The Journal of
Laryngology and Otology

(*Founded in* 1887 *by* MORRELL MACKENZIE *and* NORRIS WOLFENDEN)

August 1978

Oral cancer*

By O. H. SHAHEEN (London)

Introduction

THE number of new registrations of oral cancer each year is approximately 2,500, or 2 per cent of all neoplasms, and the number of deaths 1,200. If these figures are compared with the statistics of the common fatal illnesses, including carcinoma of the bronchus, one might be forgiven for dismissing oral cancer as a minor epidemiological problem. However, those who are familiar with the natural history of the disease and the misery experienced by its sufferers would be the first to support investigation into its aetiology with a view to reducing the incidence still further.

The ratio between the number of new registrations and deaths in a given year has for some time now been constant, and represents a crude yardstick of the lethality of the disease. The ratio of registrations to deaths varies from site to site within the mouth, being lowest for the lip, which undoubtedly has an excellent prognosis, and highest for cancer of the tongue.

In the last two decades male deaths from cancer of the mouth have decreased, but this reduction in mortality is probably due to a drop in the incidence of the disease rather than improved results of treatment. In females, registrations and deaths have remained constant and the ratio of the two has remained unchanged, supporting the concensus that the prognosis shows no signs of improving. It is probable that the drop in new registrations for males in the last four decades is responsible for the altered sex ratio from 10:1 in the thirties to the present ratio of 2:1. This is thought by some to be due to the diminished number of pipe and cigar smokers.

The object of this paper is to review the factors which are thought to be responsible for the bad prognosis of mouth cancer, to recognize specific

* Paper read to Section of Laryngology, Royal Society of Medicine, 4 March 1977.

https://doi.org/10.1017/S002221510008590X Published online by Cambridge University Press

problems which bedevil management, to summarize present-day concepts of treatment and to suggest new avenues for improving the prognosis.

Factors affecting prognosis

There is little doubt that the site of the primary lesion is an important factor affecting the prognosis. For instance, lesions of the central and posterior parts of the oral cavity carry a much worse prognosis than the anterior and peripheral parts. In the case of the tongue and floor of mouth, the high rate of metastases testifies to the richness of the lymphatic network of these structures, but more important still is the ability of these particular tumours to spread along planes, between mucous membrane and muscular partitions on the one hand, and between muscle bundles on the other. Furthermore, the phenomenon of localized embolism is responsible for the occurrence of outlying islands of tumour separated from the main mass of the tumour by areas of normal tissue. Such behaviour, related as it is to the local anatomy, can only result in a tendency to underestimate the extent of penetration of the tumour. Lesions on the under-surface of the tongue are particularly insidious in this respect, for they burrow the short distance between the under surface of the tongue and its base, rapidly fixing the organ and precluding any attempt at cure.

The size of the primary lesion is an important prognostic factor, the more so in those anatomical areas where it may be difficult to assess it with accuracy. Information on this and other factors has been obtained from the records of the Head and Neck Oncology Clinic at Guy's which have been personally compiled and kept since January 1973.

In the group of 60 patients with oral cancer seen since January 1973, 70 per cent of all tumours were 4 cm or over in the largest diameter (Fig. 1). This figure differs substantially from other reported series, particularly from North America, where lesions of this size are in a minority. In one series for instance (Krause *et al.*, 1973), lesions of this size comprised 35 per cent, and in another (Lee and Litton, 1972) they amounted to 13 per cent of the total. If these figures are accurate, then we are seeing disease which is much more advanced than in North America and the results of treatment are bound to be that much worse. It is worth mentioning in this respect that it is not uncommon to record a progressive increase in the size of the

Total number of patients	60	
Primary tumours larger than 4 cm. in one plane	41	41/60 = 68·3 per cent
Survivors with primary tumours 4 cm. or larger	19	19/41 = 46·4 per cent
Primary tumours smaller than 4 cm. in one plane	19	19/60 = 31·6 per cent
Survivors with primary tumours smaller than 4 cm.	15	15/19 = 79·9 per cent

FIG. 1

Showing the distribution of the tumours according to size and the number of survivors.

https://doi.org/10.1017/S002221510008590X Published online by Cambridge University Press

primary tumour between the initial clinical examination, the examination under anaesthesia and the eventual operation for removal of the lesion. This underlines very strongly the need for a careful examination under anaesthesia.

That the size of the primary lesion is an important prognostic factor is testified to by the frequency with which recurrence at the primary site occurs, in contrast to the less common occurrence of a controlled primary with active disease in the regional lymph nodes (Fig. 2). Perhaps it would be more accurate to define the problem as a failure to appreciate the extent of the primary lesion, and as mentioned before in the case of tongue and floor of mouth, this probably relates to spread along planes beneath the surface and micro-embolization beyond the limits of the visible and palpable tumour.

Lymph node metastasis is also an important factor prognostically but possibly less so than the size of the primary tumour (Fig. 2). The percentage of patients in the small series under review in whom it would seem that lymph node metastasis alone may have affected the eventual outcome was approximately 15 per cent as opposed to the higher figure of patients (26·6 per cent), in whom it was not possible to control the primary. Nevertheless, looking at the matter in a different way, of the 19 patients presenting with primary tumours of 4 cm or larger and surviving without evidence of disease, only two developed lymph node metastasis. The size of the primary lesion in oral cancer does not seem to affect to any great extent the rate of metastasis. The rate of metastasis from lesions of 4 cm or over was 31·6 per cent as opposed to 26·3 per cent for smaller lesions (Fig. 3). This point which has been brought out in other reports (Lee and Litton, 1972) con-

Primary disease controlled but regional node involvement not controlled	4/60
Primary disease not controlled but node involvement controlled or absent	11/60
Primary + lymph node involvement not controlled	5/60
Primary + lymph nodes controlled but death from distant metastatic disease	4/60

FIG. 2

Illustrating that cases of failure to control the primary disease outnumber those with persistent metastatic disease alone.

LYMPH NODE INVOLVEMENT

Number of patients with metastases	18/60 = 30 per cent
Number of patients dying with metastases	14/60 = 23·3 per cent
Patients with primary lesions larger than 4 cm. developing metastasis	13/41 = 31·6 per cent
Patients with primary lesions under 4 cm. developing metastasis	5/19 = 26·3 per cent

FIG. 3

Showing the effect of the size of the primary on the rate of lymph node metastasis.

https://doi.org/10.1017/S002221510008590X Published online by Cambridge University Press

tradicts the popularly held view that the size of the primary lesion should be taken into consideration when deciding about the need for elective neck dissection.

A consistent index of prognosis was found to be the nature of the histology of the primary lesion. Of the surviving patients with large lesions, that is 4 cm or over, only two had poorly differentiated tumours, whereas the vast majority had well differentiated neoplasms, and three had verrucous carcinomata. The criticism that the degree of differentiation varies from site to site in a given tumour applies more to small biopsy material and much less to the wedge biopsies which are taken from the mouth by head and neck surgeons. Small biopsies taken with cupped forceps with the patient seated in a chair are to be condemned as inadequate and sometimes dangerously misleading. We have, for example, been misled into treating a radio-insensitive neoplasm by radiotherapy on the strength of a small biopsy provided by another clinician.

Difficult management problems

There are three specific management problems over and above the considerations previously mentioned. The first of these is the patient who presents with extensive field changes. This affects the final outcome in one of two ways. The field change may be a uniform and extensive change, possibly exacerbated by previously administered radiotherapy, and presents as a dry red glazed and brittle mucosa over a wide area. This may develop *in-situ* changes in a number of different locations which subsequently mushroom out as extensive carcinoma, or as sometimes happens, presents as recurrent cancer in mucosa immediately adjacent to an excised area. The problem here is one of recognizing the limits of unhealthy tissue, for light microscopy is not always helpful in this respect and vital staining is often difficult to interpret. Field change may also create slowly growing indolent primaries, often widely separated from the initial tumour both in distance and time. More often than not the change in this type of case is one of patchy leukoplakia. These neoplasms are more amenable to control, being relatively superficial, localized and rarely exhibiting a strong tendency to metastasize. Eleven per cent of the 60 patients reviewed were cases presenting with a second primary. The field change is more obvious to the naked eye, but just as difficult to eradicate because of a constantly changing geographical distribution.

The second special problem concerns the patient who has been treated by radiotherapy, whose primary neoplasm has persisted. The initial difficulty may be one of recognizing the persistence of disease, but there may be also the difficulty of defining the boundary of the tumour, with the consequence of a strong likelihood of leaving islands of microscopical neoplasm after excision. This is likely to occur if the original primary tumour

https://doi.org/10.1017/S002221510008590X Published online by Cambridge University Press

has not been correctly mapped out, and also when a long time has elapsed between treatment and the emergence of so-called recurrent disease.

The third special problem is the patient who develops a second primary in areas other than the mouth either simultaneously or sequentially. When two primaries in separate sites exist together this is apt to signify a bad prognosis and should discourage the surgeon from performing radical procedures.

Management

The management of oral cancer has not changed basically over the last 30 years although operations have in general become more radical. Small circumscribed cancers of the mouth can be treated by either surgery or radiotherapy. Where function is not likely to be compromised or a lesion is relatively superficial, local excision with direct approximation of edges or resurfacing with a skin graft is a satisfactory form of treatment. Equally radiotherapy in the form of an implant or external beam will nearly always control the smaller lesion. The bias with small tongue lesions tends to be in favour of needles, rather than compromise the function of the organ by operation. In the case of larger lesions the decision as to which modality to choose depends in practice on a number of factors. The site of the primary lesion clearly affects the choice, for in certain situations one method of treatment may be more successful whereas it may be less so in others. Carcinoma of the alveolus penetrating bone is clearly a surgical problem, although lesions confined to the mucosa of the alveolus may be cured by radiotherapy. Carcinoma confined to the floor of the mouth, when clearly not involving the tongue or the inner aspect of the central arch of the mandible may well be successfully managed by radiotherapy. Where the inner aspect of the central arch is involved, it is probably muddled thinking to opt for radiotherapy in the hope of sparing the patient an operation requiring a complicated reconstructive procedure. The chances are that the radiotherapy will fail to control the disease, and the patient will have to undergo the operation but with repair carried out in a devitalized area.

Clearly also the age, state of health, temperament and occupation of the patient come into play when arriving at a decision regarding the type of treatment. The very old and especially those living on their own, the patient with severe liver or cardiovascular disease are bad surgical subjects. The patient whose livelihood may be imperilled by alteration of appearance or speech should be offered the alternative of radiotherapy, unless it is clear that this is obviously the wrong choice of treatment.

The histology in certain instances dictates the choice of treatment. Verrucous carcinoma for example can only be managed by surgery and for large well-differentiated tumours the bias may be towards surgery.

Surgery is the logical treatment in patients who present with cancers in an area of extensive field change. It may be indicated simply for the management of severe epithelial atypia in the absence of frank carcinoma, in which

https://doi.org/10.1017/S002221510008590X Published online by Cambridge University Press

case the diseased part is excised and resurfaced either with a skin graft or a suitably placed flap. It is often indicated in cases with a second primary, and needless to say the temptation to perform massive ablations must be resisted in view of the likelihood of further primaries. Surgery frequently becomes the inevitable sequel in those cases where radiotherapy has failed to cure the primary disease.

There is no need to describe the types of radical procedure required for the control of mouth cancer, all of which are based on a common theme and are found in textbooks of surgery. The vogue nowadays is to resurface the resultant deficit in the mouth with a flap of skin. The advantage of such a manoeuvre is to ensure rapid healing, particularly when tissues have been devitalized, but their value in lessening functional deficits is dubious. As far as the tongue is concerned, they probably do little to improve the mobility of the tongue remnant *per se* but by allowing the tongue remnant to lie in a natural position the speech impediment is lessened. Experience has shown that flaps do little to minimize the dysphagia after partial glossectomy.

The incorporation of a radical neck dissection as part of the definitive operation is clearly indicated when there is obvious metastatic disease in the regional lymph nodes. When nodes are not palpable, the value of an elective neck dissection in improving the prognosis is yet to be established. More often than not the pathologist fails to find disease in the regional nodes. When microscopical disease is present it is doubtful if the dissection will influence the outcome favourably where such disease is widespread but when microscopical disease is limited, elective dissection would probably have no advantage over a policy of waiting until the metastasis becomes clinically obvious.

There have been a number of reports purporting to show that the cure-rate after elective dissection is greater than after a wait and see policy, but the evidence is not convincing. Stell and Green (1976) were not able to demonstrate any advantage for elective dissections when they examined the results in two groups of patients paired for site, age, and sex having elective as opposed to mandatory neck dissections.

The value of combined therapy has not been properly evaluated in this country. There is some evidence to suggest that it may improve results, but this is by no means conclusive, and may only apply to the smaller rather than the larger lesions (Krause *et al.*, 1973).

One has been tempted to use this approach in one's own practice and the initial impression is favourable although the numbers are small and do not stand up to statistical scrutiny.

What of the future and how best to improve the prognosis? There is no doubt that prevention is preferable to treatment. Epidemiological surveys may well yield further clues as to the factors responsible for the disease. It is strongly suspected, for instance, that cigar and pipe smoke and certain forms of alcohol increase the risk of oral cancer (Wynder *et al.*, 1957). In Brittany where spirits containing a high proportion of impurities are con-

https://doi.org/10.1017/S002221510008590X Published online by Cambridge University Press

sumed, the incidence of oral cancer is extremely high (Schwartz *et al.*, 1962). It has become apparent also that chronic candidiasis and lichen planus are carcinogenic (Cawson, 1969), and that tobacco chewing predisposes to verrucous carcinoma (Waldron, 1970). The role of the dentist in spotting early disease cannot be over-emphasized. There is no doubt that the size of primary lesions picked up on routine dental check-up is much smaller than those lesions which eventually force the patients to go to hospital for attention.

The early identification of pre-malignant lesions and their removal would also help to improve the situation. As far as the assessment of the disease is concerned, it is possible that with the passage of time improvement in scanning techniques will help to define the stage of the disease more accurately, in regard to both the primary and lymphatic spread. Tests which are used for monitoring the efficiency of the cell-mediated response have shown that, the more advanced the disease, the poorer is the response. They also demonstrate to some extent that the immune reaction recovers after successful treatment (Shillitoe, 1976). Using the P.H.A. index of lymphocyte transformation, Parker *et al.* (1975) reported that low or consistently falling indices signified a bad prognosis. This work needs to be extended to try and differentiate those tumours which have metastasized from those which have not.

From a practical point of view, there are three or four avenues which need exploring in properly controlled trials. The first is combined therapy, the second cytotoxic adjuvant programmes, the third fast neutron therapy, and the fourth the effect of radiation therapy on the regional lymphatic fields for the control of potential metastases.

Looking far ahead into the future, it may well be that examination of a person's saliva, his blood, or his oral mucosa will yield information which will warn of a cancer risk long before such a change has occurred.

REFERENCES

CAWSON, R. A. (1969) *Proceedings of the Royal Society of Medicine*, **62**, 1300.
KRAUSE, C. J., LEE, J. G. and MCCABE, B. (1973) *Archives of Otolaryngology*, **97**, 354.
LEE, J. G., and LITTON, W. B. (1972) *Laryngoscope*, **82**, 1273.
PARKER, R., ALEXANDER, S., SHAHEEN, O. H., and PARKES, P. (1975) *Journal of Laryngology and Otology*, **89**, 687.
SCHWARTZ, D., LE CLOUCH, J., FLAMANT, R., and DENOIX, P. F. (1962) *Revue Francais des Études Clinique et Biologique*, **7**, 590.
SHILLITOE, E. J. (1976) *Proceedings of the Royal Society of Medicine*, **69**, 747.
STELL, P. M., and GREEN, R. J. (1976) *Proceedings of the Royal Society of Medicine*, **69**, 411.
WALDRON, C. A. (1970) *Thoma's Oral Pathology*, p. 837. St. Louis: Mosby.
WYNDER, E. L., BROSS, I. J., and FIELDMAN, R. M. (1957) *Cancer*, **10**, 1300.

E.N.T. Department,
Guy's Hospital
London SE1.

https://doi.org/10.1017/S002221510008590X Published online by Cambridge University Press

https://doi.org/10.1017/S002221510008590X Published online by Cambridge University Press