

*This is a study of 706 men with carcinoma of the mouth and pharynx compared with an equal number of controls who were diagnosed and treated from 1959 through 1961 in American VA hospitals. Specific findings are detailed. Survival experience is related to the size and initial location of the cancer, but not to other factors.*

## **SURVIVORSHIP WITH MOUTH AND PHARYNX CANCERS AND THEIR ASSOCIATION WITH CIRRHOSIS OF THE LIVER, MARITAL STATUS, AND RESIDENCE**

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**M**AN'S survivorship is determined by many factors. Firmly among these are his sex, age, race, residence, education, and income as well as his habits, nutritional status, diseases, and available health facilities.<sup>1-9</sup> If cancer is among his diseases, then its histological type, anatomical site, degree of differentiation and spread, and dimensions may be the crucial determinants of his survival.<sup>3,10-13</sup>

For these reasons, no single factor may be fully adequate to assess man's survival, especially from cancer, since the demographic and clinical milieu in which the cancer and the patient contemporize may so differentially influence survival that they, too, should be characterized. To this end, survival rates with standard errors in this study will derive from cancers that are histologically confirmed and anatomically specific, and from patients for whom selection, diagnosis, treatment, and follow-up are standardized.

In this study, moreover, 706 males with cancer of the mouth and pharynx will be initially characterized on the demographic variables of age, race,

marital status, religion, occupation, birthplace, and residence; then on the clinical diagnoses of cirrhosis of the liver, diabetes mellitus, rheumatoid arthritis, syphilis, and other cancers than those of the mouth and pharynx. Subsequently, cumulative five-year survival rates will be reported for all diagnoses and variables, except birthplace.

### **Veterans Administration Material**

More than 160 veterans' hospitals in the United States discharge over half a million patients each year. Routine information on their characteristics and diagnoses comprises a 20 per cent systematic sample which has repositored for many years at the Veterans Administration Central Office in Washington, D. C.

Information from this centralized data repository, and facts from other independent sources, affirm that throughout the Veterans Administration hospital system the diagnostic indexing of records is standardized; the quality and intensity of medical care are comparable; the training and qualifications of

**Table 1—Bed capacity and characteristics\* of hospitals reporting cases of mouth and pharynx cancers and other patients**

|  | A. Hospital size |                 |   | B. Hospital characteristics* |                 |
|--|------------------|-----------------|---|------------------------------|-----------------|
|  | Cancer cases     | Other patients† |   | Cancer cases                 | Other patients† |
| Number                                 | 706              | 415,953         | Number  | 706                          | 415,953         |
| Per cent                               | 100.0            | 100.0           | Per cent  | 100.0                        | 100.0           |
| 1. <100 to 499 beds<br>(54 hospitals)  | 32.2             | 44.3            | 1. Medical school affiliation and advisory committee‡<br>(67 hospitals) | 86.4                         | 72.1            |
| 2. 500 to 899 beds<br>(27 hospitals)   | 24.8             | 25.7            | 2. Neither of above<br>(28 hospitals)                                   | 8.6                          | 22.4            |
| 3. 900 to 1,499 beds<br>(15 hospitals) | 30.0             | 22.4            | 3. Medical advisory committee only‡<br>(6 hospitals)                    | 5.0                          | 5.5             |
| 4. 1,500 or more beds<br>(5 hospitals) | 13.0             | 7.6             |   |                              |                 |

\* Characteristics as determined by the hospital's medical school affiliation status.

† All patients with medical and surgical disorders treated during 1960 in 101 veterans' hospitals from which cases were discharged.

‡ A community-based committee of experts which substitutes for or complements the roles assumed by medical schools in their affiliated capacity with veterans' hospitals.

doctors, medical specialists, and graduates from leading medical schools are uniform; and the criteria for patient selection, diagnoses, and treatments are also uniform.<sup>3,14-19</sup> Thus, for comparative and epidemiological purposes, these data present distinctive advantages.

Whenever a veteran applies for hospitalization in the Veterans Administration, he is assigned a nonrecurring claim number which serves to establish his identity. According to this study, it is employed both to secure the basis for case and control selection and to ascertain follow-up for survivorship computation. Follow-up is facilitated by the estate's claim for burial allowances to which the veteran is entitled.<sup>20</sup>

### Materials and Methods

A case and its control were selected from the 20 per cent systematic sample of hospitalized veterans on whom routine information exists at the Veterans Administration Central Office for the

period 1959 through 1961, and having claim numbers terminating in one or five. Only resident veterans in the United States were selected.

A case was defined as a male with histologically confirmed squamous cell carcinoma of the tongue, floor of the mouth, mesopharynx, hypopharynx, other parts of the mouth, coexisting sites, and multiple sites. Other parts of the mouth included the relatively uncommon cancers of the alveolar ridge, buccal mucosa, retromolar pad, the gingiva, the hard palate, the uvula, and the soft palate. Coexisting site cancers were mouth and pharynx cancers diagnosed at two or more distinct anatomical sites during a three-year period. Multiple site cancers were mouth and pharynx cancers for which no single primary site could be determined. Each carcinoma corresponded to the International Classification of Disease rubric 141, 143, 144, 145, 147 or 148.<sup>21</sup> Surgical diagnoses, both histologically and anatomically, were ascertained for

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**Table 2—Marital status by race of cases of mouth and pharynx cancers and their matched controls\***

|           | Negro             |                  | White             |                   | Total             |                   |
|-----------|-------------------|------------------|-------------------|-------------------|-------------------|-------------------|
|           | Cases             | Controls         | Cases             | Controls          | Cases             | Controls          |
| Number    | 69                | 84               | 637               | 622               | 706               | 706               |
| Per cent  | 100.0             | 100.0            | 100.0             | 100.0             | 100.0             | 100.0             |
| Single    | 11.6              | 11.9             | 18.5              | 12.7              | 17.9              | 12.6              |
| Married†  | 53.6              | 63.1             | 51.0 <sup>w</sup> | 67.7 <sup>w</sup> | 51.0 <sup>w</sup> | 67.1 <sup>w</sup> |
| Widowed   | 13.0              | 15.4             | 10.7              | 9.3               | 10.9              | 10.1              |
| Separated | 5.8               | 3.6              | 2.5               | 1.9               | 2.8               | 2.1               |
| Divorced  | 16.0 <sup>z</sup> | 6.0 <sup>z</sup> | 17.3 <sup>w</sup> | 8.4 <sup>w</sup>  | 17.1 <sup>w</sup> | 8.1 <sup>w</sup>  |

\* A control matches a case on age within five years and on a hospital's bed capacity and medical school affiliation status.

† Includes, among white cases, one for whom status by marriage is not stated.

w:  $p < 0.00001$

z:  $p < 0.05$

**Table 3—Religious preference by race of cases of mouth and pharynx cancers and their matched controls\***

|             | Negro |          | White            |                  | Total            |                  |
|-------------|-------|----------|------------------|------------------|------------------|------------------|
|             | Cases | Controls | Cases            | Controls         | Cases            | Controls         |
| Number      | 69    | 84       | 637              | 622              | 706              | 706              |
| Per cent    | 100.0 | 100.0    | 100.0            | 100.0            | 100.0            | 100.0            |
| Protestants | 92.8  | 92.9     | 60.3             | 61.1             | 63.5             | 64.9             |
| Catholics   | 5.8   | 4.7      | 37.0             | 32.6             | 34.0             | 29.3             |
| Jews        | 0.0   | 0.0      | 0.3 <sup>x</sup> | 3.9 <sup>x</sup> | 0.3 <sup>x</sup> | 3.4 <sup>x</sup> |
| Others      | 1.4   | 2.4      | 2.4              | 2.4              | 2.2              | 2.4              |

\* A control matches a case on age within five years and on a hospital's bed capacity and medical school affiliation status.

x:  $p < 0.001$

**Table 4—Occupational categories by race of cases of mouth and pharynx cancers and their matched controls\***

|                 | Negro            |                  | White            |                  | Total            |                  |
|-----------------|------------------|------------------|------------------|------------------|------------------|------------------|
|                 | Cases            | Controls         | Cases            | Controls         | Cases            | Controls         |
| Number          | 69               | 84               | 637              | 622              | 706              | 706              |
| Per cent        | 100.0            | 100.0            | 100.0            | 100.0            | 100.0            | 100.0            |
| Professionals   | 4.4              | 3.6              | 5.5              | 5.3              | 5.4              | 5.1              |
| Managerials     | 1.4              | 4.8              | 3.4              | 5.6              | 3.3              | 5.5              |
| Clericals       | 5.8              | 2.4              | 8.3              | 5.5              | 8.1 <sup>y</sup> | 5.1 <sup>y</sup> |
| Sales workers   | 1.4              | 0.0              | 6.4              | 6.1              | 5.9              | 5.4              |
| Craftsmen       | 16.0             | 11.9             | 30.0             | 27.0             | 28.6             | 25.2             |
| Operatives      | 13.0             | 14.3             | 10.5             | 13.7             | 10.8             | 13.7             |
| Service workers | 31.9             | 20.2             | 16.2             | 12.7             | 17.7             | 13.6             |
| Laborers        | 16.0             | 22.6             | 12.6             | 10.1             | 12.9             | 11.6             |
| Farmers         | 8.7              | 8.3              | 5.7              | 4.5              | 5.9              | 5.0              |
| Unemployed      | 0.0 <sup>y</sup> | 9.5 <sup>y</sup> | 0.3 <sup>w</sup> | 4.2 <sup>w</sup> | 0.3 <sup>w</sup> | 4.8 <sup>w</sup> |
| Not stated      | 1.4              | 2.4              | 1.1 <sup>w</sup> | 5.3 <sup>w</sup> | 1.1 <sup>w</sup> | 5.0 <sup>w</sup> |

\* A control matches a case on age within five years and on a hospital's bed capacity and medical school affiliation status.

w:  $p < 0.00001$

y:  $p < 0.01$

z:  $p < 0.05$

**Table 5—Geographical patterns by birthplace and race of cases of mouth and pharynx cancers and their matched controls\***

|                    | Birthplace of Negro |               | Birthplace of white |                | Birthplace of total |                |
|--------------------|---------------------|---------------|---------------------|----------------|---------------------|----------------|
|                    | Cases (69)          | Controls (84) | Cases (637)         | Controls (622) | Cases (706)         | Controls (706) |
| New England        | 0.0                 | 1.2           | 8.2                 | 7.4            | 7.4                 | 6.7            |
| Middle Atlantic    | 5.8                 | 3.6           | 18.7                | 16.9           | 17.4                | 15.3           |
| East North Central | 10.2                | 3.6           | 19.0                | 18.8           | 18.1                | 17.0           |
| West North Central | 0.0                 | 1.2           | 12.2                | 14.3           | 11.1                | 12.7           |
| East South Central | 30.4                | 27.4          | 7.7                 | 8.3            | 9.9                 | 10.6           |
| South Atlantic     | 34.8                | 38.0          | 9.7                 | 9.2            | 12.2                | 12.6           |
| West South Central | 17.4                | 23.8          | 10.2                | 7.9            | 10.9                | 9.8            |
| Mountain           | 0.0                 | 0.0           | 1.6                 | 3.4            | 1.4                 | 3.0            |
| Pacific            | 0.0                 | 0.0           | 3.3                 | 3.2            | 3.0                 | 2.8            |
| Outside U. S.      | 1.4                 | 1.2           | 9.4                 | 10.6           | 8.6                 | 9.5            |
| Total              | 100.0               | 100.0         | 100.0               | 100.0          | 100.0               | 100.0          |

\* A control matches its case on age within five years and on a hospital's bed capacity and medical school affiliation status.

each malignancy by the careful review of entries in clinical records by pathologists, oral surgeons, attending physicians, and other members of head and neck tumor boards.

A control was defined as the next male—in a sequential listing of claim numbers—who matched its case on age (within five years), on hospital size (by bed capacity), and on hospital characteristics (as determined by the hospital's medical school affiliation status). Matching was effected to allow and to stabilize for variations in patient characteristics owing to age, sex, therapeutic practices (which might relate to the hospital's medical school affiliation status), and to procedures consistent with a hospital's size or bed capacity. Hence, for each of the 706 cases, there was one matched control analogously drawn from the same population and sharing the

selective factors that similarly existed for its case.

Complete clinical records were reviewed for all cases and their matched controls: in order to obtain the demographic data on race, marital status, religion, occupation, birthplace, and residence; also to confirm the clinical diagnoses of cirrhosis of the liver, diabetes mellitus, rheumatoid arthritis, syphilis, and associated neoplasms (i.e., primary neoplasms of other sites than those of the mouth and pharynx); and to determine the frequency of multiple primary body cancers. Cases and controls were compared on each of the aforementioned variables; those with cirrhosis of the liver and associated neoplasms were also compared by diagnostic sites.

Hospital utilization patterns were assessed with the use of all medical and

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surgical patients in case-reporting hospitals by their bed capacity and affiliations with medical schools. Also determined were geographical residence patterns for cases by anatomical sites in comparison with those for veterans in civil life. Subsequently, available death certificates of all cases were evaluated. For survivorship analyses, clinical records were further reviewed to ascertain the date of each patient's death and the initial place of the cancer's confirmation. These analyses employed actuarial methods which contended with additions and losses in the observation period.<sup>22-26</sup> Follow-up was terminated on December 31, 1966.

Accordingly, case survivor rates with standard errors—both cumulative over five years—were computed: for transfers and nontransfers to veterans' hospitals<sup>3</sup>; for each race, stage of disease, anatomical site, region of residence, and age

group; for those with either the absence or presence of associated neoplasms, cirrhosis of the liver, diabetes mellitus, syphilis, and rheumatoid arthritis; solely for white males by marital status, religious preference, and occupations, and for United States males of the case's age and race.<sup>9</sup> Each survivor rate and standard error were adjusted to the age distribution of all cases. Finally, five-year average death rates were determined for the general population of United States males of the case's age and race, and for the cases by race and stage of the disease.<sup>9</sup> This was done by using deaths observed within a five-year period in the numerators and person-days in the same period equated to person-years in the denominators.

To facilitate these analyses, all abstracted data were recorded on standard forms, then coded and entered on punch cards. The matched chi-square test

**Table 6—Geographical pattern by residence and race of cases of mouth and pharynx cancers and their matched controls\***

|                    | Residence of Negro |               | Residence of white |                | Residence of total |                  |
|--------------------|--------------------|---------------|--------------------|----------------|--------------------|------------------|
|                    | Cases (69)         | Controls (84) | Cases (637)        | Controls (622) | Cases (706)        | Controls (706)   |
| New England        | 0.0                | 0.0           | 8.6                | 8.0            | 7.8                | 7.1              |
| Middle Atlantic    | 14.5               | 10.7          | 19.2               | 16.9           | 18.7               | 16.1             |
| East North Central | 24.6               | 22.6          | 19.3               | 19.1           | 19.8               | 19.5             |
| West North Central | 2.9                | 2.4           | 8.2                | 10.3           | 7.7                | 9.4              |
| East South Central | 17.4               | 15.4          | 5.7                | 7.1            | 6.8                | 8.1              |
| South Atlantic     | 27.5               | 31.0          | 11.0               | 11.7           | 12.6               | 14.0             |
| West South Central | 11.6               | 13.1          | 10.0               | 8.4            | 10.2               | 8.9              |
| Mountain           | 0.0                | 2.4           | 2.0                | 4.2            | 1.8 <sup>z</sup>   | 4.0 <sup>z</sup> |
| Pacific            | 1.5                | 2.4           | 16.0               | 14.3           | 14.6               | 12.9             |
| <b>Total</b>       | <b>100.0</b>       | <b>100.0</b>  | <b>100.0</b>       | <b>100.0</b>   | <b>100.0</b>       | <b>100.0</b>     |

\* A control matches a case on age within five years and on a hospital's bed capacity and medical school affiliation status.  
z: p<0.05

**Table 7—Geographical patterns by residence of veterans in civil life and cases of mouth and pharynx cancers**

|                    | Veterans*         | Floor of mouth   | Tongue | Meso-pharynx | Hypo-pharynx      | Other parts of mouth† | Coexisting sites‡ | Multiple sites§  |
|--------------------|-------------------|------------------|--------|--------------|-------------------|-----------------------|-------------------|------------------|
| Number             | 18,383,034        | 123              | 92     | 67           | 108               | 61                    | 46                | 209              |
| Per cent           | 100.0             | 100.0            | 100.0  | 100.0        | 100.0             | 100.0                 | 100.0             | 100.0            |
| New England        | 6.4 <sup>x</sup>  | 10.6             | 5.4    | 3.0          | 14.8 <sup>x</sup> | 1.6                   | 10.9              | 6.2              |
| Middle Atlantic    | 20.5 <sup>y</sup> | 19.5             | 23.9   | 19.4         | 10.2 <sup>y</sup> | 14.8                  | 15.2              | 22.0             |
| East North Central | 20.6              | 21.1             | 19.7   | 23.9         | 14.8              | 27.9                  | 21.7              | 17.7             |
| West North Central | 8.4               | 8.1              | 8.7    | 7.5          | 5.5               | 8.2                   | 10.9              | 7.2              |
| East South Central | 5.5               | 4.1              | 6.5    | 4.5          | 9.3               | 8.2                   | 8.7               | 7.2              |
| South Atlantic     | 13.2 <sup>x</sup> | 7.3 <sup>z</sup> | 15.2   | 10.4         | 17.6              | 13.1                  | 10.9              | 12.9             |
| West South Central | 8.6 <sup>x</sup>  | 9.8              | 5.4    | 11.9         | 13.9 <sup>x</sup> | 13.1                  | 8.7               | 9.6              |
| Mountain           | 3.9 <sup>y</sup>  | 3.2              | 1.1    | 3.0          | 0.9               | 1.6                   | 2.1               | 1.4 <sup>y</sup> |
| Pacific            | 12.9              | 16.3             | 14.1   | 16.4         | 13.0              | 11.5                  | 10.9              | 15.8             |

\* Veterans living in the United States during 1960 who were 30 years or older.

† Includes the gingiva, retromolar pad, alveolar ridge, buccal mucosa, or either palate.

‡ Includes two or more distinct sites of the mouth or pharynx during the three-year period.

§ Includes combined sites for which no single primary site could be established.

x:  $p < 0.001$

y:  $p < 0.01$

z:  $p < 0.05$

(with continuity correction) was employed to determine the statistical significance accepted as the 5 per cent level of all differences between case-control pairs.<sup>27-29</sup>

## Results

### Demographic

Cases were initially treated at 101 veterans' hospitals. Within 17 per cent of these that have a thousand or more beds, there are 38 per cent of the 706 cancer patients and 27 per cent of 415,953 medical and surgical patients (Table 1A). Hospitalization rates for cancer are, therefore, significantly high in the large hospitals. Moreover, medical, surgical and cancer patients are principally diagnosed at hospitals affiliated with medical schools, which are teaching hospitals (Table 1B).

The age distribution of cases and controls is as follows: 30 to 39 years, 2.7 per cent; 40 to 49 years, 13.6 per cent; 50 to 59 years, 22.9 per cent; 60

to 69 years, 46.2 per cent; and 70 years and older, 14.6 per cent. The cases range in age from 32 to 87 years. Their median age, like the control's, is 63 years.

The married cases, in contrast to those divorced, is significantly less common than among controls (Table 2). However, the proportion separated among Negroes exceeds by twofold the separated among whites. The frequency of Protestants at 64 per cent is double that of Catholics among the combined cases and controls (Table 3). But among these, Jews comprise less than 2 per cent and are significantly uncommon as cases.

Occupational categories are based on definitions and classifications in the United States Department of Labor's Dictionary of Occupational Titles.<sup>30</sup> White collar workers, as professionals, managerials, clericals, and sales workers are twice as frequent among whites as among Negroes, but the opposite is true for service workers, laborers, and the unemployed among Negroes (Table

4). Although the proportion of clericals is significantly high among cases, this significance at the 5 per cent level might not have prevailed if the "not stated" category were otherwise classifiable.

Geographical patterns by birthplace for each race are distributed in Table 5. No one of the Negroes (69 cases and 84 controls) but 5.7 per cent of the whites (637 cases and 622 controls) were born in the West. In the South 86.3 per cent of Negroes and only 26.5 per cent of whites were born, by contrast to outside of the United States, where 1.3 per cent of Negroes and 10.0 per cent of whites were born. Hence, among all cases and controls of both races, 5.1 per cent were born in the West; nearly one-third was born in the South, and 9.1 per cent were born outside of the United States. Nonetheless, cases and controls by birthplace for each race are similarly distributed.

In Table 6 are seen the geographical patterns for the United States residence of each race. Only 3.3 per cent of all Negroes but 18.3 per cent of all whites reside in the Mountain and Pacific States of the West; yet in the South there reside 58.2 per cent of all Negroes and 26.8 per cent of all whites. Consequently, significantly more whites reside in the West and more Negroes reside outside of the South than were born in either region.

Despite the similar distributions by residence for matched controls and veterans in civil life (noted in Tables 6 and 7), the residences of all veterans will be compared with those of cases by anatomical sites, thus utilizing the parent veteran population from which cases derived. Table 7 reveals: decided deficits of floor of mouth and multiple site cancers in the South Atlantic and Mountain regions, respectively; marked excesses of hypopharynx cancers in the entire South and New England; and a result which corroborates a previous study's finding of a significant deficit

of hypopharynx cancers in the Middle Atlantic.<sup>17</sup> Tongue, mesopharynx, other parts of the mouth, and coexisting site cancers, however, are similarly distributed in veterans in civil life.

### *Clinical*

Table 8 shows cirrhosis of the liver to be associated at the 0.2 per cent level with all cancers of the mouth and pharynx, owing to its more specific association with floor of mouth cancers at the 0.8 per cent level and coexisting site cancers at the 4.5 per cent level. Cases with floor of mouth cancers comprise 41.5 per cent of the 46 patients with coexisting site cancers. Thus, the association of cirrhosis of the liver and floor of mouth cancer is again demonstrated, corroborating this same result in other studies.<sup>18-19</sup>

Rheumatoid arthritis afflicts 1.8 per cent of the cases and 1.2 per cent of the controls. Syphilis exists in 3.4 per cent of the cases and in 2.0 per cent of the controls. Diabetes mellitus is present in 5.1 per cent of the cases and in 10.2 per cent of the controls; there is therefore a difference for a negative association at the 0.1 per cent level. The negative association was further investigated by applying to each age interval of cases the corresponding age-specific rate of diabetes mellitus obtained from a 20 per cent systematic patient sample of 941 with prostatic cancers in 1961. By this procedure, 26.4 with diabetes mellitus were expected in comparison with 36 already observed, thereby affording a difference which is not statistically significant.

Primary cancers, histologically and anatomically diagnosed at other sites than the mouth and pharynx, are defined as associated neoplasms. These occur with similar frequencies of 14 per cent and 16 per cent among cases and controls, respectively (Table 9). Associated neoplasms are about half as frequent among cases with multiple site

**Table 8—Proportion with clinically diagnosed liver cirrhosis by anatomical sites for cases of mouth and pharynx cancers and their matched controls\***

| Sites                | No. | Cases |                   | Controls |                  |
|----------------------|-----|-------|-------------------|----------|------------------|
|                      |     | No.   | %                 | No.      | %                |
| Floor of mouth       | 123 | 18    | 14.6 <sup>y</sup> | 6        | 4.9 <sup>y</sup> |
| Tongue               | 92  | 7     | 7.6               | 8        | 8.7              |
| Mesopharynx          | 67  | 6     | 9.0               | 4        | 6.0              |
| Hypopharynx          | 108 | 8     | 7.4               | 6        | 5.6              |
| Other parts of mouth | 61  | 6     | 9.8               | 6        | 9.8              |
| Coexisting sites     | 46  | 7     | 15.2 <sup>z</sup> | 2        | 4.3 <sup>z</sup> |
| Multiple sites       | 209 | 22    | 10.5              | 12       | 5.7              |
| Total                | 706 | 74    | 10.5 <sup>y</sup> | 44       | 6.2 <sup>y</sup> |

\* A control matches its case on age within five years and on a hospital's bed capacity and medical school affiliation status.

<sup>y</sup>:  $p < 0.01$

<sup>z</sup>:  $p < 0.05$

**Table 9—Proportion with clinically diagnosed associated neoplasms\* by anatomical sites for cases of mouth and pharynx cancers and their matched controls\***

| Sites                | No. | Persons with associated neoplasms† |                  |          |                   |
|----------------------|-----|------------------------------------|------------------|----------|-------------------|
|                      |     | Cases                              |                  | Controls |                   |
|                      |     | No.                                | %                | No.      | %                 |
| Floor of mouth       | 123 | 13                                 | 10.6             | 16       | 13.0              |
| Tongue               | 92  | 16                                 | 17.4             | 14       | 15.2              |
| Mesopharynx          | 67  | 15                                 | 22.4             | 14       | 20.9              |
| Hypopharynx          | 108 | 17                                 | 15.7             | 21       | 19.4              |
| Other parts of mouth | 61  | 13                                 | 21.3             | 7        | 11.5              |
| Coexisting sites     | 46  | 5                                  | 10.9             | 5        | 10.9              |
| Multiple sites       | 209 | 20                                 | 9.6 <sup>z</sup> | 38       | 18.2 <sup>z</sup> |
| Total                | 706 | 99                                 | 14.0             | 115      | 16.3              |

\* A control matches its case on age within five years and on a hospital's bed capacity and medical school affiliation status.

† Associated neoplasms are primary cancers of other sites than those of the mouth or pharynx.

<sup>z</sup>:  $p < 0.05$

cancers as among their controls, yielding a significant difference at the 1.6 per cent level. The lungs and lower gastrointestinal tract are the most frequent sites of associated neoplasms (Table 10). Those notably more frequent among controls than cases involve genitouri-

nary organs and the prostate; the former's case-control frequency difference is at the significance level of 3.4 per cent.

Since no patient is diagnosed to have more than two associated neoplasms, these exist minimally in 2.0 per cent of all cases and maximally in 1.4 per cent



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of all controls as multiple primary cancers (See Tables 9 and 10). However, among cases, multiple primary cancers also exist when there are either coexisting site cancers or a single associated neoplasm. In fact, multiple primary cancers afflict 19.7 per cent of all cases, but only 1.4 per cent of all controls. Surprisingly, only five (3.6%) of the 139 cases with multiple primary cancers are Negroes. No Negroes, moreover, are among the 46 cases with coexisting site cancers, but Negroes do comprise 5.1 per cent of the 99 cases and 10.4 per cent of the 115 controls with associated neoplasms.

### *Death Certification*

At the end of follow-up on December 31, 1966, there were 601 deceased cases for whom 461 individual death certificates were available. Cancers of the

mouth and pharynx were reported as the underlying cause of death on 71.1 per cent of these, and as the associated cause of death on 10.0 per cent. On the remaining 18.9 per cent, mouth and pharynx cancers were not noted, but the underlying causes of death were ascribed to other cancers (especially of the larynx and lungs) on 11.7 per cent; to heart diseases on 2.6 per cent; to pneumonia on 1.1 per cent; to liver cirrhosis on 1.1 per cent; and to different causes, including one suicide, on 2.4 per cent. Hence, some cancer was cited as an underlying cause of death on 82.8 per cent of the death certificates for 76.7 per cent of the deceased.

### *Survivorship*

The cumulative five-year rates of survival by race, stage of disease, and transfer status to veterans' hospitals for cases

**Table 10—Proportion of associated neoplasms\* by affected sites among cases of mouth and pharynx cancers and their matched controls†**

| Sites                         | Associated neoplasms* among |                  |              |                  |
|-------------------------------|-----------------------------|------------------|--------------|------------------|
|                               | 706 cases                   |                  | 706 controls |                  |
|                               | No.                         | %                | No.          | %                |
| Skin                          | 20                          | 2.8              | 13           | 1.9              |
| Lip                           | 4                           | 0.6              | 2            | 0.3              |
| Lungs                         | 29                          | 4.1              | 22           | 3.1              |
| Larynx                        | 7                           | 1.0              | 10           | 1.4              |
| Nose                          | 4                           | 0.6 <sup>x</sup> | 0            | 0.0 <sup>x</sup> |
| Lower gastro-intestinal tract | 27                          | 3.8              | 24           | 3.4              |
| Liver or pancreas             | 2                           | 0.3              | 4            | 0.6              |
| Prostate                      | 10                          | 1.4              | 20           | 2.8              |
| Genitourinary                 | 4                           | 0.6 <sup>x</sup> | 14           | 2.0 <sup>x</sup> |
| Reticuloendothelial           | 1                           | 0.1              | 8            | 1.1              |
| Other                         | 5                           | 0.7              | 8            | 1.1              |
| Total                         | 113                         | 16.0             | 125          | 17.7             |

\* Associated neoplasms are primary cancers of other sites than those of the mouth or pharynx.

† A control matches its case on age within five years and on a hospital's bed capacity and medical school affiliation status.

x:  $p < 0.05$

y:  $p < 0.01$

**Table 11—Cumulative five-year rates of survival by race, stage of disease and transfer status to veterans' hospitals for cases of mouth and pharynx cancers**

|                              | No. | %     | Standard error |
|------------------------------|-----|-------|----------------|
| U. S. males*                 | 706 | 86.97 | ±1.26          |
| Negroes                      | 69  | 86.26 | ±3.85          |
| Whites                       | 637 | 87.06 | ±1.25          |
| Total cases†                 | 706 | 19.69 | ±1.50          |
| Negroes                      | 69  | 13.80 | ±3.67          |
| Whites                       | 637 | 20.35 | ±1.67          |
| Localized cancers            | 105 | 38.37 | ±5.90          |
| Metastasized cancers         | 601 | 16.46 | ±1.58          |
| Nontransfer to VA hospitals‡ | 576 | 21.60 | ±1.80          |
| Localized cancers            | 95  | 38.24 | ±5.22          |
| Metastasized cancers         | 481 | 18.30 | ±3.47          |
| Transfers to VA hospitals§   | 130 | 11.37 | ±2.81          |
| Localized cancers            | 10  | 39.24 | ±1.35          |
| Metastasized cancers         | 120 | 9.03  | ±2.65          |

\* United States males of cases' age and race (see reference 8).

† Cumulative five-year case rates and standard errors for each subtotal are adjusted to the age specific survival experience of all cases (see references 22 and 23).

‡ Cases first diagnosed and treated in veterans' hospitals (see reference 3).

§ Cases first diagnosed and treated in nonveterans' hospitals (ibid).

are seen in Table 11. The survivorship is better for whites, although not significantly, than it is for Negroes. Cases with localized cancers experience survival rates more than twice those for cases in whom cancers are metastasized, whether as transfers or nontransfers to veterans' hospitals. A similar result was found on survivorship by transfer status and stage of disease for 181 male veterans with primary cancer of the breast.<sup>3</sup>

Survivor rates are seen in Table 12 for cases in whom a clinical diagnosis of liver cirrhosis, syphilis, rheumatoid arthritis, associated neoplasms or diabetes mellitus is either absent or present. Cases with a presence of diabetes mellitus or an absence of liver cirrhosis,

syphilis, rheumatoid arthritis, or associated neoplasms have slightly but not significantly higher survivor rates than do their counterparts. Hence, the survival experience is not notably affected by the presence of any one of these diseases.

In Table 13 are the cumulative five-year survival rates for white males by marital status and religious preference. No significant difference in survivor rates exists within categories on either variable. Nonetheless, the lowest survivor rate for the widowed at 14 per cent and the highest for the married at nearly 23 per cent is consistent with other studies which report higher mortality rates for the widowed than for the married.<sup>31-32</sup>

**Table 12—Cumulative five-year rates of survival for cases of mouth and pharynx cancers with a clinical diagnosis of cirrhosis of the liver, syphilis, rheumatoid arthritis, associated neoplasms\* and diabetes mellitus**

|                        | No. | %     | Standard error |
|------------------------|-----|-------|----------------|
| U. S. males†           | 706 | 86.97 | ±1.26          |
| Total cases‡           | 706 | 19.69 | ±1.50          |
| Cirrhosis of the liver |     |       |                |
| Present                | 74  | 17.04 | ±3.98          |
| Absent                 | 632 | 20.01 | ±1.68          |
| Syphilis               |     |       |                |
| Present                | 24  | 12.77 | ±9.62          |
| Absent                 | 682 | 19.92 | ±1.79          |
| Rheumatoid arthritis   |     |       |                |
| Present                | 13  | 15.79 | ±8.92          |
| Absent                 | 693 | 19.76 | ±1.58          |
| Associated neoplasms*  |     |       |                |
| Present                | 99  | 17.60 | ±3.91          |
| Absent                 | 607 | 20.02 | ±1.64          |
| Diabetes mellitus      |     |       |                |
| Present                | 36  | 26.17 | ±6.83          |
| Absent                 | 670 | 19.35 | ±1.59          |

\* Primary neoplasms of other sites than those of the mouth or pharynx.

† United States males of cases' age and race (see reference 8).

‡ Cumulative five-year case rates and standard errors for each subtotal are adjusted to the age-specific survival experience of all cases (see references 22 and 23).

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Table 14 presents the survival rates for white males by occupations. Although the use of occupational titles does not intend to measure occupational risk for cancer, it does intend to delineate possible educational and income attainments which may be appropriate measures of socioeconomic status. Managerials and professionals have comparatively low survival rates at 14 per cent by contrast to farmers at nearly 29 per cent. Even so, there exists no significant difference in survival rates by occupations.

In Table 15 are shown survival rates by anatomical sites of the mouth and pharynx. When compared with the total case rate of nearly 20 per cent for all other cases, only the survival rate of 29.6 per cent for floor of mouth cases is significantly high and that of 8.5 per cent for hypopharynx cases is significantly low. Hence, the survival rate for those with tongue, other parts of mouth, multiple site, mesopharynx, or coexisting site cancers does not differ significantly from the survivor rates for all cases. Corresponding proportions of localized cancers for total cases and anatomical sites are as follows: multiple site, 2.9 per cent; hypopharynx, 6.5 per cent; total cases, 14.9 per cent; floor of mouth, 16.3 per cent; tongue, 19.6 per cent; mesopharynx, 22.4 per cent; coexisting sites, 30.4 per cent, and other parts of mouth, 41.0 per cent.

The cumulative five-year rates of survival by regions of residence are seen in Table 16 in which no significant difference between rates is evident. Yet, singly, survivor rates are highest in the Mountain regions and lowest in the South Atlantic, and may be compared with corresponding age-adjusted death rates in 1960 for the United States.<sup>9</sup> These death rates are highest in the South Atlantic, lowest in the West North Central and, unlike case survivor rates, include deaths ascribed to causes uncommon among the cases (see *Death*

**Table 13—Cumulative five-year rates of survival for white cases of mouth and pharynx cancers by marital status and religious preference**

|                                 | No. | %     | Standard error |
|---------------------------------|-----|-------|----------------|
| U. S. white males of cases' age | 637 | 87.06 | ± 1.25         |
| Total white cases*              | 637 | 20.35 | ± 1.67         |
| <b>Marital status†</b>          |     |       |                |
| Married                         | 323 | 22.59 | ± 2.49         |
| Divorced                        | 110 | 21.01 | ± 3.57         |
| Single                          | 118 | 19.49 | ± 3.85         |
| Widowed                         | 68  | 14.04 | ± 4.13         |
| <b>Religious preference‡</b>    |     |       |                |
| Protestants                     | 384 | 20.88 | ± 2.14         |
| Catholics                       | 236 | 18.82 | ± 2.67         |

\* Cumulative five-year survival rates and standard errors for this and each subtotal are adjusted to the age-specific survival experience of all cases (see references 22 and 23).

† Excludes 18 males who are either separated (16) or unknown (2) by marital status.

‡ Excludes 17 males who are either Jewish (2) or others (15) by religious preference.

**Table 14—Cumulative five-year rates of survival\* for white cases of mouth and pharynx cancers by occupations**

|                                 | No. | %     | Standard error |
|---------------------------------|-----|-------|----------------|
| U. S. white males of cases' age | 637 | 87.06 | ± 1.25         |
| Total white cases†              | 637 | 20.35 | ± 1.67         |
| Farmers                         | 36  | 28.65 | ± 7.39         |
| Operatives                      | 67  | 22.18 | ± 5.03         |
| Sales workers                   | 41  | 21.95 | ± 6.40         |
| Laborers                        | 80  | 21.17 | ± 4.67         |
| Craftsmen                       | 191 | 20.97 | ± 3.06         |
| Clericals                       | 53  | 19.42 | ± 5.39         |
| Service workers                 | 103 | 16.64 | ± 3.74         |
| Professionals                   | 35  | 14.25 | ± 6.10         |
| Managerials                     | 22  | 13.98 | ± 6.04         |

\* Cumulative five-year survival rates and standard errors for each subtotal are adjusted to the age-specific survival experience of all cases (see references 22 and 23).

† The listing excluded two who were unemployed and seven who stated they had no employment.

**Table 15—Cumulative five-year rates of survival by anatomical sites for cases of mouth and pharynx cancers**

|                      | No. | %     | Standard error |
|----------------------|-----|-------|----------------|
| U. S. males*         | 706 | 86.97 | ±1.26          |
| Total cases†         | 706 | 19.69 | ±1.50          |
| Other parts of mouth | 61  | 30.41 | ±5.71          |
| Floor of mouth       | 123 | 29.62 | ±4.17          |
| Coexisting sites     | 46  | 26.14 | ±6.02          |
| Tongue               | 92  | 21.56 | ±4.41          |
| Multiple sites       | 209 | 16.37 | ±2.63          |
| Mesopharynx          | 67  | 16.12 | ±4.45          |
| Hypopharynx          | 108 | 8.45  | ±2.77          |

\* United States males of cases' age and race (see reference 8).

† Cumulative five-year case rates and standard errors for each subtotal are adjusted to the age-specific survival experience of all cases (see references 22 and 23).

*Certification*). Combined regional rates, however, are highest in the Mountain and Pacific states of the West and are lowest in the New England and Middle Atlantic states of the Northeast.

Finally, five-year average death rates and per cent deaths by race and stage of disease are seen in Table 17 for cases and United States males of the case's age and race.<sup>9</sup> Average death rates and per cent deaths for all cases, when compared with corresponding values for United States males, are more disparate for the young than for the aged. The finding that significantly lower death rates are experienced by cases with localized than with metastasized cancers is consistent with the result in Table 12, which demonstrates that significantly higher survivor rates are experienced by cases with localized than with metastasized cancers.

## Discussion

Mouth and pharynx cancers are principally diagnosed and treated in large medical school-affiliated hospitals. Such

hospitals are less common in the Mountain States where the proportion of cases, especially with multiple site cancers, is significantly low. Nonetheless, such levels of medical detection that these hospitals might provide do not consistently explain the geographical disparities which cases manifest by anatomical sites. This is especially true for hypopharynx cancers, which are excessive throughout the South and New England, but scant in the Middle Atlantic. Neither race nor age, in addition, appears to provide the explanation that is sought. Future studies might concern themselves with elucidating these geographical disparities.

However, when compared with their matched controls, these cases are significantly more likely to be divorced than married; they are less likely to be Jews, to reside in the Mountain States, or even to have diabetes mellitus; more likely, they have cirrhosis of the liver. Only the negative association of diabetes mellitus

**Table 16—Cumulative five-year rates of survival by regions of residence for cases of mouth and pharynx cancers**

|                    | Rate of survival |       |                |
|--------------------|------------------|-------|----------------|
|                    | No.              | %     | Standard error |
| U. S. males*       | 706              | 86.97 | ± 1.32         |
| Total cases†       | 706              | 19.69 | ± 1.50         |
| New England        | 55               | 14.54 | ± 4.99         |
| Middle Atlantic    | 132              | 14.39 | ± 2.89         |
| East North Central | 140              | 21.17 | ± 3.64         |
| West North Central | 54               | 27.38 | ± 6.24         |
| East South Central | 48               | 25.30 | ± 6.52         |
| South Atlantic     | 89               | 12.21 | ± 3.49         |
| West South Central | 72               | 19.87 | ± 2.74         |
| Mountain           | 13               | 37.41 | ± 11.62        |
| Pacific            | 103              | 24.61 | ± 4.35         |

\* United States males of cases' age and race (see reference 9).

† Cumulative five-year case rates and standard errors for each subtotal are adjusted to the age-specific survival experiences of all cases (see references 22 and 23).

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with the cancer is speculated to result spuriously, since another control (i.e., patients with prostatic cancer) failed to manifest the same negative association as the matched controls.

On the other hand, the deficit of residence cases in the Mountain States is demonstrated both by the matched controls and by veterans in civil life. Further, the deficit of Jews may be explained by the very few heavy drinkers among them, as demonstrated in other related studies.<sup>16,18-19</sup>

Survivor rates are high for patients with relatively small areas of cancer (as typified by floor of mouth in contrast to hypopharynx), or with proportionately many localized cancers (as illustrated by 16.5 per cent among nontransfers versus 7.7 per cent among transfers). Whether this disparity in per cent does indeed confirm that most can-

cers in transfers were more terminal than those in nontransfers remains an open speculation.

Even so, high survivor rates might further relate both to the ease with which a cancer might be scrutinized medically or otherwise, and to physiological changes owing to its specific location. For example, if sensations arising from cancer in the hypopharynx are truly more diffuse and less intense than similarly caused sensations at anatomical sites more proximate to the body surface (such as the floor of the mouth), then patients experiencing the less diffuse and more intense sensations might seek earlier medical care.<sup>33-36</sup>

Nonetheless, the survival experience with cancers of the mouth and pharynx is not significantly altered by one's race, age, religious preference, place of residence, occupation, marital status, or by

**Table 17—Five-year average death rates ( $n_{mx}$ )\* and per cent deaths for cases of mouth and pharynx cancers by race and stage of disease and for U. S. males†**

| Age   | Five-year average death rate (100 $n_{mx}$ ) for |              |         |        |                         |              |
|-------|--|--------------|---------|--------|-------------------------|--------------|
|       | Total cases                                      | U. S. males† | Negroes | Whites | Cases in whom cancer is |              |
|       |  |              |         |        | localized               | metastasized |
| <45   | 35.3   | 0.5          | 57.3    | 29.6   | 26.3                    | 36.7         |
| 45-54 | 37.5   | 1.1          | 47.8    | 36.5   | 20.0                    | 42.4         |
| 55-64 | 40.5   | 2.4          | 38.9    | 40.6   | 22.0                    | 46.1         |
| 65+   | 43.3   | 4.6          | 59.2    | 42.3   | 18.1                    | 53.3         |
| Total | 40.4   | 2.8          | 50.7    | 39.5   | 20.0                    | 46.6         |

  

| Age   | Per cent deaths among |              |         |        |                         |              |
|-------|-----------------------|--------------|---------|--------|-------------------------|--------------|
|       | Total cases           | U. S. males† | Negroes | Whites | Cases in whom cancer is |              |
|       |                       |              |         |        | localized               | metastasized |
|       | (567)                 | (39)         | (59)    | (508)  | (65)                    | (502)        |
| <45   | 8.4                   | 1.5          | 27.2    | 6.3    | 7.7                     | 8.6          |
| 45-54 | 19.6                  | 8.2          | 22.0    | 19.3   | 20.0                    | 19.5         |
| 55-64 | 30.7                  | 26.2         | 20.3    | 31.9   | 29.2                    | 30.9         |
| 65+   | 41.3                  | 64.1         | 30.5    | 42.5   | 43.1                    | 41.0         |
| Total | 100.0                 | 100.0        | 100.0   | 100.0  | 100.0                   | 100.0        |

\*  $n_{mx}$  = (number of deaths) divided by (person-years).  
 † U. S. males of the cases' age and race (see references 8 and 25).

the presence of cirrhosis of the liver, syphilis, diabetes mellitus, rheumatoid arthritis, or other cancers. Survivorship is substantially enhanced by early medical care of the circumscribed cancers.

### Summary

A study of 706 males with squamous cell carcinoma of the mouth and pharynx and an equal number of age-matched and hospital-matched controls, who were diagnosed and treated in 101 veterans' hospitals in the United States from 1959 through 1961, demonstrates that:

1. Cirrhosis of the liver is strongly associated with cancer of the mouth and pharynx.
2. Notably few Jews have this cancer.
3. Survivorship with mouth and pharynx cancers is not significantly altered, either by one's race, religion, marital status, occupation, residence, or by the clinical diagnoses of liver cirrhosis, syphilis, rheumatoid arthritis, diabetes mellitus, or other body cancers.
4. Case survivorship is significantly better for those with a small, anatomically localized cancer than it is for others.

These findings are consistent with the conclusion that, apart from the cancer's size and its initial location, neither demographic factors nor other clinical diseases appear to influence markedly the survival experience of patients with cancer of the mouth and pharynx.

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