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PREVENTION OF TONGUE CANCER

AT AN INDIVIDUAL LEVEL

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A thesis submitted in partial requirement for the

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SUMMARY

Cancer ranked second only to heart disease as the most frequent cause of death from 1900 to 1982 in the USA.

On a global basis oral cancer ranks fourth for men and sixth for women in rank for all cancers. World-wide the incidence of oral cancer varies enormously. In most countries where data is available the incidence of cancer of the mouth, though variable, is low. But India, Bangladesh and Sri Lanka are exceptional. Cancer of the mouth accounts for approximately 40% or more of all cancer in those countries, though the incidence varies widely in different parts of this sub-continent.

In the second chapter of the thesis, the aetiology of the tongue cancer has been discussed. Among the risk factors of tongue cancer are irritations such as the use of tobacco in its different forms, oral habits like reverse smoking, betel chewing and snuff dipping, alcohol consumption, cirrhosis of the liver and different dental factors are considered as important contributors. Apart from these, industrial hazards, radiation, syphilis, virological aspects and nutrition are also some very important factors which play a role in tongue cancer.

The epidemiology of tongue cancer has been discussed briefly in the third chapter. There are considerable variations between a number of countries of tongue cancer incidence. The highest incidence rates are reported in the Indian sub-continent, Puerto Rico and Brazil. Tongue cancer affects more men than women, although this trend is less pronounced in the Scandinavian countries and in England and Wales than in other countries. Tongue cancers in patients below the age of 20 years are very rare. The highest incidence of tongue cancer occurs in the 6th to the 8th decades of life.

Apart from lip cancer, tongue cancer is the most frequent site of cancer within the oral cavity, followed by the floor of the mouth.

Mortality rates for oral cancer vary geographically as well as by sex, site and rate. Singapore and Hong Kong rank first in deaths for both males and females, followed by France in males and the Philippines in females. Honduras and Nicaragua rank lowest for oral cancer mortality in both sexes.

The fourth chapter of the thesis deals with the prevention and control. The primary goal in the management of oral cancer patients should be prevention. Nevertheless progress in the early detection of cancer is highly desirable, since the percentage of cure is increased in direct proportion to how early it is recognized. Included in the control and preventive techniques are early detection of clinically appearing signs and symptoms, as well as microscopic examination of biopsy tissue. Another form of diagnosis and investigation is exfoliative cytology, a technique used for observing the microscopic morphology of individual cells after they have been obtained from a tissue. The method of applying toludine blue is also used as an investigatory aid in distinguishing between malignant and non malignant lesions. Other measures in tongue cancer control include surgery, radiation, chemotherapy, thermotherapy, cryosurgery and palliative therapy.

Patients with unresectable cancer may be candidates for a variety of palliative approaches designed to improve the quality of life. Another type of palliative therapy is the treatment of complications that arise from the disease or its treatment.

The prevention of tongue cancer at an individual level has been briefly discussed in the last chapter of the thesis. Behaviourial change is necessary in the attempt to prevent or control oral cancer. An effective behaviour and attitude change could be obtained by proper communication and motivation in an appropriate environment. Communication is not only confined to direct association but also to indirect methods such as publications, mass media, handouts, posters and the like. Making one knowledgeable is a very basic requirement to achieve an attitude change. Cancer education programmes involve teaching recognition of signs and symptoms to the community.

Self-examination is the most economical preventive method of oral cancer. This is achieved by implementing educational programmes.

At present, total prevention of cancer before its onset is difficult, if not impossible. However, early diagnosis detection and the use of control methods can prevent mutilation of tissues and metastasis of the disease and provide the greatest chance of survival for the patient.

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1 INTRODUCTION

Carcinoma is the most common malignant tumour of the mouth but it is uncommon when compared with other sites such as bronchus, breast and gastrointestinal tract. Cancer of the mouth accounts for only about 2% of all malignant tumours in such countries as the United Kingdom and the United States. In most countries where data is available the incidence of cancer of the mouth, though variable, is low. But in India, Bangladesh and Sri Lanka are, however, exceptional and cancer of the mouth accounts for approximately 40% or more of all cancer there, though the incidence varies widely in different parts of this sub-continent.

Oral cancer is a disease that strikes children as well as adults, but it occurs with increasing frequency with advancing age. Also, it is a disease that occurs more frequently in men than in women.

Of the estimated 6950 deaths that resulted from oral cancer in 1967, according to American Cancer Society, approximately 5200 deaths occurred in men and 1750 women. Presenting symptoms are usually an ulcer or a swelling that is painful. The symptoms of more advanced stages include dysphagia, dysphonia, a lump in the neck, or a pain in the ear (Sisson & Goldstein 1960).

The prediction for new cases of oral cancer and deaths from oral cancer has steadily increased during the past decade. The following table (table 1.1) shows the estimated new cases and deaths for the years 1971, 1976, 1978 and 1980.

Twenty-five thousand five hundred new cases were predicted for 1980 as well as 9000 deaths. This estimated number of new cases for 1980 was nearly twice the estimate for 1971, and the estimated deaths totalled 2000 more than for 1971.

Table 1.1
Estimated new cases of oral cancer and estimated deaths, 1971-1980.
Source: Cancer facts and figures, American Cancer Society

YEAR	ESTIMATED NEW CASES	ESTIMATED DEATHS
1971	14200	7000
1979	23800	8300
1978	24000	8000
1980	25500	9000

Epidemiological studies attempt, by examination of such features as geographical distribution, racial prevalence, occupation, social class, diet, climate, hygiene, use of tobacco and alcohol consumption to elicit possible causative factors for the cancer of tongue. There exists a traditional list of aetiological factors some of which are habits and other host factors. These include alcohol, smoking, syphilis and oral sepsis.

Reviewing cancer of the tongue in 1918 Power concluded:

"Cancer of the tongue has always existed in both men and in animals; the actual cause as yet unknown. Its rapid increase in men within historic times is the result of two causes: The first predisposing, the second exciting. The predisposing cause is the degenerative change taking place as a result of spirochaetal infection, the change being accentuated by lapse of years and indulgence in alcohol. The form in which the alcohol is taken does not seem to be important; beer, spirits and wine are equally harmful. It is the amount consumed, not the quality which matters. The exciting cause is local irritation. The most effective irritant is tobacco although pyorrhoea and carious teeth often act as minor exciting causes".

In general, comments about the aetiology of oral cancer hold true for tongue cancer in most instances. Patients who have a primary carcinoma in this site are usually heavy smokers and often heavy drinkers. For many years syphilis was thought to be a predisposing factor in cancer of the tongue. The reduced number of patients who have tertiary syphilis has made it difficult in recent years to evaluate this factor. Trieger et al (1958) found that among 108 patients with tongue cancer 19% had positive findings for syphilis, while Deckers and Maisin (1961) found 6% with positive serological reactions.

As vital as the actual factors themselves is the concept of "cocariogenesis". Goldhaber discusses two distinct phases in the development of a malignant neoplasm of the mouth; initiation and promotion. In the initiation period, normal cells are converted to "tumour" cells (ie. a malignant potential) by a carcinogenic agent in a relatively short time interval. Promotion takes much longer and involves the frequent exposure of latent tumour cells to an agent which is not itself a carcinogen, but referred to as cocarcinogen. Tongue cancers affect more men than women, although this trend is less pronounced in the Scandinavian countries and in England and Wales than in other countries. Tongue cancers in patients below the age of 20 years are very rare and cancer of the anterior part of the tongue among Europeans is more frequent than cancer of the base of the tongue, the reverse is the case in certain parts of India.

Prevention is a major primary goal in cancer research. Nevertheless, progress in the early detection of cancer is highly desirable, since the percentage of cure is increased in direct proportion to how early it is recognized. At present, total prevention of cancer before its occurrence is difficult, if not impossible. However, cancer can be prevented from causing rapid destruction of tissues and death to the patient by early diagnosis detection and treatment. Cancer can be cured and prevented from causing sequelae and complications prior to the appearance of the classical symptoms and signs of the disease.

In thinking in terms of prevention in its truest sense, early diagnosis detection and the use of control methods can prevent mutilation of tissues and metastasis of the disease and provide the greatest chance of survival of the patient. One of the major aspects of the preventive dental philosophy involves the prevention of oral cancer because of its seriousness.

In this thesis the writer will discuss the aetiological factors and epidemiology of tongue cancer and control and preventive measures that are available. The aim of the thesis is to summarise the major factors of importance to the prevention of tongue cancer at an individual level.

2 AETIOLOGICAL FACTORS

The use of tobacco, in its different forms, oral habits like reverse smoking, betel chewing, snuff-dipping, poor oral hygiene, syphilis, inadequate diet, and chronic irritation from rough or broken teeth and ill-fitting dentures are several factors that have been considered responsible for causing tongue cancer. Other important aetiologic factors that have been associated with oral cancer are consumption of alcohol, viruses, air pollution, sunlight, heredity and endocrinology.

Wynder et al (1957) applied the terms "intrinsic" and "extrinsic" to group factors which act together in malignant transformation. Intrinsic factors infer generalized defects from such things as malnutrition from alcoholism, vitamin deficiencies, sideropenia and syphilis. Extrinsic factors are exogenous and have local effects, eg tobacco or local mechanical irritation.

Current studies of these factors, both traditional and provisional, continue to examine the multifactorial nature of the aetiology of oral cancer. The possible mechanisms by which these factors may interrelate to produce a malignant neoplasm are as vital as the study of the individual factors themselves. However, it is worthwhile to review these factors individually and assess their associations with tongue cancer.

2.1 IRRITATION

2.1.1 Smoking

Evidence accumulated over the past 200 years linking smoking habits with oral cancer was comprehensively reviewed by Clemmesen (1965). Rothman (1978) states categorically that tobacco has been well established as a risk factor in cancer of the mouth and pharynx. The assumption, bases primarily on the epidemiological association of tobacco usage with increased incidence of oral cancer should, however, obscure the as yet unresolved questions regarding the significance of the manner in which tobacco is smoked and the nature of the relationship established by combining smoking with other environmental variables.

Smoking has been estimated to increase the likelihood of developing a mouth cancer by two to four times. As early as 1859, the observation was made that out of 68 patients with cancer of the buccal cavity, 66 smoked pipes, one chewed tobacco and one apparently used tobacco in some form (Hammond 1962). Prior to World War I, tobacco consumption was primarily in the form of snuff, chewing tobacco, pipe tobacco and cigars (Peacock, & Brawley 1960). Cigarette consumption drastically increased after World War I (Moore & Bock 1956).

Nearly 36% of the oral cancer patients reported by Mills and Porter (1950) gave a history of smoking cigarettes only, while approximately 55% smoked pipes, cigars, or some combination of these.

There is ample evidence to implicate tobacco smoking as a prime aetiological factor for oral cancer and several studies have demonstrated a dose/time relationship. For instance, Mashberg et al (1981) reported an increase in the relative risk of developing oral cancer from 3.2 for those smoking 10-19 cigarettes per day to 4.5 for those smoking 20-30 cigarettes per day and 5.0 in those smoking over 40 cigarettes per day. Heavy smoking (40 or more cigarettes daily) has been found to be significant for tongue cancer and cancer of the floor of the mouth. The death rate for heavy smokers (25gms of pipe or cigar tobacco or more per day) from oral-pharyngeal cancer has been demonstrated to be more than five times that of the light smoker rate (Weir, Dunn, Buell 1969). Furthermore, the chance of developing a second primary tumour is dependent upon the quantity and duration of smoking before the onset of the first primary tumour (Wynder et al 1977). In addition several studies have suggested a synergistic effect of tobacco smoking and alcohol.

Substances present in the gas vapour phase of tobacco smoke (acrolein and cyanide) cause reduced cellular respiration which leads to malignant transformation of cells. Acrolein has been shown to produce inhibition of RNA synthesis loss of RNA, pyknosis, and

cell destruction within 24 hours after exposure of mouse kidney and slime mould cultures to cigarette smoke gas phase (Azn 1962). Polycyclic aromatic hydrocarbons (PAH), regarded as the main precarcinogens in tobacco smoke, are activated to ultimate carcinogens in cells by microsomal complex enzymes commonly referred to as aryl hydrocarbon hydroxylases (AHH) (Binwe & Rankin 1988). Analysis made of puffs of commercial cigarettes with or without sodium nitrate ($NaNO_3$) by gas chromatography showed that the addition of $NaNO_3$ reduces the components and properties of cigarette smoke that are associated with tumorgenicity. The effect is due to thermal decomposition of the nitrate into oxygen and nitrogen oxides; the fumes enhance combustion of tobacco and later inhibit free radical reactions leading to formation of benzo [α] pyrene.

The premalignant lesions leukoplakia and erythroplasia have been associated with tobacco smoking. Smokers have a significantly higher prevalence of leukoplakia compared with non smokers (Baric 1982, Silverman 1984) and the frequency of the habit has a positive dose-response relationship (Gupta 1984). Furthermore, a person with leukoplakia can have 50-100 times the risk of developing oral cancer compared with the rest of the population (Einhain & Wersall 1967).

Wynder et al (1957) presented some evidence linking cigar smoking and oral cancer. Among Danish females, it is common to smoke cheroot and Pindborg et al (1967) have shown that leukoplakia is associated with cheroot smoking.

In parts of Caribbean, South and Central America and in some parts of the Indian sub-continent, reverse smoking is practised, in which cigarettes are smoked with the burning end in the oral cavity. But, however, the Caribbeans do not suffer from oral cancer as much as the Indians. Probably the differences are due to variations in compositions or curing of the tobacco product.

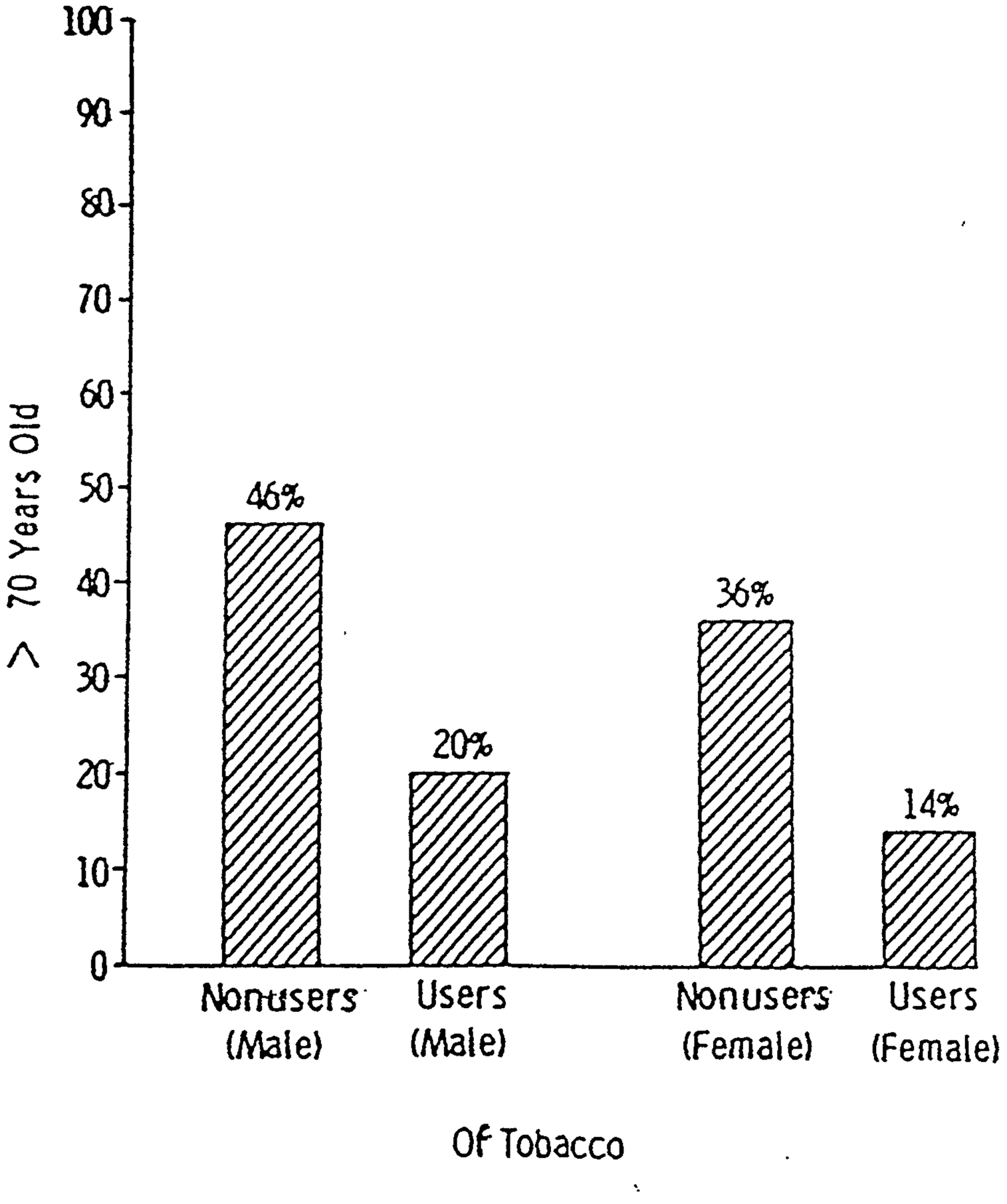
The bidi consists of a small amount of Nipani tobacco rolled up in a dried temburini leaf (Henk & Langden 1985). In 1974, Hoffman et al have shown that bidi smoke has a higher content of carbon monoxide, ammonia, hydrogen cyanide, phenol and carcinogenic hydrocarbons compared with cigarette smoke. Bidi smoking is widely practised in Bangladesh and India and Pinborg et al (1967) have shown that 16% of bidi smokers had commissural leukoplakia.

Here, Ash (1962) listed some possible aetiological factors observed over a 25-year period for oral cancer (Table 2.1). It is notable that in his series trauma (dental, mechanical) and tobacco lead the list at 14% each.

Table 2.1
Oral Carcinoma, 1929 - 1958, recorded aetiological factors.
Source: After Ash 1962

AETIOLOGY	%	
Trauma (Dental, Mechanical)	13.8	68.2
Tobacco	13.7	
Leukoplakia	8.7	
Syphilis alone	2.5	
Syphilis with other factor	2.1	
Alcohol	1.8	
Anaemia	0.8	
Chronic Inflammation	1.0	
Other, or combination	23.8	
Non stated	19.1	31.8
None	12.7	

Figure 2.1
Percentage of users and non-users tobacco who develop oral tongue cancer at age seventy years or older.
Source: Johnstone & Ballantyne 1977



2.1.2 Chewing Habits

In Asia the prevalence of oral cancer is high. Betel quid chewing is also widespread throughout this geographical area, and attempts have been made to link these two observations. Support for this hypothesis arises (Hirayama 1966, Wahi 1968) from the greater prevalence of oral cancer among individuals who chew betel quid as opposed to those who do not; in the site where the betel quid is habitually held and associated with early, prolonged or frequent usage.

Numerous epidemiological studies conducted on various Indian populations with peculiar indigenous tobacco habits have indicated that topical tobacco is a vital consideration in the evaluation of tobacco as a risk in oral cancer (Jafarey et al 1977). The tobacco is blended in various forms and the composition of the betel quid varies from area to area but usually contains tobacco, which may also be in the form of dry tobacco leaf, slaked lime, betel leaf and areca nut or betel nut. The areca nut contains tannin, gallic acid, volatile oil and alkaloids (Tennakoon et al 1968).

Khadim (1977) noted that the addition of tobacco to the betel quid known as "pan" increased the risk from 4 (without) to as much as 29 with its addition. According to Balendra (1949) the betel quid itself was not carcinogenic, but it causes gingivitis, irregularities of teeth and gums, and sepsis which give rise to chronic irritation resulting in cancer. Atkinson et al (1964), however, suggested that the possible aetiological agent involved may be the lime. This possibility is supported by observation of elevated oral cancer incidence related to endemic chewing habits in Malaysia and Papua New Guinea where it is most common to use the betel nut with lime but without tobacco. In Afghanistan and Nigeria, the incidence is contrastingly low where tobacco is chewed without lime.

Hirayama (1966) found that in India and Sri Lanka tobacco chewing was significantly associated with cancer of the buccal mucosa, anterior tongue and oropharynx. He also

stated that the effect of smoking in oral cancer was statistically significant only among non chewers and early-age chewers of tobacco in an oral cancer group than in the control group. Jafarey and Zaidi (1976) have shown that in Pakistan the combination of betel nut chewing (with tobacco) and smoking increases the risk of developing oral cancer by 23 times in men and 35 times in women.

A mixture of tobacco, ash, cotton oil and lime referred to as "nuss" is the smokeless tobacco equivalent in the USSR. An elevated incidence of oral carcinomas has been reported from several geographic areas of the USSR where this habit is known to be a common practice (Paches & Milievskaya 1980).

Mason (1977) and Mason et al (1977) supplied graphic demonstration for the need for continued evaluation of topical tobacco habits in the USA in an atlas of cancer mortality. Increased oral cancer mortality in females in the south eastern USA, which is characteristically a textile area, was identified by him where topical tobacco habits are known to be common among the workers.

In another study Jayant et al (1977) showed smoking or chewing tobacco are associated with a 70% chance for cancer of the oral cavity, an 84% chance for cancer of the oropharynx and about a 75% chance for cancer of the hypopharynx and larynx.

Three types of chemical carcinogens have been identified in smokeless tobacco (Hoffman et al 1986). A polynuclear aromatic hydrocarbon, benzo(a)pyrene, has been detected, indicating that the tobacco has been contaminated with thermal degradation products in the curing process (Hoffman 1986). Varying amounts of an α-particle-emitting metal, polonium 210, originating from a specific phosphate fertilizer used in the cultivation of tobacco, have also been demonstrated as well as several of the over 300 known carcinogenic nitrosamines (Hoffman 1986).

Jayant et al (1977) analyzed data from 2005 patients with oral, pharyngeal and oesophageal cancers and from an equal number of controls comparable in sex, age and religion. He showed that there was a higher risk of oral carcinoma among the chewers (Table 2.2).

Another study on this aspect shows that the habit of chewing and/or smoking contribute (Jayant et al 1977) to carcinoma of the mouth. Table 2.3 shows that smoking and chewing act synergistically, although in varying degrees.

Table 2.2
Chewing and smoking habits in relation to mouth cancers.
Source: After Jayant et al 1977

	HABIT				TOTAL
	CHEWERS	SMOKERS	CHEWERS OR SMOKERS	NONCHEWERS OR NONSMOKERS	
Controls	521	415	144	925	2005
Cancer cases:					
Oral cavity	192	72	90	57	411
Base of tongue and oropharynx	91	260	242	49	642
Oesophagus, hypopharynx larynx	270		260	133	935

Table 2.3
Aetiological fractions in the exposed and the overall aetiological fractions in relation to oral cavity.
Source: After Jayant et al 1977

	RISK FACTORS			OVERALL AETIOLOGIC FRACTION C &/or S
	CHEWING	SMOKING	SMOKING AND CHEWING	
AETIOLOGIC FRACTION	0.83	0.65	0.90	
				0.70
CASE FRACTION	0.47	0.18	0.22	

2.1.3 Alcohol

The role of alcohol consumption in oral cancer aetiology is complicated by several factors. The most common reason to be cited is the difficulty in isolating heavy alcohol consumption from smoking. Individuals who drink large quantities of alcohol also smoke heavily; this may produce a synergistic potential for the initiation or promotion of oral cancer (Rothman & Keller 1972, Bross & Coombs 1976). In three studies it has been shown that combined exposure to alcohol and tobacco lead to the onset of oral cancer 15 or more years earlier than would be expected for individuals who do not use either alcohol or tobacco (Feldman et al 1975, Fortier 1975, Bross & Coombs 1976). Lemon et al (1964) found a significantly reduced mortality from oral cancer among Seventh Day Adventists, a group who abstain from both alcohol and tobacco.

Schwartz et al (1962), however, in 3937 French males in an analysis of association between alcohol consumption and cancer of the tongue, hypopharynx, larynx, oesophagus, buccal cavity and oropharynx exclude the possible overlapping influence of smoking and showed a definite relationship.

Young and Russell (1926) were the first to note the mortality statistics in the UK showed an association between death from oral cancer and occupations in the liquor trade. Wynder et al (1957) calculated that heavy drinkers (more than six ounces daily of spirits or equivalent) had a 10 times higher risk of developing oral cancer than did occasional drinkers. A similar relationship between the amount of alcohol consumed and oral cancer risk was found by Graham et al (1977). In 1957 (Wynder et al) a positive correlation between excessive drinking habits and oral cancer has been demonstrated in the USA. Herity et al (1981) in their Irish study showed an increase tongue cancer risk of 4.6 for light drinkers and a 9-fold risk for heavy drinkers. They also made the point that a significant excess of alcohol-related occupations (eg bartenders) among the cases was represented. Study of the prevalence and consumption of illegally produced spirits indigenous to certain parts of the world shows there is a possible significance of carcinogenic congeners or

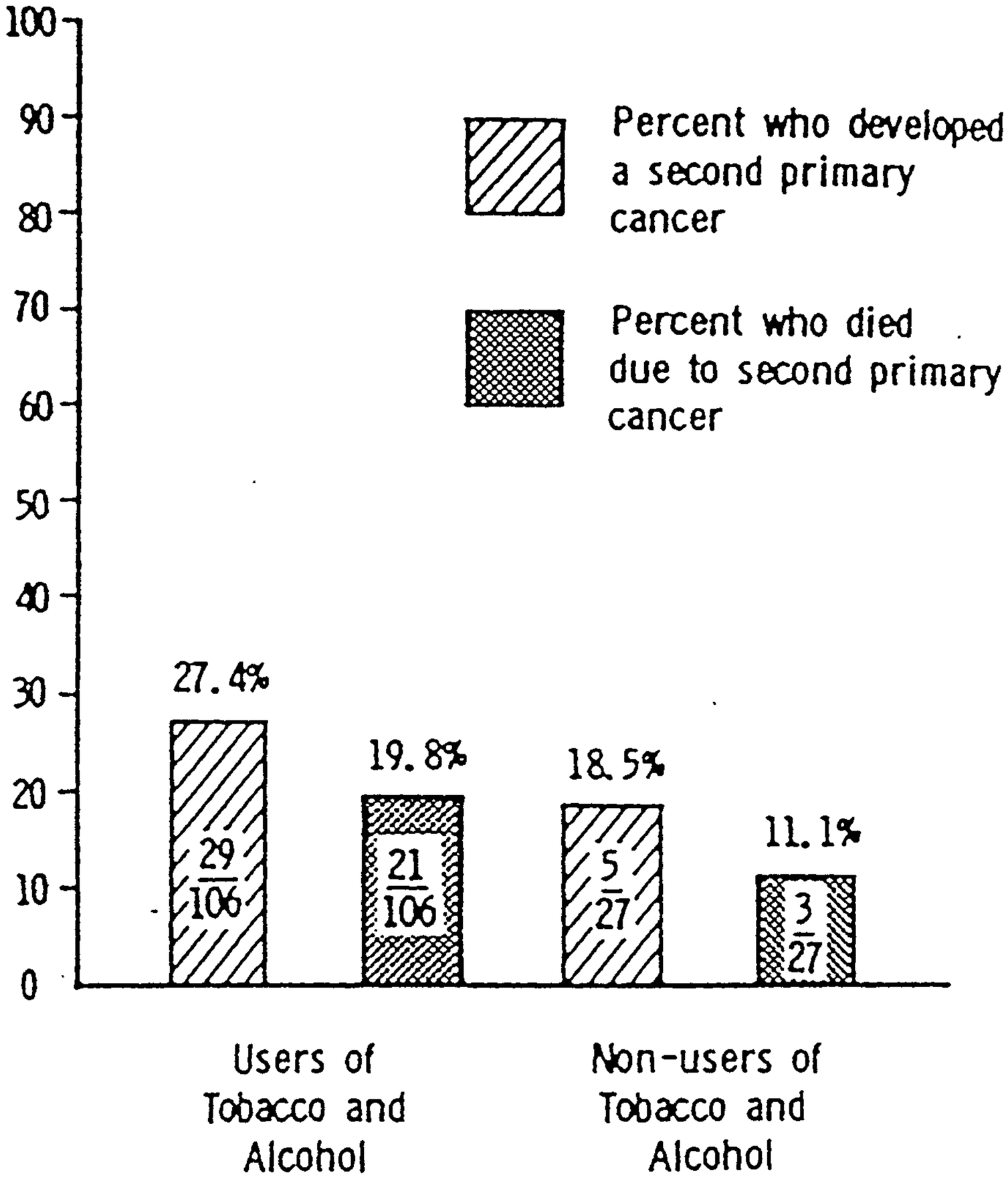
contaminants. There is also a possibility that a similar geographic pattern applies to oral cancer. Fischman and Martinez (1977) suggested after contrasting the incidence of oral cancer in Puerto Rico with the mainland USA, that prevalence of home-processed rum might in part account for the higher incidence reported in Puerto Rico. In another study Mashberg et al (1981) surprisingly reported a greater relative risk for beer and wine drinkers than for whiskey drinkers.

According to McCoy (1978) there is a possibility that the entry of carcinogens into exposed cells is facilitated by alcohol. He suggests, "The effect of alcohol may be more readily explained by alterations in metabolism in the oral cavity and oesophageal epithelium". McCoy (1978) elaborating on the localized alcohol effects, further proposed, "The oxidation of ethanol by epithelial cells of the target tissues could alter intercellular metabolism, creating a more favourable environment for metabolic activation of procarcinogens".

Compiled from data of Johnston and Ballantyne (1977), Figure 2.2 shows the incidence of second primary cancer. There was a greater incidence of second primary cancer in users of tobacco and alcohol than in non users.

FIGURE 2.2

Incidence of second primary cancer in five to twenty year follow-up after treatment of primary cancer.
Source: After Johnston and Ballantyne 1977



2.1.4 Cirrhosis of Liver

Protzel et al (1964) have shown in animal experiments that alcohol may be an aetiological factor in oral cancer through a systemic effect, and they have also shown that other substances which damage the liver can potentiate the action of carcinogens on the oral mucosa. The systemic impact of alcohol, the link between a high level of alcohol consumption, liver cirrhosis and oral cancer, has been shown by several authors such as Vincent and Merchetta (1963), Trieger et al (1958, 1959), Keller (1967), Vincent et al (1969) and Martinez (1969). They have all suggested that alcohol-induced liver damage helps to initiate or accelerate malignant changes in the oral mucosa. McCoy (1978) tried to explain the possible connection and suggests the possibility that the alcohol compromised liver could have a decreased ability to detoxify potential carcinogens. Observations of 276 cases with squamous cell carcinoma of the mouth and compared with a control group, are shown in Table 2.4.

Table 2.4
Proportion with clinically diagnosed liver cirrhosis by anatomical sites for cases of mouth cancers and their matched controls.
Source: After Keller 1969

		CASES		CONTROLS	
SITES	No.	No.	%	No.	%
Floor of mouth	123	18	14.6	6	4.9
Tongue	92	7	7.6	8	8.7
Other parts of mouth	61	6	9.8	6	9.8
TOTAL	276	31	11.2	20	7.2

2.1.5 Dental Factors

Poor oral hygiene, rough or faulty restorations, ill-fitting dentures and sharp edges of teeth have often been incriminated in tongue cancer aetiology. Browne et al (1977) reported a higher incidence of poor oral hygiene and ill-fitting dentures in an examination of aetiologic factors related to an increased incidence of oral cancer in Stoke-on-Trent, England. A topographic coincidence of tumour development and chronic mechanical trauma from dental prostheses in 44% of cases of oral cancer examined by Thumfart et al (1978). Among cancer therapists in the UK it is a commonly held belief that the decrease in oral cancer incidence is due to improved dental health.

In experiments with animals, Renstrup et al (1962) demonstrated that chronic irritation does enhance carcinogenesis. Graham et al (1977) created a 'dentition index' to assess dental status and found association with developing oral cancer and poor dental status. They found that men who smoked heavily, drank large quantities of alcohol and had an inadequate dentition had a risk 8 times higher than controls without these characteristics.

Thumfart and coworkers (1978) examined oral cavity tumours in a series of 1160 cancer patients and correlated the site of the tumours or epithelial lesions with results of a biopsy and possible aetiologic components. The tongue was the site of 62% of the oral cavity tumours (Table 2.5). In this study the population was predominantly of farmers and labourers. Most of these patients had poor oral hygiene, abuse of both alcohol and tobacco and persistent mechanical irritation at the site of cancer.

The mechanical irritation was caused by sharp teeth edges, or projecting fillings, ill-fitting dentures or deficient clasp devices or partial dentures (Table 2.6). In 44% of cases of oral-cavity carcinoma, tumour development was related to sharp remaining teeth, deficient dental fillings, badly finished edges of dentures, loose anchoring element and unsuitable denture-bearing tissue. Chronic habits like prolonged exposure to an inert substance may also terminate in malignant transformation.

Table 2.5
Site of the oral cavity carcinomas (n=86).
Source: After Thumfart et al 1978

Tongue and floor of the mouth	53 (62%)
Isolated involvement of the floor of the mouth	12 (14%)
Palate	10 (12%)
Gum	7 (8%)
Cheeks/vestibule of the mouth	4 (4%)

Table 2.6
Dental status of the patients with signs of mechanical irritation of the tumour region (n=38).
Source: Thumfart, Weidenbecher, Waller and Pesch 1978

Ill-fitting Complete Denture	10
Partial Denture	8
Teeth remaining	14
Sharp teeth remaining	6

2.2 INDUSTRIAL HAZARDS

Vogler et al (1962) in a small series of patients noticed that among women textile workers in the Southern USA oral cancer was at least twice as common as cancer in other sites. Many of these workers chewed tobacco while working but the number of patients was small. The authors concluded the finding was not significant.

In 1972, Binnie et al noted a high incidence of oral cancer in male textile workers. Excess deaths (77%) from oral and pharyngeal cancers in male textile workers of England and Wales (1959 to 1963) involved the tongue, mouth and pharynx. Predominantly the excess was concentrated in fibre prepares (wool).

According to Moss (1976) another study was made including male and female patients from two main textile regions in England; Northwest region (cotton) and West Yorkshire (wool). Along with age matched controls, fifty seven women with squamous cell carcinoma in oral and pharyngeal sites were interviewed during 1973 and 1974. An association was found between oral and pharyngeal cancers and industrial exposure to textiles that could not be accounted for by the wearing of dentures, by smoking or drinking habits, or by tobacco chewing.

Moss and Lee (1974), confirmed that there was an increased risk of developing oral cancer for people employed in certain subgroups of the cotton and woollen textile industry; workers exposed to the dust created by the initial 'carding' of raw cotton and wool appeared to be particularly at risk.

Some investigators have suggested that oral cancer may be associated with high degrees of industrialization, atmospheric pollution by coal smoke, and exhaust fumes containing benzopyrene and other polycyclic hydrocarbons (Moore & Bock 1956). A lower incidence of oral cancer in rural areas add some support to the evidence (Hammond & Horn 1955).

2.3 RADIATION

Alpha, beta and gamma rays - these ionizing radiations are known as recognized human environmental carcinogens acting of susceptible cells in the body (Heuper 1961). Human clinical studies and animal research investigations have verified that radiation under certain conditions related to dosage and duration can produce cancer (Mottram 1938, Chase et al 1961, Southam 1963, Hamner 1964, Jablon 1975, Hutchison 1977).

It is recognized that one of the high risk groups for developing cancer are those individuals who received therapeutic doses of X-radiation or radium applications to the head, neck or upper thorax for various benign conditions during infancy and childhood (Hamner 1986). Beverley in 1978 stated that the more the exposure, the greater the susceptibility to carcinoma.

2.4 SYPHILIS

Syphilis, infection by Treponema pallidum, has a long established relationship with oral cancer, particularly cancer of the tongue, and this was reviewed by Clemmesen in 1965. Late stages of syphilis involving the tongue are often complicated by cancer of the tongue (Moertal & Foss 1958). Martin (1946) found syphilis in 24% of patients with oral cancer. Vitamin B deficiency and use of tobacco are some additional factors which were also related to many of these cases. A positive Wasserman test was reported in 18% of negro patients with oral cancer.

The relationship between syphilis and oral cancer is variable. It is dependent upon the population sample and the site of involvement. A high incidence of cancer and syphilis of the tongue has been reported (Trieger et al 1958, Lund 1938). The relative risk of cancer of the tongue in patients with a positive Wassermann was found to be 3.1. Wynder et al (1957) reported a similar figure of 2.6 and the investigators managed to eliminate the possibility of other factors, i.e. alcohol and smoking, confusing the issue. Trieger et al (1958) found positive serology in 19% of 108 patients with tongue cancer and Deckars and Maisin (1961) found 6% of tongue cancer patients to have positive serology.

Levin et al (1942) compared registrations of syphilis with registrations of cancer, of many sites, in white males in New York state. There was serological and clinical evidence five times greater in patients with lingual cancer than in those with other forms of malignant neoplasms, despite a low overall incidence of syphilitic infection. The expected number of cases of lingual cancer was exceeded fourfold by the actual numbers found among the registered syphilitics. Further evidence of a specific association is suggested between the two diseases by the fact that syphilitic-linked leukoplakia or carcinoma occurs predominantly on the dorsum of the anterior two thirds of the tongue, which is an unusual cancer site nowadays. The majority of tongue cancers occur on the lateral border, ventral surface, or posterior third of the tongue.

Smith (1973) has raised the possibility that various preparations of arsenicals and heavy metals, the substances used in the treatment of syphilis before the use of antibiotics, may have been more influential carcinogenic agents that the infection itself.

2.5 VIROLOGICAL ASPECT

Gross (1953) isolated a virus from a murine parotid tumour, a virus which produced tumours in many organs if injected into newborn mice. This virus termed as 'polyoma' virus has been shown in animals to produce tumours in the head and neck, including oral neoplasms similar to the ameloblastoma and salivary gland tumours, but there is little evidence for such an association in humans.

Cancer viruses are nucleoprotein macromolecules. They consist mainly of DNA with a covering of protein (Cowdry 1968). It is accepted that at least in the early stage of cervical cancer the cells carry a fragment of the herpes simplex virus type 2 (HSV-2) genome and express some, but not all, HSV-2 antigens (Dressman et al 1980). Both HSV-1 and -2 can cause malignant transformation of cells in vitro, and the transformed cells continue to express some HSV antigens. Some attention has been directed towards the possibility that HSV-1 might be associated with oral cancer as a result of these findings. A change in humoral immunity in a high risk group of population, who are likely to develop squamous cell carcinomas of the head and neck region, was demonstrated by Smith et al (1976). They showed that cigarette smoking and the use of alcoholic beverages were associated with heightened humoral immunity to HSV-induced antigens, particularly IgA.

Human Papilloma Virus (HPV) play a role in a range of diseases and they are increasingly being implicated in the aetiology of squamous cell carcinoma. Syrjanen et al (1983) studied 40 biopsies of oral squamous cell carcinoma and found that 16 showed histological features suggestive to HPV. In 1984 Loring et al stated that nodular leukoplakia demonstrating HPV viral antigens progressed to squamous cell carcinoma. Scully (1988) stated that HPV antigens and HPV DNA have been found in oral carcinoma and in premalignant lesions. He also showed that an unusual HPV type related to HPV-16 is found in oral squamous carcinoma but, in verrucous carcinoma, HPV-2 is the main agent.

2.6 NUTRITION

Iron metabolism is important in maintaining the health of the oral mucosa, and many disease states, including carcinoma, are associated with iron depletion (Rennie et al 1984). The best known example of oral carcinogenesis attributed to a dietary imbalance in humans is the Plummer-Vinson iron deficiency syndrome (Hamner 1977). The Plummer-Vinson syndrome, first described by Plummer (1914) and then by Vinson (1922), is one of the main manifestations of iron deficiency anaemia. Usually the symptoms include cracks at the corners of the mouth, a yellow tinted skin, smooth, red painful tongue and dysphagia. Ahlbom (1936, 1937) in Scandinavia, as well as confirming the importance of the syndrome in the development of carcinoma of the meso and hypopharynx, showed in his studythat this also applied to the buccal mucosa, tongue, and all levels of the oesophagus.

Other series have been reported of patients with Paterson-Kelly syndrome who have developed single or multiple oral cancers (Wynder et al 1958, Shamma et al 1958, Watts 1961). Prime et al in 1983 in their study which used a rat palate model painted with 4-nitroquinoline-N-oxide have shown that animals with iron deficiency anaemia, induced by venesection and a low iron diet, develop carcinomas after a mean of 183 days as opposed to a mean of 229 days in control animals. Furthermore, the early tumours are not on the palate but on the tongue. Joynson et al (1972) demonstrated an impairment of cell mediated immunity in iron deficient patients and stated that this condition carries important implications with regard to the pathogenesis of malignant disease.

According to Krieshover and Salley (1957) avitaminosis has a possible role in the the aetiology of oral cancer. In many patients with oral cancer a lower vitamin B excretion level has been found (Waravdekat et al 1950). Low serum vitamin A was found in 76.2% of patients with oral carcinomas in a series and was considered as an adjuvant in the carcinogenic process (Wahi et al 1965).

Peto et al (1981) reviewed the role of ß-carotene and retinol in cancer and showed that blood retinol and dietary ß-carotene are inversely proportional to cancer risk. An Indian study revealed (Wahi et al 1965) 76.2% of patients with oral and oropharyngeal carcinoma were found to have subnormal levels of serum vitamin A. Ibrahim et al (1977) showed plasma vitamin A and ß-carotene levels to be significantly lower in oral cancer patients than in controls in Pakistan.

3 EPIDEMIOLOGY

It is a fundamental principle of epidemiology that disease does not occur randomly, and it is the province of epidemiology to identify the characteristics of these non-random occurrences (Hutchison 1982). The epidemiology of cancer, especially oral cancer, is unique in its long latent period and relatively low incidence which renders a direct cause and effect relationship more difficult to identify, particularly if the premise of multifactorial aetiology is accepted.

In 1900 cancer ranked eight, in the United States of America, as a cause of death. Because of the successful treatment of infectious diseases, mainly due to antibiotic therapy and national immunization programmes, cancer ranked second only to heart disease as the most frequent cause of death from 1900 to 1982. On a global basis oral cancer ranks fourth for men and sixth for women in rank for all cancers (Waterhouse et al 1982). In the USA, malignant neoplasia of the oral cavity comprises only 2 to 4% of total malignant tumours (American Cancer Society 1983). A similar incidence of 2% was reported by Binnie et al (1972) in England and Wales. A range of 2 to 6% applies to most of the Western countries (Pindborg 1977). In incidence, however, there are tremendous variations, internationally. A figure approaching 50% has been reported for different parts of the Indian sub-continent (Mehta et al 1971) and over 40% in Sri Lanka (Lucas 1976).

Oral cancer prevalence varies from state to state among different populations. In 1969, Doll showed in his report that the highest occurrence was in India at 61.3% of all cancers and the lowest in Iceland at 1.3% (Table 3.1). A relatively high frequency of oral cancer in most of the countries in Southeast Asia was noted by Pindborg in 1977 (Fig 3.1). Although living in the same country the prevalence might vary between different ethnic groups as well. Shanmugarathnam (1973) showed differences in the condition in Singapore, which has Chinese, Malays, Indians and Pakistanis (Fig 3.2). Different habitual patterns among the groups suggested by Pindborg (1977) are responsible for such a variation.

In Switzerland, the incidence of oral cancer was determined in two cities - Neuchatel and Geneva (Obradovic et al 1979). The highest incidence in males was seen for cancer of the lip, tongue and buccal cavity. The level of mortality from cancer of tongue and pharynx is one of the highest in the world in Switzerland. A 1965 cancer incidence survey by site and status revealed 26,542 cases of cancer in Western Canada and among the 616 new cases of oral cancer 100 were of tongue. During the years 1962-67 in England and Wales the average annual registration for cancer of the oral cavity was 2628 from a total of 138123 of all malignant neoplasms (Binnie et al 1972).

Within Europe, the incidence varies from 16.9 in Malta to 2.5 in the southern UK in males per 100,000 population (Waterhouse et al 1976). Exceptionally high mortality has been reported by Binnie et al (1972) from oral cancer in France. He postulated an association between oral cancer, cirrhosis and the consumption of immature pot-still spirits containing toxic by products of distillation. In the Americas, there are even greater differences in incidence rates than in Europe. Newfoundland has the highest rate for oral cancer in the western world. The incidence of oral cancer varies considerably between states and between whites and blacks in the USA.

Oral cancer has been one of the two most common cancers reported to the Papua New Guinea Tumour Registry with 668 cases being reported between 1958 and 1970 (Atkinson et al 1974). Statistical information from the Union of Soviet Socialist Republics (USSR) shows that the incidence of oral cancer is higher in their Central Asian Republics, as would be expected, than in other regions of the USSR. For example, the age adjusted incidence rate for oral carcinoma in Uzbek was 2.3, whereas by contrast, the rate was only 0.4 in Byelorussia (Paches & Miliesvkaya 1980). The manner of preparation and degree of use of "nuss" in the Central Asian Republics might have attributed to the difference.

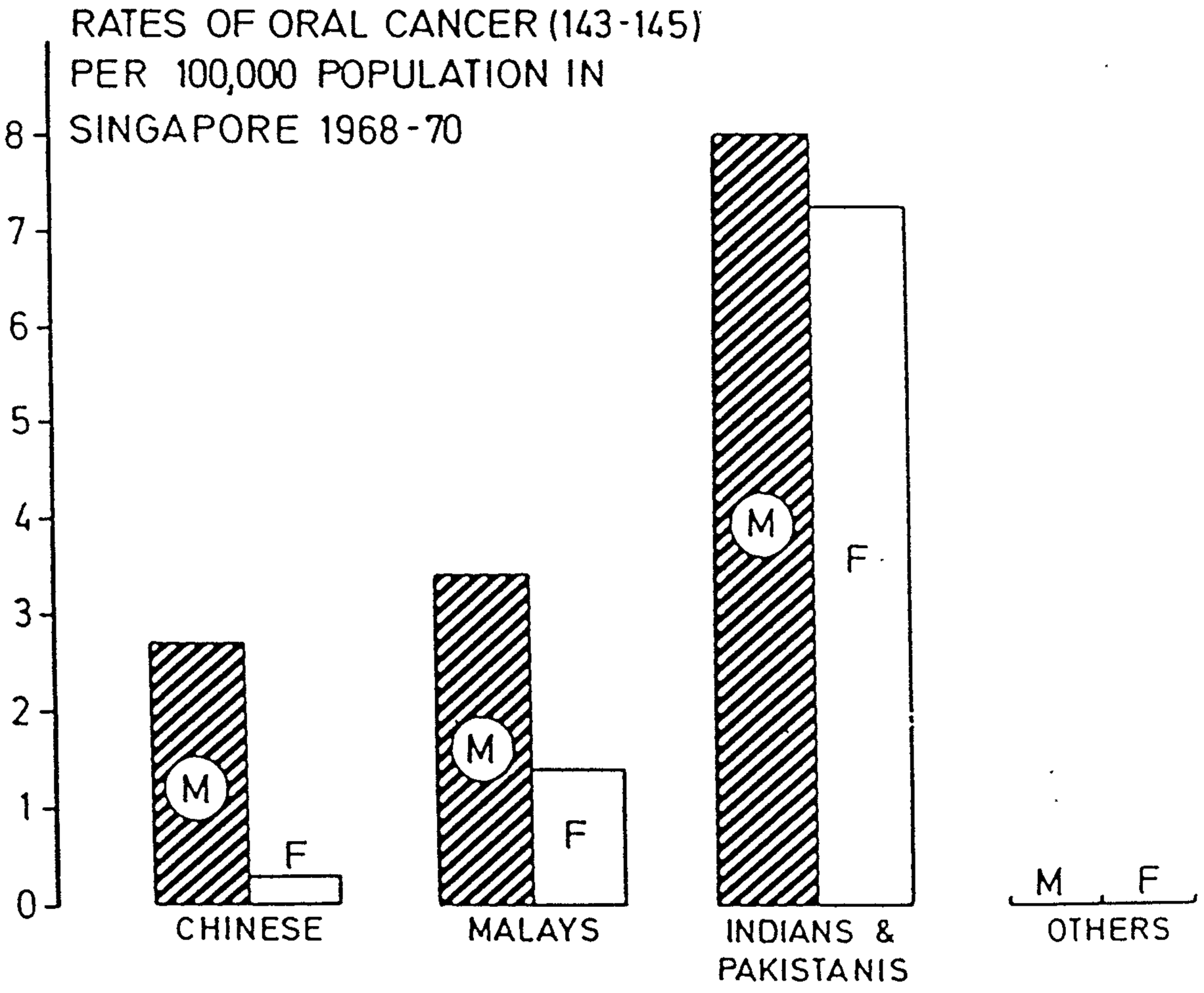
Table 3.1
Incidence of oral cancer in different populations: Annual rates per 100,000 persons aged 35-64 years, standardized for age
Source: After Doll 1969

POPULATION	
AFRICA	
Mozambique	
Lourenco Marques	8.5
Nigeria, Ibadan	2.3
S Africa	
Durban	
(African)	10.9
(Indian)	3.3
Johannesburg	
(African)	7.9
Unganda, Kyadondo	1.9
AMERICA	
Canada	
Alberta	4.5
Manitoba	2.9
New Brunswick	5.4
Newfoundland	3.8
Saskatchewan	3.2
Chile	2.3
Columbia, Cali	9.0
Jamaica, Kingston	7.9
Puerto Rico	26.6
USA	
Connecticut	11.5
New York State	7.7
ASIA	
India, Bombay	61.3
Israel	3.0
Japan, Miyagi	1.9
Singapore (Chinese)	4.6
EUROPE	
Denmark	2.2
England and Wales	
Birmingham region	4.4
Liverpool region	3.7
S Metropolitan region	3.1
S western region	2.5
Finland	2.4
Ireland	1.3
Netherlands (3 provinces)	3.1
Norway	3.1
Sweden	2.6
Yugoslavia, Slovenia	5.0
OCEANIA	
New Zealand	3.9
USA, Hawaii	
(Caucasian)	16.8
(Hawaiian)	5.9
(Japanese)	1.9

Figure 3.1
Histogram showing oral cancer as a percentage of all cancers on a global basis.
Source: After Pindborg 1977

* Figures from "Epidemiological and Vital Statistics Report"

Figure 3.2
Rates of oral cancer per 100,000 population in Singapore 1968-70.
Source: After Shanmugarathnam 1973



Very low incidence rates for oral cancer are found among African blacks, in general. In Asia and Oceania and Australasia group, the lowest incidence rates are found in Japan and among the Maoris in New Zealand. The highest incidence rate is found in Bombay of 19.6 (Waterhouse 1976). But this figure is considerably lower than the rates found in other studies, from different areas in India (Table 3.2).

Table 3.2
Annual incidence rates for oral cancer per 100,000 population in three Indian surveys
Source: After Wahi 1968, Bhargava et al 1975, Pindborg et al 1975

LOCATION	INCIDENCE RATE
Mainpuri, Uttar Pradesh	21.4
Ahmedabad, Gujrat	25.2
Ernakulam	33
Srikakulam	22

The South Australian cancer registry data for the 1977-1980 period demonstrated that 3.2% of malignant neoplasms occurs in the mouth (Roder & Wilson 1983). A total of 16,028 cases of cancer recorded in South Australia in 1977-1980, shows that among the 506 oral cancers (3.2%) that of the lip was highest (285 cases, 56.3%) followed by 79 cases of the tongue (15.6%).

In England and Wales, Binnie et al (1972) in their study showed that 98% of cases of oral cancer occurred in persons over the age of 40 and the peak incidence for individual sites occurs in the 60-70 year age group. Waterhouse in 1974 quotes a mean age for oral cancer of 63.5 for males and 60.6 for females. Langden et al (1977) showed very similar figures - 63.6 for males and 63.7 years for females. When the incidence of oral cancer is compared to the world population between the ages of 35 to 64 years of age, it can be shown that in the populations of Bombay, Puerto Rico and Hawaii, Caucasians have the higest incidence of oral cancer. Roder and Wilson (1983) showed in South Australia that the incidence of oral cancer increased with age.

Oral cancer is more common in males than females. In the USA the total incidence is 17.4/100,000 males and 6.2/100,000 females (Young et al 1981), and this 3:1 ratio represents an average ratio for most parts of the world. Without exception, for all sites, the ratio is changing towards equality for males and females. The Cancer Control Branch (CCB) has stated that the risk of oral cancer is highest at ages 45 to 54 males and 65 to 74 for females.

Apart from lip cancer, the tongue is the most frequent site of cancer within the oral cavity, followed by the floor of the mouth (Langdon 1985). The frequency at which oral cancer may occur at any intraoral site has been tabulated by the Cancer Control Branch (CCB) of the United States Public Health Service and shows that the incidence of tongue cancer was 22% in 1965. In 1977-80, a total of 16,028 cancer cases were recorded in South Australia and among the 506 (3.2%) of oral cancers, 79 (15.6%) was of tongue cancer cases. In the white male population of the USA (American Cancer Society 1983) and the UK (Binnie et al 1972) the lower lip is the most common oral site for squamous cell carcinoma to develop, and this is followed by the tongue (lateral and ventral surfaces). In 1973, Smith showed among selected different countries that Puerto Rico scored the highest in tongue carcinoma distribution and Sweden was seen at the end of the list (Table 3.3). Studying tongue cancer Lucas (1977) found the prevalence highest in Bombay and lowest in Israel. The difference shown by female to male ratios in different countries, at the same time, revealed the geographical distribution of the pathology.

Comparison of incidence figures in the four volumes of Cancer Incidence in Five Continents (Waterhouse et al 1982) shows that tongue cancer is increasing, particularly in USA Alameda blacks, New York State, the German Democratic Republic, Israeli Jews and Slovenian and Hungarian males while falling slowly or remaining static in over one half of the 32 population groups reported.

Table 3.3
Age-standardized average annual incidence rates for malignant tumours of tongue, per 100,000 individuals, males only.
Source: After Smith 1973

Country or region	Tongue		Floor of the Mouth	
	Period I	Period II	Period I	Period II
Puerto Rico	7.1	6.7	7.1	7.8
Connecticut, USA	3.6	3.2	3.7	4.0
Liverpool, England	1.5	1.3	2.0	1.8
Birmingham, England	1.9	1.3	1.7	1.4
Sweden	0.5	0.6	1.1	1.0

Period I

Puerto Rico	Connecticut	Liverpool	Birmingham	Sweden
1962-63	1960-62	1959-63	1960-62	1959-61

Period II

Puerto Rico	Connecticut	Liverpool	Birmingham	Sweden
1964-66	1963-65	1963-66	1963-66	1962-65

A study of cancer of the tongue in Australia for 1959-1964 was carried out from the Department of Preventive Dentistry, University of Sydney in 1967 (Tan 1970). There were 490 men and 214 women with the disease to give a ratio of 2.3:1 (Table 3.4). With malignancy of the posterior third of the tongue, the male to female ratio for 137 patients was 5.2:1, whereas that for 97 patients with cancer of the anterior two thirds of the tongue was 1.6:1. The average age of 691 patients with tongue cancer was 64.7 years and the median age 65.6 years. For women, the average age (66.4 years) and median age (67.9 years) were slightly higher than those for men (average age 63.9 years, median age 64.9 years). The youngest man was aged 21 and the oldest 93, whereas for women the age range was from 23 to 91 years. Only about 4.8% of the patients were below the age of 40 years and about 13.3 % above 80 years, in contrast to 72.1% who were between 50 and 80 years of age.

Table 3.4
The location of 704 cancers of the tongue in 490 men and 214 women in Australia.
Source: After Tan 1970

Site	Number of men	Number of women	Total men + women	Male to female ratio
Posterior 1/3 (base)	115 (83.9)	22 (16.1)	137	5.2:1
Anterior 2/3	60 (61.9)	37 (38.1)	97	1.6:1
Multiple parts (base and anterior 2/3)	4 (50.0)	4 (50.0)	8	1:1
Unspecified	311 (67.3)	151 (32.7)	462	2.1:1
TOTAL	490 (69.6)	214 (30.4)	704	2.3:1

(Percentage figures in brackets)

According to volume III of Cancer Incidence in Five Continents (Waterhouse et al 1976), the tongue cancer incidence shows considerable variation in a number of countries. The highest incidence rates were found in India (Bombay), Puerto Rico, and Brazil (Sao Paulo). Tongue cancer affects more men than women, although this trend is less pronounced in the Scandinavian countries and in England and Wales than in other countries. The male:female ratio decreased rapidly and steadily from 3.9:1 in 1940-9 to 2.2:1 in 1965-9 in the USA (Axtell et al 1972). In England (Manchester) it fell from 7.8:1 in 1932-9 to 1.7:1 in 1960-9 (Easson & Palmer 1976). Tongue cancers in patients below the age of 20 years are very rare. The highest incidence of tongue cancer occurs in the 6th to the 8th decades of life.

Flamant et al (1964) studied the case histories of 904 patients with cancers of the tongue in France between 1943 and 1959. The ratio of male and female patients was 6.7 with 87% male and 13% female patients (Figure 3.3). The average age of the patients was 59 years with the largest percentage being in the 55 year age group (Figure 3.4).

Shedd et al (1968) using data of 973 patients in Connecticut 1935-1959 (Table 3.5) showed that the squamous cell carcinoma is the most frequent malignant lesion of the tongue and men are more frequently involved than women except in Sweden (Table 3.6). Cancer of the tongue was most commonly seen in men in the lower income bracket, in Britain and the mean age at diagnosis was 62 years. Approximately one half of the patients seen at diagnosis have a primary neoplasm still confined to the tongue; two fifths of these are two cm in size or smaller. In about 40-50% of patients nodal metastasis occurs and 20% are more likely to develop (Shaheen 1969).

Flamant et al (1964) showed out of 904 tongue cancer patients 513 cases of tumours originated in the mobile portion of the tongue, 368 tumours in the tongue base, and the origin of the remaining 23 cases were not determined because of poor anatomic description. Among the 513 tumours of the mobile portion of the tongue 396 cases had the site of origin in the lateral border of the tongue, anterior to the insertion of the anterior pillars, 37 in the dorsal surface anterior to the circumvallate papillae; 16 cases in the tip of the tongue and 64 cases on the ventral surface of the tongue, excluding the borders. Of these originating in the base of the tongue, 274 cases were in the posterior portion posterior to the circumvallate papillae. In 94 cases, there were instances of massive or total involvement of the tongue base.

Figure 3.3
Sex ratio of tongue cancer in France between 1943 - 1959.
Source: After Flamant et al 1964

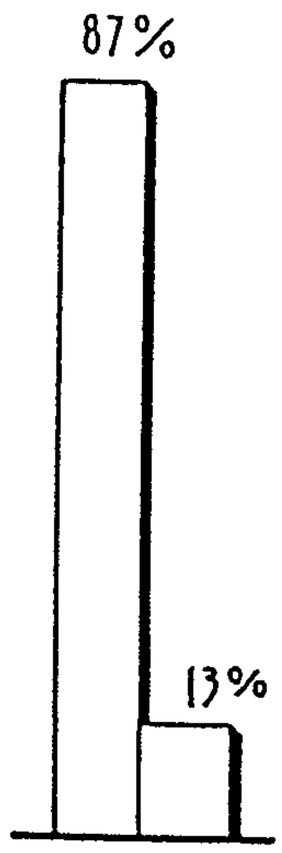


Figure 3.4
Age of patients with tongue cancer.
Source: After Flamant et al 1964

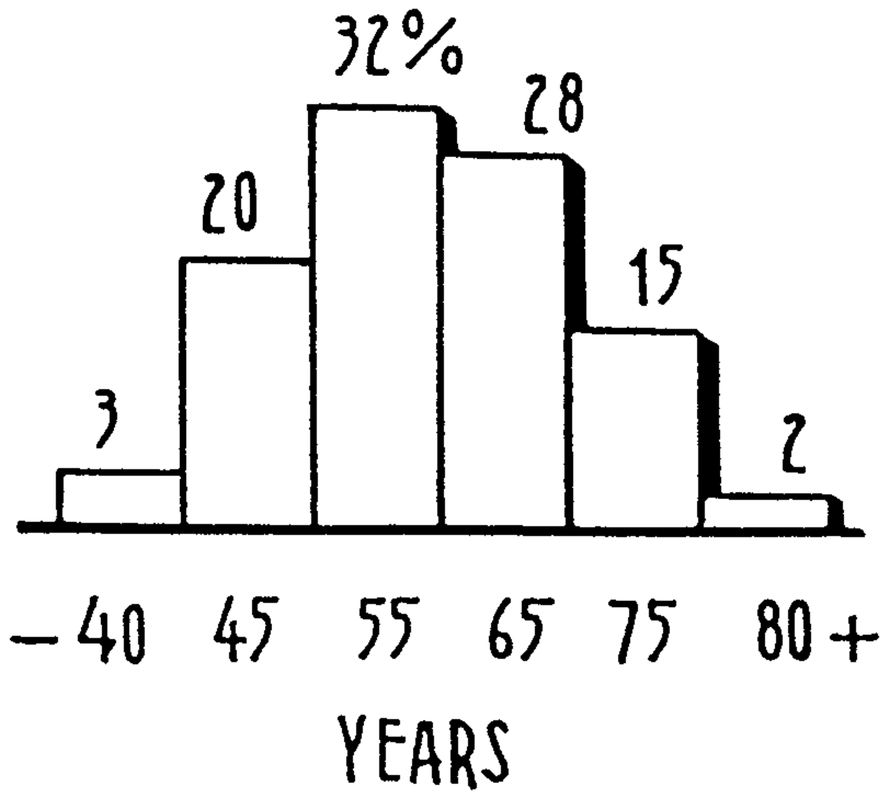


Table 3.5
Number of patients and per cent histologic type distribution by sex - cancer of the tongue in Connecticut, 1935 - 1959.
Source: After Shedd et al 1968

	TOTAL		MALE		FEMALE	
Histologic Type	No.	%	No.	%	No.	%
Squamous cell carcinoma	722	74.2	590	73.1	132	79.5
Carcinoma, NOS	104	10.7	85	10.5	19	11.4
Other specified types	22	2.3	18	2.2	4	2.4
Unspecified types	125	12.8	114	14.1	11	6.6
All types	973	100.0	807	100.0	166	100.0

Table 3.6
Age adjusted rates for incidence of cancer of tongue per 100,000 population, by sex and geographic area.
Source: After Shedd et al 1968

Geographic Area	Period	Male	Female
10 US cities	1947	4.2	0.8
Finland	1953-62	1.0	0.6
Sweden	1958-61	0.6	0.6
Norway	1953-61	0.9	0.5
New York	1958-60	2.4	0.7
Puerto Rico	1950-61	6.6	2.2
Denmark	1943-57	0.8	0.6
S E England	1960-62	1.4	0.6
Connecticut	1935-59	3.3	0.6

The primary tumours tended to favour the left side, (Figure 3.5) with a significantly higher percentage originating on the left (56%) than on the right (44%). The figure 3.6 shows, however, the majority (69%) were in the central area, while 19% were in the intermediate area, and only 12% were situated laterally. The primary tumour was larger at the base of the tongue and smaller at the tip (Flamant et al 1964).

In Australia, the survey performed by Tan (1970), showed of 704 cases analysed, there were 462 patients (65.6%) in whom the specific site of involvement of the tongue was not recorded in the case histories (Table 3.4). Of the remainder, 137 patients (19.5%) had lesions sited on the posterior third of the tongue, 97 (13.8%) had cancer involving the anterior two thirds of this organ and 8 (1.1%) had lesions on the posterior third and anterior two thirds of the tongue.

Tongue cancer in Connecticut is more often found on the anterior two thirds of the tongue (Table 3.7) without inclusion of the base. Classification, based on localized regional spread and distant or remote spread, shows females have a more favourable stage distribution (Table 3.8).

As with incidence, mortality rates for oral cancer vary geographically as well as by sex, site and rate. The number of deaths from oral cancer is an indication of the absolute occurrence of oral cancer as this type of cancer will be lethal in many cases. The American Cancer Society (1983) demonstrated the global variation in mortality from oral cancer and showed Hong Kong and Singapore rank first in deaths for both males and females, followed by France in males and the Philippines in female. Honduras and Nicaragua rank lowest for oral cancer mortality in both series.

In the US (excluding Puerto Rico) the Surveillance, Epidemiology and End Results programme by the National Cancer Institute Bethesda Md reports an overall mortality rate of 3.8/100,000 for cancer of the buccal cavity (including tongue, lip, salivary gland and gum) for the years 1973 to 1977 (Young et al 1981).

Figure 3.5
The laterality of the primary tumours showing a significantly higher incidence of tumours on the left side.
Source: After Flamant et al 1964

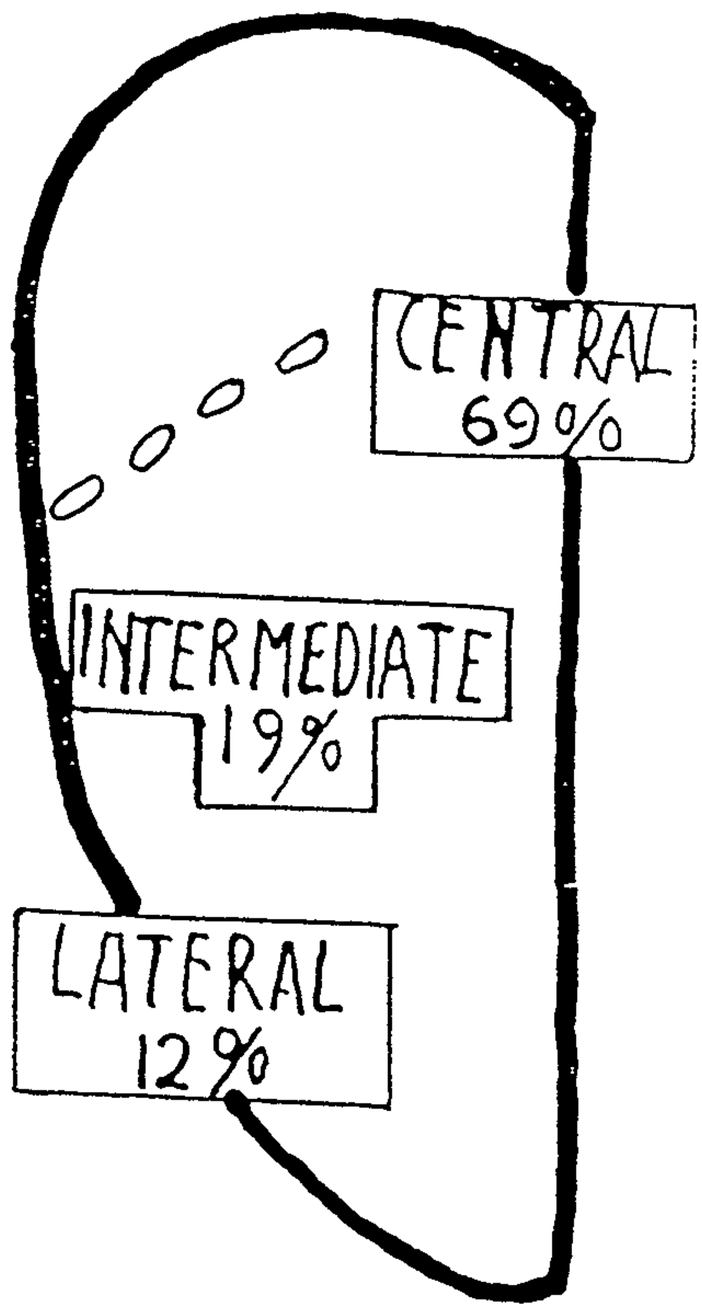


Figure 3.6
Sites of origin of neoplasms of tongue.
Source: After Flamant et al 1964

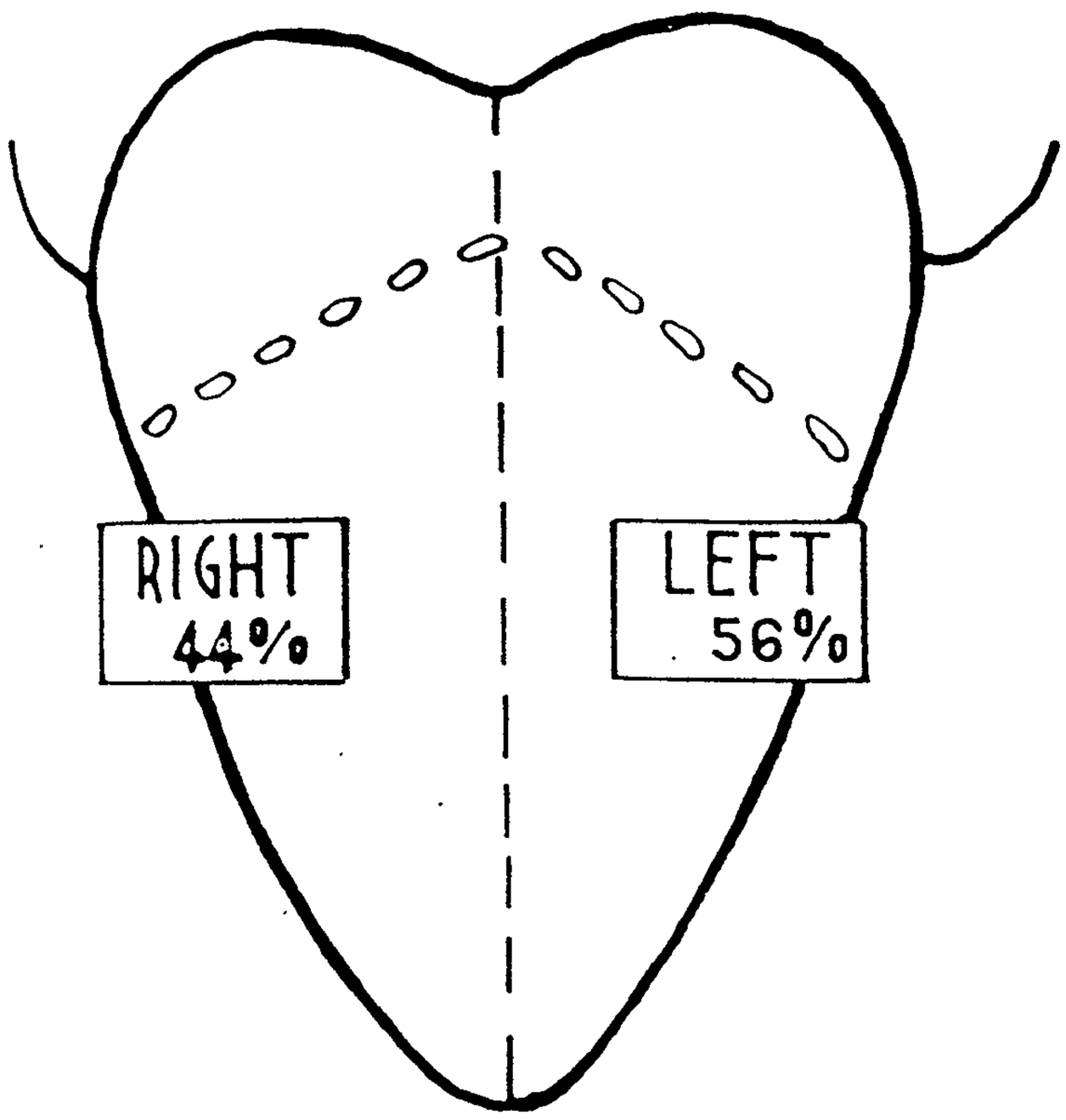


Table 3.7
Number of patients with cancer of the tongue and per cent sub-site distribution by sex.
Source: After Shedd et al 1968

SUB-SITE	TOTAL		MALE		FEMALE	
	No.	%	No.	%	No.	%
Base plus other locations	151	15.5	124	15.4	27	16.3
Base only	203	20.9	172	21.3	31	18.7
Other than base	398	30.9	323	40.0	75	45.2
Tongue, NOS	221	22.7	188	23.3	33	19.9
All locations	973	100.0	807	100.0	166	100.0

Table 3.8
Number of patients with cancer of the tongue and per cent stage distribution by sex
Source: After Shedd et al 1968

STAGE OF DISEASE	TOTAL		MALE		FEMALE	
	No.	%	No.	%	No.	%
Localized	399	47.4	306	44.5	93	60.4
Regional	313	37.2	273	39.7	40	26.0
Distant	47	5.6	39	5.7	8	5.2
Other and unknown	82	9.7	69	10.0	13	8.4
All stages	841	100.0	687	100.0	54	100.0

In England and Wales, the annual mortality rate from lip cancer (males and females) and tongue cancer (males only) were in the latter part of the nineteenth century to a peak in the early part of the twentieth century, after which there has been a steady decline. For females with tongue cancer there has been a steady decline during the past century (Langdon 1985) (Figure 3.7).

In Victoria (Australia), the annual death rate from cancer in the mouth and pharynx over a 30 year period (1928-58) showed a striking decrease in men (Eddy 1960). Tan (1969) continued the work of Eddy (1960) in Australia, using morbidity figures and found that during the period 1959-64 there was a significant decrease in the number of new cases of oral cancer in men (20%) and women (18%).

Phillips (1961) found a decreasing male mortality and a steady female mortality rate of oral cancer incidence in Canada. In the Federal Republic of Germany, Freudenberg (1959) showed a marked decrease in mortality rates during 1933-56, particularly in men. In Czechoslovakia, the incidence of oral cancer decreased in both men (by 34%) and women (by 38%) curing the period 1959-68 (Svejda &d Kosut 1971). During 1947-70, in Texas (USA), a significant decline in the incidence of oral cavity cancer was shown by Szpak et al (1977).

The only exceptions to the worldwide fall in oral cancer incidence are reported by Pindborg (1963) in Denmark where no change in oral cancer mortality from 1943-1956 was found and in Finland where Sainio (1977) found no change from 1953 to 1962.

Easson and Palmer (1976) studied the distribution of intraoral cancer according to the sites and sex compared to the distribution in two different decades (Figure 3.8). The figure shows that the tongue is the most frequent site in the United Kingdom.

Figure 3.7
Death rates in England and Wales from cancer of the lip and tongue, in those aged 35 and over: (a) male tongue (b) female tongue (c) male lip (d) female lip.
Source: After Henk and Langdon 1985, p 10

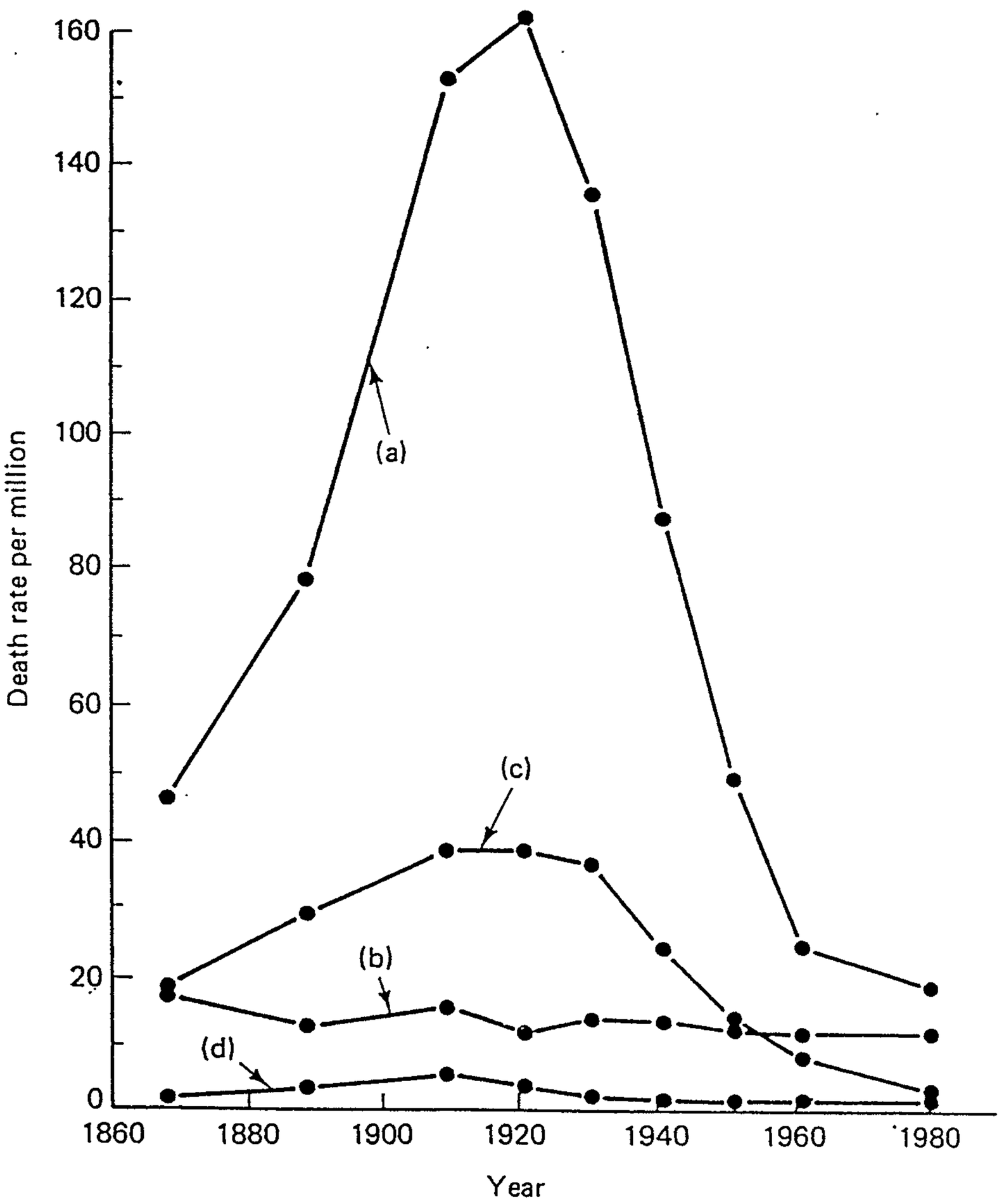
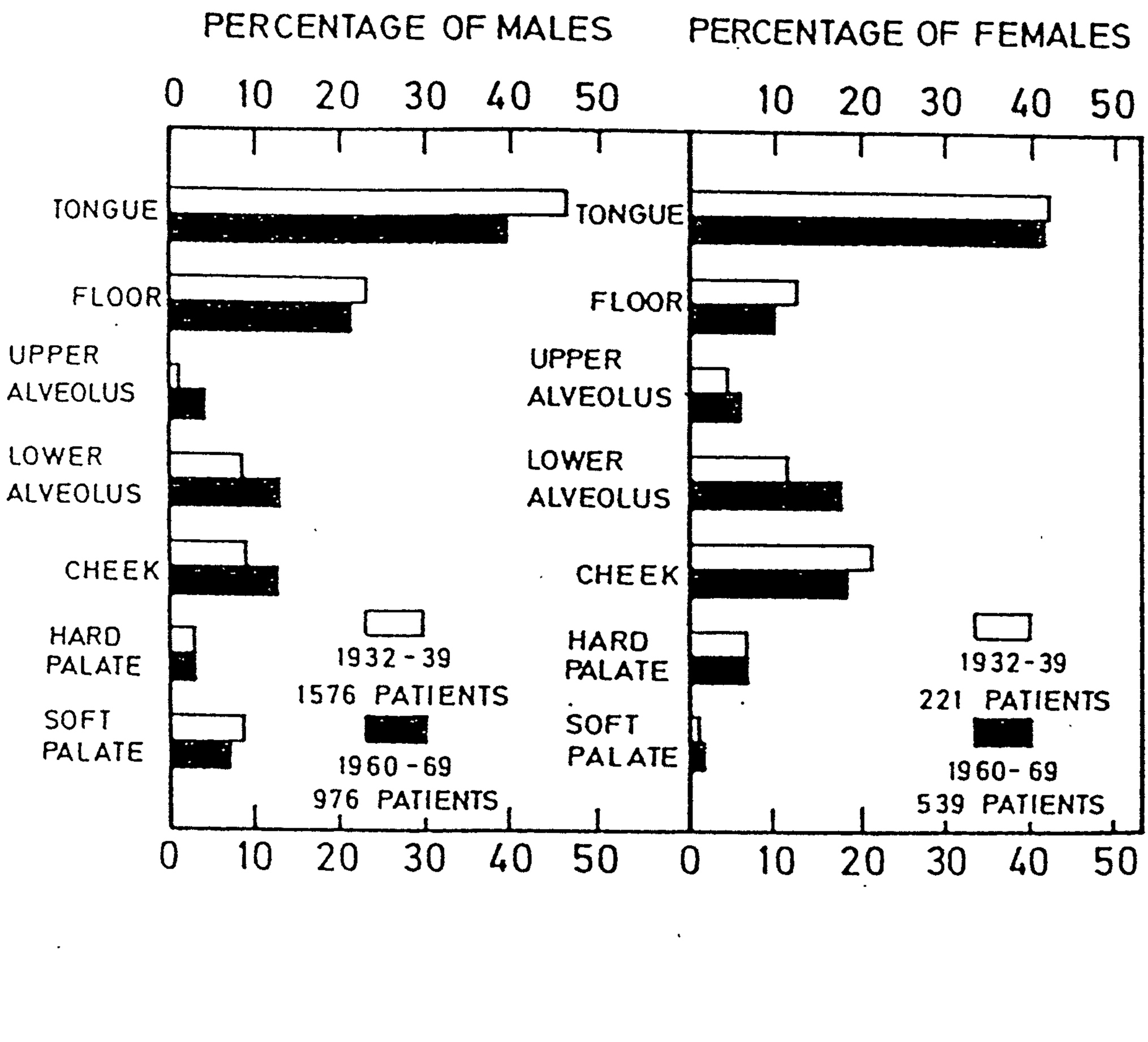


Figure 3.8
Percentage of all registered patients with different tumour sites at Christie Hospital and Holt Radium Institute, Manchester, England.
Source: After Easson and Palmer 1976



In California (USA) the case incidence rate of cancer of the tongue is twice that of cancer of the floor of the mouth. Mean annual deaths from tongue cancer are more than two times that from cancer of the floor of the mouth (Table 3.9).

Tan in 1970 showed that the rate per 100,000 population of patients with tongue cancer (Table 3.9a). It had progressively increased from 0.05, for those in the age groups of 20-24 years, to 13.0 for patients over 85 years of age. He also pointed out the prognosis of patients (Table 3.9b) with cancer of the tongue was poor, the crude cumulative five year survival rate of 479 men was 24.9% (relative survival ratio 0.324) and that for 212 women was 33.7% (relative survival ratio 0.426).

Smith stated in 1968 that the survival experience was related to the extent of metastasis. The American joint committee in Philadelphia in 1968 further suggested that the size of the primary tumour and depth of the penetration are two important factors to measure mortality (Table 3.9c). It was established that smaller lesions with no invasion had better results than lesions which were growing in size along with intrusion. Langdon (1977), depending on variation in local anatomy, demonstrated the significance of the size, fixation and likelihood of early lymph node involvement, which varied significantly according to the site. A lesion of the posterior third of the tongue was shown to have a graver prognosis than that of arising in the lower lip.

In 1977, Fishman and Martinez noted that cancer of the tongue had a 5 year survival for 32.7% patients, with early lesions, and 18.5% for all lesions in Puerto Rico. In the USA male and female survival was found to be 53 and 58% for early lesions and 29 and 52% for all (Figure 3.9). In Britain the five year survival rate amongst the patients varied from 31% to 54% in the anterior two thirds and 22% to 32% for the base of the tongue, during 1943 to 1959. This difference in anatomical locations had been confirmed by certain other studies (Table 3.9d).

Table 3.9
Oral cancer mortality and morbidity by specific sites.
Source: After Weir et al 1969

Oral Cancer Site (ICD Code)	Mean No. of Annual Deaths, California (1960-1962)	Age adjusted average annual case incidence rates/100,000 population (Alameda county, Calif)
Lip (140)	10.33	4.7
Tongue (141)	106.33	3.6
Salivary (142)	26.67	0.9
Floor (143)	42.33	1.6
Other mouth (144)	50.33	1.5
Mesopharynx (145)	47.00	1.7
Nasopharynx (146)	33.00	0.7
Hypopharynx (147)	25.67	1.2
Unspecified pharynx (148)	67.00	0.7
TOTAL (140-148)	408.66	16.6

Table 3.9a
Morbidity of cancer of the tongue in Australia by sex and age groups.
Rate per 100,000 population Australia.
Source: After Tan 1970

Age group	Men	Women	Total
< 20	-	-	-
20-24	0.05	0.05	0.05
25-29	0.1	-	0.05
30-34	0.4	0.2	0.3
35-39	0.5	0.1	0.3
40-44	0.7	0.4	0.5
45-49	1.5	0.8	1.2
50-54	2.8	1.0	1.9
55-59	3.6	1.0	2.3
60-64	6.1	2.7	4.3
65-69	7.9	1.9	4.6
70-74	9.0	3.9	6.2
75-79	12.5	3.8	7.5
80-84	17.6	7.0	11.1
85-	17.9	10.3	13.0
All ages	1.5	0.7	1.1

Table 3.9b
Prognosis of 479 men and 212 women with cancer of the tongue - Australia.
Source: After Tan 1970

SITE	Total Number patients		Crude Cumulative 5 yrs survival rate		Expected 5 yrs survival rate		Relative 5 yrs survival ratio	
	Men	Women	Men	Women	Men	Women	Men	Women
Posterior 1/3 (base)	113	22	13.4	*	77.6	*	0.172	*
Anterior 2/3	60	37	37.9	*	76.8	*	0.494	*
Multiple parts	4	4	*	*	*	*	*	*
Unspecified	302	149	38.4	37.1	76.6	77.2	0.371	0.481
TOTAL	479	212	24.9	33.7	68.2	79.1	0.324	0.426

* Group too small for calculation

Table 3.9c
Survival from primary tumours of anterior 2/3 tongue with no metastasis.
Source: After Smith 1968

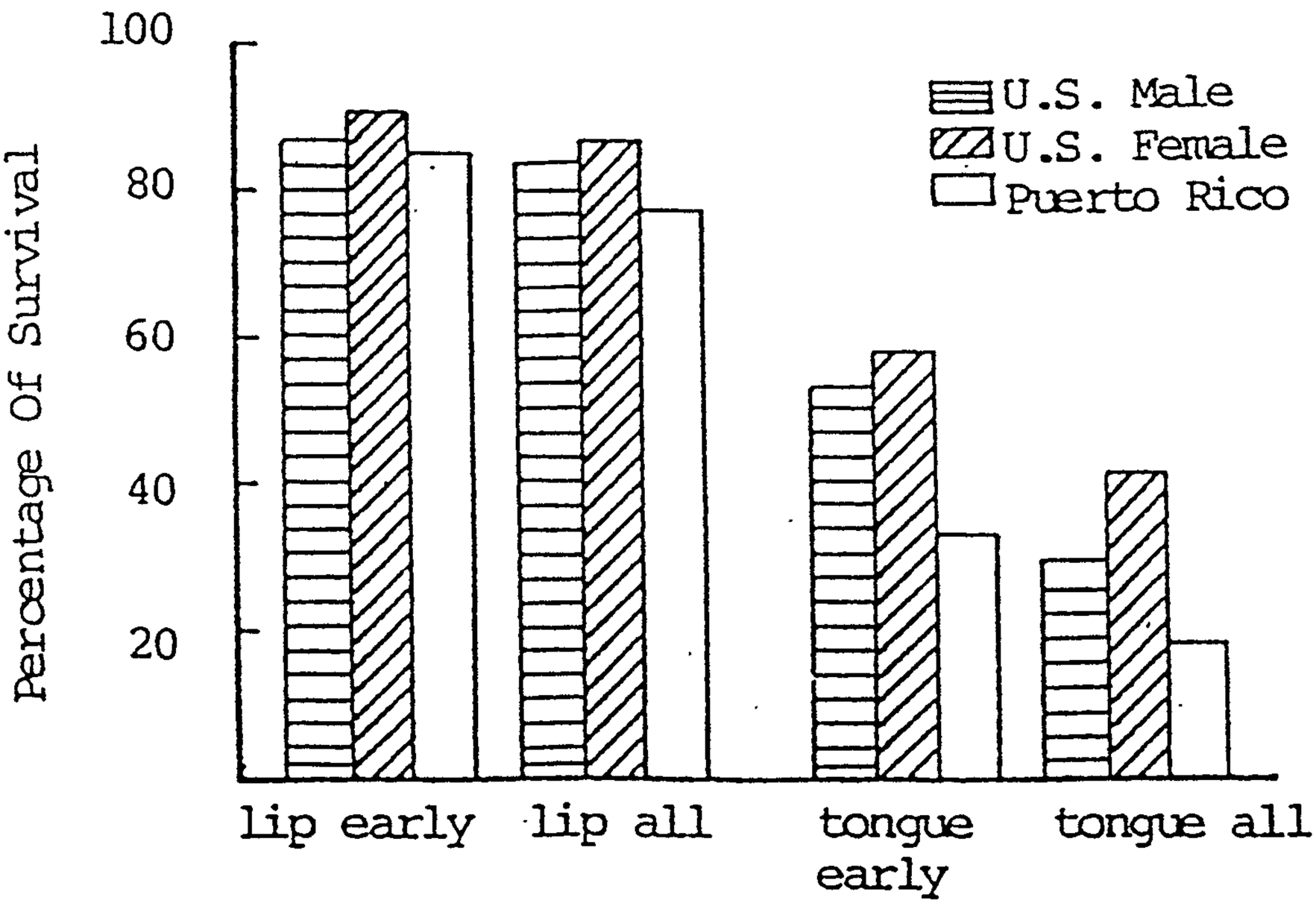
	TONGUE	
Carcinoma	Patients	Survival
T1 0-2 cm	46	76%
T2 2.1 - 4 cm	35	60%
T3 +4 cm	24	50%

T - primary tumours
T1 - tumours 2 cm or less in greatest diameter
T2 - tumours greater than 2 cm but not greater than 4 cm in greatest diameter
T3 - tumours greater than 4 cm in greatest diameter

Table 3.9d
Five year observed survival rates by anatomical location of the tumour tongue cancer in Connecticut, 1935-1959.
Source: After Shedd el al 1968

		Survival Rates (per cent)		
Author	Period	All patients	Location of tumour Base	Anterior 2/3
Cade & Lee	1925-55	27	11	35
Frazell & Lucas	1939-53	35	21	42
Fletcher et al	1948-59	44	32	51
Latourette & Myers	1940-59	21	17	24
Pappe	1932-58	22	13	25
Shedd et al	1935-59	23	13	29

Figure 3.9
Five year survival rate of tongue cancer in USA and Puerto Rico.
Source: Compiled from Fischman 1977



Weir et al (1969) pointed out that the mean annual deaths from cancer of the tongue are more than two times that of cancer of the tongue are more than two times that of cancer of the floor of the mouth, in California (USA). Johnston et al (1977) in a comparison study showed that, patients with oral tongue cancer who have chronically used tobacco and alcohol had an increased rate of death due to intercurrent disease or second primary carcinoma, whereas those who never used tobacco or alcohol enjoyed a little longer life span.

Cancer ranked second only to heart disease as the most frequent cause of death from 1900 to 1982 in the USA. On a global basis oral cancer ranks fourth for men and sixth for women in rank for all cancers. Worldwide the incidence of oral cancer varies enormously. The highest reported rates are in India. Although living in the same country the prevalence might vary between different ethnic groups due to different habitual patterns. The incidence of oral cancer increases with age and is more common in males than females. Apart from lip cancer, the tongue is the most frequent suite of cancer within the oral cavity.The tongue cancer incidence shows considerable variations between a number of countries. The highest incidence rates are found in India (Bombay), Puerto Rico and Brazil (Sao Paulo). Tongue cancer affects more men than women, although this trend is less pronounced in the Scandinavian countries and in England and Wales than in other countries. The highest incidence of tongue cancer occurs in the 6th to the 8th decades of life.

Mortality rates for oral cancer vary geographically as well as by sex, site and race. Singapore and Hong Kong rank first in deaths for both males and females, followed by France in males and the Philippines in female. Honduras and Nicaragua rank lowest for oral cancer mortality in both sexes.

4 PREVENTION AND CONTROL

Even though the improved and sophisticated methods of treating oral cancer in the last decade could not decrease the oral cancer mortality rate, the figure is unsatisfactory, when it is realized that the oral cavity can be readily examined and requires no special facilities. Early oral lesions, unlike tumours of many other sites, give rise to symptoms. About 85% of oral cancers are visible either directly or indirectly with a mirror and the rest, 11%, are palpable on careful clinical examination (Laskin 1974).

Nevertheless, despite the advantage of the visibility of oral cancers, between 27% and 50% of patients present with late lesions (Binnie et al 1972, Langdon et al 1977). Cook and Tapper-Jones (1977) analysed the delay in diagnosis and treatment and cite the fact that many of these patients are elderly and frail and as a result delay making the effort to visit their doctor or dentist. Many wear dentures and are accustomed to discomfort and ulceration in the mouth and show no urgency in seeking treatment. Furthermore, the practitioner himself is not often suspicious that the lesion is malignant, so may initially treat it with antifungal therapy, antibiotics, steroids and mouthwashes, thus contributing further delay in ultimate diagnosis and treatment.

4.1 EARLY DETECTION

Early diagnosis of oral cancer is of utmost importance in improving survival. Delays in diagnosis can only lead to local extension of a lesion and increase the risk of metastatic spread, thereby causing greater morbidity and mortality. A good history and physical examination, including inspection and palpation of the oral cavity, oropharynx and the neck by the dentist are the best methods of early detection of these tumours.

The decision to remove an organ or part of an organ for prophylaxis/prevention requires consideration of several factors. The presence or absence of symptoms, statistical evidence of future cancer, the risk from surgery and the postoperative functional impairment and alteration in appearance.

Oral cancer, clinically, may present as an ulcer, a swelling, a fungating mass, an osteolytic radiolucency, a pathologic fracture, facial asymmetry, a white indurated zone, an area of hyperpigmentation, an oro-antral fistula, an oro-facial fistula, a fluctuant mass, zones of erythema or extraction sites which do not heal. Pain may present depending upon if there is any secondary infection or if there is impingement on growth during mastication. Halitosis, haemorrhage, ulceration, rapid growth, rapid change in colour, trismus, difficulty in eating and difficulty in swallowing are some of the more prevalent signs and symptoms of advanced pathology noted by Bolden (1977).

The tongue is frequently a site of oral carcinoma, and this site always signifies a serious prognosis. The majority of the tongue cancers occur in the middle third of the lateral margins, extending early in the course of the disease onto the ventral aspect and floor of the mouth. Approximately 20% occurs on the anterior third and only 4% on the dorsum (Frazell & Lucas 1962). Those rare cases occurring on the dorsum of the tongue are usually associated with a history of syphilitic glossitis. Cancer of the tongue usually starts as a small ulcer and gradually infiltrates deeply and extensively, resulting in the tongue losing its normal motility (Guralink 1984). It may occur as an ulcer in the depths of a fissure or as an area of superficial ulceration with unsuspected infiltration into the underlying muscle. However, if the filiform and the fungiform papillae undergo atrophy, leaving a smooth denuded surface on the dorsal surface of the tongue, this region becomes highly susceptible to leukoplakia and results in a greater risk of the development of carcinoma. Later in the course of the disease often a more typical malignant ulcer of several centimetres in diameter usually develops. The ulcer is hard in consistency with heaped-up and often everted edges. The floor is granular, indurated and bleeds readily. Often there are areas of necrosis. The growth infiltrates the tongue progressively, with increasing pain and difficulty with speech and swallowing. By this stage pain is often severe and constant, radiating to the neck and ears (Guralink 1984).

Ulcers on the tongue may be associated with rough, sharp or irregular restorations and, if

there is any doubt about their possible implication, careful smoothing of any offending tooth or restoration should result in rapid resolution of such a traumatic ulcer. Failure to heal must raise immediate suspicion and further investigation should be carried out. If the ulcer does not fit the clinical picture, then this should strike a discordant note. Although apthous ulcers, for example, are common in the younger age groups, they become less of a problem with age, and the sudden appearance of ulceration in an older person, particularly if isolated, is clearly unusual and should be a stimulus to further investigation. Erythema migrans (geographical tongue) may frequently present with a most alarming appearance, but is, nevertheless, benign. Erosive lichen planus, once it affects the tongue may, on superficial examination, be mistaken for erythema migrans, but is potentially more sinister and a cause for anxiety (Williams 1990). Median rhomboid glossitis, on the other hand, which is in the past has sometimes been mistaken for carcinoma (Ogus & Bennett 1978) is now thought to be a manifestation of candidiasis and not associated with a malignant potential.

The tragic aspect of carcinoma of the tongue is that it metastasizes early in its course of development. Both submandibular and jugular nodes become involved. Owing to the relative early lymph node metastases of tongue cancer, some patients present with no symptoms other than "a lump in the neck" (Frazell & Lucas 1962).

Much of the current research in oral cancer is devoted to improving methods of detection, diagnosis and prognostication (Howell & Wright 1988). Several substances have been investigated as possible biochemical serum markers of oral cancer which would be useful for screening and early detection as well as for following patients after treatment. The biochemical markers which have been studied and show some potential include carcinoembryonic antigen (CEA), ferritin, ß2- microglobulin, thymidine kinase, alkaline deoxyribonuclease, IgA, and IgE. Serum CEA levels have been found to be elevated in head and neck cancer patients and to correlate with tumour burden; however, they were not predictive of survival and are also elevated in smokers without tumours (Silverman et

al 1976). Elevated CEA levels have also been detected in the saliva of oral cancer patients. Serum ferritin may be a useful marker as it was found at elevated levels in head and neck cancer patients. These levels were higher in more advanced stages of disease, returned to normal within 5 months after successful treatment, but remained at high levels in patients with a poor prognosis (Maxum & Jeltri 1986). Some 8.5-12% of oral cancer patients have elevated ß-2 microglobulin concentration in tumour tissues (Wennerberg et al 1984). Serum thymidine kinase activity had been found to be elevated in oral cancer patients (Scully 1982) as has serum alkaline deoxyribonuclease. Serum IgA and IgE levels were shown to be elevated in head and neck cancer patients (Scully 1982, Katz et al 1978) and have been noted as useful markers.

Specific histochemical staining methods of enzyme systems have been applied to oral smears, in order to differentiate malignant and benign status. Camilleri in 1968 observed changes in acid phosphatase reaction. Histochemical studies evaluated the presence of acid phosphatase in epidermoid carcinoma and the absence of alkaline phosphatase. A positive activity for alkaline phosphatase and aminopeptidase is showed by tumour stroma. Non specific estarase, ß glucuronidase, aminopeptidase, succinate dehydrogenase, lactate dehydrogenase, malate dehydrogenase, ß hydroxybityrate dehydrogenase, NADP dependent dehydrogenase, glucose-6-phosphate dehydrogenase, isocitrate dehydrogenase (Mori 1968) are the name of the enzymes found in histochemical analysis. If the alkaline phosphatase gives the negative reaction, it is a definite prediction in oral carcinoma, and valuable in preventive measure (Mori 1968).

Toto and Garginlo (1985) stated that continuing research in finding histochemical markers that may distinguish premalignant or malignant epithelium from non malignant mucosal lesions. Some promise is shown in cell surface glycoconjugates, which specially bind to plant lectins. A number of different lectins are available which bind to different terminal sugar residues that are generally located on the cell surface (Toto & Garginlo 1985). The lectins can be conjugated with markers such as fluorescein or biotin to allow visualization

by standard immunohistochemical methods (Toto & Garginlo 1985, Dobelsteen & MacKenzie 1978, Prime et al 1985).

The distribution of fibronectin and laminin in leukoplakia and squamous carcinoma of the oral cavity was found to be essentially the same as that in normal oral mucosa, with the exception that laminin was lost around islands of deeply invasive carcinoma (Meyer et al 1985). Henokinase, an important enzyme in glucose metabolism, was found by histochemical studies to have the same distribution in oral squamous carcinoma as in leukoplakia or normal oral carcinomas than in adjacent normal appearing epithelium (Matsumura et al 1983).

Mashberg noted the evaluations of the usefulness of tolonium (toluidine blue) rinses for screening of patients for oral cancer in 1981 and 1983. The research which has been done in the file of colposcopy of premalignant and malignant neoplasms of the cervix may have applicability to oral cancers. The colposcope is essentially a stereoscopic operating-type microscope which can differentiate between benign lesions, varying degrees of dysplasia, and squamous cell carcinoma with great accuracy (Kolstad 1983, Javaheri & Fegjin 1980).

4.2 DIAGNOSIS AND INVESTIGATIONS

4.2.1 Biopsy

The first emphasis for early diagnosis must be on clinical suspicion. Once the suspicious lesion is identified perhaps the next most important step is biopsy. In most instances oral malignancies can be adequately biopsied under local anaesthetic with little or no resultant morbidity. Mashberg in 1983 reviewed the use of tolonium chloride (toludine blue) oral rinse as a screening method for suspicious oral lesions. Combining the results of both toludine blue staining with clinical suspicion Mashberg was able to reduce his false-negative (under diagnosis) rate to 1.9%. It seems, therefore, a very useful adjunct to the clinical evaluation of oral mucosal lesions and helpful in the selection of biopsy sites. A positive result with toludine blue rinse makes biopsy mandatory (Mashberg & Meyers 1976).

When it is proposed to take tissues for diagnostic purposes, it must be decided whether the whole lesion is to be removed and submitted (excisional biopsy) or a portion of the lesion (incisional biopsy). Excisional biopsy is carried out where the lesion is small and it, together with an area of normal tissue around it, can be removed and repaired without mutilation. In incisional biopsy, a representative sample together with some adjacent tissue is taken, rather like a slice of cake, and the incised normal tissue repaired by a suture (Bramley & Smith 1990). The biopsy specimen should be adequate and be obtained from a representative portion of the tumour so that the pathologist can examine the tissue properly.

Although biopsies of intraoral lesions ordinarily present no difficult technical problems, tumours in the base of the tongue may escape detection even by an experienced examiner. For tumours in this site, it is frequently necessary to examine the patient and perform the biopsy with the patient under general anaesthesia. Even if the cervical lymph nodes are palpable and suspected of being involved in metastatic carcinoma, the biopsy specimen should always be obtained from the primary lesion.

Other than the excisional and incisional biopsy methods the other several biopsy techniques available are aspiration, punch and Silverman needle biopsy.

Excisional Biopsy

Excisional biopsy refers to the total removal of the lesion surgically. It is the method of choice when the size and the location of the lesion permit a wide margin of normal tissue (not less than 0.5cm in all directions from the periphery of the lesion) to be included in the specimen. The depth of the lesion is also an important factor in its removal. If excisional biopsy is performed, however, exact mapping of the site is essential for future planning of curative surgery. The placement and the extent of the surgical incision should also be taken into consideration. It should be placed within the site of future curative surgical approach.

Incisional Biopsy

Incisional biopsy involves removal of a wedge of tissue that contains normal and suspected malignant cells. It gives the pathologist the ability to differentiate a metastatic lesion from a primary one where changes can be seen at the interface between the normal and malignant tissues. If the lesion is extensive, several representative portions may be removed and should be marked with proper identification to indicate the area from which they were taken. After the section of the tissue has been cut with a sharp knife, a dissemination of the malignant cells may be prevented by immediately cauterizing the wound to coagulate the tissue fluid and the blood in the exposed vessels that have been cut.

Aspiration biopsy is the utilization of a thin needle to aspirate cells and occasional small fragments of tissue for cytologic examination. Aspiration biopsy is specially designed for fluid containing lesions and widely used in obtaining bone marrow specimens. Punch biopsy obtains a small portion of the tissue by hitting or punching out a piece of tissue, by the punch forcep. The oral cavity and the surrounding area rarely require use of the punch biopsy technique. The procedure of Silverman needle biopsy is useful in deep seated lesions. With this needle, one can remove a strip of intact tissue, 1.5mm wide and about 1.5cm long, which can be sectioned and studied like an ordinary surgical biopsy.

For accurate histologic interpretation biopsy tissues should be obtained very carefully to preserve details. Bently in 1974 suggested sharp, cold scalpel excision with minimal crushing and manipulation. Tearing, mutilation, anaesthetic application and antiseptic application should be avoided. Cautery should be performed only after surgery for controlling bleeding. Haemorrhage is usually arrested by pressure, cautery or with a suture. The specimen is immediately immersed in a wide-mouthed bottle of fixing solution containing ten times its volume of 10% buffered formalin or formal saline. The fixatives of the biopsy specimen also include Helly's fluid (potassium dichromate and bichloride of mercury) or formalin-alcohol-calcium acetate combination. After the fixation is completed the specimen is processed in paraffin, sectioned at six microns, stained with haematoxylin and eosin and read under microscope.

4.2.2 Exfoliative Cytology

In 1940, Weinmann was the first to study the keratinization of the oral mucosa in smears taken from different areas of the oral cavity. After the publication of the monograph by Papanicolaou and Traut (1943), which created a basis for the cytodiagnosis of gynaecologic cancer by the examination of exfoliated cells, the development of oral cytology slowly began, but was and is still the subject of many controversies (Banoczy 1976).

Exfoliative cytology is a technique used for observing the microscopic morphology of individual cells after they have been obtained from a tissue, spread on a slide, fixed and stained. Because the oral epithelium renews fairly rapidly (probably within two weeks) and most superficial cells of the mouth contain nuclei, surface scraping may be reliable indicators of dysplastic or neoplastic changes. The usefulness of cytology is increased in oral cancer detection by the fact that over 95% of oral cancers are epithelial in origin. Direct smears allow for accurate sampling of a lesion and aid complete screening (Silverman et al 1977). Numerous reports show the fact that use of oral cytology has accelerated biopsy of lesions which did not clinically appear to be oral cancers, thus

leading to the early diagnosis of malignancies which would otherwise have remained temporarily unsuspected (Sander 1964, Hayes et al 1969, Folsom et al 1972, Allegra et al 1973).

A clean cotton-tipped applicator or wood spatula is used for collection of specimens. If the area to be scraped is dry, the applicator or spatula should be moistened. Saliva or tissue excretions are usually sufficient to prevent dehydration. The scraping should be immediately smeared on the centre area of the slide. For fixation, 70% alcohol is adequate. Commercial spray fixatives or hair sprays are satisfactory and also make it easier to handle the specimen. .The smear is stained by a modified Papanicolaou-Traut technique using Mayer's hematoxylin, orange G, eosin and light green. After staining, the nuclei appear blue and epithelial cells range from non keratinized blue cells to precornified red cells and highly cornified orange cells, according to their origin from various areas of the oral mucosa (Table 4.1).

In Table 4.2, general features of normal intraoral squamous cells are shown. The criteria upon which cytologic interpretations of malignant cells are based are as follows:

A. Enlarged nuclei.
B. Variation in nuclear size and shape (pleomorphism).
C. Prominent and irregular nuclear border.
D. Increased nuclear-cytoplasmic ration (decreased cytoplasm).
E. Multiple prominent and irregular nuclei.
F. Hyperchromatism (increased nucleoproteins).
G. Abnormal chromatin pattern and distribution.
H. Discrepancy in maturation (extreme variations).

Cells from benign lesions may have atypical appearances, but they seldom display enough criteria to cause them to be misinterpreted as malignant (Silverman 1965) (Table 4.3).

Summarising the use and place of exfoliative cytology in the early diagnosis or oral carcinomas, the method might serve as an important aid to diagnosis if its limitations are taken into consideration. Exfoliative cytology is effected in early ulcerated oral carcinomas and erosive leukoplakias, in these cases the early diagnosis and indication for a biopsy is of great importance.

Table 4.1
Cell distribution according to staining reaction of cytoplasm of oral cancer.
Source: Watnabe 1968

	Blue	Blue-Red	Red	Orange
Hard Palate	1	6	15	78
Gum	8	5	26	61
Tongue	14	2	51	33
Buccal Mucosa	52	7	35	6

Figures showing %.

Table 4.2
Appearance of surface cells in relation to location of oral cancer.
Source: Silverman 1981

Hard Palate, Gingiva, Dorsal Tongue	Mature Cells: High degree of cornification and some cells anucleated.
Buccal and Labial Mucosae	Intermediate Maturity: Nucleated basophilic and acidophilic staining cells.
Floor of Mouth, Ventral Tongue, Soft Palate, Oropharynx	Least Maturity: Preponderantly basophilic cells with large nuclei.

Table 4.3
Report of smears of oral cancer.
Source: Silverman 1965

Positive	Criteria for malignant cellular change are observed.
Negative	No malignant cells are observed in the specimen. These cells may appear atypical but do not demonstrate malignant criteria. In the event of continued clinical suspicion or persistence of a lesion, a negative report should not be taken as conclusive. This is particularly true in hyperkeratotic lesions (Sandler 1966, Stahl et al 1967, Shklar et al 1970, Rovin 1967).
Suspicious or Inconclusive	Cells seen that do not fulfil the malignant criteria adequately to allow a positive report, yet reveal enough deviation from normal to indicate follow-up studies should be performed.
Inadequate	Either cellular morphology is not preserved adequately for interpretation, or the presented material is too scanty to be representative specimen.

In the course of serial examinations, clinically unsuspected early oral carcinomas might be detected by the use of exfoliative cytology, and in extensive lesions the site of the biopsy might be selected. In 1972, Folsom et al concluded that the oral cytology should be used as an adjunctive measure in the evaluation of visible oral lesions; but it should not be used in preference to, or as a substitute for, biopsy, unless biopsy is specifically contraindicated.

4.2.3 Toluidine Blue

Toluidine blue (tolonium chloride) is an acidophilic metachromatic dye which is fixed by cellular DNA and RNA (Mashberg 1980, 81, 83, 84; Silverman et al 1984). Because of chromatin aberrations, malignant cells, unlike normal cells, will retain the dye following attempted decolourization with acetic acid. This property enables toluidine blue to be used as an aid in distinguishing between malignant and nonmalignant lesions.

The technique is that the suspicious area is painted with a 1% aqueous solution of toluidine blue for ten seconds. The mouth is then thoroughly rinsed with a 1% solution of acetic acid. The toluidine blue is bound to DNA present in the superficial cells and resist decolourization by the acetic acid. Dye binding is, therefore, proportional to the amount of DNA present and the number and size of superficial nuclei in the tissues. When the dye is applied to the epithelium of a malignant lesion and viewed clinically, the area will appear dark blue.

A toluidine blue mouth rinse can be used as a screening procedure for the detection of asymptomatic, clinically occult epidermoid carcinoma of the mouth and oropharynx in high-risk patients. Silverman et al in 1989 stated that the sensitivity of the toluidine blue rinse in detecting asymptomatic lesions with poor clinical signs is as high as 91%. This is impressive considering that lesions of this type would most likely remain undetected until they become symptomatic. The sensitivity of the dye for detecting noninvasive dysplastic lesions is considerably less. False-positive findings occur with traumatised tissue, ulceration and granulomatous disease, as well as normal filiform papillae. Sabes et al in 1972 criticize the technique and condemn its use on the grounds that false-negatives occur so frequently as to render the test unreliable. In their report they showed, in an experimentally induced carcinoma in the hamster cheek pouch, 65.6% false-positives and 21.4% false-negatives in early carcinomas, and 12.1% false-positives and 39.6% false-negatives in old tumours. Still several authors like Shedd et al (1967), Strong et al (1968) and Meyers (1970) found this test valuable.

4.3 SURGERY

The literature on treatment of tongue cancer is both voluminous and controversial. It reveals not only differences in approach from one country to another, but also changes in modalities within the same country or within the same hospital. Frazell in 1971 discussed some of these problems and concluded that early cancer of the anterior two-thirds of the tongue can be controlled by either local surgery or local radiation in a high percentage of cases.

Most clinicians prefer surgery for cancers of the anterior part of the tongue. In France, however, these tumours are, to a large extent, treated by interstitial therapy with iridium, ^{192} Ir (Pierquin et al 1971). Cancer of the base of the tongue are usually treated either by surgery or by irradiation. The 5 years survival rates are much lower than for anterior tongue cancers, varying from 11% to 32% (Shedd et al 1968).

Frazell and Lucas in 1962 in their study (1939-1953) state that treatment methods of cancer of the tongue have varied considerably throughout the years. Factors influencing the choice of one method over another have been numerous but have in common the aim to cure more patients. Such choice was based on the clinical evaluation of the individual patient, as his probable response to treatment. Although the series as a whole, irradiation or surgery was employed almost equally as the initial treatment for the primary lesion, the proportion of patients treated by this method differed according to the anatomic site of involvement (Table 4.4). It is significant that four-fifths of the surgically treated patients had lesions involving the anterior two-thirds of the tongue. It should also be noted that 22% of the surgically treated patients were secondary cases, who for the most part had been prior irradiation failure (Frazell & Lucas 1962).

A small superficial lesion can be excised completely an intraoral approach, leaving a normally functioning tongue. A margin of at least 1cm, preferably 1.5cm, around the entire visible and palpable disease must be controlled by frozen section at the time of surgery. Even excisions as great as hemiglossectomy result in little postoperative deformity when healing is complete. The remaining tongue musculature hypertrophies, and after some months form and function are virtually completely restored (Henk 1984).

Table 4.4
Choice of initial treatment of the primary lesion * of tongue cancer.
Source: Frazell and Lucas 1962.

Site or Condition Primary Lesion	Type of Treatment Irradiation	Surgery
Anterior 1/3	81	204
Middle 1/3	294	357
Posterior 1/3	282	90
Dorsum	20	39
Entire tongue	5	6
Primary healed ☼	1	4
	683	700

* The total of primary lesions that were treated was 1383.

☼ Recurrence after previous treatment.

Following excision of a small lesion, traditionally the cut surface of the tongue is either closed primarily by direct suture, or if this is not possible, the defect is covered by a split skin quilted graft (McGregor 1975). Direct suture often distorts the remaining tongue and owing to postoperative oedema is very painful initially. Split skin within the oral cavity is unsightly and often becomes infected with Candida albicans. A better technique is to perform the surgical excision with a cutting diathermy and then, after tying off any major bleeding points, to go over the raw surface with a ball-shaped coagulator.

The advantage of surgical excision is promptness of treatment and completion within a short period of time. The excised specimen is available for microscopic evaluation of the margins. The major disadvantage of surgical excision are tissue loss and the required removal of adjacent functioning structures (Murray 1984).

4.4 RADIATION THERAPY

Radiation therapy is the treatment of diseases with ionizing radiation. Ionizing radiations are electromagnetic and particulate high energy that cause the dislodgment of electrons from the atoms of the tissue and the production of electrically charged ion pairs. The types of ionizing radiations most commonly used in radiation therapy are x-rays, gamma rays and beta rays (Chen 1986).

X-rays and gamma rays, also called photons, are electromagnetic radiation. Beta rays are beams of electrons, particulate radiation.

Interstitial irradiation with needle implant is commonly employed for the treatment of the anterior two thirds of the tongue. Needles are inserted vertically to the dorsum of the tongue. The usual dosage is 5000 to 7000 rad in five to seven days. For advanced tumours, a combination of external irradiation and interstitial irradiation is necessary: external radiation, 5000 rad in five weeks, followed by interstitial irradiation, 3000 rad in four days.

The dose required to sterilize a given neoplasm depends upon the microanatomy, size, and location of the tumour. The advantage of radiation therapy is its ability to treat a larger volume than may conveniently be removed surgically. The disadvantages related to the prolonged treatments, radiation injury to normal tissue traversed by the beam, and depression of salivary gland function and resultant radiation caries, osteomyelitis and soft tissue necrosis.

Tan (1970) in his survey showed in the treatment of primary cancer of the tongue, radiotherapy was used more frequently than surgery in the hospitals in Australia. Of 663 patients who received treatment for the primary disease, 73.8% were treated by radiotherapy; 17.5% by surgery and 8.7% by a combination of two methods (Tan 1970).

Combinations of Surgery and Irradiation

With the extreme radiosensitivity of lymphomas combined treatment is unnecessary. However, the need for doses exceeding normal tissue tolerance in some squamous and adenocarcinomas of the oral cavity often necessitates a combination of radiation and surgery. Surgery is able to remove the major bulk of the tumour and the resistant central portion, and radiation is then able to sterilize the microscopic routes of spread in the lymphatics and tissue planes not resected in the standard excisional procedures (Galant et al 1981).

4.5 CHEMOTHERAPY

Both systemic and regional (perfusion, infusion) use of cytotoxic chemotherapeutic agents in oral cancer have been actively explored. Chemotherapeutic agents may attack widespread disease and may augment the local effects of surgery and radiation therapy. To date (Murray 1984), most chemotherapeutic programmes have been palliative or adjunctive. Recently, the increasing use of multiple agents in combination with chemotherapy has produced dramatic decreases in tumour bulk and, therefore, its effects seem promising.

The exploitable difference between cancer cells and normal cells is very small. The interference by a drug in the metabolic process of the cancer cells occurs also in the normal cells. However, the effect on the normal cells is slightly less, thus allowing them to recover. Because of the relatively low therapeutic index of most of these drugs, toxicities may become cumulative during administration.

The dosage of the chemotherapeutic agents are commonly based on body surface area or body weight. Dosage is expressed as mg/m^2 (milligrams per square meter of body surface) or mg/kg (milligrams per kilogram of body weight). Body surface can be calculated easily from a body surface nomogram chart using height and weight measurements.

Chemotherapeutic agents can be classified into groups according to their mechanism of action. They include alkylating agents, antimetabolites, antibiotics, plant alkaloids, hormones and miscellaneous agents. Of the 46 agents currently in use, the following are clinically effective in the treatment of oral cancer. They are used singly or in varying combinations. The agents are methotrexate, 5-fluorouracil, hyroxyurea, cyclophosphamide, vincristine, bleomycin, doxorubicin hydrochloride (adriamycin), and cis-diamminedichloroplatinum (cis-platinum). Of the mentioned drugs the most active chemotherapeutic agents are cis-platinum, bleomycin and methotrexate (McAndrew 1990).

Methotrexate

Methotrexate, a folic acid antagonist, is the most extensively studied drug in head and neck cancer (Goldsmith & Carter 1975, Bleyer 1978). Response rates in the range 20-80% have been reported ever since its introduction in the early 1950s. Methotrexate has been given extensively by intra-arterial (IA) infusion as well as by intravenous (IV), intramuscular (IM), and preoral routes. The conventional dose and schedule of 40mg/m^2 of body surface intravenously once or twice weekly gives a response rate up to 50%.

Its mechanism of action is by inhibiting the folate-reducing enzyme, dihydrofolate reductase, which catalyzes the reduction of folates to dihydro- and tetrahydro-forms and thereby inhibits DNA synthesis. At high doses of methotrexate, the drug will enter the normal cells by the transport system and diffusion, but it will enter the tumour cells only by diffusion because the tumour cells lack the transport mechanisms. Calcium leucovorin rescue has been used at varying time intervals after administration of methotrexate in an effort to improve its therapeutic index. Leucovorin can enter and rescue normal cells but not the tumour cells (Frei et al 1975).

Bleomycin

Bleomycin is a glycopeptide antitumour antibiotic isolated from Streptomyces verticillis in Japan, and found to have activity against a variety of squamous cell neoplasms. It has been widely used in the treatment of head and neck neoplasia, with a very wide range of reported response rates. Bleomycin has a remarkable spectrum of side effects, different from those seen with other cytotoxics. Bone marrow toxicity is mild or absent, probably on account of a 'bleomycin hydrolase' enzyme present in normal bone marrow which deactivates the drug. Immediate toxicities which may be seen are fevers, skin reactions and abdominal pain, while most troublesome long-term effect is pulmonary fibrosis (Calvert 1985). Bleomycin usually has been given at a dose of 15 units/m^2. It may be given subcutaneously, intramuscularly, or intravenously twice weekly (Sako & Razack 1986).

Cis-Platinum

Cis-platinum is a new agent (Galant et al 1981) which has demonstrated activity in head and neck cancer. Structurally it is an inorganic complex formed by a central atom of platinum surrounded by chlorine and ammonia ions in the 'cis' position in the horizontal plane. Cis-platinum appears to cause irreversible cross-linking of DNA strands and transient inhibition of DNA synthesis (Rozencweig et al 1977). In recurrent tumours, the overall response rates have been approximately 31% (Wittes et al 1977, Sako et al 1978). The duration of response is also relatively short, in the range of four months. Dosages commonly used are 80 to 120mg/m^2 given intravenously every three to four weeks.

Patients on cytotoxic drugs are prone to infection and haemorrhage as a result of depression of the white cell component of the blood. Poor gingival condition can lead to profuse gingival bleeding and attention should be directed towards high standards of oral hygiene. Regular use of chlorhexidine gluconate 0.2% is recommended (Morton & Roberts 1990).

4.6 THERMOTHERAPY

Ultrasound, radiofrequency, microwaves and heat perfusion solutions are among the several methods of the induction of hyperthermia. Ultrasound can be easily generated, focussed and localized but air, fluid and bone interfaces can limits its application. The microwave method provides convenient and readily controlled local heating with relative simplicity. Radiofrequency may require multiple electrodes and heating occurs at lower frequencies than microwaves.

There have been other 'advances' in the treatment of oral cancer which represent new techniques rather than improvement upon traditional methods. Oner of these has been the carbon dioxide laser. The CO_2 laser has wide application in the management of premalignant dysplastic lesions using vaporisation, and the laser can also be used for excision. Vessels less than 0.5mm in diameter are sealed by the laser beam and vapourisation of the wound surface is limited to a depth of about 200 microns so that the tumour margins can be accurately assessed. The great advantage of the laser is that wounds heal and epithelialise with minimal slough and little scar formation or contracture (Frame et al 1988).

Another advanced technique is haematoporphyrin derivative and photodynamic therapy. Photodynamic therapy uses a light source (for example the argon pumped dye laser) to destroy cells sensitized by haematoporphyrin derivatives (HPD). HPD is given intravenously to patients 48-72 hours before light exposure and preliminary reports have produced exciting results in advanced disease (Edge & Carruth 1988).

4.7 CRYOSURGERY

Cryosurgery is a technique which uses extreme cold for the destruction of tissues. Robert Boyle in 1683 first demonstrated that cells were destroyed by freezing (Henk 1985).

During freezing, ice crystals of pure water form within the cells, and during this phase the concentration of electrolyte solutes within the remaining liquid phase rises. This rising concentration of ions produces large osmotic changes which destroy the intracellular protein structures, thus killing the cell (Farrant 1971). Cell killing is also produced by cellular compression caused by extracellular ice, attainment of minimum cell volume by loss of water and increased membrane permeability, membrane rupture, pH changes, mechanical disruption of cell organelles by intracellular ice, and microvascular changes leading to post-thaw ischaemic necrosis (Green 1981).

It has also been claimed that following cryosurgical destruction auto-antibodies may be formed which may help the destruction of the original lesion.

Cryosurgery using liquid nitrogen (-196°C) has been used in the treatment of small primary oral cancers using tissue temperatures, monitored with thermocouples, of at least -50°C. Cooling should be rapid and the thaw cycle slow; post-treatment biopsies are used to check the tumour response. Survival figures in selected patients are similar to conventional treatment (Gage 1976), but the treatment can produce significant oedema and tracheostomy may be needed.

In the palliation of some patients with painful recurrent disease, cryosurgery may help and treatment can sometimes be carried out without anaesthesia. Cryosurgery may have an immunological effect by stimulating a specific humoral and cellular response in patients already demonstrating an immune response to their tumours (Ablin & Bradley 1986).

4.8 PALLIATIVE THERAPY

Patients with unresectable cancer may be candidates for a variety of palliative approaches designed to improve the quality of life. In this type of procedure, the surgeon removes as much as possible of gross tumour, leaving minimal disease for the chemotherapy that will follow. Another type of palliative therapy is the treatment of complications that arise from the disease or its treatment (Elias 1986).

5 PREVENTION AT AN INDIVIDUAL LEVEL

5.1 BEHAVIOURAL CHANGE

The primary goal in the management of oral cancer patients should be prevention. Ideally, these patients should be seen for complete dental evaluation soon after diagnosis and, if possible, prior to instituting chemotherapy or radiotherapy. If the patient's blood counts and overall condition permit, teeth that cannot be saved should be extracted and those remaining should be restored to prevent an acute situation at a time when dental manipulation may be contraindicated.

Attitude change is necessary in the attempt to prevent or control oral cancer. An effective behaviour and attitude change could obtained by proper communication and motivation in an appropriate environment. The level of awareness, vary from individual to individual. Therefore, not all are immediately cooperative or receptive. Prior to attempts to correct oral habits and inadequacies, an understanding of behaviour patterns and attitudes held is necessary.

At first, the dentist may intercede as he keeps a one-to-one relationship with clients. Working in groups may achieve a favourable result within a shorter period. Depending on the community concerned, different numbers and types of personnel will be required. The principal officers responsible may be dentists, assistants or hygienists. They may attempt to achieve attitude change by different approaches. Audio-visual accessories, mass media, posters, hand-outs, publications and the like, help to meet this responsibility.

Listing of danger signals which are published repeatedly, help the public to avoid what is harmful. The list has to stress the moderate use of alcohol (if used), maintaining balanced adequate nutritious diet, correction of dental deficiencies, avoidance of too much exposure to sunlight, using tobacco sparingly, smoking to a moderate degree (if smoking), avoid using lime and tobacco as a chew and regular check-ups by professionals (Bolden 1977).

Patients, especially those most susceptible, should be reminded of relationships between the frequent use of tobacco, alcohol, betel quid and the incidence of tongue cancer. It is often difficult to discourage the use of irritants, but is possible to significantly reduce their use to at least tolerable levels, both to the oral tissues and individuals.

No one should unreasonably and carelessly introduce proven carcinogens into the human environment. Whenever the substitutes for carcinogens are not available, the World Health Organization (1977) stressed that there should be appropriate legislative action, to ensure that occupational exposure to these carcinogens is strictly controlled.

5.2 PROMOTION OF PREVENTIVE EDUCATION

Making one knowledgeable, is a very basic requirement to achieve an attitude change. Prevention and cntrol of oral cancer has been approached from a wider point of view in recent years. Various chewing, smoking and similar oral habits, which have been part of certain cultures over the centuries, are only subject to valid changes, by the altered mode of planning by the authorities.

Cancer education programmes involve teaching recognition of signs and symptoms to communities. Further emphasis is provided by the House of Delegates of the American Dental Association taking a stand against smoking at its sessions. A similar action was taken by the American Society of Oral Surgeons (Laskin 1974). Moreover, it should go one step further and ban the smoking at all scientific meetings. The same routine can be applied to other possible risk factors. Thus the professional concern of the problem will be emphasized to the public, opening a channel of easy access to change attitudes. Legislation could then be implemented for public places and extended to include public transport and the like, to achieve behavioural changes. Providing cancer education material will reinforce these actions. High quality epidemiological network is necessary to provide reliable information on environmental cancer risks.

The patient with oral cancer may experience a variety of emotions following diagnosis. Loss of independejnce and control will also be experienced to some extent by all patients. The nurse can help them regain both of these by involving them in an education and self-care programme. Patients with oral cancer will often need to learn how to cope with disfigurement or dysfunction as a result of their treatment. Educating them to cope with their problems will not only achieve the acquisition of new skills, but will encourage them to visualise their defects and enable the nurse to assess their acceptance of altered body image (Morton & Roberts 1990).

5.3 SELF-EXAMINATION

Despite extensive research into the aetiology of oral cancer, and vast improvement in its management, the most important factor in effecting a cure still remains early recognition. When detected early, the five-year cure rate for oral cancer increases from 16-31% depending upon its location. Fortunately for the patient, 75% of oral lesions are directly visible, 10% can be seen with the aid of a mirror and 11% are palpable. Thus, if one follows the old adage about seeing the dentist twice a year, and a proper examination is performed, an event better cure rate than currently exists might be expected (Laskin 1978).

It has been proposed that careful examination by the dentist during routine dental checkups would help to reduce the proportions of late-stage diagnoses of oral cancer (Glass et al 1975). In the United States of America, over 70% of oral cancer are in persons over the age of 55 years. Furthermore, 41% of the population older than 55 are edentulous, and in most cases rarely visit a dentist. As long as dentures fit reasonably or can be made comfortable by various devices advertised and sold over the counter, the edentulous person seems to have little motivation to seek dental care. Therefore, until persons at high risk for oral cancer visit their dentist regularly for a thorough oral examination, it is essential to find other ways of achieving early detection.

By familiarizing the public with techniques of self-examination, early signs suggestive of cancer, or lesions with a malignant potential, can be detected and brought to the attention of a clinician before the disease develops beyond capabilities for local control.

Instruction in self-examination for early signs of orofacial cancer was given to over 450 persons attending a large country fair in western New York State. The participants received one-to-one instruction from dentists, or specially trained dental hygienists, according to a protocol designed to detect abnormalities of the oral cavity, cervical lymph nodes, and major salivary glands, as well as facial skin cancers. The method of personal instruction was judged feasible for large-scale application (Grabau et al 1978).

As with other techniques taught to patients, simplicity is the key to self-examination of the oral cavity and head and neck. It was found helpful to teach the procedure as a part of the overall preventive education programme. The patient is either given a hand mirror or, preferably, is seated in front of a large mirror. The patient is asked to go through the technique under the watchful eye of the instructor. The instruction continually points out normal colour, texture, and anatomy as the patient examines each area. The abnormalities for which the patient is examining can be reduced to lumps and bumps, and red, white or blue colour changes in the mucosa or skin. The patient can be given a printed order of examination, but an awareness of all areas to be examined is of greater importance.

Examination: The patient is asked to check the mobility of the tongue by moving it from one corner of the mouth to the other. The patient is given a 2x2 gauze and is asked to view the lateral borders of the tongue as far back as the patient can see. The colour and areas of vascularity are pointed out. In addition to this visual examination, the patient is asked to palpate the dorsum and lateral borders of the tongue, feeling for lumps and bumps.

After the initial examination, the patient should be aware of what is normal for one. The patient is then instructed to perform the examination once a month. It should be emphasized that abnormalities will appear as raised lesions (lumps or bumps) or as changes in colour (red, white or blue). The patient is told to observe any lesion for two weeks and if healing has not occurred within this time span, to call the dentist immediately (Glass et al 1975).

Storer (1972) pointed out that the group of patients with the highest risk of development of oral cancer are those in their sixth through eighth decade of life. It is also noted that these are also the patients who tend to be edentulous and do not seek routine dental care. Oral self-examination in this group of patients is of the greatest importance.

DISCUSSION

In dentistry, prevention of oral cancer is a major problem yet to be solved. Oral cancer is easy to detect on close inspection, a characteristic which is not shared by most other cancers, though its nature of onset is insidious. At present, total prevention of cancer before its occurrence is difficult, if not impossible. However, cancer can be prevented from causing rapid destruction of tissues and death to the patient by early diagnosis, detection and treatment. Cancer can be cured and prevented from causing sequelae and complications prior to the appearance of the classical symptoms and signs of the disease.

Oral cancer can be caused by a wide variety of agents (carcinogens), which may be chemical, physical viral and/or hormonal. No single, clearly recognisable cause has been found for oral cancer. Several of the factors implicated in its aetiology have, however, emerged from studies among well defined population groups. Cancer has been induced in laboratory animals and in humans by many agents, including chemicals, viruses and irritation. It is thought that these carcinogenic agents may interact with one or more human host factors, including age, sex, hormonal balance, immune status or genetic structure to cause cancer. However, many cancers would not develop if certain substances were not present in the host's environment. Some investigators believe that environmental factors, such as work place or occupational exposure, life-style habits, iatrogenic exposures and general environmental exposures, are implicated and may contribute to 80% of all cancers.

Any discussion of this mix of internal and external factors that may induce cancer in various combinations leads to the concept of cocarcinogenesis. Cocarcinogenesis is the enhancement of the potency of a carcinogen by another substance, which may or may not produce cancer when used alone.

Among the main possible predisposing factors in the formation of tongue cancer are tobacco, radiation, nutrition, cirrhosis of liver, viruses, industrial hazards, syphilis and traumatic irritation. Tobacco consumption can take many forms and the primary cause of

the very high incidence of oral cancer in South East Asia is the widespread habit of chewing a betel quid to which tobacco is added. The longer the quid is kept in the mouth, the higher the risk. If chewing is combined with smoking tobacco, then the risk is even higher. All form of smoking tobacco carry a risk of oral cancer and particularly high rates occur when reverse smoking, with the lighted end inside the mouth, is practised. Alcohol is another major risk factor for oral cancer as well as for cancers of the pharynx, oesophagus, larynx and liver. Alcoholics and other heavy users of alcohol are at much higher risk and conversely, populations with a low alcohol intake have very low risk. There is also strong evidence that alcohol acts synergistically with tobacco to multiply the risk of tongue cancer. Some investigators suggested that oral cancer may be associated with high degree of industrialization, atmospheric pollution by coal smoke and exhaust fumes containing benzopyrene and other polycyclic hydrocarbons. The ionizing radiations - Alpha, Beta and Gamma rays are known as recognised human environmental carcinogens acting on susceptible cells in the body. Trauma to the soft tissues resulting from poor dentition and ill-fitting denture may play a role in localising a site where tumours develop. People whose diets have low levels of vitamin A, vitamin C, iron and possibly other trace elements are at a high risk of developing oral cancer which may be one reason why the highest incidence rates are found in the poorest countries.

In 1900 cancer ranked eighth as a cause of death in the USA. Because the successful treatment of infectious diseases has greatly improved from 1900, due mainly to antibiotic therapy and national immunization programmes, cancer currently ranks second only to heart disease as the most frequent cause of death. On a global basis oral cancer ranks fourth for men and sixth for women in rank for all cancers. World-wide the incidence of oral cancer varies largely. The highest incidence rates of tongue cancer are reported in the Indian sub continent, Puerto Rico and Brazil. It affects more men than women. The sex ratio has decreased as male rates have been falling proportionately more than female rates. The highest incidence of tongue cancer occurs in the 6th to the 8th decades of life and patients below the age of 20 years are very rare. Apart from lip cancer, tongue cancer is the most frequent site of cancer within the oral cavity followed by the floor of the mouth.

The size of the primary tumour and depth of the penetration are two important factors to measure mortality. The rate is more favourable in young age groups. In recent years the incidence and mortality rates have started to increase for cancer of the tongue and mouth, especially in younger men. Mortality rates for oral cancer vary geographically as well as by sex, site and race. Singapore and Hong Kong rank first in deaths for both males and females, followed by Frances in males and Philippines in females. Honduras and Nicaragua rank lowest for oral cancer mortality in both sexes. Survival rate is dependent on the size and the extent of metastasis. Nodal involvement is of particular importance as mortality is increased when lymph nodes of both sides are affected by malignancy. Patients with oral tongue cancer who have chronically used tobacco and alcohol had an increased rate of death due to intercurrent disease or second primary carcinoma, whereas those who never used tobacco or alcohol enjoyed a little longer life span.

Prevention is a major primary goal in cancer research. Nevertheless, progress in the early detection of cancer is highly desirable, since the percentage of cure is increased in direct proportion to how early it is recognized. One of the great contributions the public health dentist can make to the public health team, and which draws him more closely to his medical colleagues, is the early recognition of systemic disease or neoplasm. All dental inspections or examinations should be made with a watchful eye for abnormalities in soft tissue or bone. This is particularly true when examining the mouths of the older patients, now constituting an ever-increasing proportion of the population. Patients whose cancer is detected at an early stage generally have much longer survival times and also very importantly, treatment will be less radical.

In thinking in terms of prevention in its truest sense, early diagnosis detection and the use of control methods can prevent mutillation of tissues and metastasis of the disease and provide the greatest chance of survival for the patient. Included in the control and preventive techniques are early detection of clinically appearing signs and symptoms, as well as microscopic examination of biopsy tissue. Exfoliative cytology, a technique used

for observing the microscopic morphology of individual cells after they have been obtained from a tissue, is another form of diagnosis and investigation. The method of applying toluidine blue is also used as an investigatory aid in distinguishing between malignant and non-malignant lesions. Other measures in tongue cancer control include surgery, radiation, chemotherapy, thermotherapy, cryosurgery and palliative therapy. All of these different treatment procedures have their own advantages and disadvantages.

Before treatment is started for a patient with oral cancer, two important factors must be considered: firstly, the precise objectives of treatment, ie exactly what it is we are trying to achieve for a particular patient; and secondly the limitations of treatment and how to reconcile limitations with objectives. Whenever such patients are treated a balance must be achieved between overall length of survial and the quality of life remaining. It is worth repeating in this context the advice of the Arabian physician and philosopher Avicenna: "The cure of a disease must never be worse than the disease itself".

Behavioural change is essential in the attempt to prevent and control oral cancer at any individual level. Ideally, the patients should be seen for complete dental evaluation soon after diagnosis and, if possible, prior to instituting chemotherapy or radiotherapy. Patients, especially those most susceptible, should be reminded of relationships between the frequent use of tobacco, alcohol, betal quid and the incidence of tongue cancer. An effective behaviour and attitude change could be obtained by proper communication and motivation in an appropriate environment. Communication is not only confined to direct association but also to indirect methods such as publications, mass media, handouts, posters and the like. Lists of things to be done and not to be done would help patients, by placing stress on urgent factors such as periodic visits to dentists. The responsible members of society should assist in formulating relevant legislation. Making one knowledgeable is a very basic requirement to achieve an attitude change. Cancer education programmes involve teaching recognition of signs and symptoms, to the community. When detected early, the five-year cure rate increases from 16-31% for oral

cancer, depending upon its location. By familiarizing the public with the techniques of self-examination, early signs suggestive of oral cancer, or lesions with a malignant potential, can be detected and brought to the attention of a clinician before the disease develops beyond the capabilities for local control. Self-examination is the most economical preventive method of oral cancer. This is achieved by implementing educational programmes. Professional qualifications are not essential in a self-education programme. Para-professionals and non-professionals are of equal value, once they gain experience. Those countries that lack facilities for any sort of sophisticated work, could very well follow this path.

CONCLUSIONS

In recent years the incidence and mortality rates have started to increase for cancer of the tongue and mouth, especially in younger men. In North America the increase in tongue cancer has been linked to the growth in smokeless tobacco consumption, but this is very unlikely to be the main cause in the UK, as consumption of smokeless tobacco is very low. World-wide the incidence of oral cancer varies widely.

Generally the highest rates of oral cancer are found in the developing world where oral cancer and pharynx (combined) is the third commonest site of cancer causing over 272,000 new cases each year. Unfortunately, the improved and sophisticated methods of treating oral cancer in the last decade could not decrease the oral cancer mortality rate. The figure is very unsatisfactory, when it is realized that the oral cavity can be readily examined and requires no special facilities. Early oral lesions, unlike tumours of many other sites, give rise to early signs. About 85% of oral cancers are visible either directly or indirectly with a mirror and the rest 11% are palpable on careful clinical examinations.

It is very important for the public health worker to be alert to those factors which predispose to oral cancer. Among these may be noted ill-fitting dentures, broken or rough teeth, excessive use of tobacco, excessive alcohol consumption, poor diet and syphilis. With such well-known risk factors as tobacco and alcohol, it is theoretically possible to prevent a substantial proportion of oral cancer. The benefits of eliminating tobacco use and reducing alcohol intake are well documented in Western countries and would reduce mortality from many cancers, as well as other diseases such as ischaemic heart disease. Studies have shown that dietary supplements play a protective role against the development of oral cancer. One method of lowering the risk of oral cancer would be to give dietary supplements or better still to ensure a balanced diet which would also reduce the risk of many other diseases.

Patients whose cancer is detected at an early stage generally have much longer survival times and also very importantly, treatment will be less radical. Delay by the patient in seeking consultation was the main reason for late referral. This indicates the need for more public education about the early signs of oral cancer. Screening programmes are recommended for the early detection of oral cancer and pre-cancer in high risk areas of the Third World and in high risk groups in Western countries.

Dentistry has played an important role in directing the attention of the health profession toward the prevention of disease. Dental health education activities should be designed to lead to improvements in desired dental health behaviour rather than simply increasing dental knowledge. Before beginning a dental health education programme, more consideration should be given to the explicit behaviour change goals intended to be achieved by the programme. A fuller understanding of motivational theory should be gained by professionals engaged in dental health education so that greater effectiveness in changing dental health behaviours can be attained.

Glaring by their absence have been measures that the patient might use to decrease morbidity and mortality from neoplastic diseases of the head and neck. A simplified self-examination procedure can be taught to the patient as a part of preventive programme. It is hoped that this procedure would permit earlier detection and treatment of both neoplastic and non neoplastic disease of the head and neck area. One study shows (Laskin 1974) that the five-year survival rate increased more than 45% when the diagnosis of oral cancer was made before metastasis occurred. This is the challenge that faces dentistry and oral surgery today. What greater service can we render than to help save the life of a fellow human being?

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