

CARCINOMA OF
THE URINARY BLADDER
IN ZAMBIA

by

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A project report submitted in partial fulfillment of the
requirements for the award of the
MASTERS OF MEDICINE (SURGERY)
degree of
the University of Zambia.

School of Medicine.

University of Zambia.

April, 1987.

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INTRODUCTION

Every cancer has a beginning and in the beginning every cancer is more likely to be curable. Early diagnosis may allow the possibility of cure.

The prime objective, therefore, should be to discover cancer in its incipiency. But how early and at what stage in cell proliferation does a cancer become clinically detectable? Urinary cytology is becoming widely accepted as a diagnostic and follow up procedure in bladder cancer (Morrison et al). Carcinoma may be cytologically detectable months or years before it becomes endoscopically or histologically visible (Murphy 1984). Urinary cytology using cytocentrifuge specimens of voided urine stained with Giemsa, Oil Red or Papanicolau stains have been used with good results revealing cells shed from the tumour (Theodorou 1984). It has been found in previous studies that sensitivity of exfoliative cytology increases with repeated specimens on consecutive days. While certainly more laborious, observation with the scanning electron microscope by revealing pleomorphic microvilli, provides the earliest morphological evidence of irreversible malignant transformation.

It is almost 100 years since Nitze invented the light bearing cystoscope which, with subsequent improvement, became the "magic lantern" that illuminated the dark, dank, murky diagnostic jungle of the bladder interior. The cystoscope exposed for the first time in history of man, living intravesical pathology, including cancer.

It is postulated that neoplastic transformations are continuously induced by an ever increasing exposure but the changes are shortlived or vitiated by a constant cell-mediated immunological mechanism (Melicow 1974). The tumour is no longer regarded as an independent microcosm of cells and evidence is accumulating that there is an interaction between the neoplastic cells and the host, and that an immunal response mediated through lymphocytes is operating. This response probably accounts for some of the differences in growth and spread of tumours and also individual host response differences (Melicow 1974).

Cystoscopy and Cytology are the least invasive yet most effective of tests necessary in making early diagnosis of Bladder Cancer. These two tests are more accurate in diagnosis of tumour and for obtaining specimens for histology. The objective in the ensuing report is to highlight some of the facets and the significance of the problems in making an early diagnosis of Carcinoma of the Urinary Bladder.

"No other system or organ of the human body gives us so much diagnostic information by its excretion as does the urinary tract."

Corpus Hippocraticum - Hippocrates, 5th century BC ,
founder and pioneer of Urology.

EPIDEMIOLOGY

Demographic factors of Bladder cancer.

Carcinoma of the urinary bladder varies in frequency in different geographical regions throughout the world. The different aetiological factors associated with histologically different tumours play a major role in the incidence of the tumour worldwide.

The frequency of Carcinoma of the bladder in Egyptians suffering from vesical bilharziasis is probably much higher than that reported from other countries (Ferguson 1911, Gillman and Prates 1963) It is the commonest solid tumour in the Egyptian male (Aboul Nasr, et al 1963, Badr 1964.)

In the same subregion, Bladder cancer in the Sudan shares some features with both bilharzial and non-bilharzial bladder cancer in other countries and transitional cell carcinoma is more common (Ebrahim et al 1977)

Bilharziasis is known to be endemic in Egypt and Iraq and in areas along the River Nile and bilharzial bladder cancer is common though variations occur within the same region (Makhyoun 1971).

The incidence of bladder cancer in many African countries with endemic Schistosomiasis is not known.

Carcinoma of the bladder is one of the commonest tumours in Zambia. Bhagwandeem and Carruthers from histopathology and hospital records reported it was the third commonest tumour. (Bhagwandeem 1976, Carruthers 1976) According to Histology records at the UTH. it is the fourth commonest tumour with cancer of the cervix being the commonest (Elem, personal communication).

At Katete in the Eastern province of Zambia where Schistosomiasis is endemic in a mostly rural population it is the commonest tumour diagnosed (Cairns 1979)

According to distribution by county in the United States bladder cancer mortality seems to be more common in the more industrialized cities eg. New York City, New Jersey and the industrialized areas around the great Lakes. (Wynder 1977). Table 1 shows Age adjusted Incidence rates for malignant neoplasms of the bladder by sex (per 100,000 Population)

Country	Male	Female	M:F
England and Wales,	21.1	3.5	6.0
U.S.A. Connecticut	19.9	5.9	3.4
Canada	10.9	3.6	3.0
South Africa	9.6	3.0	3.2
Japan, Miyagi	4.7	1.6	2.9
India, Bombay	2.3	0.8	2.9

(Data from Doll, Muri, Waterhouse, 1970)

Age and Sex distribution.

Carcinoma of the bladder varies in age and sex distribution depending on the type of tumour and occupation in various regions of the world.

The average age in Egypt is 46.7 for males and 44.6 for females and 46.3 for the whole group (Boulkany 1972). In Iraq 73% of the patients are between 40-60 years of age (Morton 1957). In the U.S.A. the average age is 60.1 years with 80% of the patients above 50 years of age (Liebermann 1968). In England (Payne 1959) gave an average incidence of 63.5 years for males and 66.5 for females.

The peak age in the Sudan is between 40 and 50 years of age (Ibrahim 1977).

In Zambia Bladder Cancer presents most commonly in the fourth to fifth decades (Carruthers, 1976 Cairns 1979) and that bilharzial bladder tumours occurs in a younger age group. The male to female ratio varies considerably. In Egypt the M:F ratio is 7:1 and in the Sudan 6.6:1. This may be due to the fact that in these countries most of the field work is done by Males along the river Nile therefore men are more exposed to the Schistosome parasite. In Industrialized areas the ratio is still in favour of males. Males are employed more often than females in the chemical and dye industry. In England a 3:1 sex ratio of non-bilharzial bladder cancer suggests that males are more exposed to industrial carcinogens.

AETIOLOGY.

Since 1895 when Rehn demonstrated an increased risk of Bladder Cancer in dye industry employees, several industrially used aromatic amines have been identified as Bladder carcinogens (Wynder 1977). Workers in the textile, printing, plastic, rubber and cable industries have been found to be at an elevated risk for bladder cancer.

Industrial Aromatic Amines suspected or known to induce Transitional Bladder Cancer in Man are :

Benzidine

1-Naphthylamine, 2-Naphthylamine

4-Aminobiphenyl

4-Nitrobiphenyl

Auramine

Magenta

Dianisidine

3,3'-Dichlorobenzene

O-Tolidine.

* Wynder, Cancer 40, 1977.

The contribution of other factors to the incidence of carcinoma of the bladder has not yet been fully determined. Most studied among these are cigarette smoking and coffee consumption. An international study of smoking and Bladder cancer in Boston, Massachusetts, Manchester, United Kingdom and Nagoya, Japan revealed a positive association between smoking and bladder cancer. (Morrison et al 1984).

A substantial amount of evidence has accumulated in support of a relationship between cigarette smoking and bladder cancer (Morrison 1984 , Wynder 1977) A direct effect of cigarette smoke constituents and /or their metabolites may be indicated by the presence of potent bladder carcinogen, 2-Naphthylamine, in the smoke. Other factors include Chronic urinary tract infection , urethral strictures, bladder stones and leukoplakia which may be contributory in the pathogenesis of bladder cancer (Wynder 1977).

The essential amino acid Tryptophan, was implicated in the genesis of bladder cancer by Dunning et al. 1966 who reported a high incidence of bladder carcinoma in rats fed supplemental DL-tryptophan and 2-acetylaminofluorene, whereas no bladder tumours were present in rats fed with only 2-acetylaminofluorene. Several primary aromatic amine metabolites, structurally similar to known environmental human bladder carcinogens, are derived from Tryptophan and are present in human urine. The mutagenicity of tryptophan metabolites 3-hydroxykynurenine and 3-hydroxyanthranilic acid for mammalian cells was demonstrated and proposed as the probable mechanism for carcinogenicity. (Price 1966, Bryan 1977).

It appears reasonable to conclude that the experimental production of bladder cancer is a complex process that requires the participation of two or more factors, and that tryptophan metabolites may be only one of the participants in this series of coordinated events.

Both *Schistosoma Haematobium* and *Mansoni* are Endemic in Zambia and in many of the African countries. Lack of research facilities and funds have resulted in inadequate documentation, and a lack of an accurate National Cancer Registry making it difficult to determine the exact incidence of Bladder Cancer.

TABLE 2 Reported histological incidences of associated Schistosomal infection in Bladder Cancer from Zambia and neighbouring countries.

Year	Authors	Country	Histological evidence of <u>Schistosoma inf.</u>
1959	Prates and Gillman	Mozambique	30%
1966	Chapman	South Africa	57%
1969	Fine	Zambia	40%
1969	Hinder and Schman	South Africa	45%
1969	Philip	Tanzania	25%
1976	Bhagwandeem	Zambia	60%
1981	Lucas	Malawi	67%

Tissue digestion in Potassium hydroxide is an accurate method for detecting schistosomal ova, and provides a reliable quantitative indication of the intensity of infection in the bladder (Cheever 1968). Both calcified and non-calcified eggs resist digestion (Cheever 1970).

Using this method the incidence of schistosomal infection in 50 malignant bladders was found to be 94% (Elem 1983) as compared to a control group of non malignant bladders which was 45%. This was by far the highest recorded incidence of associated schistosomal infection in Bladder cancer compared with previously reported series in Zambia (Fine 1969, Bhagwandeem, 1976) and its neighbouring countries (Prates and Gillman, 1959; Chapman, 1966; Hinder and Schman, 1969; Philip, 1969; Lucas, 1981). This figure is also higher than incidences in Egypt where it was 73.6% in one study (Makhyoun, 1971) and in the Sudan (Ibrahim 1977). It was also observed that the overall severity of infection was not the sole factor in the pathogenesis of bladder cancer if one is to accept a causal role of *S. Haematobium* in Bladder carcinoma (Elem 1983). Factors supporting a bilharzial role in Bladder cancer are:

- 1) A known tendency of bilharziasis to induce Squamous metaplasia in the bladder mucosa.
- 2) A high incidence of Squamous cancer in a relatively younger age group.
- 3) Locality of a village environment (more exposed).

Pathology.

In a review of 910 cases of Bladder cancer over a period of ten years at Columbia University 91.8% were Urothelial tumours, 6.4% were Squamous cell carcinoma, 1.3% glandular and 0.5% miscellaneous (Melicow 1974). This is in an area where schistosomiasis does not exist. (Payne 1959) records 962 cases of Bladder tumour of which 92.5% were transitional cell carcinoma.

In a study of 304 patients at the cancer institute in Cairo, showed that Squamous cell carcinoma accounted for 66.7% of tumours, transitional cell 23.4%. Adenocarcinoma 8.1% and 1.8% were miscellaneous tumours. In 1971, 91 cases of bladder cancer were registered at the Lusaka cancer registry covering the southern half of Zambia of which 69% were Squamous cell carcinoma, (Carruthers 1976). At Katete in the Eastern province of Zambia 262 cases were seen between 1968 to 1977, of which 75% were Squamous cell carcinoma (Cairns 1976).

SITE OF TUMOUR

The most frequent site of involvement are the posterior and lateral walls of the bladder affected in 60-70% of the tumours of both the urothelial and Squamous cell varieties. Squamous cell metaplasia is rare in the region of the trigone in the bilharzial bladder (El Sebai 1961) and in one study in Cairo constituted only 5.7% at the trigone (Boulkany 1972). On the other hand the trigone is a common site of involvement in Transitional cell tumour. (Mostofi 1956) gave a figure of

21% in his study. The dome of the bladder gives an equal percentage of 10% in both types of tumour. Figure 1 shows usual sites and shapes of Bladder Neoplasms.

Macroscopically the tumours are either solid, papillary, infiltrating or fungating. (Boulkany 1972, Melicow 1974). Figure 2 shows the types of Bladder Neoplasms.

Spread of the tumour may be local involving perivesical tissue and the pelvic walls. Massive involvement of the retroperitoneal tissue with involvement of the ureters leading to obstructive uropathy is frequently the cause of death in many patients. Visceral metastases most commonly involve the liver, lungs, adrenals and kidneys. Bone metastases most frequently involves the pelvic bones, vertebrae and ribs. Lymph nodes commonly involved are the retroperitoneal, periaortic and most commonly are the regional pelvic lymph nodes. (Results of 125 consecutive autopsies in bladder cancer patients - Melicow 1974)

USUAL SITES & SHAPES OF BLADDER NEOPLASMS

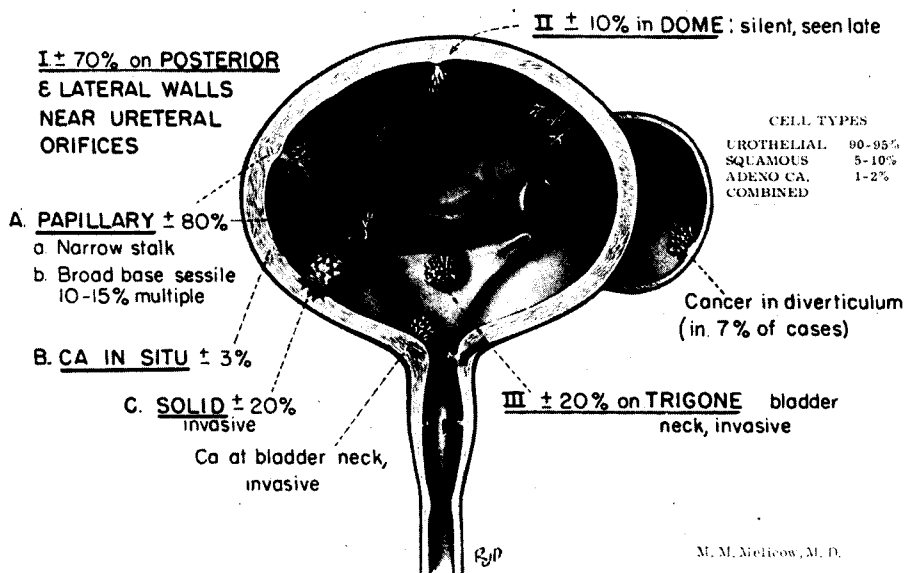


Figure 1. Composite diagram displays Gamut of vesical neoplasms from the point of view of site, shape, and cell contents,

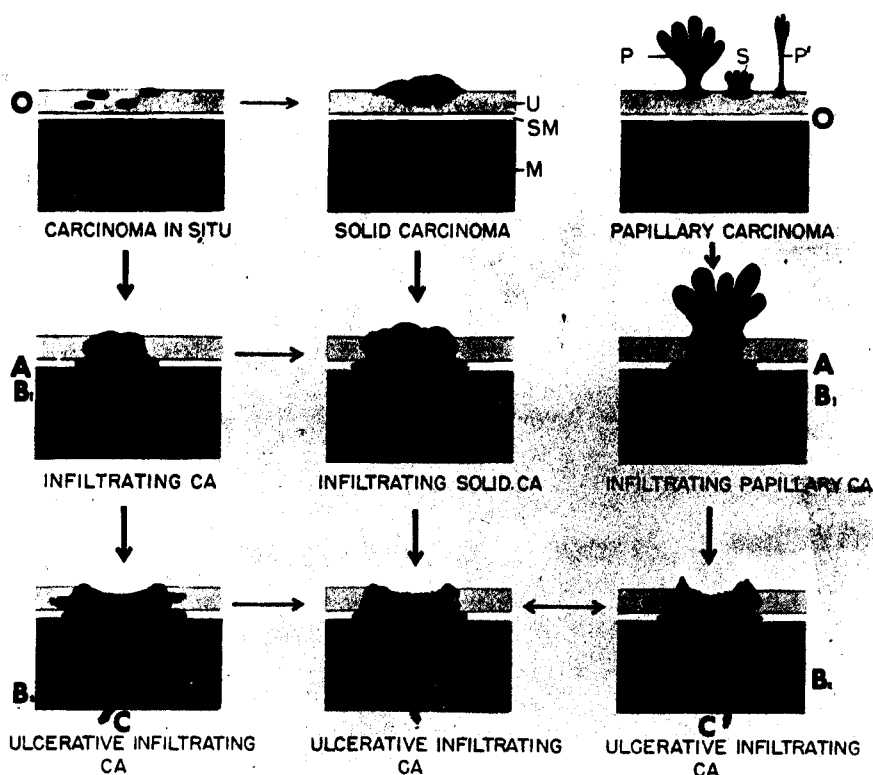


Figure 2. Probable life cycle of untreated bladder tumours. Eventually all types may become ulcerated and infected and may be difficult to determine whether they were originally solid or papillary.
 U - urothelium SM - submucosa M - muscularis
 P - papillary Ca, S - sessile tumour PI - papilloma.

Hyperplasia of the urothelium and von Brunn's nests, and the developments of cystitis cystica and glandularis were frequently encountered in a study of more than 1000 bladder tumours. They were found in close proximity to neoplasms, in areas between tumours, in association with foreign bodies and in infected bladders (Melicow 1974)

This tetrad fascinated pioneers in pathology, including Von Limbeck in 1887 and von Brunn in 1893, who discussed their relationship to irritation and the possibility of their being forerunners of neoplasia.

Squamous cell metaplasia and leukoplakia - the latter was first reported by Rokitansky in 1881 are also often seen in association with chronic irritation. Carcinoma in situ is a fascinating and probably extremely important event in oncology. It is quite possible that many solid tumours, not only of the bladder but of other organs, start as carcinoma in situ. In 1970 Cifuentes and in 1974 Koss and associates reviewed carcinoma in situ and credited Melicow with being the first to report this lesion in the bladder in 1952 . That carcinoma in situ is a threat to the patients life is a well established fact.

Whatever the source of the carcinogen(s), external or internal, basically it is the interaction between [cellular neogenesis] and the hosts immunological mechanism which is important, either in progression or in their retardation or liquidation.

BIOLOGICAL MARKERS.

Increased levels of lactic dehydrogenase LDH5 and Beta glucuronidase have been detected in the urine of Bladder cancer patients. The levels of these biologic markers in urine have been used for evaluation and early detection of bladder cancer. (Wassef 1969).

Urinary levels of alpha-esterases have been found to be high in bladder cancer patients and may have a possible role in detection of bladder cancer in early stages. (Sewedy 1978).

A diagnostic - prognostic test for bladder cancer using a monoclonal antibody based, enzyme linked immunoassay to detect Fibrin degradation products was found to be effective in several studies (McCase 1984, Wajzman Z. 1978,).

Several tests have been suggested over the years to assist in detection of bladder cancer using biologic markers and found to have some value, Carcinoembryonic antigen, chromosome mapping, creatinine kinase, cytotoxicity tests, karyotyping, Muramidase and polyamines in urine (Lessing 1978).

Clinical staging of Bladder Cancer.

The staging system by Jewett & Strong (Jewett 1946) as modified by Marshall (Marshall 1952) has been used widely for the categorisation of bladder carcinoma. The details of this system are given in figure 3. Stage 0 tumours are limited to the mucosa. In stage A, tumour infiltration does not extend beyond the submucosa, in stage B not beyond the detrusor muscle layer and in stage C into the perivesical tissue whereas stage D indicates metastases and/or invasion of adjacent organs or the pelvic or abdominal wall.

The Jewett-Strong-Marshall system is convenient and still used in many centres especially in the USA. The system is based on histopathological examination of operative specimens. There is therefore a need for a staging system based solely on clinical and radiological examinations and possibly on biochemical tests. The TNM system, proposed by the international union against cancer (WHO 1973), fulfils these requirements. T indicates the extent of the local tumour, N involvement of regional and juxta-regional lymph nodes, and M indicates metastases in distant organs and tissues, including remote lymph node areas. Figure 4 illustrates the T stage of the local tumour which is the 1978 appraisal of the TNM system by the UICC. This classification should remain unchanged for the next ten years.

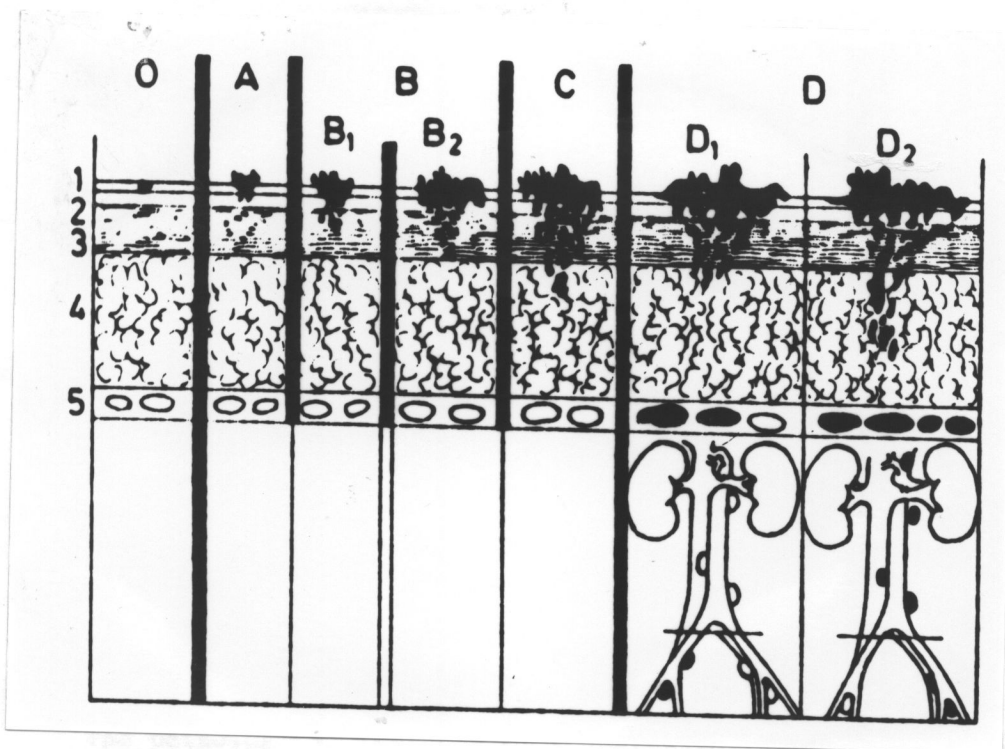


Figure 3, The Jewett-Strong-Marshall classification for tumours of the urinary bladder,

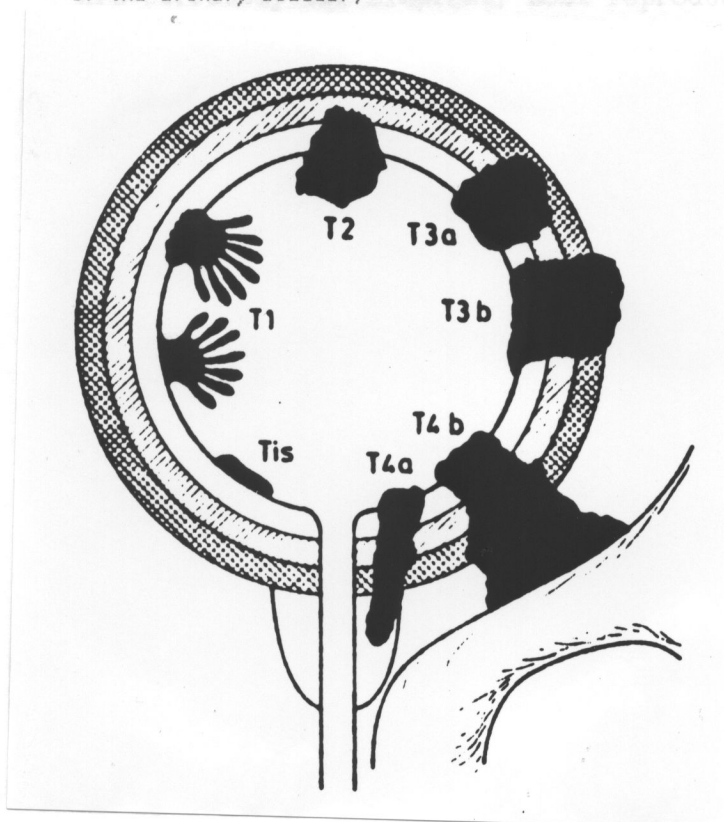


Figure 4, TNM system for Staging of Bladder Tumours,

TREATMENT .

Geographically, modalities of treatment vary. These variables are important factors in the end results but are difficult to assess. The many problems posed by bladder cancer demand an early recognition, correct topographical localization and thorough evaluation of cell potential (pathological-grade) , and as accurate a preoperative assessment of spread as is feasible (clinical and pathological staging). This should then be posed against the host's age, sex, physical, mental and emotional status after which therapy is instituted.

The pathological features of grade, stage, and multicentricity are currently the simplest, most reproducible, most therapeutically relevant, and most prognostically significant characteristics. (Whitmore 1977). Options are Surgery, irradiation, chemotherapy, and immunotherapy.

At present immunotherapy is an experimental modality without an established place in treatment. Attempts at manipulation of the immune mechanism are of interest, but they are a long way from being accepted as part of standard surgical practice. (Symes et al 1978).

CHEMOTHERAPY.

Cytotoxic Chemotherapy has for long been used in Bladder cancer patients. Systemic Chemotherapeutic agents have included drugs like Adriamycin, Bleomycin, cyclophosphamide, 5-fluouracil, cisplatinum, and Methotrexate. Unfortunately, no consistently good response to systemic treatment with chemotherapeutic agents has yet been found (Hall R. 1983). It does not seem to be clinically useful in squamous cell carcinoma of the bladder (Gad-el-Mawla, 1978). The ideal application of chemo-therapy is in the adjuvant treatment of cancer following potential curative surgery or irradiation. Intravesical therapy with Doxorubicin Adriamycin, thiotepa etc has been used as an adjuvant to surgery (Nijiima, Edsmyr 1978) Current use of chemotherapeutic agents in conjunction with radiotherapy and radical surgery on a pre-operative and post-operative basis is now being evaluated with promising results (Pavone-Macaluso 1978)

RADIOTHERAPY.

For patients with high grade tumours infiltrating the superficial bladder wall musculature or with tumours of any grade invading deep muscle or the perivesical space, the evidence is now substantial that integrated treatment with irradiation and cystectomy or a lesser resection if possible in selected cases results in a significantly higher survival rate than does either approach alone (Caldwell 1977). Usually the whole pelvis is irradiated preoperatively.

SURGERY.

The surgical procedures that carry the potential for cure for the patients with invasive bladder carcinoma are segmental resection, various types of cystectomy and occasionally, endoscopic fulguration. The three broad operative treatment groups are the flat carcinoma in situ (Tis), the superficial carcinoma (Ta T1) and the invasive carcinoma of the bladder (T2,T3,T4) (Macaluso 1978)

Transurethral Resection and fulguration of Bladder Carcinoma.

The tumour must be localized to the bladder and the failure rate increases as the size of the tumour and depth of penetration increases and skill in selection plays a great role in the outcome of treatment. Most resections do not do well in invasive bladder cancer (Barnes et al 1967)

Segmental resection of Bladder Cancer.

It is easy to perform ,preservation of sexual and vesical function being its attractive features. The following criteria is to be met before segmental resection is performed.

1. At least 3cms of normal bladder are available to be excised around the tumour.
2. Patient has no previous history of bladder tumour.
3. The tumour is solitary and removal will not require ureteroneocystostomy.
4. Biopsies of bladder at sites distant from the tumour reveal normal, not atypical epithelium.

Partial cystectomy has been practically abandoned now.

CYSTECTOMY.

Very little was known about the effect of cystectomy on survival of patients until Marshall began a systemic evaluation of the procedure. The Brunschwig philosophy that an effective operation for a pelvic carcinoma should follow the pelvic wall where possible removing peritoneum, lymph nodes and fat associated with the offending organ. Jewett and Strong established the clear relationship between the depth of the invasion of the bladder wall, lymph node involvement, and curability. The reported incidence of positive lymph nodes observed during radical cystectomy is 35 per cent without preoperative radiotherapy and 8 per cent following preoperative radiotherapy (Wallace and Bloom 1976) The difference in lymph node involvement demonstrates the efficiency of pre-operative pelvic field Radiotherapy. Pre operative radiotherapy has doubled the five year survival figure for Surgery alone. (Werf-Messing 1971, Wallace and Bloom 1976, Whitmore 1980).

Total cystectomy is indicated in more advanced lesions of bladder tumour (T3) where there is no evidence of widespread metastatic disease and necessitates the transplantation of the ureters.

Surgery for Bladder cancer has made no substantial progress over the last 30 years. Disregarding partial cystectomy as being practically abandoned, we can say total cystectomy gives only moderately good results (Pavone-Macaluso 1978).

OBJECTIVES

1. A study of the epidemiology of bladder cancer in Zambia to analyse the incidence, age, sex, tumour histology, and survival parameters.
2. To study the clinical presentation, pathology and management of bladder cancer in Zambia.
3. Microscopic Analysis of cells in quantitative centrifuge sediment of voided urine as a means of making an early diagnosis of carcinoma of the bladder, as an alternative to more expensive and invasive techniques.



PLAN OF STUDY

This study was divided into three phases

PHASE 1

- 1) A retrospective analysis of cases of carcinoma of the bladder documented at

- a) Saint Francis mission hospital in Katete,
- b) University Teaching Hospital in Lusaka,

during the period January 1st 1984 to December 31st 1985.

A retrospective analysis was done using case notes of these patients.

PHASE 2

A case controlled study of patients at

- a) Saint Francis mission hospital in Katete for the period of September 1985 to February 1986.
- b) University Teaching Hospital for the period of March 1986 to March 1987.

PHASE 3

Microscopic analysis of centrifuged sediment of voided urine of patients with proven carcinoma of the bladder both cystoscopically and histologically to establish a statistically significant index of making an early diagnosis of bladder cancer. Urine specimens were taken from all patients in Phase 2 both at St. Francis and at the UTH.

A protocol was made which was considered and approved by the medical research and ethical committee of the University of Zambia.

METHODOLOGY

PHASE 1 - Retrospective analysis

This phase was aimed at recording the incidence of Bladder cancer and

to document the following parameters:

- Age of the patient
- Sex
- Tribe
- Geographical location of village, district.
- Water source
- history of haematuria in childhood
- Symptoms
- Histological / cystoscopical diagnosis.
- Grading / staging of tumour
- Treatment and outcome of management.

A retrospective analysis of all the available case notes of patients both at Saint Francis Hospital and at the University teaching hospital were made for the period of 1st January, 1984 to December 31st 1985.

Data was extracted into data sheets (Appendix 1).

The data obtained was used to extract the relevant information and reported as percentages of the total. Statistical correlation was not sought.

METHODOLOGY

PHASE 2 - Case control study

1. DEFINITION OF CASE

Any patient with a cystoscopically and histologically confirmed Carcinoma of the Urinary Bladder.

2. QUALIFICATION OF CASE

Any of the above cases presenting during the study periods from 1st September 1985 to 28th February 1986 at Saint Francis hospital in Katete and from 1st March, 1986 to 30th March, 1987 at the University Teaching hospital in Lusaka.

3. INFORMATION AND ASSESSMENT

All cases within this study were interviewed, examined and followed up personally by the investigator to ensure consistency in data recording. All the data were entered into data sheets prepared for this purpose. (Appendix 1)

The following details were sought:

PERSONAL DETAILS - Name, age, sex, occupation, tribe, village
and district where patient spent most of his
life.

WATER SOURCE - rivers, dams, or water reservoirs

SMOKING - Most of the villagers who smoke usually
cannot afford commercial cigarettes and have
to do with unprocessed home made cured tobacco leaves.

- SYMPTOMS** - Initial symptoms were recorded
- Haematuria - the commonest symptom in carcinoma of the urinary bladder. Duration and extent were recorded.
- Pain on micturition
- suprapubic pain
- Pieces in the urine - usually epithelial debris due to necrosis of tumour tissue.
- Nocturia or frequency
- Other symptoms were also noted like pyuria.etc
- EXAMINATION** - All patients were examined and a record of Nutritional status, Karnofsky's status, whether a palpable abdominal mass was present, and a Wallace's staging of the tumour was made.
- INVESTIGATIONS**- A record of the various investigations including urea, cystoscopy, and cytology.
- HISTOLOGY** - This was recorded after the Histology results were obtained and categorised accordingly as Squamous cell tumour, Transitional cell tumour, Incidence of histologically demonstrable ova.
- SITE** - The site was recorded whenever it was possible depending on the cystoscopy results.
- Right and left lateral walls
 - Dome of the bladder
 - posterior bladder wall
 - Trigone of the bladder.

KARNOFSKY'S PERFORMANCE STATUS (Halnan 1982)

- 100% - No sign or symptoms
- 90% - Trivial signs and symptoms not interfering with activity.
- 80% - Definite signs and symptoms but able to work with effort.
- 70% - Able to care for self but not to work.
- 60% - Requires assistance but fit to be at home.
- 50% - Requires more assistance but able to get out of bed and sit in the sun.
- 40% - Requiring hospitalization and active treatment.
Chooses to stay in bed. Can walk to toilet.
- 30% - More incapacitated, but stands out of bed briefly.
- 20% - Bedridden.
- 10% - Moribund.

WALLACE'S STAGING (after D.M. Wallace 1975)

- T1 - Tumour is confined to the mucosa- tumour is impalpable.
- T2 - Penetrating the bladder wall - a localised thickening is palpated but the tumour is mobile.
- T3 - Penetration of the bladder wall - the tumour is mobile but the mass is larger than suggested by its cystoscopic appearance.
- T4 - fixed to adjacent structures (pelvis or prostate) the mass is immobile.

TREATMENT PROFILE

An attempt was made to record the treatment and follow up of the patients in the study but was difficult in that follow up records are poor probably due to poor patient compliance. Most of the patients however present late and there was not much that could be done for them.

4. CONTROL MATCHING

Each of the cases was matched for age and sex among the hospital in-patients. The matched controls were patients admitted into the surgical wards for diseases other than cancer of the urinary bladder.

5. STATISTICAL ANALYSIS

The results obtained from the case controlled studies were analysed and subjected to a Chi squared analysis. The Chi-squared test was utilised for grouped data.

METHODOLOGY

PHASE 3 - CYTOLOGY

All the patients used in the prospective study were subjected to cytology of their urine specimens. All these cases were cystoscopically and histologically proven cases of carcinoma of the bladder. This was to establish a statistically significant index of cytology in proven cases of carcinoma of the bladder and to test the accuracy of the method.

This included all the cases in the prospective study at Katete and the

cases at the University Teaching Hospital in Lusaka.

CONSENT

Informed verbal consent was obtained from all the patients used in the study.

TECHNIQUE

1. All patients were seen in mid- morning period. All patients were interviewed and information filled on the data forms (Appendix 1 and 3).
2. Informed verbal consent was obtained from the patients.
3. Patients were made to exercise by walking up and down the ward several times. They were accompanied by a student nurse.
4. Mid morning whole urine specimens were collected in sterile containers.
5. Urine samples were divided and put through a centrifuge for 10 minutes.
6. The sediment was collected and smeared onto separate slides.

7. The slides were then stained by the two different techniques, the papanicolau method and the Romanowsky's stain (Giemsa).

If any problems were encountered during the collection period or during the time of staining the urine sample collection was repeated later.

A) PAPANICOLAOU METHOD

1. Fix the smear in 3% alcohol for twenty to thirty minutes.
2. Rinse briefly in absolute alcohol or 74 o.p.spirit - 5 sec.
3. Rinse briefly in 70% alcohol for 5 seconds.
4. Rinse briefly in distilled water for 5 seconds.
5. Stain with Harris's haematoxylin (ortho modification) 1 min.
6. Run gently in running tap water till blue - 1 to 2 minutes.
7. Run briefly in 70% alcohol - 5 seconds.
8. Rinse briefly in absolute alcohol or 74 O.P. spirit - 5 secs.
9. Stain with Orange G. solution (O.G.6) for 1 minute.
10. Rinse briefly with absolute alcohol or 74 O.P. spirit - 5 s.
11. Rinse briefly with absolute alcohol or 74 O.P. spirit - 5 s.
12. Stain with Eosin-azure 50 mixture (E.A.50) - 2 minutes.
13. Rinse briefly in absolute alcohol or 74 O.P. spirit and repeat three more times for 5 seconds.
14. Clear in Xylene.
15. Mount in balsam or D.P.X.

RESULT - Nuclei stains blue. Cytoplasm varies from Orange to green depending on the maturity of cells and the amount of Keratin present.

B) ROMANOWSKY'S STAIN (GIEMSA)

1. Slide is smeared with sediment and dried in air.
2. Immerse the film in Giemsa stain for 20 - 45 minutes.
3. Remove the stain and allow the excess stain to drip off.
4. Wash in buffered distilled water (pH 6.8 to 7.0) 3 dips.
5. Dry in air and then examine under oil immersion.

EXAMINATION OF SLIDES.

The slides were examined and read by a trained cyto - technician with several years of experience of the cervical Pap smear.

Problem: The university Teaching hospital has no specially trained cytologist for Bladder cytology. The pathologist at the U.T.H. have limited experience in cytology, Nonetheless the prepared slides were counter checked by a pathologist with an interest in the subject.

REPORTING

Each cytological smear was assessed for the following changes:

- Inflammatory changes
- Dysplasia
- Malignant changes.

CONTROL MATCHING

To get a statistically significant index of the cytological result each proven case of bladder cancer was matched for age and sex among hospital in-patients. Urine specimens were also taken from this control group and sent for cytology without a diagnosis to avoid bias.

RESULTS

PHASE 1 - Retrospective Analysis

Incidence in Zambia

The average annual incidence of Urinary bladder cancer in Zambia according to the Cancer Registry is 92 and according to the records at the ministry 235, representing a crude incidence of 1.5 and 3.9 per 100,000 population respectively. This wide variation in incidences recorded by the two registries reveal the inadequacy of the reporting system. The higher figure recorded by the ministry is due to the fact that many peripheral hospitals send their returns only to the ministry. This higher figure when comparing incidences of other tumours appears more accurate. According to these records Carcinoma of the bladder is the third commonest tumour in Zambia.

Table No. 3

CARCINOMA OF THE URINARY BLADDER

INCIDENCE 1983 - 1986

<u>YEAR</u>	<u>CANCER REGISTRY</u>	<u>MINISTRY</u>
1983	98	197
1984	90	273
1985	88	197
1986	95	205

The UTH had a total of 12,395 surgical admissions from January, 1984 to December 1985, the period of study.

Incidence at the UTH.

The average annual incidence of carcinoma of the bladder at the UTH is 26 patients. Histology records from the pathology laboratory reveal that Carcinoma of the Bladder is the 5th commonest tumour seen in Lusaka at the UTH. During the study period January 1984 to December 1985 there were 44 new cases admitted at Saint Francis mission hospital in Katete. The case notes of all these patients were reviewed. At the UTH case notes studied were from January, 1984 to December 1985 making a total of 46 new cases. Several cases were seen in the clinic but not admitted and it is possible that these were not included in the study.

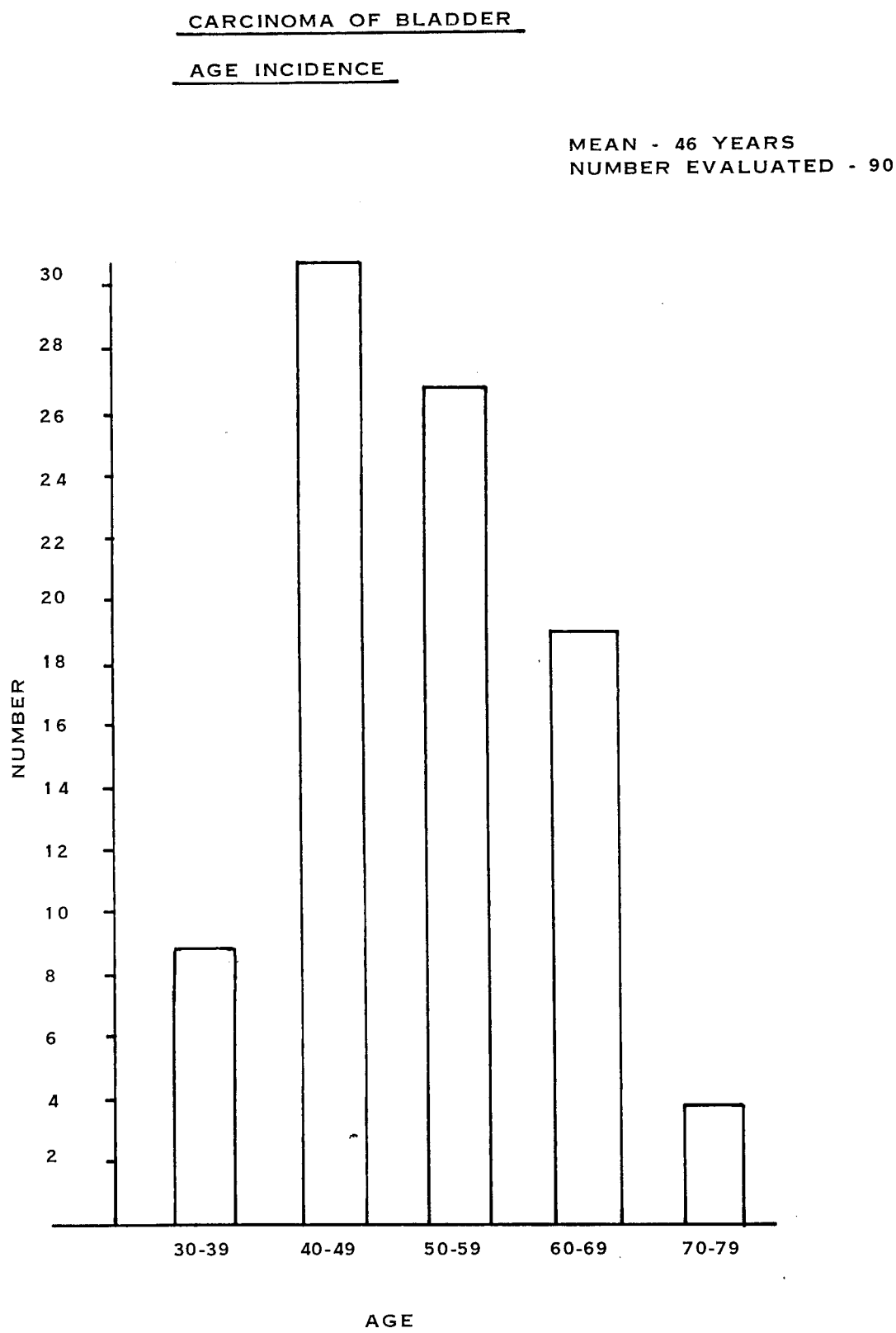
Age and Sex Incidence

The mean age of presentation at Saint Francis Hospital was 45.3 years with the majority of patients falling in the 45 to 55 year age group and with six patients presenting in the third decade of their life (fig. 5) There was a male preponderance with a male to female ratio of 1.4 : 1.0. The mean age in the UTH study was 47.4 with majority of patients in the 40 to 50 year age group with one patient presenting at 29 years.

Occupation

The occupation of some of the patients were not recorded but it was interesting to note that most of the patients were peasant farmers or that most of them had at one stage in life been in a rural setting.

FIGURE 5



Geographical distribution

The locality of patients in the Katete group showed that most had come from around Katete and Petauke districts which is an endemic area for schistosomiasis. The UTH group also showed the majority of patients had stayed for most of their lives in the Eastern province and had later migrated to another area. The equal number of cases of Cancer of the bladder seen at Katete annually in comparison to a much larger centre such as the UTH suggests it may be a commoner cancer in the Eastern province. However most cases seen at the UTH Urology clinic have their origin from the Eastern province. A total of 24-25 Bladder cancer patients are seen at Ndola every year and probably at Kitwe. This may mean that patients from other provinces are not seen at the UTH (Elem - personal communication).

Symptoms and Signs

The main presenting symptoms in order of frequency were:

- | | |
|--------------------------|---------------------------------|
| 1) Haematuria (terminal) | 4) Frequency |
| 2) Dysuria (pain). | 5) Necroturia (pieces in urine) |
| 3) Suprapubic pain | |

Histology of Tumour

Of the 90 Bladder cancer patients seen at Katete and UTH the histology was as follows:

- | | |
|-----------------------------|-------------------------------------|
| 55 Squamous cell carcinoma, | 6 Adenocarcinoma, |
| 3 Leiomyosarcoma, | |
| 11 Transitional cell, | 14 cases no histology was obtained. |

Table No. 4.

Site of TumourSite of Tumour in bladder as seen on cystoscopy

<u>Site</u>	<u>No of cases</u>	<u>%</u>
Right and Left lateral walls	52	(40)
Whole bladder	6	(4)
Bladder base	3	(2)
Bladder Neck	3	
Vault		
Trigone	2	
Not determined	24	

() squamous.

Social Habits

Most of the patients came from a locality where the water supply was from reservoirs which was untreated and probably infested with bilharzial parasite. No significant history of smoking was obtained although a few patients did have records of smoking home grown tobacco.

TREATMENT PROFILE

No proper records were made of the follow up due to poor patient compliance . Only six of the cases had Surgery, namely Total Cystectomy with Ureteric transplants into the Sigmoid Colon. Three of these patients died within two weeks of Surgery. The majority of cases were deemed inoperable and no proper follow up was done except for those who were readmitted in their terminal stages.

RESULTS

PHASE 2 - Case controlled Study

AGE INCIDENCE

Table No. 5	<u>CASES</u>	<u>CONTROLS</u>
Number Evaluated	40	40
Mean age	46.6	46.4
Age range (Years)	36-70	35-65

SEX INCIDENCE

Number Evaluated	40
Male / Female ratio	1.2 : 1.0

OCCUPATION

Most of the patients evaluated belonged to the lower socio-economic strata of the society. The majority were subsistence farmers and the remaining were employed in low paying jobs like Driver, Gardener, watchman etc.

There were 27 subsistence farmers among the 40 cases evaluated and all of them from a locality in the rural area. This is important in the aetiology of Bladder cancer in that most of this rural population is dependent on a water supply from either dams or rivers which are not treated and infested with the Schistosome parasite and is therefore statistically significant.

Table No. 6	<u>FARMERS</u>	<u>NON FARMERS</u>
CASES	27	13
CONTROLS	25	15

$p > 0.05$, Chi Squared corrected

TRIBAL ORIGIN

Twenty four out of the forty cases studied (60 percent) belonged to the tribes from the Eastern Province (Chewa, Ngoni and Nsenga). This correlates with previous reports from Katete that Carcinoma of the Bladder is the commonest tumour seen in the Eastern province (Cairns 1981). Data from the cancer registry also reveals the higher incidence of the tumour in people from this locality. Four patients were from the Central province (Soli), three were from the Southern province (Tonga and Ila) and two Bemba from the Northern province. Seven were not classified.

Table No. 7

	<u>EASTERN TRIBES</u>	<u>NON EASTERN TRIBES</u>
CASES	24	16
controls	20	20

$p > 0.05$, Chi Squared corrected.

HISTORY OF HAEMATURIA

Although some patients gave a definite history of Haematuria some of which was in childhood, the majority could not remember having had haematuria. This could be because most of them had believed haematuria was a normal phenomenon as the majority of the villagers at one stage or another had had haematuria during their lifetime.

CHEMICAL CONTACT

This was not significant in this study because the majority were a rural population and had not worked in industries for them to come in contact with carcinogens (aromatic amines etc)

WATER SOURCE

Most of the villagers came from a locality where the water source was from rivers and dams. Even though some villages had wells this was used for drinking and cooking, and they still would have to go to the river or dam to bathe and wash their clothes. This explains the high rate of infection with the Schistosoma parasite in these people. Most people in the Eastern province are still rural while in provinces like the copperbelt a lot of people are urbanised and their water source are from treated reservoirs provided by the councils.

TOBACCO CONSUMPTION

The patients in this study either smoked home grown tobacco or commercial cigarettes. Two female respondents took snuff on a long term basis. Those that admitted to smoking gave a history of smoking approximately 5 cigarettes per day with only three people admitting to smoking for over ten years and more than five cigarettes a day.

Only twelve of the forty cases admitted to smoking regularly, mostly home made cigarettes while in the controls only ten were regular smokers. No significant difference in tobacco consumption was found in the two groups, patients with Carcinoma of the bladder and the matched controls.

DURATION OF HAEMATURIA

Thirty one out of the forty patients presented with terminal Haematuria with an average duration at time of presentation at 4 months. Most patients did not seek medical advice at the time of initial haematuria and only sought advice at a more advanced stage especially when associated with dysuria which was between 2 to 6 months.

Number evaluated	=	40
Mean duration	=	24 weeks
Range	=	8 - 24 weeks.

OTHER SYMPTOMS

Pain on micturition was the second most commonest symptom followed by suprapubic pain and frequency of urine in almost the same frequency.

SYMPTOMSPERCENTAGE

Haematuria (terminal)	73
Pain on micturition	72
Suprapubic pain	60
Frequency	60
Necroturia / pieces in urine	46

WALLACE'S STAGING

Sixteen of the forty patients were on initial cystoscopy labelled as Stage 4 tumour because of perivesical spread to the pelvic walls. Six of the tumours were deemed operable and only four underwent cystectomy with Ureteric transplant.

KARNOFSKY'S PERFORMANCE STATUS

At the time of presentation the mean Karnofsky's performance status was recorded as 60 percent. This is equivalent to a patient who is " Fit to be at home but requires assistance ".

Number Evaluated	=	40
Mean K-Status	=	60
Range of K-Status	=	30 - 90 percent

TUMOUR SITE

The majority of the tumours were found in the lateral walls, either left, right or both.

Table No. 8 : Site of Tumour in Bladder as seen on Cystoscopy

Site	No. of cases	%
Lateral Walls	12	30
Whole Bladder walls	6	15
Bladder base	6	15
Trigone	2	5
Not assessed	14	35
	40	100 %

The tumour which was detected at the trigone was a transitional cell carcinoma. This confirms the theory that Squamous cell metaplasia is rare at the trigone.

HISTOLOGICAL ASSOCIATION OF SCHISTOSOME OVA IN BLADDER TUMOUR

Only 40% of cases on histology had schistosome ova.

HISTOLOGY

43.

Squamous cell carcinoma of the bladder is by far the commonest histological type of tumour found in this study

Histological type of Bladder Cancer in 40 cases

Table No. 9

Histological Type	No. of cases	%
Squamous cell Carcinoma	22	55
Transitional Cell Carcinoma	5	12.5
Adenocarcinoma	4	10
Poorly differentiated carcinoma	2	5
Not determined	6	15
TOTAL	40	100 %

TREATMENT PROFILE

Eleven patients who on initial cystoscopy were labelled as Wallace's Stage 4 tumour were managed conservatively. Of nine patients who were deemed operable only five underwent total cystectomy with ureteric transplants into the sigmoid colon. Two patients had transurethral resection of the tumour to relieve the obstruction as a palliative procedure.

Table No. 10

<u>TREATMENT</u>	<u>NO.</u>
TOTAL CYSTECTOMY + DIVERSION	5
PALLIATIVE TRANSURETHRAL RESECTION	2
CONSERVATIVE MANAGEMENT	33

RESULTS

PHASE 3 - CYTOLOGY

A Microscopic Analysis of centrifuged sediment of voided urine in a single divided one urine specimen was performed in all the cases in the Phase 2 of the study.

All patients subjected to this study were cystoscopically and histologically proven cases of Carcinoma of the bladder. All the controls were cytologically negative

Table No. 11

HISTOLOGY	NO.	INFLAMMATORY CHANGES	DYSPLASIA	CYTOLOGICAL CONFIRMATION.
-----------	-----	-------------------------	-----------	------------------------------

Katete

Squamous Ca.	9	8	2	0
Transitional	2	2	0	0
Poorly diff.	1	1	0	0

UTH

Squamous Ca.	18	18	12	6
Transitional	3	3	1	1
Adeno. Ca.	3	2	0	0
Poorly diff.	1	1	0	0

TOTAL	38	36	15	7
-------	----	----	----	---

Two cases were omitted because the results were misplaced.

All thirty eight cytological smears showed various degrees of cell morphology with inflammatory changes. All the thirteen cytological smears done at Saint Francis Hospital were poorly stained and no mitotic changes were noted even though they were read by the same cytology technician reading the smears at the UTH.

Of the twenty five cytological smears done at the UTH. most of these showed varying degrees of inflammation and seven specimens revealed malignant changes on microscopy.

These results reveal that in spite of cytological and histological confirmation of bladder tumour only seven of these cases showed cytological confirmation of the tumour. The differences in results between the two hospitals signify the importance in collection, staining techniques and careful evaluation on microscopy of the smears.

Each of the cases in this study was matched with in-patient controls without, urinary problems. All the cytologic smears of the controls were negative.

An attempt to correlate the cytology results with the cystoscopy appearance was made. There was no definite correlation observed.

DISCUSSION

PHASE 1 - Retrospective Analysis

METHODOLOGY

The wide discrepancy in incidences recorded by the two main registries in the country reveals the inaccuracy and incompleteness of returns from the hospitals and health centres in various parts of the country. The returns from all the provinces are prepared by clerks who are not trained in that aspect, and who rely on case notes which are inadequately completed. The figures from the records in the Ministry of Health are much higher than those from the National Cancer Registry. This may be because many of the centres still send their records to the ministry as they are not aware of the Cancer registry. Records at the UTH are however more accurately obtained from the Histopathology records. Retrospective analyses have a drawback in that records have to be traced in retrospect sometimes with great difficulty. These records are often inaccurate and may not contain relevant data which is required. Fortunately case notes at Katete regarding cases of carcinoma of the bladder were better recorded than other general cases due previous studies carried out at the hospital on that subject. Most of the case notes at the UTH were traceable though three could not be traced. Twenty percent of the case notes were inadequate. This therefore cannot be the complete picture of the events at the UTH.

Retrospective studies rely on the accuracy of record keeping. Many of the records were made by different individuals and are therefore biased. Incomplete data retrieval make results less representative of the objectives of the study.

On the other hand, retrospective studies are relatively easy to carry out. Data retrieval is easy and cheap with rapid assembly of the information required to make a variety of hypothesis.

Prospective studies are more time consuming, expensive, yet more elaborate and effective

RESULTS

Carcinoma of the bladder is the third commonest tumour in Zambia. The exact incidence of this tumour is difficult to tell due to poor records and difficulty in diagnosing as only a few hospitals have cystoscopes. This study shows that the prevalence has remained constant.

It appears to be more common in the Eastern part of Zambia and in a population with its origins in the East.

Bladder cancer in Zambia as in other endemic regions of Schistosomiasis is predominantly of the Squamous cell variety. (Chapman 1966, Makhyoun 1971, Lucas 1981, Elem 1983). As in other African countries the tumour was found to be a disease of a younger age group around forty to fifty years with an almost equal sex ratio.

The majority of the patients in the study came from the locality of a village or had spent the greater part of their lives in a village environment. This suggests that this population is at greater risk of being infected with the schistosome parasite from infested waters in dams and rivers. Only 30% of the cases showed evidence of *Schistosoma* infection on histopathology in this part of the study.

History of haematuria in childhood was difficult to assess. Haematuria and dysuria were present in over ninety percent of the cases and were the commonest symptoms as reported in other studies. (Carruthers 1976, Cairns 1978).

The late presentation of these cases to the hospital was responsible for the poor survival rates. Most of the patients were treated conservatively as inoperable Bladder cancer and only very few patients had surgery. Surgery was not considered in many of the cases due to the advanced nature of the disease and also in many instances due to the patients refusal to undergo surgery. Males were more reluctant to undergo surgery as total cystectomy results in impotence. There was a much better compliance to surgery in females and therefore the majority of the total cystectomy patients were female. Palliation was the mainstay of treatment consisting of pain relief with narcotics and sometimes catheterisation to relieve an obstruction.

DISCUSSION

PHASE 2 - Case control Study

METHODOLOGY

Case controlled studies are analytical studies in patients known to have a specific disease with comparison of specific criteria against matched individuals not having the disease. These prospective studies are used to analyse a theory or hypothesis based on previous observations and studies. Its validity is based on assumptions that if some of several criteria are controlled than other non-controlled criteria can be tested against matched individuals not suffering from the disease. Prospective studies can be more accurate and can be carried out by a single examiner who can enquire for relevant information concerning the particular study. Disadvantages include cost and time consumed.

This study comprises of forty cases from Saint Francis hospital in Katete and the UTH in Lusaka. All these patients had matched controls. All these patients were also used for Phase 3 of this study using Urine cytology. These forty cases were seen at the two hospitals in just over a year and was possible because of the common occurrence of the tumour. The relatively simple technique of collecting urine samples and staining centrifuged specimens made it possible for all these patients to be included in the Phase 3 study. Follow up was unfortunately inaccurate.

RESULTS

This study confirms our previous findings that Carcinoma of the Urinary bladder occurs in a relatively younger age group in Schistosoma endemic areas (Boulkany 1972, Ibrahim 1977) in comparison to the West (Liebermann 1968, Payne 1959).

The average age in this study was 46.6 years with an almost equal ratio of Males to females.

Although occupation has not definitely been linked to Bladder cancer in Zambia it seems that it affects a mostly rural population in subsistence farming. This population have greater contact with bilharzia infested waters, with women and children doing their washing and bathing in these waters. There is absolutely no evidence to link other occupations with the causation of bladder cancer in Zambia.

It was also noted that the majority of patients were either from or had previously been in the locality of a village in the Eastern province of Zambia. This supports the finding that Bladder cancer is the commonest type of cancer diagnosed at Katete in the Eastern province of Zambia. (Cairns 1969).

As records from many other centres have not been analysed one cannot make a definite conclusion as to the prevalence of the tumour in other geographical areas.

The prognosis of bladder cancer in this country is generally poor

Low survival rates associated with bladder cancer in Zambia may be due to the following factors :

- 1) Late presentation of the patient for treatment. Belief in witchcraft and traditional healers may be a factor.
- 2) Late detection due to inadequate diagnostic facilities in the rural health centres.
- 3) Lack of awareness by the patient and the medical assistant of the significance of Haematuria etc.
- 4) The tumour in most situations appears to be rapidly progressive.

Many of these patients have had haematuria in childhood which was passed off as normal. As chronic infection develops the haematuria may not be significant or noticeable. Re-occurrence at later stages of life may indicate a more sinister origin of the haematuria. Haematuria and pain on micturition were the commonest symptoms found in these patients.

There was no association between smoking and bladder tumour in this study nor was there any evidence of a chemical link.

The lateral walls of the bladder were most commonly affected with the least findings at the trigone on cystoscopy.

Majority of the patients were at initial cystoscopy labelled as Wallaces Stage 4 tumour which was inoperable. In the few patients who had surgery consisting of a total cystectomy with transplant of ureters into the sigmoid colon most did not survive the first few months. Chemotherapy was not used at all in these patients.

Carcinoma of the urinary bladder is a major problem in Zambia and can be listed in the top five cancers afflicting Zambians. Within the constraints of this study Bladder cancer can be summarised as follows :

1. It is a fairly common tumour in Zambia.
2. In this study it seems to be more common in the Eastern tribes of Zambia.
3. It occurs in a relatively younger age group as compared to bladder cancer in the West.
4. Male to female ratio appears to be almost equal, and has recently been diagnosed more often in females due to increased awareness among gynaecologists (Elem, personal communication). This makes the ratio equal.
5. Occurs more often in a village population whose water source is from untreated reservoirs.
6. Schistosomiasis is associated with bladder tumour in a high proportion of cases. Forty percent of the cases had schistosome ova on histology. No other causative link could be established.
7. Has the same pattern of behaviour and prognosis as is other bilharzia endemic areas in Africa.
8. It is a fairly rapidly growing tumour with the majority being of the Squamous cell variety.
9. It is not amenable to cure most likely due to the advanced nature and late presentation to the hospital.

DISCUSSION

PHASE 3 - CYTOLOGY

Hayward S. Cox in his book entitled, 'Medical Cyto-Technology' (Laboratory Aid services) states, that as long ago as 1902, at the Royal Northern Hospital, London, a correct diagnosis of a Malignancy was made from a specimen of urine (Clayden 1981). The urine of 104 patients with bladder cancer was examined by exfoliative cytology. Three staining methods were used (Giemsa, Papanicolaou and oil red). Giemsa was found to be superior to the other two methods but the highest sensitivity sensitivity (which was statistically significant) was obtained by a combination of the three methods (Theodorou 1984). A case report of Bladder cancer first detected by urinary cytology 20 years before a definite cystoscopic diagnosis could be established was reported by Marshall J-Urol 1977.

A study initiated in September 1976 to detect early bladder cancer by selective cytologic screening in a rural Egyptian population gave a yield of 2.3 per 1000 in a high risk group of the population. This indicated that cytologic screening is feasible and effective in high risk group populations in endemic areas of schistosomiasis (Boulkainy 1982).

Microscopic Analysis of cells is the principal non-invasive method of diagnosing and detecting cancer of the lower urinary tract. The sediments contain several populations of cells of unequal diagnostic value.

This study was undertaken using centrifuged sediment of voided urine with simple commonly used staining techniques with an aim which is three fold:

- 1) Early detection of bladder cancer favorably modifies the prognosis.
- 2) Accuracy and consistency of the technique when used by the average cytology technician.
- 3) Whether cytology can replace cystoscopy as the diagnostic test, especially in rural centres where cystoscopy and more expensive investigation are not available.

The conclusion drawn from this study is that the technique is not suitable for the early diagnosis of bladder cancer in the Zambian patient for the following reasons.

- 1) Cytology demands a very accurate and infallible technique if bladder tumours are not to be missed. This may not be possible in our environment where we do not have the cytocentrifuge and proper collection bottles etc.
- 2) An experienced and highly proficient cytologist can make cytology a very accurate investigation. The UTH does not have a specially trained bladder cytologist.
- 3) Bladder tumours in Zambia are the 'squamous' cell type, which are more rapidly growing with much cell necrosis and distortion making reading of slides difficult with wrong interpretation.
- 4) Most patients present late or are missed on first visit to centres that lack diagnostic facilities.

Even though several of the Bladder cancers were detected by cytology using voided urine obviously the technique was not perfect, because all the specimens were taken from proven Bladder cancer patients. This may be because cytology has a greater role to play in diagnosis of early tumour, and most of these tumours presented late. This implies that cytology cannot replace cystoscopy as a means of making early diagnosis of bladder cancer but may be used as an adjunct which is likely to aid the development of this technique. Even then cystoscopy would be far superior as far as localizing and staging the tumour is concerned. Repetition of cytology and the use of several staining techniques improve statistically the chances of diagnosing the tumour earlier.

Cytology is likely to play its role in the screening of the population at large. Trott and Edwards (1973) suggested improving the technique by irrigating the bladder with saline, and found this technique superior to a similar study of voided urine.

Even though cytology can be used in rural hospitals and in hospitals where facilities do not exist. A negative result however does not rule out the presence of malignancy in the urinary bladder.

CONCLUSIONS.

The conclusions drawn from this study in relation to carcinoma of the urinary bladder in Zambia are :

1. Carcinoma of the urinary bladder is a fairly common tumour in Zambia. The Urinary bladder can be classified as being in the top five sites of occurrence of cancer in Zambia.
2. It has a high incidence in the Eastern Province of Zambia and in a population that had its origins in the Eastern province.
3. The predominant histology is of the Squamous cell variety as in other areas of Africa where Schistosomiasis is endemic.
4. An association with Schistosomiasis of the urinary bladder evident on cystoscopy or on radiology as calcification.
5. No other risk factors could be identified in the patients in this study.
6. The disease is seen in a much younger population than in bladder cancer in Europe and elsewhere.
7. The tumour which is of the Squamous cell variety seems to be a rapidly growing tumour with a poor prognosis.
8. The most common site of involvement is the lateral walls of the urinary bladder.
9. The disease has similar clinical features and progression as in other Schistosoma endemic African countries.

10. Late presentation is a common feature in the various regions with a poor prognosis.
11. Conservative non-surgical management forms the mainstay of treatment in advanced bladder cancer .
12. Cytology of centrifuged sediment of voided urine is not practical for routine diagnostic use though it may be used as an adjunct to cystoscopy.
13. Cystoscopy is the most accurate method of diagnosing bladder cancer.
14. Cytology may play a big role in bladder cancer if the technique is standardized.
15. Cytology is useful in screening large populations to detect early tumour but in the clinical situation its value is limited.

APPENDIX 1

DATA SHEET - PHASE 1,2, and 3

CARCINOMA OF THE BLADDER - DATA FORM

NAME: AGE: SEX:

WEIGHT: HEIGHT: NO.

VILLAGE: CHIEF: DISTRICT:

OCCUPATION:

INITIAL SYMPTOMS:

- 1) Haematuria..... duration/type/extent
- 2) Suprapubic pain.....OTHER SYMPTOMS.....
- 3) Pain on micturition.....
- 4) Pieces in the urine.....
- 5) Frequency/nocturia.....

HISTORY.

EXAMINATION.

Haematuria in childhood.....Nutrition.....

Chemical contact.....Karnofsky performance.

water source.....Abdomen.....

Others.....Wallace's stage.....

INVESTIGATIONS

Blood Urea

Cystoscopy

Cytology

Others

PROGRESS.....

.....

.....

APPENDIX 2

CARCINOMA OF THE BLADDER

PHASE 3 - URINARY CYTOLOGY

NAME :

AGE:

SEX:

WEIGHT:

HEIGHT:

VILLAGE:

DISTRICT:

FILE No:

TYPE OF SPECIMEN: mid morning divided whole urine

HISTOLOGICAL DIAGNOSIS:

CYSTOSCOPIC FINDINGS:

.....

CYTOLOGY:

.....

.....

.....

.....

ACKNOWLEDGEMENTS

I would like to extend my thanks to my Moderators ,

Baha Elem, consultant Urologist at the University Teaching Hospital for his able guidance and criticisms.

James Cairns, consultant surgeon and Superintendent at Saint Francis Hospital in Katete for his assistance in obtaining information in the Katete part of the study.

Professor Anne Bayley for her encouragement.

I am indebted to Carl Regisford, consultant surgeon at the UTH for his invaluable advice and persistant encouragement.

My special thanks go to David Watters, consultant surgeon at the UTH. for pushing me at the right time.

I am grateful to Afzal Ansari of the medical illustration unit for his advice on layout of the dissertation and his help in making the photographs.

I am also indebted to Mr Locha, cytology technician without whose skills in preparing and reading of the slides would not have been possible.

Finally I extend my thanks to my wife Fazila whose patience was a major force and my children Khadija and Akil who made it worthwhile.

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FUTURE RESEARCH.

Cytology may play a major role in the future if :

1. The technique is standardized and improved.
2. Cytology may be more effective if applied to screening of larger population groups.
3. Repeated cytology may improve results.
4. Use of cytology after bladder irrigation with different staining methods may increase significance.
5. Use of a cytocentrifuge may be an important factor.

The role of *Schistosoma Haematobium* in causation of bladder cancer must be further looked into.