative balance between cellular and humoral responses may be the major factor in determining the over all outcome of a tumour.
(J. Vivian Wells et al, 1981).