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CARCINOMA OF THE LIP

A series of 869 cases

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A total of 869 cases of carcinoma of the lip were treated during the period 1946—1966 but those cases with recurrences following primary treatment elsewhere as well as those with a doubtful histologic diagnosis were excluded from the analysis. The object was first and foremost to determine the occurrence of metastases in regional lymph nodes; as such spread is low a 20-year period had to be reviewed in order to obtain a reasonably representative series. Various other data of interest, especially concerning the primary tumour, became apparent in the course of the analysis and are presented for discussion.

The series cannot be said to be representative of the incidence of the condition in a given geographic area, as some cases were treated at other centres. A greater tendency to centralize the treatment appears also to have occurred during recent years. It is possible to trace only a slight increase in the number of newly referred cases, in other words no major change in the incidence of the disease was evident. Publications from the Danish Cancer Registry (CLEMMESSEN 1965) have also indicated merely a moderate increase in the annual number of new cases.

Material. This consisted of 869 cases, 845 (97.2 per cent) of which were males and 24 (2.8 per cent) females. The highest mean range lay in the 60 to 70 year group (Fig. 1). The lesion was always an epidermoid cell carcinoma, except-

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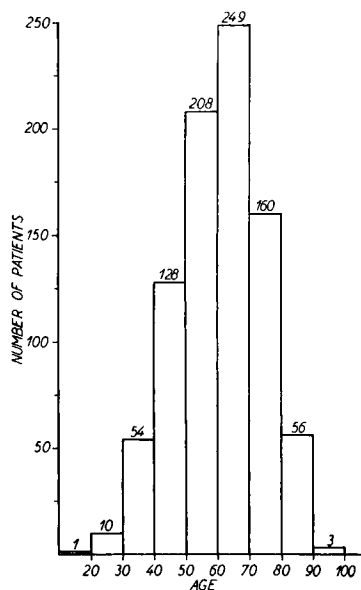


Fig. 1. Age distribution at time of histology.

ing 6 cases of basal cell carcinoma; the records in these stated that the growths seemed to have arisen from the epithelium of the vermillion border.

The primary sign was a tumour, ulcer, or blister that was possibly crusting; the duration before their confirmation by histology was 0 to 4 months in 43 per cent, 4 to 8 months in 20 per cent, 8 to 12 months in 20 per cent, and more than 12 months in 17 per cent of the cases; an appreciable number of the cases thus had a relatively long history.

Localization and classification. Only those tumours arising from the vermillion area were included in the analysis; 853 (98.2 per cent) affected the lower lip and 16 (1.8 per cent) the upper lip.

The series was classified in retrospect by the TNM system in the UICC formulation (UICC, Geneva 1968):

- T1S pre-invasive carcinoma, so-called 'in situ'
- T0 no evidence of primary tumour
- T1 tumour measuring 2 cm or less in its largest dimension, strictly superficial or exophytic
- T2 tumour measuring 2 cm or less in its largest dimension, with minimal infiltration in depth
- T3 tumour measuring more than 2 cm in its largest dimension or one with deep infiltration, irrespective of its size

Table 1*The 869 cases of carcinoma of the lip grouped according to the TNM system (UICC)*

	N0	N1	N2	N3	Total
T1	443	1	0	0	444
T2	337	1	0	1	339
T3	75	6	0	2	83
T4	0	0	1	2	3
Total	855	8	1	5	869

T4	tumour involving bone
N0	no palpable nodes
N1	movable homolateral nodes
N2	movable contralateral or bilateral nodes
N3	fixed nodes
M0	no evidence of distant metastases
M1	distant metastases

The rules thus fail to give a sharp distinction to the T groups. As a criterion of distinguishing between T2 and T3 infiltration 5 mm in depth was chosen. The classification was based upon fairly detailed descriptions in the records and by clinical photographs.

Table 1 indicates the distribution within the TNM groups. All the cases were M0. A notable preponderance of cases in the early stages is apparent with only 14 N1, N2, and N3 cases, or 1.6 per cent (14/869). The records contained no information regarding the aetiology.

Treatment. The primary treatment was radium intubation in 766 of the 869 cases. The principle consisted in puncture of the part of the lip involved transversely and longitudinally with 10 mg radium needles varying in number with the extent of the growth; the active length of the needles was 10 mm. The needles were interspaced at 5 mm but in order to secure the dose at the margins of the neoplasm, the corresponding needles were placed in healthy tissue 5 mm from its macroscopic border. The needles were usually in situ for four hours to yield a dose halfway between two needles ranging from 2 500 to 5 600 rad.

Seventy-four cases received primary external roentgen irradiation, 48 with a single large dose at 26 kV. Fifteen cases were treated by fractionated irradiation with somewhat more deeply penetrating rays, and 9 cases by various other methods and different qualities of irradiation; only 3 cases were treated by a radium mould, either alone or supplementary to external irradiation. One case had combined treatment in the form of low voltage irradiation and concomitant wedge-

Table 2*Frequency of recurrences and residual tumours in the entire series with primary treatment*

	No. of cases	Residues and first recurrence	
		No.	Per cent
Radium intubation	766	84	11
26 kV 5 000 R or 5 100 R at one sitting	38	3	8
Other radiation therapy	36	11	31
Surgical treatment	29	1	1

shaped excision. Twenty-nine cases underwent primary operation, consisting in wedge-shaped excision in 27 cases combined with an Estlander plastic operation in one case while the entire prolabium was excised in another case.

Table 2 represents the frequency of recurrence and residues in relation to the primary therapeutic principle. Residues are taken to mean remnants of the neoplasm within the first two months of the primary treatment. Recurrence signifies a malignant process arising more than 2 months after the treatment, and less than 10 mm from the primary lesion. A fresh primary, on the other hand, is a malignant lesion at a distance of over 10 mm.

The groups in Table 2 are not intercomparable, but the table perhaps affords

Table 3*Grouping by therapeutic method of 165 cases of recurrences, residues and fresh primary lesions*

Irradiation	
Lip intubation	82
26 kV at one sitting	4
Other radical irradiation	4
Palliative irradiation	3
Surgery	
Wedge-shaped resection	51
Estlander-type operation	9
Bernard-type operation	5
Diefenbach-type operation	2
Other types of resection	3
No treatment	2
Total	165

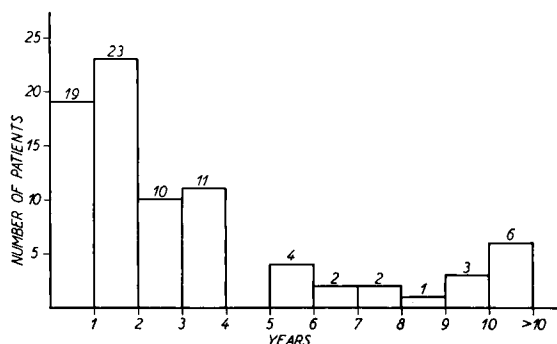


Fig. 2. Time of occurrence of 81 local first recurrences.

some impression of the level of the recurrence rate. Fig. 2 illustrates the time at which local recurrences arose. Most appeared within the first 2 years. It is remarkable that quite a few occurred after the 6th year and some more than 10 years after the primary treatment.

A number of the patients, however, had more than one recurrence while several developed fresh primaries. Of the 81 patients with one local recurrence 19 also had 2, 4 had 3, one had 4 and one patient had 5 local recurrences. A total of 106 local recurrences occurred in these 81 patients. Eighteen patients had 20 residues, 33 patients developed 39 fresh primaries. Thus, in 132 cases, there were 165 local recurrences, residues, and fresh growths. Table 3 indicates how these 165 cases were treated, that is generally either by radium intubation or wedge resection. The most interesting thing about these figures is that by utilizing every therapeutic possibility it proved possible to control the primary lesion in all but 7 cases; of these, 5 cases also had regional lymph node metastases.

The frequency of recurrence and residues in the group treated by radium intubation is related to the T classification (Table 4). As might be expected, with radium intubation of the lesions with deep infiltration, i.e. in the T3 group, the

Table 4

Frequency of residues and first recurrences after primary treatment with radium intubation in 766 cases grouped according to the T classification

	No. of cases	No. affected	Per cent
T1	378	28	7.4
T2	331	42	12.7
T3	57	14	24.6
T4	0	0	—

Table 5*Complications of treatment of local lesions*

After radium intubation and external irradiation	
Cicatricial changes and tissue loss	17
Chronic ulceration treated by wedge excision	9
Chronic ulceration, untreated	5
Necrosis of bone	2
After surgery	
Microstoma	8
Wound rupture	1
Severe local infection (contributory cause of death on the 5th day in one case)	5
Total	43

recurrence rate was high, viz. almost 25 per cent. In such cases, therefore, it is wise to choose other forms of primary treatment.

Complications. All complications are included even if they are only just mentioned in the records, regardless of their severity. As a whole, the rate was low (Table 5). Of 37 patients who received two radium intubations in the same area 7 had disturbing sequelae: 4 developed a chronic ulcer which had to be excised, 1 recurrent ulceration and 2 patients fairly marked, disfiguring radiation-induced changes. Of 3 patients who received a third intubation in the same area one is suffering from intermittent ulceration, one from chronic ulceration and one developed a further recurrence, treated surgically. These values are low but it seems beyond doubt that the complication level is higher after re-intubation, in particular as regards disturbing complications that require treatment.

Radium intubation affords satisfactory therapeutic results in cases with small, not deeply infiltrating tumours, mainly T1 and T2. Re-intubation should not be used for treating recurrences following primary radium intubation, as this involves a considerable risk of complications such as chronic ulceration requiring treatment; such cases necessarily demand secondary surgery.

The present material fails to permit of conclusions regarding external roentgen irradiation; this was administered by a varying technique, and the results are scarcely comparable with the others.

Metastases. The prognosis of primary, localized carcinoma of the lip would appear to be excellent and could be controlled in all but 7 cases of the present material.

The degree of malignancy of this condition is determined first and foremost by its tendency to produce metastases partly to the regional lymph nodes and partly

Table 6*Localization of presumed and confirmed regional lymph node metastases, primary and secondary, in 59 cases*

Submental	Submandibular	Submental + subman- dibular	Submental + subman- dibular + sup. jugular	Submandi- bular + inf. jugular	Sup. jugu- lar
3	38 3 contralateral	8 1 bilateral	8 1 bilateral	1	1 Boeck's disease

beyond this barrier. Distant metastases were extremely rare and occurred in only 5 cases. The prognosis depends on the whole primarily on the treatment of regional lymph node metastases in the neck.

The frequency of regional nodal metastases confirmed or presumed in this series of 869 cases with primary metastases was 1.6 per cent (14/869) and with secondary metastases 5.2 per cent (45/869), i.e. rather low.

The localizations of presumed and confirmed regional lymph node metastases, primary as well as secondary, appear in Table 6. Most involved the submandibular nodes with only a few in the submental nodes alone. Doubtful bilateral or contralateral nodes were present in 5 cases. Only one case had palpable superior jugular nodes without simultaneously questionable submandibular or submental nodes; histology however proved this to be a case of Boeck's sarcoid. It must be said therefore that in this series the regional metastases have accurately followed the paths of lymph drainage from the lips without missing any 'stations'.

It would be of interest to find a group or groups particularly exposed to developing metastases in the cervical lymph nodes, and in which special measures might be considered, e.g. follow-up at shorter intervals than usual or possibly prophylactic neck dissections.

The age distribution in the group with metastases, related to that in the entire series, perhaps represented a somewhat greater tendency to embrace metastases in the 70 to 80 year group, although this failed to amount to a definite bias.

By far the largest number of metastases occurred within the first 30 months after the primary tumour was diagnosed, most being detected either at the first examination (14 cases) or at subsequent controls (28 cases). Seventeen patients had themselves noticed the metastases. Five of the patients sought further advice immediately whereas 12 came at the appointed time, up to 8 weeks later.

The cases of metastases, as well as the distribution of the entire series by the T classification, are presented in Fig. 3. This indicates a distinct bias, the metastatic rate being, as expected, highest in the T3 and T4 groups (100 per cent

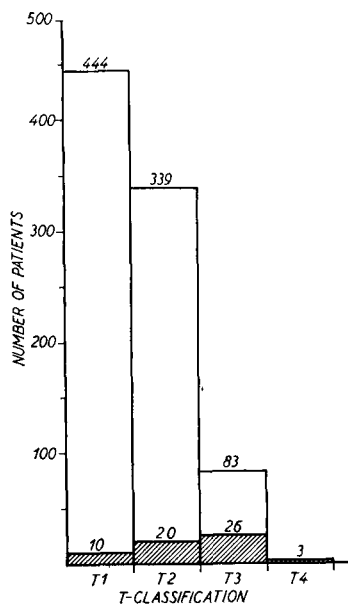


Fig. 3. T classification of the entire series and of 59 cases with metastases.

in T4); metastases also occurred however in the T1 and T2 groups.

The secondary metastatic rates, partly in the group without recurrence of the primary tumour and partly in that with recurrence, residues, or further lesion, related to the T classification, appear in Table 7. The secondary metastatic rate in the latter group of patients reveals that about 38 per cent in the T3 group developed metastases.

Treatment of regional lymph node metastases. Thirty-seven cases were treated by surgery and 22 by radiation therapy, with curative intention in 10, and as a palliative measure in 12 cases (Table 8). The two groups are not comparable, inter alia, because a relatively far larger number of cases, 18 and 12 respectively, in the irradiated group than in the surgically treated group, had fixed nodes. Five of the irradiated patients were alive at five years (from the diagnosis of the primary tumour) although a further 3 died of the condition later. One patient is alive with recurrence at five years. Thus, within this group only one patient is living without signs of recurrence.

Thirty-seven patients were treated by surgery; 25 (68 per cent) were alive at 5 years, but in 10 of these no signs of carcinoma in the lymph nodes were revealed at microscopy; if these cases be excluded, the 5-year survival rate becomes 56 per cent (15/27) in the group with confirmed lymph node metastases. The nature and number of operations appear in Table 9. This also gives the 5-year survival

Table 7

Frequency of secondary metastases in relation to T classification and occurrence of local recurrence, residues or fresh primaries

	No recurrence of primary tumour	Frequency of secondary metastases	Number of local recurrences, re- sidues or fresh primaries	Frequency of secondary metastases
T1	389	6 (1.6 %)	54	3 (6 %)
T2	287	9 (3.1 %)	50	9 (18 %)
T3	54	10 (18.5 %)	21	8 (38 %)
T4	0	0	0	0
Total	730	25 (3.4 %)	125	20 (16 %)

Table 8

Grouping, by method of treatment, of 59 cases with presumed and confirmed regional lymph node metastases

	No.	Died of carcinoma of the lip	Died of other causes	Alive at end of 5 years	Died of carcinoma of the lip after 5 years
Surgical treatment	37	9	3	25 (68 %)	1
Irradiation	22	16	1	5* (23 %)	3
Total	59	25	4	30 (51 %)	4

* 1 patient alive with recurrence at 5 years.

Table 9

Grouping of 27 cases with lymph node metastases by nature of treatment

Nature of operation	No. of cases	No. of recurrences	5-year survival		
			After first operation	After operation for recurrence	Total
Radical neck dissection	8	3/8	4/8	0/2	4/8
Bilateral neck dissection	4	2/4	1/4	1/1	2/4
Partial neck dissection	15	9/15	5/15	4/15	9/15
Total	27	14/27	10/27	5/8	15/27

56 %

of the 27 cases with positive histology grouped by the nature of the surgery; the recurrence rate was relatively high following partial neck dissections. A retrospective analysis of the recurrences in this group fails to elucidate whether the rate would have been lower if the surgical procedures had been more radical, although there is reason to believe that it would have been.

The prognosis depends upon whether the nodal metastases were movable or fixed. Only 2 of the 25 patients with the former died of carcinoma of the lip, whereas death occurred in 8 of the 12 with fixed nodes. Invasion by the neoplasm into or fixation of the lymph nodes to the mandible spells a particularly poor prognosis. All such patients (a total of 22) died.

Cardiac arrest at 24 hours constituted a postoperative complication in a patient with ischaemic heart disease. As for other sequelae it may be mentioned that one patient developed vagal paralysis and another peripheral palsy of the facial nerve. In addition, a few cases of postoperative haemorrhage required secondary haemostasis.

Most of the cervical metastases appear within the first 30 months; during this period therefore the patients should be seen at brief intervals and should be told to present themselves before their appointments if in doubt about anything. The metastatic rate in the T4 group was 100 per cent. The rate was then, as expected, highest in the T3 group and in the group with recurrence of the primary tumour, residue or a fresh primary. Accordingly, these two groups should be followed with particular care. The metastatic rate in the T3 group with any malignancy in the primary area is so high (in the present series about 38 per cent) that in this group it must be reasonable to perform prophylactic neck dissection simultaneously with the treatment of the first recurrence. Suprahyoid and supraomohyoid neck dissections appear to be followed by a high recurrence rate and should, therefore, as far as possible be omitted in favour of radical neck dissections. Invasion into the mandible is a serious prognostic sign and indicates a particularly extensive surgical procedure. Irradiation of cervical node metastases in 22 cases (with a curative intention in 10) led to presumed cure in only one case.

Special results. The series included 24 women, the ratio for carcinoma of the upper lip being 5/24, or 21 per cent. By comparison, it may be mentioned that the corresponding ratio for men was 1.3 per cent (11/845). This difference is significant. Two of the cases affecting the upper lip of women were of basal cell carcinomas.

Four of the 16 cases of carcinoma of the upper lip were basal cell carcinomas. Prognostically, this group failed to differ from the entire series, with only one death within the control period.

Survival calculations. The survival curve for the entire series is illustrated in Fig. 4. The 5-year crude survival was 84 per cent with a 2 times standard devia-

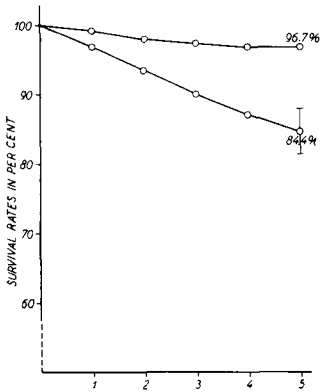


Fig. 4

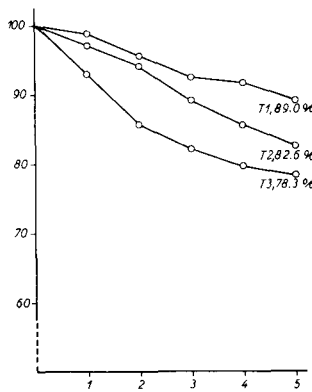


Fig. 5

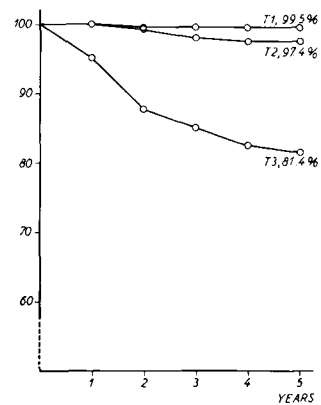


Fig. 6

Fig. 4. Survival curves for the entire series. The bottom curve is uncorrected, whereas the top curve is corrected for mortality from causes other than carcinoma of the lip.

Fig. 5. Uncorrected survival curves for T1, T2 and T3 cases.

Fig. 6. Survival curves for T1, T2 and T3 cases corrected for mortality from causes other than carcinoma of the lip.

tion of only 2.5 per cent due to the large number of patients. After correction for mortality from causes other than malignancy the 5-year survival became 96.7 per cent. In other words, only 3 to 4 per cent of the patients succumbed to carcinoma of the lip. Compared with other materials, these values are high but it must be borne in mind that the greater part of the series represents relatively early stages of the disease. Fig. 5 gives the 5-year survival curves for the T1, T2 and T3 groups. After correction for causes of death other than carcinoma (Fig. 6) the difference between T1 and T2 on the one hand and T3 on the other is more marked; it is mainly in the T3 group that the cancer deaths occur and, as already mentioned, is due to a higher tendency to lymph node metastases rather than to local factors per se.

Discussion

A surprising variation in the sex ratio has been reported, from 2 per cent women in the series of MARTIN et coll. (1941) to 28 per cent in that of PLAZA & AVELLO from Peru (1966). MALMIO (1967) reported 7 per cent (151/2138), and LYNCH (1968) in a series from Northern Ireland, 2.7 per cent. In the present material only 2.8 per cent of the patients were women.

The histology reports contained nothing of great interest. Six cases of basal cell carcinoma were included. Other authors (MARTIN et coll.) have excluded

this condition in their belief that it cannot arise from the vermilion border; owing to the small number of cases in the present series this problem is however of little importance.

The duration of symptoms and signs has varied within wide limits in the series reported. MARTIN *et coll.* gave an average of 15 months, KENNEDY (1934) 9 to 10 months and RATZKOWSKI *et coll.* (1966) a little under 6 months. The mean duration of signs in the present series was around 6 months, an indication that the afflicted patients appeared early; indeed this is reflected in the staging of a relative preponderance of T1 and T2 cases.

Poorly defined classification rules make a distinction between the T groups somewhat difficult. The present authors selected 5 mm infiltration in depth as a distinction between T2 and T3; this proved easy to administer. Quite often the records gave data such as "about 0.5 cm infiltration in depth"; these cases were assigned to the T3 group. It is thus apparent that the T3 group differs completely from the T2 group, both in respect to metastases and prognosis; a 5 mm criterion of distinction therefore seems reasonable.

A few only of the series published have been TNM classified; in a large series of more than 2 000 patients, MAHONEY (1969) reported TNM distribution little different from those now presented.

Only about 2 per cent of cases affected the upper lip, whereas an incidence of 5 to 10 per cent has been recorded in most other series.

The present analysis cannot contribute much to the aetiology considerations but others have been able to demonstrate important factors: EBENIUS (1943) in his thesis has suggested the importance of pipe smoking as an aetiological factor. BERNIER *et coll.* (1951) demonstrated that exposure to sunlight as well as the degree of skin pigmentation are decisive factors in the production of carcinoma of the lip; LYNCH also discussed the aetiological role of exposure to the sun.

It is apparent from the account of local therapy that the tumour could be controlled in all but 7 cases, 5 of which had lymph node metastases. Radium intubation produced satisfactory results, both from the curative as well as the cosmetic points of view. However, the recurrence rate in the T3 group was high, 25 per cent, and this group should not be treated by radium implantation but better by fractionated roentgen irradiation or primary surgery. The latter is the choice, if an operation is to be carried out simultaneously on the cervical nodes. Roentgen irradiation with a low tube potential at a single sitting has afforded good results in the early stages, but has now been completely abandoned. KÁPÁTI *et coll.* (1966) and RATZKOWSKI (1966) appeared satisfied with radium intubation, whereas others (STANLEY LEE & WILSON 1970, JESSE 1967) inclined to the view that fractionated roentgen irradiation is preferable. No previous authors appear to have advocated primary surgical treatment.

The frequency of lymph node metastases in the present series was low — only 5.6 per cent (49/869). Fairly high frequencies of metastases have been reported in early publications. KENNEDY (1934) gave 24 per cent while from Canada (WATSON & BURKELL 1955) the figure was 8.5 per cent. It appears to be widely agreed that neck dissection is the correct treatment, with most authors recommending standard radical neck dissection. MAHONEY (1969) suggested that contralateral partial neck dissection be performed at the same stage.

Several authors have advocated prophylactic neck dissection (FIGI 1932, KENNEDY 1934); many have taken an interest in this problem, and in recent years it has been widely agreed that this procedure was not justified, a view that the present authors of course share in general. However, the fact that about 38 per cent of those cases of the T3 group that developed one or more local recurrences also had metastases of the cervical nodes suggests that this group should be subjected to cervical dissection.

Conclusion

The material comprised 869 cases with histologically confirmed carcinoma of the lip primarily treated during the period 1946—1966. The cases were TNM classified. The primary treatment consisted of radium intubation in 766 cases; the recurrence rate was low and the cosmetic results satisfactory. However, the incidence of residues and recurrence was 25 per cent in the T3 tumour group, so that for this group primary surgery is suggested. Although 132 patients had either residues, recurrences or else developed fresh primaries, the condition could be controlled in all but 7 patients, 5 of whom had lymph node metastases.

Primary metastases in regional lymph nodes were present only in 14 cases (1.6 per cent) while 45 (5.2 per cent) had secondary metastases. These appeared never to have missed primary lymph node stations. Radiation therapy of the nodal metastases produced poor results, but after neck dissection the 5-year survival was 68 per cent (25/37). A transverse analysis indicated that of T3 cases recurring for the first time 38 per cent had, or later developed lymph node metastases. Prophylactic neck dissection thus appears to be suggested in this particular group.

The 5-year survival for the entire series was 84.5 per cent, and after correction for mortality from causes other than malignant disease, was 96.7 per cent; in other words, under 4 per cent of the patients died of the condition.

SUMMARY

A total of 869 cases of carcinoma of the lip were reviewed. The 5-year crude survival was 84.5 per cent. Primary treatment consisted of radium intubation in most cases. Recurrence

rate was low and the cosmetic results satisfactory. For T3 tumour group primary surgery is suggested. After neck dissection in cases of nodal metastases the 5-year crude survival became 56 per cent.

ZUSAMMENFASSUNG

Insgesamt 869 Fälle von Lippenkarzinomen wurden behandelt. Die gesamte 5-Jahres-Überlebensrate betrug 84,5 Prozent. Die primäre Behandlung bestand in einer Radium-intubation in den meisten Fällen. Die Rezidivfrequenz war niedrig und die kosmetischen Resultate zufriedenstellend. Für die T3 Tumorguppe wird die primäre chirurgische Behandlung vorgeschlagen. Bei Fällen mit Lymphmetastasen betrug nach Halsdissektion die gesamte 5-Jahres-Überlebensrate 56 Prozent.

RÉSUMÉ

Les auteurs ont passé en revue un total de 869 cas de cancer de la lèvre. Le taux brut de survie à 5 ans était de 84,5 pour-cent. Le traitement primaire a consisté en implantation de radium dans la plupart des cas. Le taux de récurrence était bas et les résultats esthétiques satisfaisants. Les auteurs proposent un traitement chirurgical primitif pour les tumeurs du groupe T3. Après dissection cervicale dans les cas de métastases ganglionnaires le taux brut de survie à 5 ans est de 56 pour-cent.

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