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CARCINOMA OF THE OESOPHAGUS
IN ZAMBIA

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FOREWORD

This dissertation has been submitted in partial fulfillment of the requirements for the award of the Master of Medicine (Surgery) degree of the University of Zambia.

INTRODUCTION

Galen in the second century suggested the possibility of a tumour obstructing the passage of food down the gullet. The disease has been known in the Chinese for 2000 years.

EPIDEMIOLOGY

Desophageal cancer is characterised by a wide variation in geographical distribution both world wide and regionally (1). Marked variations in incidence rates also occur in neighbouring regions within the same country (2). Very high incidence rates have been reported from Northern China (2), the Caspian Littoral of Iran (3), and the Transkei (4). In these areas incidence rates exceed 100 per 100,000 population per annum in contrast to West Africa where it is an uncommon tumour (5). In most of Africa the incidence of this disease has not been studied (1).

The consistent feature of this disease is its propensity for the lower socioeconomic groups. This is particularly evident among the Negro population of South Carolina (6) where it is the most common malignant disease in the male Negro. Whether this is a reflection merely of the low socioeconomic in the Negro population or a reflection of the increasing incidence among urban black populations such as those in South Africa whose dietary and social habits are comparable to those of the western world (31).

Although the disease was not common in the Bantu before World War II, it is now the commonest cancer in Bantu males of Natal (7). It is therefore an emergent disease in certain areas of Africa (Table 1).

The incidence of oesophageal cancer in Zambia is not known.

TABLE 1

INCIDENCE OF CARCINOMA OF OESOPHAGUS

<u>COUNTRY</u>	<u>M:F RATIO</u>	<u>PER 100000</u>	
TANZANIA	5.0	0.26	(27)
KENYA	8.0	0.67	(28)
UGANDA	3.0		(29)
ZIMBABWE	2.0	55.85	(1)
MOZAMBIQUE	26.0		(30)
TRANSKEI	2.3	83.0	(31)
NATAL	5.0	26.1	(1)
NIGERIA	1.6	0.65	(1)
JAMAICA	2.5	8.1	(1)
ENGLAND	1.7	1.8	(7)
FRANCE	24.5	29.4	(1)
U.S.A. Blacks	4.3	9.1	(1)
IRAN (Gonbad)	0.78	122.0	(3)
CHINA	1.6	139.8	(2)

Carcinoma of the Oesophagus is classically a disease of the elderly male with the average age approximately 60 years (8). However, in areas of high incidence, it is not uncommon to see patients below the age of 30 years (9). Another peculiar characteristic of the disease is its variable male to female ratio. Although the tumour is commoner in men with an average reported male to female ratio of 3:1, in Iran, Finland and Alaska females predominate (3)(10). A lower male to female ratio in areas with high incidence rates has been reported (2).

AETIOLOGY

A number of aetiological theories have been proposed. Despite reports of high incidence Chinese families (11), there is no evidence of a genetic basis for the disease. However, tylosis which is a genetic disease, is frequently associated with oesophageal cancer (17).

The association of chronic oesophagitis, mucosal atrophy and dysplasia has been proposed by Munoz et al (32) to be precancerous in that they represent the natural progression to oesophageal cancer. Animal studies have shown that dysplasia is a precancerous condition (21)(32)(57).

Corrosive damage to the oesophagus, Plummer-Vinson Syndrome and achalasia of the cardia are considered to be premalignant .

Although excessive alcohol and tobacco consumption appear to be important predisposing factors in Africa, France and America, they certainly are not implicated in the Near and Far East (1). In these areas hot food and drinks appear to be important.

Dietary deficiencies have been variously implicated in relation to high incidences amongst the low socioeconomic groups. Reports from the Carribean (1), the Transkei (12) and Iran (3) have shown an association between dietary deficiencies and an increased risk of oesophageal cancer. Diets deficient in protein, vitamin A, vitamin C, riboflavin, nicotinic acid, and zinc have been implicated (1)(12)(33)(36). Increased consumption of zinc and iron through indigenous preparations of alcoholic spirits have likewise been implicated (34)(35).

The nitrosamine content of food samples taken in high incidence areas of China was found to be significantly higher than those found in low incidence areas. This has correlated with the nitrosamine content of gastric juice from the same area (2). Nitrosamines have been found in animal studies to induce dysplasia and oesophageal cancer (14). Nitrosamines have also been found in the environment of high risk populations of China but its precise relationship with oesophageal cancer is not known and is still under investigation (14).

Fungal contamination of maize and cereals have been recognised in populations with a high risk for oesophageal cancer (2)(13) but these appear to be promoters rather than initiators.

Recently, contamination of the diet with silica fragments have been discovered in all three areas of high incidence (Iran, Transkei and China) (15), but its role needs further study.

Herpesvirus has been known to be related to various cancers in man and has been identified in oesophageal cancer tissue in one case (16).

In summary, the aetiology of oesophageal carcinoma is unknown although many associated factors have been recognised. These factors are complex and multifactorial. Perhaps many more factors are yet to be recognised.

PATHOLOGY

The most frequent site of involvement is the middle third of the oesophagus (50%), followed by the lower third (30%) and the upper third (20%). Macroscopically, the tumours are either fungating, ulcerative, or infiltrative.

Squamous carcinomas constitute 95 percent of all primary malignancies of the oesophagus, adenocarcinomas a further 3 percent and miscellaneous malignancies 2 percent (17). The degree of cellular differentiation has no bearing on the rate of spread and prognosis (18).

Spread of the tumour is predominantly by the submucosal lymphatics and this may extend 4 to 8 cms beyond the gross margin of the tumour (19). The absence of a serosal covering, extensive submucosal lymphatics and close proximity of other structures contribute to early spread of the tumour to adjacent structures.

Oesophageal tumours involve adjacent structures in relation to the level of the tumour. Upper and middle third tumours may involve trachea, bronchi, recurrent laryngeal nerve or aorta. Lower third tumours may involve pericardium, diaphragm or cardia and fundus of stomach. In one study, 18 percent of 184 patients had a tracheo respiratory fistula (37).

Growths of the upper third of the oesophagus drain to the perihilar, paratracheal and external jugular lymph nodes. The mid thoracic oesophagus is drained by paraoesophageal and tracheal bifurcation nodes. The lower third and gastro-oesophageal junction is drained by the paracardiac, left gastric and celiac nodes (19).

Cancer cells may spread proximally or distally via the submucosal lymphatics producing satellite lesions and, rarely, double carcinomas separated by normal epithelium. In one study of 417 patients (17), only 20 percent had disease localised to the oesophagus and 60 percent had lymph node metastasis. Distant metastasis to liver, tracheo-bronchial tree, lungs, pleura and bones occur.

DIAGNOSIS

The only hope of improving the prognosis of oesophageal carcinoma lies in early diagnosis. Dysphagia, recent weight loss, voice changes, regurgitation and vomiting should arouse suspicion of the cancer and further tests be ordered to confirm the diagnosis. Unfortunately, by the time the patient seeks help his tumour is likely to be inoperable.

A barium swallow has a reported accuracy of 92 percent. Confirmation is usually obtained by oesophagoscopy, resulting in 96 percent yield (19). Fibre-optic endoscopy has enabled early diagnosis in high risk populations. Computed Tomography may improve the pre-operative staging of the cancer thereby determining the optimum treatment option (20) and reducing unnecessary exploration. However, CT scanning was not found to be helpful in staging carcinoma of the oesophagus in an African context (38) possibly because of reduced fat in the tissues of African patients.

Bronchoscopy should be done particularly for tumours in the upper and middle third of the oesophagus to rule out involvement of the respiratory tract (39), which occurs in more than 30 percent of the patients in Durban (53).

Cytological techniques are invaluable both in the confirmation of diagnosis and for mass screening in high incidence areas. Cytological smears can be obtained either directly through an endoscope or blindly by the passage of a tube into the oesophagus. The Chinese have used inflatable balloons with a mesh net to collect the smears in mass screening exercises. They report 90 percent accuracy rates for detecting premalignant and early lesions (21). More recently, South African workers have reported equally good results using a suction abrasive technique for detecting early oesophageal cancer in high risk populations (40).

TREATMENT

The treatment options are surgery (resection, bypass or intubation), radiotherapy and chemotherapy; used either singly or in combination. For cancers of the lower third of the oesophagus, if cure is the objective, resection is advocated (17). No single treatment modality offers significantly better survival rates (22). The aim of treatment is to cure occasionally and to provide a swallowing mechanism often.

SURGERY

The basis of curative surgery is resection of the tumour and offers the best palliation. Until 40 years ago, the results of surgery were disastrous. But today, in China, resectability rates have increased to almost 90 percent with operative mortalities of less than 5 percent (41). These impressive figures are a reflection of vigilant efforts towards early diagnosis and treatment. In most other series, 50 percent of patients are considered operable but only about 39 percent are actually resectable (23). In Africa, patients present late and the resectability rates are correspondingly poor (42).

The criteria for resectability (for cure) are: (17)

- 1.No clinically detectable lymphatic or distant spread of the tumour
- 2.No respiratory involvement
- 3.Tumour less than 6 cms on Barium Swallow
- 4.No deviation of the oesophageal axis on Barium Swallow examination

The criteria for fitness for resection are:

- 1.Serum albumin greater than 25g/l
- 2.Total lymphocyte count greater than 1000
- 3.FEV1 greater than 1 litre

The world-wide average 5 year survival after surgical resection is only 4 percent with an operative mortality of 29 percent (23). However, a Chinese series of 850 patients reported a significantly higher 5 year survival rates of 22 percent with an operative mortality of 10 percent (54). This may in fact represent the fruits of detecting the cancer in the early stages.

Palliative surgery is indicated for unresectable tumours, oesophago-airway fistula and failed intubation (24). This takes the form of a bypass utilising the stomach, colon or jejunum. The use of the stomach is preferred due to the low mortality rates (10 - 20 percent) associated with its use (43)(55). The average survival after gastric bypass is 4 months. For lower third tumours the bypass is retrosternal upto the neck. For upper and middle third tumours the presternal route is preferred by Mannell (43) although Conlan et al (56) prefer the retrosternal route for all bypass procedures of the thoracic oesophagus. The primary tumour is not resected and is left in situ. Most of the patients undergoing bypass surgery are followed up with radiation therapy to control the growth of the tumour. The average survival after gastric bypass and radiotherapy is 7 months (43).

RADIOTHERAPY

This is the acceptable form of therapy for high cervical tumours and for patients who are unfit for surgery. It is also suitable for upper and middle third tumours.

The criteria for curative radiotherapy are:(44)

- 1.Squamous or undifferentiated carcinoma
- 2.No distant metastasis
- 3.Tumour less than 5 - 7 cm
- 4.No invasion of airways, thyroid, stomach or vertebrae
- 5.Good general health

The maximum dose for cure is 6000 rads given over a period of 4 - 6 weeks. The average 5 year survival is only slightly better at 6 percent (25), but treatment mortality is less than 1 percent (44). Unfortunately, local recurrence of the tumour occurs in 50 - 80 percent of patients treated by radical radiotherapy (45). In view of these results curative radiotherapy is used only in selected patients.

Palliative radiotherapy is advocated for patients not suitable for curative radiotherapy. The recommended dose is 4500 rads over 4 weeks (44)(45). The palliation for pain is better than the palliation for dysphagia. It is useful for recurrent disease after resection and after bypass surgery.

CHEMOTHERAPY

The role of Chemotherapy in the treatment of oesophageal cancer is not defined. Chemotherapy has often been used in combination with either surgery or radiotherapy where enhancement is the objective.

The cytotoxic agents that have been found to be useful in the treatment of squamous carcinoma of the oesophagus are bleomycin, adriamycin, 5-fluouracil, methotrexate, mitomycin-c, cisplatin and vindesine. Conflicting results of single agent chemotherapy abound (45) but good response rates, though not cures, have been reported with most combination chemotherapeutic regimes (46)(47).

Recently, very promising results have been reported using chemotherapy with preoperative radiotherapy (45). Initial results indicate an average survival of 24 months. Follow up data is awaited.

PALLIATIVE PROCEDURES

The most commonly used method of palliation in unresectable tumours is intraluminal intubation.

These may be either :

1. Pulsion Tubes - not requiring a gastrotomy
 - may be inserted with a
fibre-optic or rigid endoscope
 - suitable for upper thoracic
lesions
2. Traction Tubes - require a gastrotomy
 - suitable for lower third
lesions

The techniques carry a hospital mortality of 27 percent and median survival time of 11 weeks (48).

Tumours in the cervical portion of the oesophagus are not amenable to palliation by intubation. These tumours are sometimes treated by dilatation but results are unsatisfactory.

Gastrostomy as a means of palliation for advanced disease has also been found to be unsatisfactory.

A new palliative treatment using endoscopic laser therapy shows promise but needs further evaluation (26).

Despite the technological advances in medical care, the survival rate of oesophageal cancer still remains dismally poor. Oesophageal cancer remains a depressing disease both to the patient and the clinician.

The only hope of improving this gloomy outlook is to find what causes the cancer and minimise its exposure in risk groups. Early diagnosis of the condition has already shown its worth and screening methods in high risk groups should be improved and expanded.

OBJECTIVES

1. To record the incidence of Carcinoma of the Oesophagus in Zambia.
2. To study the incidence of accepted risk factors in Zambia by means of a case controlled study.
3. To study the clinical presentation, pathology and treatment of carcinoma of the oesophagus in Zambia.
4. To assess the suitability of the suction abrasive cytological technique for the diagnosis of Carcinoma of the Oesophagus.

PLAN OF STUDY

The study was divided into 3 Phases:

PHASE 1

1. Figures were obtained from the Ministry of Health, Statistical Unit to ascertain the reported annual incidence of carcinoma of the oesophagus in Zambia.
2. A retrospective analysis of case notes at the University Teaching Hospital (UTH) for the period 01 January 1981 to 31 December 1982.

PHASE 2

A case controlled study of patients at:

- a) St. Francis Hospital in Katete for the period 01 January to 30 June 1984 ; and
- b) University Teaching Hospital (UTH) for the period 01 January to 30 June 1985.

PHASE 3

A single blind analysis on the suitability of the suction abrasive cytological technique in the diagnosis of Carcinoma of the Oesophagus. This study involved all patients with dysphagia presenting at Katete from 01 January to 30 June 1984 and at the UTH from 01 January to 30 June 1985.

All three phases of the study were considered and approved by the Medical Research and Ethical Committee of the University of Zambia.

METHODOLOGY

PHASE 1 - Retrospective Analysis

The aim of this phase of the study was to record the incidence of Carcinoma of the Oesophagus and to note the following information:

- Age of the patient
- Sex of the patient
- Occupation of the patient
- Tribe of the patient
- History of alcohol intake
- History of tobacco intake
- Duration of dysphagia
- Anatomical site of tumour
- Histological diagnosis
- Type of treatment
- Outcome of treatment

All the available case notes for the period 01 January 1981 to 31 December 1982 were perused and data extracted and recorded on prepared data sheets. (Appendix 1)

The data obtained was then analysed to obtain the relevant information. The results have been reported as percentages of the total. No specific statistical correlation was sought.

METHODOLOGY

PHASE 2 - Case Control Study

1. DEFINITION OF CASE

Any patient with a histologically confirmed SQUAMOUS carcinoma of the oesophagus.

2. QUALIFICATION

Any case presenting in the study periods 01 January 1984 to 30 June 1984 at St Francis Hospital, Katete or 01 January 1985 to 30 June 1985 at UTH Lusaka.

3. ASSESSMENT

All cases were interviewed, examined and followed up by the investigator personally to ensure consistency in recording data. All records were entered on prepared data sheets. (Appendix 2)

The following details were sought:

PERSONAL DETAILS - Age, sex, occupation, tribe,

DIET - Inquiry was made into habitual diet and whether or not there was a period of famine in the history

SMOKING - The type of tobacco was categorised into whether the patient smoked commercial cigarettes or home made cigarettes. Home made cigarettes are made by rolling home grown and home cured tobacco leaves in a piece of scrap paper, usually a piece of old newspaper. The amount consumed was

calculated from the amount consumed per week and the frequency. A cut off point of 20 sticks per week for 10 years was chosen as this represented the minimum among the smokers.

ALCOHOL - The type of alcohol consumed was categorised into Kachasu, home brewed beer and commercial beer. Kachasu is a beer brewed from maize husks and sugar and fermented together. This is drunk at communal gatherings where a container containing the spirit is passed around for each to drink from.

Local Brew is a cereal based brew and goes by the names of Chibuku, Mowa and Seven Days; the latter signifying the number of days required for fermentation.

The amount consumed was calculated from the amount consumed per week and the duration. A cut off point of 50 litres per year for 10 years represents the minimum consumed by the drinkers.

DYSPHAGIA - The duration of the dysphagia was recorded in weeks. This is arbitrary as most of the patients do not have a sense of time.

OTHER SYMPTOMS - Hoarseness, cough, weight loss

KARNOFSKY'S PERFORMANCE STATUS (58) -

- 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 some assistance but fit to be at home
- 50% - Requires more assistance but can get out of bed to talk with friends and sit in the sun
- 40% - Requiring hospitalisation and active treatment. Chooses to stay in bed. Can walk to toilet
- 30% - More incapacitated - Can stand out of bed very briefly.
- 20% - Bedridden
- 10% - Moribund

HISTOLOGY - This was categorised according to whether the tumour was squamous, adenocarcinoma, anaplastic or other.

SITE - Upper Third 15 to 25 cms from incisors
 Middle Third 25 to 33 cms
 Lower Third 33 to 40 cms

4.CONTROL MATCHING

Each case was matched for age and sex only among hospital in-patients. The matched controls were patients admitted in the surgical wards for diseases other than cancer.

5.STATISTICAL ANALYSIS

The results obtained in the case controlled study were analysed and subjected to Chi Squared Analysis or Fisher's Exact Test. The Chi Squared Test was utilised for grouped data except in those instances where the expected values were smaller than 5 in the 2 x 2 tables. In these instances, Fisher's Exact Test was utilised (59).

METHODOLOGY

PHASE 3 - CYTOLOGY

Fourteen consecutive patients were available for study. Three of these were studied in Katete and eight at UTH. Three other eligible patients were excluded because the patients had already been subjected to oesophagoscopy and biopsy and it was felt that this procedure would spill malignant cells into the oesophageal lumen.

CONSENT

Informed verbal consent was obtained from all patients studied.

TECHNIQUE

The technique described by Tim et al (40) was employed. A standard 14F nasogastric tube was employed to obtain cells from the oesophagus. The same tube was employed for all the patients in the study with prior cleansing and renewing the abrasive swabs. The abrasive surface was provided by a small guaze-swab wrapped twice around the circumference of the tube to cover the three side holes and held in place by an adhesive tape.

After an overnight fast, cytology was performed before a scheduled oesophagoscopy. The oropharynx was sprayed with xylocaine 2% spray and the tube passed with the patient in the left lateral position. The tube was introduced to the 40cm mark or up to the obstructive lesion. Constant suction was maintained with a 20ml syringe as the same was rotated and withdrawn. The abrasive material was smeared over a glass slide and fixed by immersing the slide in 95 percent Ethanol. The material was stained by the Papanicolaou method (60).

SCRUTINY

All cytological smears were examined by the investigator and a particular pathologist (Dr N.Nkanza) in one batch. The pathologist was not aware of the diagnosis. The cytological smears were then compared with slides of the histological specimen taken at oesophagoscopy.

REPORTING

Each cytological smear was assessed for the following:

- Inflammatory changes
- Dysplasia
- Cytological Evidence of tumour cells

EXCLUSIONS

Three patients were excluded from the study because the patients had already been subjected to oesophagoscopy and biopsy.

RESULTS

PHASE 1 - Retrospective Analysis

Incidence in Zambia

The average annual incidence of oesophageal cancer in Zambia is 105, representing a crude incidence of 1.84 per 100000 population. Of the total cancers reported, oesophageal cancer accounts for 3.3 percent.

Incidence at UTH

The average annual incidence of carcinoma of oesophagus at UTH is 38 patients (Table 2).

TABLE 2 CARCINOMA OF OESOPHAGUS - UTH

<u>INCIDENCE 1980 - 1984</u>	
<u>YEAR</u>	<u>NOS.</u>
1980	38
1981	30
1982	34
1983	48
1984	42
MEAN	38.4

The total hospital admissions for 1984 were 91,802. Of these, 16,644 (18%) were surgical admissions.

During the study period January 1981 to December 1982 there were 64 new cases recorded but only 29 case notes were available for retrospective analysis - the rest of the case notes could not be traced.

Age and Sex Incidence

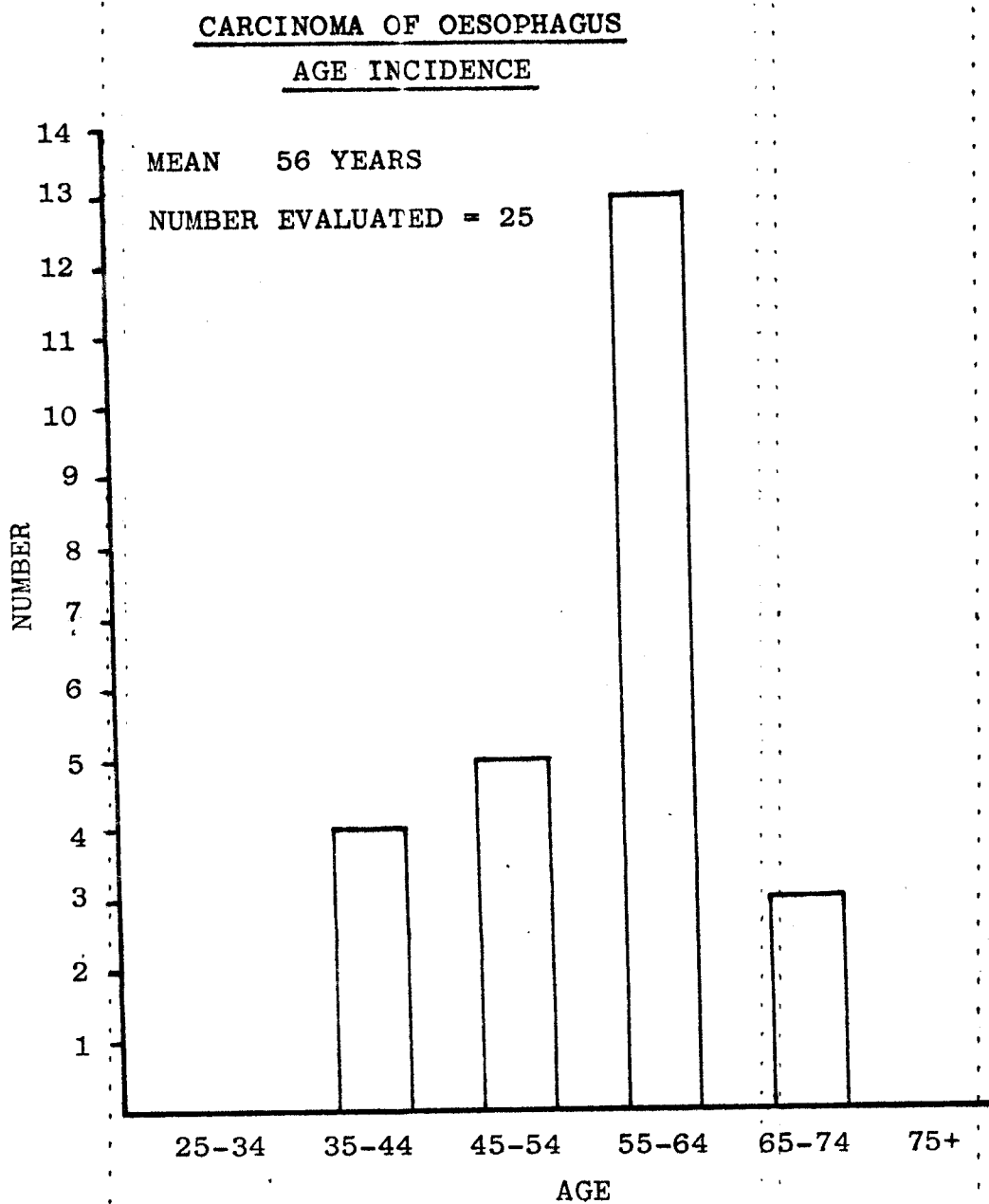
The mean age at presentation at the UTH was 56 years with the majority of patients falling in the 55 to 64 age group (fig 1). There is a male predominance with a sex ratio of 3.14:1 .

Duration of Dysphagia

Dysphagia was the main presenting symptom with the average length of history 17.5 weeks and range of 2 to 104 weeks. The other presenting symptoms were not recorded in the notes.

Histology of Tumour

Of the 17 histologies reviewed, 16 were squamous carcinomas and one adenocarcinoma.

FIGURE 1

Site of Tumour

Fifteen tumours (55.5 percent) were in the middle third of the oesophagus, 10 tumours (37.1 percent) were in the lower third and the remaining 2 tumours (7.4 percent) were located in the upper third of the oesophagus. The single adenocarcinoma was in the lower third.

Social Habits

Sixteen patients (84 percent) admitted to regular alcohol consumption and 14 patients (74 percent) admitted to regular tobacco use. Fourteen patients (74 percent) also admitted to both regular smoking and drinking.

Treatment Profile

Ten out of the 29 patients reviewed had oesophageal Celestin intubation - of these 3 died within a week in hospital. Another 2 patients had simple oesophageal dilatation - there was no mortality amongst these. No details of their subsequent ability to swallow was recorded in the case notes. Only 3 patients underwent resection of the tumour and one of these died. Two others had feeding jejunostomies. A total of 12 patients had no surgical treatment, either because they refused treatment or because they were unfit for general anaesthesia.

RESULTS

PHASE 2 - Case Control Study

AGE INCIDENCE

	<u>CASES</u>	<u>CONTROLS</u>
No Evaluated	14	14
Mean Age (Years)	59.2	59.1
Age Range (Years)	51-70	48-68

SEX INCIDENCE

No Evaluated	14
Male / Female Ratio	3.66

OCCUPATION

All the occupations stated belonged to the low socio-economic strata of society (table). Unfortunately, no specified working socio-economic scales are identified for the Zambian society and therefore these cannot be classified as such.

<u>TABLE 3</u>	<u>OCCUPATION</u>	<u>CASES</u>	<u>CONTROLS</u>
	FARMERS	10	5
	DRIVER	2	1
	GARDENER	1	0
	HOUSEBOY	1	3
	WATCHMAN	0	2
	MESSENGER	0	2
	BREWER	0	1

There were 10 subsistence farmers among the 14 cases studied. However, the role this occupation plays in the aetiology of Carcinoma of the Oesophagus is not statistically significant.

	<u>NON FARMERS</u>	<u>FARMERS</u>
CASES	4	10
CONTROLS	9	5

$p > 0.05$, Chi Squared corrected

TRIBAL ORIGIN

Eight out of the 14 cases studied (57 percent) belonged to tribes from the Eastern Province (Chewa, Ngoni and Nsenga). Three were Tonga / Ila (Southern Province), 2 were Soli (Central Province) and one was Bemba (Northern Province).

Analysis of this data also contradicted the belief that this tumour was found predominantly in people from the Eastern Province.

	<u>NON EASTERN TRIBES</u>	<u>EASTERN TRIBES</u>
CASES	6	8
CONTROLS	7	7

$p > 0.05$, Chi Squared corrected

DIETARY HISTORY

All the Cases and Controls studied reported eating a diet of Nshima and a 'relish'. The relish was variable being a vegetable or meat based stew.

Nshima is a thick porridge made of maize meal and water with added salt to taste. The vegetables were mainly rape, pumpkin, pumpkin leaves, beans and cabbage. Meat was chicken, goat, beef or fish.

Of the 14 Cases studied, five reported eating a predominantly non-meat diet and the other nine reported eating a mixed meat and vegetable diet. There was no significant difference in the diet of patients with Carcinoma of the Desophagus and matched controls.

	<u>MEAT & VEG.</u>	<u>VEGETARIAN</u>
CASES	9	5
CONTROLS	8	6

$p > 0.05$, Chi Squared corrected

HISTORY OF FAMINE

Only two of the Cases studied admitted to a period of starvation and famine in their lives. One of the Control patients also admitted to period of starvation. All the three reported eating wild berries and roots during the period of famine.

ALCOHOL CONSUMPTION

The common varieties of alcohol consumed by the patients in the study are Kachasu and local brewed beer.

Kachasu

In the analysis of the data obtained, it was observed that those Cases who admitted to drinking Kachasu did so in excess of ten years and each consumed more than fifty litres per year. There was no significant difference in the Kachasu consumption of patients with Carcinoma of the Oesophagus and matched controls.

	<u>NO KACHASU</u>	<u>KACHASU</u>
CASES	12	2
CONTROLS	11	3

$p > 0.05$, Fisher's Exact Test

Local Brew

Eleven of the fourteen Cases studied admitted consuming this local brew in quantities exceeding fifty litres per year and for more than 10 years. Here too, none of the respondents consumed less than these arbitrary amounts specified. There was no significant difference in local brew consumption of patients of Carcinoma of the Oesophagus and matched controls.

	<u>NO LOCAL BREW</u>	<u>LOCAL BREW</u>
CASES	3	11
CONTROLS	4	10

$p > 0.05$, Fisher's Exact Test

Alcohol (general)

In this category are included all respondents who admitted to consuming any alcoholic beverage in excess of fifty litres per year for more than ten years.

As in the previous two categories, there was no significant difference in the consumption of alcohol of patients of Carcinoma of the Oesophagus and matched controls.

TOBACCO CONSUMPTION

The respondents in this study consumed either commercial cigarettes or home made cigarettes. None of the respondents took snuff. Those that admitted to smoking both types gave a history of smoking for more than ten years, each smoking an average of twenty sticks per week.

Eight of the 14 Cases admitted smoking in excess of this amount. Only 5 of the Controls were regular smokers. There was no significant difference in tobacco consumption of patients of Carcinoma of the Desophagus and matched controls.

	<u>NON SMOKERS</u>	<u>SMOKERS</u>
CASES	6	8
CONTROLS	9	5

$p > 0.05$, Chi Squared corrected

HOUSING TYPE

Nine of the Cases lived in substandard housing made of mud with a thatched roof (hut). The remaining 5 Cases lived in a cement based house with sheet iron roofing. Housing standards were similar in both groups.

	NON HUT	HUT
CASES	5	9
CONTROLS	9	5

$p > 0.05$, Chi Squared corrected

HOUSING SIZE

As most Cases reported living in substandard housing the number of rooms per household were noted. Eight of Cases lived in one roomed dwellings together with their families. There was no significant difference between the two groups.

	>1 ROOM	ONLY 1 ROOM
CASES	6	8
CONTROLS	11	3

$p > 0.05$, Chi Squared corrected

DURATION OF DYSPHAGIA

The average duration of dysphagia at presentation to hospital was 17.5 weeks.

No EVALUATED = 14

MEAN DURATION = 17.5 weeks

RANGE = 3 - 50 weeks

TRADITIONAL TREATMENT

At the time of presentation, seven patients (50 percent) had consulted the traditional healer before consulting a qualified doctor for the dysphagia.

No EVALUATED = 14

No WHO SOUGHT TRADITIONAL TREATMENT = 7

BELIEF IN WITCHCRAFT

All the patients did not have an insight into their illness and 4 patients (29 percent) actually attributed the illness to witchcraft.

KARNOFSKY'S PERFORMANCE STATUS

At the time of presentation the mean Karnofsky's performance status was recorded as 71 percent. This is equivalent to "able to care for oneself but unable to work..".

No EVALUATED	=	14
MEAN K-STATUS	=	71 percent
RANGE OF K-STATUS	=	30 - 100 percent

LYMPHADENOPATHY

Of the 14 Cases studied, only one had cervical lymphadenopathy. Unfortunately lymph node biopsy was not performed in this case.

HEPATOMEGALY

Of the 14 Cases studied, only one had a palpable liver which was 2 cms below the costal margin. The result of the liver function tests in this patient was normal. A liver scan was not performed in this case.

VOICE CHANGES

Of the 14 Cases studied, only one complained of a change in voice but further investigations were not performed to define the abnormality.

TUMOUR SITE

The majority of tumours were in the middle third of the oesophagus, followed by the lower third (table 4).

TABLE 4

<u>SITE</u>	<u>NO</u>	<u>PERCENT</u>
UPPER THIRD	3	21
MIDDLE THIRD	6	43
LOWER THIRD	5	35
<hr/>		
TOTAL	14	

TREATMENT PROFILE

The majority of patients had palliative oesophageal intubation (table 5). Only two patients underwent resection.

TABLE 5

<u>TREATMENT</u>	<u>NO</u>	<u>HOSP MORTALITY</u>
INTUBATION	10	0
Celestin 6		
Livingston 4		
RESECTION	2	0
DILATATION	1	1
NIL	1	1
<hr/>		
TOTAL	14	2 (14%)

All 10 patients who had intubation and both patients who underwent resection could swallow a light diet (dilute nshima) well and were eventually discharged from hospital. Length of hospital stay and survival figures of these patients are not available.

RESULTS

PHASE 3 - CYTOLOGY

Eleven patients were subjected to the Suction Abrasive Cytological technique (table 6).

TABLE 6

HISTOLOGICAL DIAGNOSIS	NO	INFLAM CHANGES	DYSPLASIA	CYTOLOGICAL CONFIRMATION
SQUAMOUS CA	8	5	Ø	Ø
ADENOCAR	2	1	Ø	Ø
NO CAUSE	1	Ø	Ø	Ø
TOTAL	11	6	Ø	Ø

All eleven cytological smears showed normal exfoliated squamous cells of varying degrees of maturity. The nuclei of the squamous cells were also normal. No mitotic changes were observed.

All eleven patients tolerated the tube well and there were no complications. In spite of both histological and radiological evidence of tumour in eight patients the cytology specimens failed to obtain malignant cells.

DISCUSSION

PHASE 1 - Retrospective Analysis

METHODOLOGY

The incidence figures for Zambia obtained from the Ministry of Health are not true figures because they rely on reports from various hospitals. These reports are made by clerks who rely on case notes which are usually far from adequate. However, these figures are probably more reliable than the figures made available by the National Cancer Registry whose figures of incidence are much lower.

As with all retrospective analyses, this study showed that accuracy of hospital records is far from what is expected of them. The original intention to analyse retrospective cases from Katete was discarded because case notes were inadequate with respect to the information that was required. Hence, in this phase of the study only case notes from U.T.H. were analysed. Here, too, not all the desired information was forthcoming and many of the case notes could not be located. In essence, therefore, this is not a complete picture of the status of events at the U.T.H.

This study like most retrospective studies puts a lot of emphasis on accurate record keeping. Records made by different individuals are subject to bias which may not be evident at the time of study. Incomplete data retrieval may make results less representative of the population under study.

On the other hand, retrospective studies are relatively quick, easy and cheap. They enable rapid assembly of data which can be screened rapidly to make a variety of hypotheses. These hypotheses can then be tested by more elaborate, time consuming and reliable prospective studies.

RESULTS

Carcinoma of the oesophagus is not a common tumour in Zambia; the incidence rate is certainly less than that reported from neighbouring countries (27) (29). The U.T.H. manages about a third of all reported cancers of the oesophagus in the country and this study shows that the prevalence of the disease has remained constant.

As elsewhere, this is a disease of the elderly male with a male to female sex ratio of 3.14:1. These figures are in keeping with sex ratios published from areas of low incidence.

Alcohol and tobacco have been implicated in the aetiology of oesophageal cancer in southern Africa (1). Seventy-four percent of patients in the retrospective series smoked and drank alcohol but in the Phase 2 study a similar proportion of controls smoked and drank alcohol.

As in Natal, Squamous carcinoma accounts for almost 95 percent of all primary oesophageal neoplasms (17). The most common site of involvement is the middle third of the oesophagus, in keeping with most reported series (7) (19) (27) (28) (29) (31).

The delay between the onset of symptoms and presentation is borne out and is responsible for the low resection and poor survival rates. As with most other series, palliation was the mainstay of treatment, aiming to restore the patients ability to swallow food and relieve pain without necessarily prolonging life. This has been achieved in most cases by the passage of a Celestin Tube. The 30 percent mortality with Celestin intubation is similar to other series (37) (48) (49) (50).

DISCUSSION

PHASE 2 - Case Control Study

METHODOLOGY

Case controlled analysis are a means of testing a hypothesis based on impressions made from previous non-controlled studies. Its validity is based on assumptions that if one or several criteria are controlled, other non controlled criteria can be tested against matched individuals not suffering from the disease.

Case controlled analyses are analytical studies based on patients already known to have the disease and comparing criteria suspected of being important with matched individuals not having the disease. Being retrospective, such studies do not give direct risk estimations as would a prospective or cohort analysis.

This study, unfortunately, comprises only 14 patients and 14 controls. Its value in deriving a conclusion is therefore limited by the small number in the study. This shortfall was due to the low incidence of carcinoma of the oesophagus in Zambia and by the short period of study. A study involving 50 patients and 50 controls would be more representative.

RESULTS

This phase of the study also shows that Carcinoma of the Oesophagus is a disease of the elderly male as in many other countries. The sex ratio of 3:1 is similar to that reported from South Africa (31), Tanzania (27) and Uganda (29) but contrasts with reports from Kenya (28) and Iran (1).

Although occupation has not been associated with cancer of the oesophagus, it provided an indication of the socio-economic status, though arbitrary. It appears that the low socio economic groups are more vulnerable to this cancer but data to substantiate this is not available.

McGlashan (34) noted in the mid 1960's that this cancer was more common in the Eastern Province of Zambia. The present study failed to confirm this although details of migration was not considered. It should also be noted that Lusaka caters predominantly the Eastern, the Southern and the Western provinces in terms of hospital referrals. This may introduce a bias in analysis as most of the northern regions are catered for at other hospitals.

Diet has been known to be associated with Carcinoma of the Oesophagus in Iran (3), China (15) and the Transkei (13). Most of the available data implicate mechanical trauma, micronutrient malnutrition or fungal contamination of foods. The staple food in Zambia is maize and maize is known to be prone to fungal contamination especially in rural areas (51). Ten of the fourteen patients in this study were subsistence farmers who did not have special storage facilities for their maize harvest. Further studies in this direction may yield vital clues. A history of drought or famine was not evident in this study.

Excessive alcohol intake and tobacco smoking has been variously implicated elsewhere (1) but has been found not to be statistically significant in our population. McGlashan (34) postulated that drinking Kachasu may be significant in Zambia but that was not supported by this study. McGlashan also found variable quantities of zinc in the Kachasu. The zinc content of Zambian soil is not known.

Environmental factors have also been variously cited and low socio economics stressed to varying extent (10). Both the type and size of houses have not been found to be of importance in Zambia.

As has been emphasised previously (52), cancer of the oesophagus is a lethal disease in rural and urban blacks. This may in fact be a reflection of the state of medical services available to the underprivileged communities in Africa where the highest incidences are reported (10). In addition, the lack of insight of the disease and belief in witchcraft is also responsible for the late presentation to hospital.

The most common site of involvement was the middle third of the oesophagus in conformity with most reported series (17)(19)(27)(29).

The long delay between onset of symptoms, the poor general health, and poor overall survival figures has laid emphasis on palliation as the principal modality of treatment. Radical treatment is attempted only on a small number of patient who are not considered anaesthetic risks. Palliation, especially intubation has the advantage of a short hospital stay, immediate improvement in swallowing and requires little expertise. Unfortunately, these do little in terms of prolonging life.

Surgical resection and bypass surgery, on the other hand requires considerable surgical skill and ancillary services of expert anaesthesia. The overall survival data of these procedures in non expert centres does not merit its use unless a cure is anticipated.

In summary, within the constraints of this study it can be said that cancer of the oesophagus in Zambia :

1. is not a common tumour.
2. is usually a disease of the elderly male.
3. is predominantly seen in the low socioeconomic strata of society.
4. has no tribal or provincial predilection.
5. has no identifiable aetiological risk factors.
6. has the same pattern of behaviour and prognosis as in the surrounding regions of Africa in spite of its low incidence in Zambia.
7. is predominantly not amenable to cure due to the advanced stage of disease at presentation to hospital.

DISCUSSION

PHASE 3 - CYTOLOGY

METHODOLOGY

Prospective single blind studies are valuable for testing both specificity and sensitivity of a particular test. However, double blind and randomised studies supercede these in objective analysis.

In this study, double blind analysis is not possible because the aim was to ascertain the accuracy of this test in comparison to oesophagoscopy and biopsy.

Again the limitations in the study period and the small number of patient limit the validity of any observations made.

RESULTS

Exfoliative cytological techniques have long been established in the armamentarium of the clinician. Oesophageal cytological techniques have been developed in the hope of making an early diagnosis of oesophageal cancer and improve the dismal survival and cure rates.

Blind techniques employ lavage or abrasion cytology. Chinese workers have reported on the use of an inflatable balloon (11), and South African workers have devised a suction abrasive method (40). Both methods are highly effective in detecting dysplasia and early cancers which would otherwise not be detected.

The present study was undertaken using the latter technique due to its simplicity in design. The aim of the study was to establish its sensitivity in detecting cancer cells in patients already complaining of dysphagia and if suitable, to apply it for use in peripheral hospitals where oesophagoscopic and x-ray facilities do not exist.

The conclusion drawn from this study is that this technique is not suitable for the diagnosis of oesophageal cancer in the Zambian patient. The explanation for this apparent contradiction to other studies is that our patients presented for treatment very late. The obstruction in the oesophagus did not permit contact between the abrasive surface and the tumour. In the other studies, the technique has been used exclusively for mass screening in areas of high incidence. Tim et al (40) utilised the technique solely for mass screening.

However, it must be emphasised that UTH does not run a regular cytology service nor is there a full time cytologist in the department. These reasons may contribute to the failure of the suction abrasive method.

The suction abrasive cytological method is of no value once there is dysphagia. This is not a method to be advised for general doctors wishing to make a diagnosis without performing oesophagoscopy.

CONCLUSIONS

The conclusions drawn from this study relating to carcinoma of the oesophagus in Zambia are:

1. Carcinoma of the oesophagus is not a common tumour in Zambia - the reason for the low incidence was not established.
2. The disease is usually seen in the elderly male.
3. Alcohol and tobacco play an insignificant role in the aetiology of oesophageal cancer in Zambia.
4. The disease is seen in the low socio-economic group of the population.
5. The study failed to identify any risk factors.
6. The disease has no tribal or provincial predilection.
7. The predominant tissue type is Squamous cell carcinoma.
8. The most common site of involvement is the middle third of the oesophagus.
9. The disease presents with similar clinical features and at a similar stage to other African countries. The outcome of treatment is also similar to other countries.
10. Palliation is the mainstay of treatment being achieved in most cases by intraluminal intubation.
11. Suction abrasive cytological technique is not advised for diagnostic use once there is dysphagia.

APPENDIX 1PHASE 1 Data Sheet

NAME		STUDY NO
AGE	SEX	HOSP NO
OCCUPATION		TRIBE
HOME ADDRESS		
DIET	NORMAL-	
	NOW -	
GEOGRAPHICAL HIST-		
ALCOHOL	TYPE:	AMOUNT: REG:
TOBACCO	TYPE:	AMOUNT: REG:

TUMOUR

TYPE:	ULCERATING / ANNULAR / POLYPOID	
SITE:	UPPER / MIDDLE / LOWER	cms
HISTOLOGY NO:	XRAY:	
HISTOLOGY:		

HISTORY

FIRST SYMPTOM:
 DURATION:
 DYSPHAGIA YES/NO
 " DURATION
 " TYPE
 " EXTENT
 COUGH
 HOARSENESS
 WT LOSS
 APPETITE

EXAMINATION

NUTRITION
 K-STATUS
 PALLOR
 JAUNDICE
 LYMPH NODE
 CHEST
 ABD
 VOICE

TREATMENT

DISCHARGE
 DEATH
 RELATED/UNRELATED

APPENDIX 2PHASE 2 Data Sheet

NAME:		STUDY NO
AGE:	SEX:	CASE/CONTROL
HT:	WT:	HOSP NO:
OCCUPATION:		TRIBE:
HOME ADDRESS:	BIRTH	
	HISTORY	
	NOW	
DIET:	STAPLE--	
	CROP--	
	NOW--	
	FAMINE--	
ALCOHOL:	STARTED--	
	TYPE--	AMOUNT--
	REGULARITY--	
	BREWING--	
TOBACCO:	STARTED--	
	TYPE--	AMOUNT--
	REGULARITY--	
	MANUFACT--	
HOUSING:	TYPE--	
	ROOMS--	
	OCCUPANTS--	

HISTORY

FIRST SYMPTOM:
 DURATION:
 DYSPHAGIA: YES/NO
 " DURATION:
 " TYPE:
 " EXTENT:
 COUGH:
 HOARSENESS:
 WT LOSS:
 APPETITE:
 DYSPEPSIA:
 TREATMENT:
 BELIEF:
 OTHER SYMPTOMS:

EXAMINATION

NUTRITION:
 K-STATUS:
 PALLOR:
 JAUNDICE:
 LYMPH NODES:
 CHEST:
 ABD:
 VOICE:
 OTHER:

TUMOUR TYPE: ULCERATING / ANNULAR / POLYPOID
 SITE: UPPER / MIDDLE / LOWER
 HIST NO: XRAY:
 HISTOLOGY:

cms

PROGRESS

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