

# Distant Metastases and Local Recurrence in Head and Neck Cancer \*

MARVIN S. ARONS, M.D., D.M.D., ROBERT R. SMITH, M.D.

*From the Surgery Branch of the National Cancer Institute, National Institutes of Health,  
Public Health Service, U. S. Department of Health, Education, and Welfare,  
Bethesda, Maryland*

TRADITIONALLY, it has been held that cancer of the head and neck seldom, if ever, spreads below the clavicle.<sup>8, 12, 13, 15-17</sup> Current cancer textbooks<sup>2, 18</sup> still employ the terms "rare," "exceptional," and "uncommon" in this regard, and most of the recent papers on head and neck cancer, with several exceptions,<sup>11, 20, 23</sup> have little, if any, reference to distant metastases. The problem of postoperative wound recurrence in these cases has been more widely recognized.<sup>4, 19, 20, 23, 25-27, 32</sup>

In the various types of cancer of the head and neck, cervical lymph nodes are thought to function as an early protective barrier, confining metastatic growth and allowing time for treatment. Once there is local wound recurrence or distant metastases or both, treatment is of limited benefit.

This paper presents a clinical study of a group of patients, designed with the following objectives: 1) to stress the incidence of distant metastases occurring during a clinical study; 2) to determine the value and need of preoperative and postoperative chest and bone x-rays in demonstrating distant metastases (spread below clavicle); 3) to re-emphasize the early appearance and frequency of local recurrence; 4) to correlate cervical lymph node metastases with local recurrence and distant metastases; and 5) to illustrate the use of life-table analysis of data on cancer of the head and neck.

## Materials and Methods

The 89 patients in this study were admitted to the Surgery Branch of the National Cancer Institute between July 1953 and January 1960. None was lost to follow up which closed on August 1, 1960 giving a minimum follow up period of six months and a maximum of 76 months. All cases had extensive epidermoid carcinoma except for two with adenocarcinoma of the paranasal sinuses. The location and number of tumors studied are listed in Table 1 and represent consecutive admissions. Cancer of the lip, skin, salivary glands, nasopharynx, thyroid and neck with an unknown primary were excluded. Also omitted were three cases of cancer of the head and neck with a second primary at a different anatomic location (pancreas, colon, myeloma).

All patients had chest x-rays, and 86 per cent had x-rays of the skeleton for metastases (skull, spine, pelvis). None had radiologic evidence of pulmonary or skeletal metastases on admission.

Table 2 lists the primary therapy given on admission. The number of patients treated by operation, x-ray therapy, or a combination prior to admission was 35 (39%). Definitive operation is that performed with an attempt to cure. Exploratory operation refers to two craniotomies performed as the initial procedure in a combined neurosurgical-surgical approach to cancer of the sinuses and where tumor was found to be irresectable. Radiation was em-

\* Submitted for publication January 16, 1961.

TABLE 1. *Location and Number of Primary Head and Neck Cancers*

Location	No.
Paranasal sinuses	13
Tongue	12
Larynx	12
Floor of mouth	11
Tonsil-pharynx	10
Pyriiform sinus	8
Multiple intra-oral (2 or more)	6
Alveolar ridge	5
Buccal mucosa	5
Buccogingival	4
Palate	3
Total	89

ployed primarily when the cancer was considered inoperable. Four patients in the definitive group were admitted on a special study to radiate primary intra-oral cancers in conjunction with radical neck dissection. Residual tumor remained in five patients after attempted resection and supplemental x-ray therapy was given to those four patients not previously radiated.

The data in Figure 1 is based on 55 cases where neck dissection was performed and on 17 cases without neck dissection. In all 72 cases, no residual tumor remained and no doubt existed in differentiating between local recurrence and new primary tumor.

An attempt was made to secure follow up chest and bone x-rays on all cases every six months. All patients now living, except two, have had such metastatic surveys. It is realized that what was diagnosed as a pulmonary metastasis in some may actually have been a primary lung tumor or a metastasis from an unrecognized second primary elsewhere. In one instance even after thoracotomy and resection of a lung tumor, pathologic examination did not resolve the question of whether this was a new primary or a metastasis. When skeletal or pulmonary metastases were discovered, 50 per cent of the patients had symptoms referable to these systems.

Local recurrence refers to recurrence in the operative field following definitive op-

eration and includes six cases with contralateral cervical node metastases. The data excludes five cases with residual tumor and three with multiple intra-oral cancer in whom recurrence could not be distinguished from a new primary.

## Results

**A. Distant Metastases.** Of all patients studied, 21 per cent developed x-ray evidence of distant metastases. Metastatic spread to the lungs occurred in 16 of the 19 cases (Table 3). In 72 cases where all tumor was removed by definitive operation and no doubt existed in differentiating between a local recurrence and a new primary, 19 per cent developed distant metastases. As plotted in Figure 1, 27 per cent of distant metastases occurred within four months from the time of operation done at this hospital, 60 per cent by eight months, and all but one case within 24 months. It was also noted that the occurrence of distant metastases approximated the time of the development of local recurrence. When plotted by the life-table method (Fig. 1), the cumulative percentage living and dead with distant metastases after definitive operation was 23 at two years.

**B. Local Recurrence.** Local recurrence was encountered in 31 of the 72 patients receiving definitive surgical therapy. Median time interval from operation to recurrence was five months. Data in Figure 1

TABLE 2. *Primary Treatment on Admission*

Treatment	Cases
Definitive surgery	77
Surgery alone	70
Surgery + x-ray	7
Exploratory surgery	2
Radiation	5
Refused surgery	4
Refused x-ray	3
Accepted x-ray	1
No treatment	1
Total	89

reveal that 48 per cent of recurrences occurred within four months, 71 per cent by eight months, and all by 36 months. When calculated by life-table analysis (Fig. 1), the cumulative percentage living and dead with local recurrence after definitive operation was 47 at three years.

**C. Cervical Metastases.** Neck dissections were performed for two reasons: 1) when surgical treatment of necessity involved the neck without palpable nodes; and 2) where there were operable palpable cervical nodes with a resectable primary tumor and no distant metastases. When these dissections were done, 39 cases had microscopically positive lymph nodes and 16 had negative nodes (Table 4). Based on these 55 cases, there appeared to be no statistically significant correlation between positive nodes and either local recurrence or distant metastases as determined by the chi-square significance test on two-by-two tables at the .05 probability level (Table 4). No apparent difference could be detected in survival rates in those cases with either positive or negative nodes or in the 17 cases where no neck dissection was per-

TABLE 3. X-ray Evidence of Distant Metastases

Location	No. with Metastases	
	All Cases (89)	Surgical Cases (72)
Lung	14	10
Bone	3	2
Lung and bone	2	2
	—	—
Total	19 (21%)	14 (19%)

TABLE 4. Correlation of Cervical Lymph Nodes with Local Recurrence and Distant Metastases \*

	Positive Nodes	Negative Nodes
Local recurrence	16	3
Distant metastases	6	0
Local recurrence and distant metastases	5	2
Neither	12	11
	—	—
Totals	39	16

\* Data based on the 55 cases where neck dissection performed, no residual tumor remained, and no doubt existed between local recurrence and a new primary tumor.

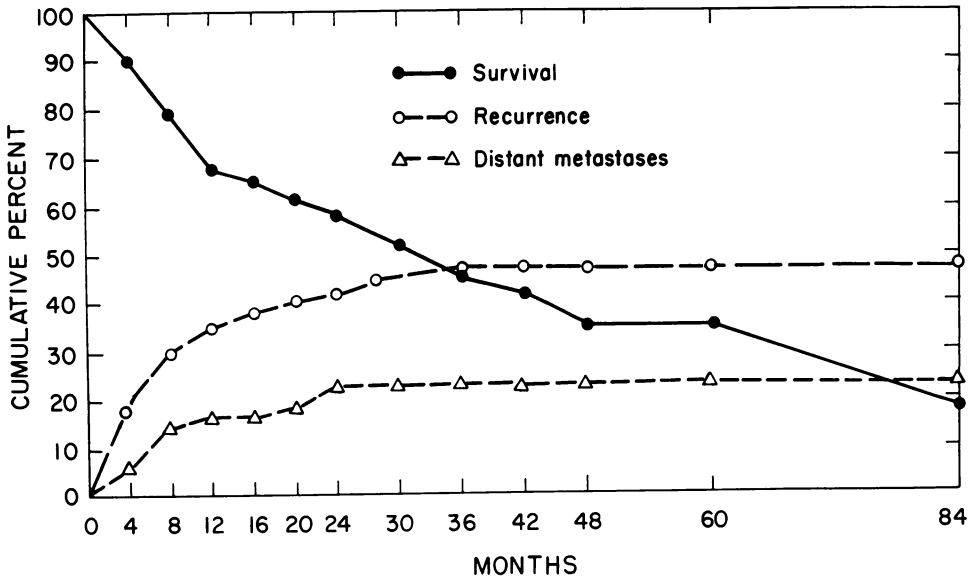


FIG. 1. Life-table analysis of distant metastases, local recurrence, and survival data in 72 cases treated by definitive surgery.

formed. However, it must be noted that these groups represent only a small series and that significant differences might be found in larger groups.

**D. Survival Data.** The cumulative percentage of patients surviving after definitive operation was 35 at five years by life-table analysis (Fig. 1). This was calculated for reference with the data on local recurrence and distant metastases.

### Discussion

Contrary to the usually accepted concept of limited local spread of cancer, this clinical study of living patients with cancer of the head and neck demonstrated a 23 per cent incidence of metastatic spread below the clavicle. It is of both clinical and practical significance to report the incidence of distant metastases in living<sup>11</sup> rather than in autopsied cases.<sup>1, 7, 9, 22, 28-30</sup>

Although admission x-rays failed to reveal distant metastases in this and another reported series of cases,<sup>11</sup> the hazards of diagnostic radiography are considered small enough to be outweighed by the expectation of potential benefit.<sup>31</sup> However, the chance of x-ray detection of distant spread of cancer of the head and neck appears to be minimal or nonexistent when a patient first presents for treatment.

Postoperative pulmonary and skeletal x-ray films are usually of more academic than practical value in terms of therapy except in the instance of finding a solitary lung lesion.<sup>24</sup> Since 50 per cent of patients in this study with postoperative pulmonary or skeletal metastases had symptoms referable to these systems, only one in ten of all patients followed after definitive operation would have benefited from routine x-ray follow up.

This study supports routine chest roentgenograms as a means of postoperative follow up. Twelve of 14 patients with distant metastases after definitive operation had metastases confined to the lungs. The most important time for obtaining these x-rays

would be during the first two years of follow up.

The interpretation of chest x-rays occasionally is a problem. In this series, eight x-rays initially read as metastases were found later to be negative, while three originally judged negative showed tumor on retrospective examination. There were five autopsied cases with lung or bone metastases not evident radiographically even though the x-rays were taken one day to one week prior to death. It is important to recall this x-ray negative stage of metastases.<sup>6, 21</sup>

The problem of early local recurrence has been well recognized. It has been reported<sup>10, 19</sup> that no correlation existed between recurrence and tumor cells found in operative cancer wounds of the head and neck. Analysis of data in a series of patients undergoing definitive operation for various types of cancer, including 48 per cent of the head and neck, showed no correlation between wound washings for tumor cells and local recurrence or distant metastases, nor between positive lymph nodes and the incidence of local recurrence or distant metastases.<sup>3</sup> This latter finding is in agreement with the present study. The accumulation of such data emphasizes the need to explore new methods of therapy to control the implantation and growth of tumor emboli both locally in the wound and systemically at distant sites.

Attention should be directed to the advantages of life-table analysis of this data. It is an actuarial method that gives a better statistical estimate of distant metastases, local recurrence, and survival rates than the direct or five-year method with small numbers of cases.<sup>5</sup> It also makes possible the use of all data accumulated up to the closing date of the study including all patients who entered observation even six months prior to this closing date.<sup>14</sup> Finally, the life-table method takes into account the effective number exposed to the risk of develop-

ing distant metastases or local recurrence and to the risk of dying during the study.

### Summary

A group of 89 patients with cancer of the head and neck was studied to determine the incidence of distant metastases and local recurrence as demonstrated by radiological and clinical examination.

As determined by life-table analysis of 72 cases treated by definitive operation, the cumulative percentage with distant metastases was 23 at two years, the cumulative percentage with local recurrence was 47 per cent at three years, the cumulative percentage surviving was 35 at five years. No patient had radiologic evidence of pulmonary or skeletal metastases on admission. After operation, 60 per cent of distant metastases developed by eight months and all but one case by two years. Since 50 per cent of those with postoperative pulmonary or skeletal, metastases had symptoms referable to those systems, only one in ten of all patients followed after definitive operation would have benefited from routine metastatic surveys. Median time interval from operation to local recurrence was five months with 71 per cent recurring by eight months and 100 per cent by three years. No statistical correlation could be found between cervical lymph node metastases and local recurrence or distant metastases in this small series. Finally, the advantages of life-table analysis of cancer data were noted.

### Acknowledgment

The authors wish to thank Mr. Max H. Myers of the Biometry Branch, National Cancer Institute, for his statistical assistance.

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