MANUAL FOR staging OF cancer

Second edition

American Joint Committee on Cancer

MANUAL FOR STAGING OF CANCER

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SECOND EDITION

AMERICAN JOINT COMMITTEE
ON CANCER

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The authors and publisher have exerted every effort to ensure that drug selection and dosage set forth in this text are in accord with current recommendations and practice at the time of publication. However, in view of ongoing research, changes in government regulations, and the constant flow of information relating to drug therapy and drug reactions, the reader is urged to check the package insert for each drug for any change in indications and dosage and for added warnings and precautions. This is particularly important when the recommended agent is a new or infrequently employed drug.

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Dedicated to the memory of
Murray M. Copeland, M.D.

The first chairman of
The American Joint Committee on Cancer
Staging and End-Results Reporting

A native of McDonough, Georgia, Murray Copeland received his medical degree from Johns Hopkins University School of Medicine in 1927, followed by training in surgery and oncology at the Mayo Clinic, Memorial Hospital in New York City, and Union Memorial Hospital in Baltimore.

Among Dr. Copeland's numerous distinctions were his leadership positions as national president of the American Cancer Society in 1965 and secretary-general of the 1970 UICC Cancer Congress.

He was known and loved by physicians around the world for his willingness and ability to support organizations designed to facilitate the spread of knowledge about cancer.

Murray Copeland was internationally acclaimed for his superior knowledge of and efforts against large bowel cancer and bone cancer.

Introduction

This manual brings together all currently available information on the state of the art of staging cancer at various anatomic sites as developed by the American Joint Committee on Cancer (AJCC). Although not all of the schemes included here are uniform in design, and some are more firmly established than others, the manual permits consistency in describing the extent of the neoplastic diseases of different anatomic parts, systems, or organs.

Proper classification and staging of cancer will allow the physician to determine treatment for the patient more appropriately, to evaluate results of management more reliably, and to compare statistics reported from various institutions on a local, regional, and national basis more confidently.

Staging of cancer is not an exact science. As new information becomes available about etiology and various methods of diagnosis and treatment, the classification and staging of cancer will change. Periodically, this manual will be revised so that it reflects the changing state of the art. However, revisions will occur only at reasonable periods. At the present time the anatomic extent of the cancer is the primary basis for staging; the degree of differentiation of the tumor and the age of the patient are also factors in some cases. In the future, biologic markers and other factors may also play a part.

It is hoped that the staging recommendations included in this manual may be used as published—or at least modified only minimally—so that consistency in data gathering will be possible. The recommendations in the manual are to be used in the cancer programs approved by the Commission on Cancer of the American College of Surgeons. Also, future reports by the Statistics, Epidemiology, and End-Results group (SEER) of the National Cancer Institute (NCI) will be based on the staging recommended by the AJCC.

The AJCC was first organized on January 9, 1959, as the American Joint Committee for Cancer Staging and End-Results Reporting (AJC), for the purpose of developing a system of clinical staging of cancer by site acceptable to the

American medical profession. The sponsoring organizations are the American College of Surgeons, the American College of Radiology, the College of American Pathologists, the American College of Physicians, the American Cancer Society, and the National Cancer Institute. Each of the sponsoring organizations designates three members to the Committee. The American College of Surgeons serves as administrative sponsor. Subcommittees, called "task forces," have been appointed to consider malignant neoplasms of selected anatomic sites in order to develop classifications. Each task force is composed of committee members and other professional appointees whose special interests and skills are appropriate to the site under consideration.

During its 22 years of activity, various special consultants have worked with the Committee, as well as liaison representatives from the American Academy of Pediatrics, the American College of Obstetricians and Gynecologists, the American Urological Association, the Association of American Cancer Institutes, and the SEER program of the NCI. More than 400 individuals have contributed to the work of the various task forces appointed by the Committee. Dr. Murray Copeland was Chairman from the inception until 1969, Dr. W.A.D. Anderson from 1969 to 1974, Dr. Oliver H. Beahrs from 1974 to 1979, and Dr. David T. Carr from 1979 to 1982. The current Chairman is Dr. Harvey W. Baker.

Pioneer work on the clinical classification of cancer was done by the League of Nations Health Organization (1929), the International Commission on Stage Grouping and Presentation of Results (ICPR) of the International Congress of Radiology (1953), and the International Union Against Cancer (Union Internationale Contre le Cancer, UICC). The latter organization became most active in the field through its Committee on Clinical Stage Classification and Applied Statistics (1954), later known as the TNM Committee.

The AJC decided to use the TNM system, where applicable, to describe the anatomic extent of the cancer at the time of diagnosis (before the application of definitive treatment), and from this to develop classification into stages, which would be useful as a guide to treatment and prognosis and in comparing the end results of treatment. Subsequently, the system has been extended to other points during the natural history and treatment of a cancer. Task forces to accomplish this extension were appointed to focus on particular sites of cancer. Retrospective studies have resulted in recommendations for stage classifications for cancer at various sites or systems, which have been published and distributed in separate fascicles and articles.

The TNM Committee of the UICC and the AJC have been working along similar lines and with similar objectives, although points of view and methods sometimes have differed. Cooperation between the two groups is necessary if the same internationally used classification systems are to be achieved. Toward this goal a meeting of representatives of the UICC and the AJC was held in Toronto on November 21 to 22, 1969. As a result of this meeting, consultation between the two groups was agreed upon before publication of a classification scheme by either group, and a joint exhibit was presented at the UICC International Cancer Congress in Houston in 1970. Several joint meetings of representatives of the UICC and the AJC on the classifications for specific cancer sites have been held in Houston and Geneva.

The AJC sponsored a National Cancer Conference on Classification and Staging in Atlanta on March 27 to 28, 1976. This conference delineated the accomplishments to that time and brought into focus future needs and activities.

In January 1970 a revised statement of the "Objectives, Rules and Regulations of the American Joint Committee" was adopted. Among other things, it broadened the scope of the Committee by including in its objectives the formulation and publication of systems of classification of cancer not limited to but including staging and end-results reporting.

It was recognized that for cancer of certain sites the information made available by observation at the time of a surgical procedure, as well as information from the pathologic examination of the operatively removed cancer, could form the basis of useful classifications. From this evolved a "surgical-evaluative staging" and a "postsurgical treatment-pathologic staging." These are often useful supplements to the clinical-diagnostic staging; for a few sites where a purely clinical classification is not feasible, they may be the only classifications recommended.

It also became evident that in certain organs (*e.g.*, thyroid) the biologic potentiality of different histologic types of cancer is such that different types cannot be mixed together in a meaningful classification. Therefore, cases should be analyzed separately by histologic type. In some kinds of cancer, such as soft-tissue sarcomas, grading is of such significance that it becomes a necessary component of the classification system. For certain cancers, widely used and accepted classifications, such as the Ann Arbor classification of Hodgkin's disease and the FIGO classification of carcinoma of the cervix, were adopted.

The various data in previously published individual-

site fascicles, with revisions and the addition of other material, were brought together to form a *Manual for Staging of Cancer,* the first edition of which was published in 1977. A second printing, slightly revised, appeared in 1978.

The importance of a data-collecting form for use in the staging system of each site has been realized for some years. Such forms ensure the recording of the data necessary for stage classification. Recent emphasis has been given to the development of a checklist for each cancer site for which there is a stage classification and to the availability of such checklists as a part of each staging recommendation.

The expanding role of the Committee in a variety of cancer classifications, including their significance and value and the promotion of indicated usage in cancer diagnosis and therapy, suggested that the original name of the Committee no longer portrayed the broader scope of its interests and activities. The name was therefore changed in 1980 to the American Joint Committee on Cancer (AJCC). The publication of this new edition of the *Manual* reflects the widening interests and activities of the Committee.

The AJCC attempts to develop classifications that are compatible, as far as possible, with those published by the UICC* and that are within the current standards of practice in American medicine. In developing its classifications, the AJCC has employed the principles of the TNM system as described by the UICC where appropriate, but not if other staging recommendations are already accepted and widely used.

The TNM Committee and the AJCC have attempted to come to agreement on staging of cancer at many anatomic sites. The differences in the recommendations of the two committees are gradually decreasing.

Members of the AJCC, its task forces, and its committees, as well as the sponsoring organizations, owe a debt of gratitude to the many physicians and others who have voluntarily contributed so greatly to this effort in the hope that in the future more patients with cancer would survive and that the quality of life of the cancer patient could be as near normal as possible. The contributions of the TNM Committee of the UICC and other international organizations with the same purposes are gratefully acknowledged.

Staging recommendations are included in the *Manual* for cancers at most anatomic sites. However, there are several regions or organs as yet not considered, such as the adrenal, small intestine, urethra, and penis. Several of the recommendations are preliminary, based on earlier studies by the AJCC, current studies now under way but not yet completed, or expert opinion by specialists in the field. These include cancer of the pancreas, brain, and bone. Last, when in certain instances data are not available to arrive at preliminary recommendations, none are given, but reference to other studies and protocols for prospective studies is made.

Under any circumstance, a cancer at any anatomic site can be recorded as localized, regional, or distant, depending on the findings, until a more refined classification and staging are developed.

*TNM Classification of Malignant Tumors, Third Edition, 1978. International Union Against Cancer, 3 Rue du Conseil-General, 1205 Geneva, Switzerland

Introduction to the Second Edition

Sixty thousand copies of the first two printings of the *Manual for Staging of Cancer 1977* and *1978* have been distributed. Based on the demand for the manual and for the subsequently published separate pamphlets on Reporting of Cancer Survival and End Results and Staging for Cancer of Head and Neck Sites, and Melanoma, Lung, Gynecologic Sites, and Soft-Tissue Sarcoma, there is an indication that the staging of cancer at the time of diagnosis and management is more universally applied now than previously. The Commission on Cancer of the American College of Surgeons, with 900 approved cancer programs, has recently requested that the recommendations of the American Joint Committee on Cancer (AJCC) be used in their programs and cancer registries. This will lead to further uniformity in recording the extent of cancers at the time of diagnosis and treatment and will make statistical data on follow-up and end results more meaningful.

This second edition of the *Manual* contains some revised recommendations based on new and added information. In a few instances, arbitrary changes have been made to make the recommendations of the AJCC consistent with those of the TNM Committee of the International Union Against Cancer (UICC). Consistency at all anatomic sites has not as yet been achieved.

The data-collecting forms have been modified to reflect more usefully the information required to stage cancer. These forms can become part of the patient's record but are not considered to be a replacement for history, treatment, or follow-up data forms. In some instances they list the information essential for staging as well as data that may be useful for future staging systems or research studies.

The AJCC wishes to thank all of those physicians, nurses, registrars, and others who have made suggestions regarding the contents of this manual, but in particular all of the more than 400 persons who, over 20 years, have contributed so greatly to the evaluation of the material and recommendations made in this revision. Likewise, great credit and thanks go to Mr. Robert Rowan and J.B. Lippincott Company for their cooperation and help in undertaking this *Manual for Staging of Cancer* for the American Joint Committee on Cancer.

Contents

MANUAL FOR STAGING OF CANCER

PART I

GENERAL INFORMATION ON CANCER STAGING AND END-RESULTS REPORTING

1

Purposes and Principles of Staging

Philosophy of Classification and Staging by the TNM System

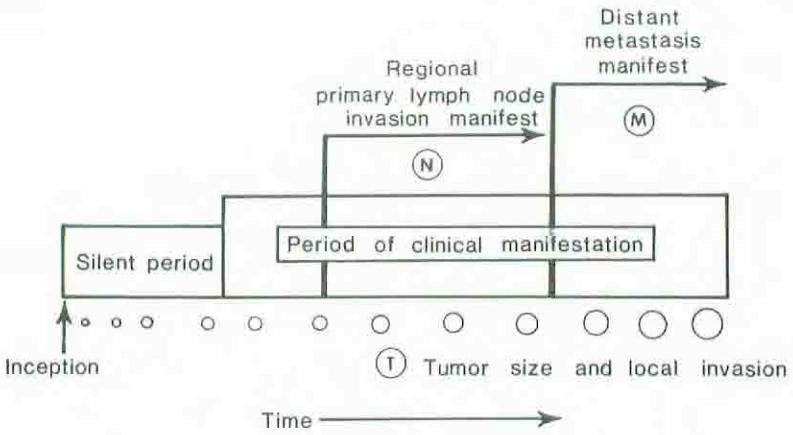
A classification scheme for cancer must encompass all attributes of the tumor that define its life history. The American Joint Committee on Cancer (AJCC) classification is based on the premise that cancers of similar histology or site of origin share similar patterns of growth and extension.

The size of the untreated primary cancer or tumor (**T**) increases progressively and at some point in time regional lymph node involvement (**N**) and, finally, distant metastases (**M**) occur. A simple classification scheme, which can be incorporated into a data form for staging and universally applied, is the goal of the TNM system as proposed by the AJCC. This classification is largely consistent with that of the Union Internationale Contre le Cancer (UICC) and is a distillate of several existing systems.

For most cancer sites the staging recommendations in this manual are concerned only with anatomic extent of disease, but in several instances, grade (soft-tissue sarcoma) and age (thyroid cancer) are factors that must be considered. In the future, biologic markers and other parameters may have to be added to those of anatomic extent in classifying cancer, but they are not necessarily components of stage.

As the primary tumor increases in size throughout its time span, at some point (probably early) local invasion occurs, followed by spread to the regional lymph nodes draining the area of the tumor. The period when this spread is manifest or discernible by available methods of clinical examination is thus another significant marker in the progression of the cancer (N). It is usually later, and often in the middle or older period of the life span of the cancer, that distant spread or metastasis (M) becomes evident from clinical examination. Thus metastasis (M) is the third and usually the latest time marker.

These three significant events in the life history of a cancer—tumor growth (T), spread to primary lymph nodes (N), and



metastasis (M)—are used as they appear (or do not appear) on clinical examination, before definitive therapy begins, to indicate the degree of extension of the cancer. This shorthand method of indicating the extension of disease at a particular designated time is the stage of the cancer in its evolution. However, it may be used, sometimes with other features added, in a scheme of stage classification. When retrospective or prospective studies of cases show that certain groupings of TNM or other features can be made that have valid significance for staging, a stage classification may be devised.

Events such as local spread, including spread to primary lymph nodes, and metastasis sometimes occur before they are discernible by clinical examination. Thus, examination at the time of a surgical procedure and histologic examination of the surgically removed tissues may identify the significant markers of the life history of the cancer (T, N, and M) as being different from what could be discerned clinically before therapy. Although this may be the basis of a stage classification (surgical-evaluative or pathologic, based on examination of a surgically resected specimen), it cannot be mixed with clinical diagnostic staging for evaluative and reporting purposes. Nevertheless, it may be a more accurate depiction of the period in the life history of the cancer and may be valuable for prognostic purposes.

Therapeutic procedures, even if not curative, may alter the course and life history of cancer. Although cancers that recur after therapy may be staged with the same markers as are used in pretreatment clinical-diagnostic staging, their significance may not be the same. Hence the stage classification of recurrent cancer must be considered separately for therapeutic guidance, prognosis, and end-results reporting.

The significance of the marker points in their life history differs for tumors of different sites and of different histologic types. Hence the marker points, even if T, N, and M, must be defined for each type of tumor in order to be valid and to have maximum significance. In certain types of tumors, such as Hodgkin's disease and lymphomas, a different system for designating the extent of the disease and for classifying its stage is necessary to accomplish the goal of usefulness. In these cases other symbols or descriptive markers are used rather than T, N, and M.

Classification and stage-grouping is thus a method of designating the state of a cancer at various points in time and is related to the natural course of the particular type of cancer. It is intended to provide a way by which this information can be readily communicated to others, to assist in decisions regarding treatment, and to be a factor in determining prognosis. Ultimately, it provides a mechanism for comparing like or unlike groups of cases, particularly in regard to the results of different therapeutic procedures.

In addition to anatomic extent, the histopathologic analysis and grade of the tumor are important determinants in classification. The type of tumor and the grade are also most important variables affecting choices of treatment. For sarcomas the tumor grade may prove to be the most important index.

Nomenclature in Morphology of Cancer

Cancer therapy decisions are made after an assessment of the patient and tumor, using many methods that often include sophisticated technical procedures. For most types of cancer, the extent to which the disease has spread is probably the most important factor determining prognosis and must be given prime consideration in evaluating and comparing different therapeutic regimens.

Staging classifications are based on description of the extent of disease, and their design requires a

thorough knowledge of the natural history of each /pe of cancer. Such knowledge has been and continues to be derived primarily from morphologic studies, which also provide us with the definitions and classifications of tumor types.

An accurate histologic diagnosis, therefore, is an essential element in a meaningful evaluation of the tumor patient. In certain types of cancer, biochemical or immunologic measurements of normal or abnormal cellular function have become important elements in typing tumors precisely. Increasingly, definitions and classifications should include function as a component of the pathologist's anatomic diagnosis. One may also anticipate that special techniques in histochemistry, cytogenetics, and tissue culture will be used more routinely for typing and characterizing tumor behavior.

The most complete and best known compendium of tumor definitions and illustrations in English is the *Atlas of Tumor Pathology*, published in many volumes by the Armed Forces Institute of Pathology. These are under constant revision and are used as a basic reference by pathologists throughout the world.

In 1956, the World Health Organization initiated a program designed to provide an internationally acceptable histologic classification of tumors. For ach tumor site, a draft classification is prepared by a mall group of international experts. A reference center and several collaborating laboratories are then designated by the World Health Organization. After intensive review of large amounts of histologic and clinical material, the proposed classification is revised and tested in the field. The product is the "blue book" publication, which includes the definition of the tumors in a given organ site or system, along with numerous illustrations. The terms used for each tumor type represent the preferred nomenclature, and their arrangement may be considered a working classification.

In the interest of promoting national and international collaboration in cancer research, and specifically to facilitate cooperation in clinical investigation, the AJCC recommends that the International Classification of Diseases for Oncology (ICD-O) be accepted and its use encouraged for coding neoplasms by topography and histology (morphology) and for indicating behavior (malignant, benign, *in situ*, uncertain, or metastatic). This coded nomenclature is based on the *Manual of Tumor Nomenclature and Coding* (MOTNAC), published by the American Cancer Society in 1968.

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General Rules for Staging of Cancer

To facilitate the use of the TNM system and to standardize its application in the classification of various cancers, the AJCC has adopted the following general rules:

1. The TNM system provides a basis for categorizing the extent of disease and, when appropriate, it will be used. When the TNM system is used, the letter **T** represents the primary tumor, with appropriate suffixes to describe increasing sizes of the tumor, involvement by direct extension, or both. The letter **N** represents the regional lymph node involvement, with appropriate suffixes to describe the absence of involvement or increasing degrees of such involvement. The letter **M** represents distant metastasis, with appropriate suffixes to describe the absence of such metastasis or increasing degrees of such dissemination of the tumor. The various categories of T, N, and M may be grouped into appropriate combinations to create a small number of stages of the disease.
2. All available evaluative evidence for classifying the extent of disease at different sites and at different points during the natural history and treatment should be used. Histologic confirmation of cancer is mandatory if a case is to be included in a series for evaluation. The chronology of classification and terms are as follows:

   cTNM *Clinical-diagnostic staging:* using all information available prior to first definitive treatment, including pathologic confirmation of extent of disease by biopsy or invasive techniques

   pTNM *Postsurgical resection-pathologic staging:* using all data available at the time of surgery and on examination of a completely resected specimen

   sTNM *Surgical-evaluative staging:* using all clinical information available plus that obtained on surgical exploration; usually done for a few inaccessible tumors that are not amenable to definitive resection

   rTNM *Retreatment staging:* classification when restaging is necessary for additional or secondary definitive treatment after a (disease-free) interval following first treatment

   aTNM *Autopsy staging:* used only when the cancer is first diagnosed at autopsy

3. Clinical-diagnostic staging. For cancers at certain accessible sites, especially those that can be treated in an appropriate manner by more than one treatment modality, the extent of the cancer should be determined and recorded before definitive treatment is carried out. Included is pathologic information available from biopsies for confirmation of disease. This provides a clinical-diagnostic stage classification and makes it possible to compare the results of different modalities of treatment of certain accessible lesions.
4. Postsurgical resection-pathologic staging. This term *postsurgical resection-pathologic staging* is to be used to describe the known extent of the disease following the complete examination of the therapeutically resected specimen. Residual tumors, if any, following surgical resection should be recorded (see rule 9).
5. Surgical-evaluative staging. The term *surgical evaluative stage classification* is to be used to describe the known extent of disease after a major surgical exploration to identify the extent of a cancer for which definitive surgical resection is not the anticipated or appropriate treatment.
6. For cancers of some sites it may be desirable to record a clinical-diagnostic stage classification, a surgical-evaluative stage classification and/or a postsurgical resection-pathologic stage classification.
7. Varying amounts of information may be used in determining each stage classification for each primary site. Specific recommendations about which information should be used for each type of staging is given in the recommendations for each primary site.
8. Once the extent of disease has been established, the stage classification should not be modified as a result of information obtained either during follow-up or from more definitive observation. For example, clinical diagnostic staging should not be influenced either by the fact that a patient experienced early recurrence or by information from surgical notes or a pathology report. The cancer, however, can be staged cTNM and, if treated surgically, it can then also be staged pTNM. Data comparison must be based on cases with comparable available information on extent of disease.
9. At the time of surgical resection of a cancer, all gross evidence of cancer may have been removed. On the other hand, gross residual cancer may have been left behind. This residual tumor must be identified under **R** to facilitate and aid in additional or further treatment of the patient. R does not enter into the staging of the tumor.

10. Retreatment staging. Cases in which a cancer recurs after a period of freedom from disease may be described by TNM but must be identified by the symbol **r** before the appropriate TNM category. Such cases should not be combined with a primary treatment series but should be grouped together and evaluated and reported separately. However, they must not be deleted from the original primary treatment series.
11. Autopsy staging. At times it might be desirable to stage cancer when it is first diagnosed at autopsy. Staging at this time period should be designated aTNM. All available clinical and pathologic information may be used.
12. Histologic or cytologic verification of cancer is always necessary for classification and to establish the extent of tumor or stage.
13. The degree of anaplasia, whether well differentiated, moderately well differentiated, or undifferentiated, should be recorded as determined on histologic study under the letter **G**. If grading is well accepted at an anatomic site by numbers 1 through 4, then four groups may be used.
14. The performance index of the host, considering all cofactors, should be recorded at the time of each stage classification and at follow-up examinations. This should be done on the data record form under the letter designation **H**. This factor may be an influencing one in determining treatment.

In stage classification of cancer at various anatomic sites, an attempt has been made to simplify the staging as much as possible, consistent with accuracy. Also an attempt is made to have definitions of the various symbols as similar as possible from one site to another.

Definitions of Symbols

Three capital letters are used to describe extent of cancer

T Primary tumor
N Regional lymph nodes
M Distant metastasis

Chronology of classification

c Clinical-diagnostic
p Postsurgical treatment-pathologic
s Surgical-evaluative
r Retreatment
a Autopsy

This classification is extended by the following designations:

Tumor

TX The minimum requirements to assess the primary tumor cannot be met.
T0 No evidence of primary tumor
Tis Carcinoma *in situ*
T1, T2, T3, T4 Progressive increase in tumor size or involvement

Nodes

NX The minimum requirements to assess the regional lymph nodes cannot be met.
N0 No evidence of regional node involvement
N1, N2, N3, N4 Increasing degrees of demonstrable abnormality of regional lymph nodes

Metastasis

MX The minimum requirements to assess the presence of distant metastasis cannot be met.
M0 No evidence of distant metastasis
M1 Distant metastasis present
Specify sites of metastasis _____

The category M1 may be subdivided according to the following notations:

Pulmonary	PUL
Osseous	OSS
Hepatic	HEP
Brain	BRA
Lymph nodes	LYM
Bone marrow	MAR
Pleura	PLE
Skin	SKI
Eye	EYE
Other	OTH

Histopathology

Histopathology refers to the histologic type of cancer.

Grade (G)

GX Grade cannot be assessed.
G1 Well-differentiated
G2 Moderately well-differentiated
G3-G4 Poorly to very poorly differentiated; use whichever indicator is most appropriate (term or G + number).

In certain sites further information regarding the primary tumor may be recorded under the following headings:

Lymphatic invasion (L)

LX Lymphatic invasion cannot be assessed.
L0 No evidence of lymphatic invasion
L1 Evidence of invasion of superficial lymphatics
L2 Evidence of invasion of deep lymphatics

Venous invasion (V)

VX Venous invasion cannot be assessed.
V0 Veins do not contain tumor.
V1 Efferent veins contain tumor.
V2 Distant veins contain tumor.

Residual Tumor (R)

This information does not enter into establishing stage of tumor but should be recorded on data form for use in considering additive therapy. When the cancer is treated by definitive surgical procedures, residual cancer, if any, is recorded.

Residual tumor following surgical treatment

R0 No residual tumor
R1 Microscopic residual tumor
R2 Macroscopic residual tumor
Specify _____

Host Performance Scale

The host performance status is determined at the time of classification. The condition of the patient does not enter into determination of stage of the tumor but may be a factor in deciding type and time of treatment. Three suggested scales are illustrated. The simplified AJCC scale is preferred because of simplicity. The other scales are shown so comparisons can be seen.

Host (AJCC)

H The physical state (performance scale) of the patient, considering all cofactors determined at the time of stage classification and subsequent follow-up examinations
H0 Normal activity
H1 Symptomatic and ambulatory; cares for self
H2 Ambulatory more than 50% of time; occasionally needs assistance
H3 Ambulatory 50% or less of time; nursing care needed
H4 Bedridden; may need hospitalization

The Karnofsky scale and the Eastern Cooperative Oncology Group (ECOG) scale are frequently used to record the physical state of patients and are listed for information and comparison

Karnofsky Scale: Criteria of Performance Status (PS)

Able to carry on normal activity; no special care is needed.	100	Normal; no complaints; no evidence of disease
	90	Able to carry on normal activity; minor signs or symptoms of disease
	80	Normal activity with effort; some signs or symptoms of disease
Unable to work; able to live at home and care for most personal needs; a varying amount of assistance is needed.	70	Cares for self; unable to carry on normal activity or to do active work
	60	Requires occasional assistance but is able to care for most of own needs
	50	Requires considerable assistance and frequent medical care
Unable to care for self; requires equivalent of institutional or hospital care; disease may be progressing rapidly.	40	Disabled; requires special care and assistance
	30	Severely disabled; hospitalization indicated although death not imminent
	20	Very sick; hospitalization necessary; active supportive treatment necessary
	10	Moribund, fatal processes progressing rapidly
	0	Dead

Eastern Cooperative Oncology Group Scale (ECOG)

GRADE
0 Fully active, able to carry on all predisease activities without restriction (Karnofsky 90-100)
1 Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature; for example, light housework, office work (Karnofsky 70-80)
2 Ambulatory and capable of all self-care but unable to carry out any work activities. Up and about more than 50% of waking hours (Karnofsky 50-60)
3 Capable of only limited self-care, confined to bed or chair 50% or more of waking hours (Karnofsky 30-40)
4 Completely disabled. Cannot carry on any self-care. Totally confined to bed or chair (Karnofsky 10-20)

Data Forms for Cancer Staging

Each site-specific data form is to be used fo recording the classification of the tumor and the stage of the cancer. The anatomic site of the cancer

should be indicated, as well as the histologic cell type and grade. The appropriate period of the chronology of classification must be recorded. If a cancer is staged during several time periods in the chronology, separate forms must be used for each time period.

The T, N, and M classification can be checked opposite the appropriate definitions of the extent of the primary tumor, the regional nodes, and distant metastasis. The lesion(s) can be marked on the diagram and, finally, the stage can be checked according to the grouping of TNM. In some instances information regarding other characteristics of the tumor (not leading to stage) might be asked for. This data may be pertinent in deciding management of the cancer. On the obverse side of the data form is information and definitions that are important in proper classification of a cancer.

The data form for cancer staging is not a replacement for history, treatment, or follow-up records but might become part of the patient file.

Screening for the Early Detection of Cancer

The entire concept of cancer staging is built upon the foundation of progression of disease from clinically undetectable cancer to very limited disease, to involvement by direct extension of immediately adjacent organs or tissues, to metastatic spread of disease into regional lymph nodes or into distant sites or lymph nodes. The literature on cancer patient survival is filled with reports reflecting the survival advantage of patients whose cancer was diagnosed before direct extension or metastatic spread has taken place. Thus, one approach to improving overall survival for patients who develop cancer is to diagnose it while it can be managed more effectively with currently available therapeutic modalities. This idea has led to the search for methods of detecting cancers that heretofore could not be identified by routine clinical examination. The Pap smear for detection of cervical abnormality or cancer, mammography for detection of breast cancer, sputum cytology for detection of lung cancer, and the fecal occult blood test for early diagnosis of colon cancer are examples of methods currently being used.

There is substantial evidence that the Pap smear has been instrumental in reducing mortality due to carcinoma of the cervix. Mammography, in addition to clinical examination, has been shown by means of a randomized trial to be effective in reducing mortality due to breast cancer. The other two methods are currently being evaluated by controlled trials. Results from these studies are demonstrating that earlier detection is possible for cancers of the lung and colon, two of the most frequently occurring cancers.

The American Joint Committee on Cancer supports efforts to develop and evaluate early detection methods for these and other cancers as rapidly as possible, so that screening can be offered to a wide segment of the population. Thus, persons who are unaware of the existence of small cancers could have them identified and treated before the cancers have had the chance to grow and disseminate.

2

Reporting of Cancer Survival and End Results

To evaluate the efficacy of treatment and to provide a sound base for therapeutic planning for cancer patients, it is necessary to describe the survival and the results of treatment of different patient groups in comparable form. The objective of this report is to define a method of reporting end results that may have wide application. Throughout this chapter, the term *survival time* is used, although the guidelines apply equally to reporting length of response time, time to recurrence of disease, time to development of tumor, or any other function of response time.

Certain basic information must be included in every report on cancer survival and end results. Such information should include the following:

1. A description of the cancer patients whose survival experiences are to be summarized
2. A definition of the starting time or "zero" time for the measurement of survival
3. An explanation of the method used in calculating survival rates

The specific definitions and methods used in a particular study depend on the nature and purpose of that study.

DESCRIPTION OF CASE MATERIAL

Before any meaningful interpretation of survival data can be made, the case material from which the data are derived must be described. A fact not adequately appreciated is that the description of case material is quite independent of the actual mechanics of handling the data and determining survival rates.

In organizing the material for presentation, consideration should be given to the following:

1. Reports should account for every case diagnosed as having the particular cancer under consideration. If some cases are excluded, the characteristics and number of these cases should be stated. The report should give the dates during which the patients were studied and should state whether the results are based on the experience of an entire institution,

on the experience of a single clinic or hospital service, or on the experience of a single physician or group of physicians. The general nature of the institution and the general characteristics of the patients should be indicated, because factors such as race and socioeconomic status may influence end results.

2. All diagnoses should be confirmed histologically or cytologically. Those not confirmed at any time during the course of the disease or at autopsy should be reported and tabulated separately. Where indicated, the findings for histologically distinct types of cancers should be reported separately. So that the effects of morphology on survival may be appreciated, reports should be stratified by histologic type where indicated.
3. The clinical stage or anatomic extent of disease at the time of diagnosis is of particular importance in evaluating treatment and in making valid comparisons of end results reported from different sources. Where it is applicable, patients should be stratified by stage of disease. The TNM system provides a common language for categorizing the primary lesion and the extent of involvement.

   The TNM assignments are grouped into appropriate combinations to create a small number of stages, usually four, such that the force of mortality increases from one stage to the next.

   Specific criteria modify this system according to the primary site. The clinical-diagnostic classification for cancer at certain accessible sites, such as the uterine cervix, includes all diagnostic and evaluative information obtained up to the date that tumor-directed treatment begins or the decision for no treatment is made. Information obtained by surgical exploration or histopathologic studies, or both, may be used in describing extent of disease at sites inaccessible to clinical evaluation, such as carcinoma of the ovary, kidney, and stomach. These cancers are reported in terms of surgical-evaluative stage or postsurgical treatment-pathologic stage of disease.
4. Data on groups of patients previously treated should be presented separately from the data on new patients who have not been previously treated. Such patients are classified according to the stage at time of retreatment.
5. The number of groups into which a patient series is subdivided depends on the total number of patients, the purpose of the study, and the nature of the case material. For example, in reporting on cancer of the prostate, the patients might be grouped into three age groups, such as: under 60, 60 to 69, and 70 and over. An entirely different age grouping would be used in reporting on patients with leukemia. Generally, it is desirable to subdivide with respect to histologic type, sex, stage and treatment.

DEFINITION OF STARTING TIME

The starting time for determining survival of patients depends on the purpose of the study. For example, the starting time for studying the natural history of a particular cancer might be defined in reference to the appearance of the first symptom. Various reference dates are commonly used as starting times for evaluating the effects of therapy. These include: (1) date of diagnosis; (2) date of first visit to physician or clinic; (3) date of hospital admission; and (4) date of beginning treatment. If the time to recurrence of a tumor after apparently complete remission is being studied, the starting time is the date of apparently complete remission. The specific reference date used should be specified clearly in every report.

The date of initiation of therapy should be used as the starting time for evaluating therapy. For untreated patients, the most comparable date is the time at which it was decided that no tumor-directed treatment would be given. For both treated and untreated patients, the above times from which survival rates are calculated will usually coincide with the date of the initial staging of cancer.

VITAL STATUS

At any given time the vital status of each patient is defined as alive, dead, or unknown (*i.e.*, lost to follow-up). The end point of each patient's participation in the study is (1) a specified "terminal event" such as death, (2) survival to the completion of the study, or (3) loss to follow-up. In each case *survival time* is the time from the starting point to the terminal event, or to the end of the study, or to the date of last observation. This survival time may be described further in terms of patient status at the end point such as the following:

Alive, tumor-free; no recurrence
Alive, tumor-free; after recurrence
Alive with recurrent or metastatic disease
Alive with primary tumor
Dead; tumor-free
Dead; with cancer (primary, recurrent, or metastatic disease)
Dead; postoperative
Unknown; lost to follow-up

Completeness of the follow-up is crucial in any study of survival time because even a small number of patients lost to follow-up may bias the data.

SURVIVAL INTERVALS

The total survival time is broken up into arbitrary units or intervals in terms of days, months, or years. This provides a description of the population under study, with respect to the dynamics of survival, over a specified time. The time interval used should be selected with regard to the natural history of the disease under consideration. In diseases with a long natural history, the duration of study could be 5 to 10 years and survival intervals of 6 to 12 months will provide a meaningful description of the survival dynamics. If the population being studied has a very poor prognosis (*e.g.*, patients with carcinoma of the esophagus or pancreas), the total duration of study may be 2 to 3 years and the survival intervals described in terms of 1 to 3 months. In interpreting survival rates one must also take into account the number of individuals entering a survival interval. *Survival rates probably should not be computed for intervals in which fewer than 10 patients enter the interval alive.*

CALCULATION OF SURVIVAL RATES

A properly calculated survival rate is the best single statistical index available for measuring the efficacy of cancer therapy. The basic concept is simple: Of a given number of patients, what percentage will be alive at the end of a specified interval, such as 5 years? For example, let us begin with 1000 patients in a defined diagnostic category such as localized carcinoma of the uterine cervix. If we observe each member of this group until death and enumerate those alive 5 years, 10 years, and 15 years after initiation of therapy, then the ratios of these numbers to the original 1000 patients give, respectively, the 5-year, 10-year, and 15-year survival rates. In practice, however, we do not begin literally with a given group and follow them all continuously until death before calculating survival rates. In a body of actual data, the group considered generally contains persons who were treated at different times, so that different persons are observed for different lengths of time. On the closing date of the study, some are known to be dead, others are known to be alive, and some have been lost to follow-up and it is not known whether they are alive or dead.

To illustrate the approach to dealing with this type of situation, let us consider in detail a moderately small series of patients. Table 2-1 lists 50 patients with melanoma of the skin treated in one hospital during the 15-year period from October 1952 to June 1967. The survival experience of these patients is to be assessed on the basis of information available through the end of 1969, that is, the *nominal closing date* of the study is December 31, 1969. For each patient, the list provides the following basic information:

1. Sex
2. Age at initiation of treatment
3. Date treatment started (month and year)
4. Date of last contact (month and year)
5. Vital status at date of last contact (alive or dead)
6. Presence of melanoma at date of last contact (yes or no)

Patients are listed consecutively by date of first treatment.

Calculation by the Direct Method. The simplest procedure for summarizing patient survival is to calculate the percentage of patients alive at the end of a specified interval such as 5 years, using for this purpose only patients exposed to the risk of dying for at least 5 years. This approach is known as the *direct method.*

In this set of data there were contacts with patients during 1969, but these contacts occurred during different months of the year. We know that all patients last contacted in 1969 were alive on December 31, 1968, but we do not know whether they were all alive at the end of 1969. Thus, we will designate December 31, 1968, as the *effective closing date* of the study. Consequently, all patients first treated on January 1, 1964, or later were not at risk of dying for at least 5 years as of the closing date. This means that 20 of the 50 patients (numbers 31 to 50) must be excluded from the calculation by the direct method.

Examining the entries in the "vital status" column in Table 1 for the 30 patients at risk for at least 5 years, we find that 16 patients were alive at last contact and 14 had died before December 1968. However, patient 2, although known to have died in January 1960, had been alive on his fifth anniversary. Therefore we have 17 of the 30 patients alive 5 years after their respective dates of first treatment and, thus, the 5-year survival rate is 57%.

Calculation by the Actuarial Method. The direct method for calculating a survival rate does not use all the information available. For example, we know that patient 31 died in the fourth year after treatment was started and that patient 32 lived for more than 4 years. Such information should be useful, but we were unable to use it under the rules of the direct method because the patients were diagnosed after December 1963.

The *actuarial,* or *life-table,* method provides a means for using all follow-up information accumulated up to the closing date of the study. The actuarial method has the further advantage of providing

Table 2-1. Listing of 50 White Patients With Melanoma of the Skin

PATIENT NUMBER	SEX	AGE	DATE TREATMENT STARTED	LAST CONTACT			INTERVAL OF LAST OBSERVATION (YEARS)
				Date	*Vital status**	*Melanoma present?*	
1	M	63	Oct. 1952	Nov. 1952	D	Yes	1
2	M	42	Jul. 1954	Jan. 1960	D	Not†	6
3	M	41	Mar. 1955	Apr. 1955	D	Yes	1
4	F	57	Jun. 1955	Jul. 1956	D	Yes	2
5	M	35	Sep. 1955	Oct. 1969	A	No	15
6	F	48	Oct. 1955	Aug. 1956	D	Yes	1
7	M	43	Apr. 1956	Feb. 1959	D	Yes	3
8	F	27	Jan. 1957	Jan. 1957	D	Yes	1
9	F	56	Dec. 1958	Oct. 1969	A	No	11
10	F	33	Jan. 1959	Nov. 1969	A	Yes	11
11	F	37	Apr. 1959	Apr. 1969	A	No	11
12	F	58	Sep. 1959	Aug. 1969	A	No	10
13	M	21	Feb. 1960	May 1960	D	Not†	1
14	M	71	Feb. 1960	Nov. 1968	A	No	9
15	F	66	Jun. 1961	Aug. 1961	D	Yes	1
16	F	35	Jul. 1961	Dec. 1969	A	No	9
17	F	31	Oct. 1961	Nov. 1969	A	No	9
18	M	35	Mar. 1962	Jun. 1969	A	No	8
19	F	44	Apr. 1962	Jul. 1969	A	No	8
20	M	26	Apr. 1962	Oct. 1969	A	No	8
21	M	57	Oct. 1962	Jun. 1963	D	Yes	1
22	M	54	Dec. 1962	Feb. 1963	D	Yes	1
23	M	63	Jan. 1963	Jan. 1964	D	Yes	2
24	F	32	Jan. 1963	Oct. 1965	D	Yes	3
25	F	43	Apr. 1963	Feb. 1969	A	No	6
26	F	76	Jul. 1963	Feb. 1968	D	Yes	5
27	M	31	Sep. 1963	Nov. 1969	A	No	7
28	M	77	Nov. 1963	Feb. 1969	A	No	6
29	F	59	Nov. 1963	Apr. 1969	A	No	6
30	F	76	Dec. 1963	Sep. 1969	A	No	6
31	M	39	Mar. 1964	Aug. 1967	D	Yes	4
32	F	50	Jul. 1964	Apr. 1969	A	No	5
33	F	38	Sep. 1964	Jun. 1969	D	Yes	5
34	F	82	Mar. 1965	Dec. 1969	A	No	5
35	M	65	Apr. 1965	Jul. 1965	D	Yes	1
36	M	40	Apr. 1965	Oct. 1969	A	Yes	5
37	M	22	Jun. 1965	Feb. 1969	A	No	4
38	F	25	Jan. 1966	Nov. 1969	A	No	4
39	M	33	Apr. 1966	Nov. 1969	A	No	4
40	F	51	May 1966	Jul. 1969	A	No	4
41	F	40	Jul. 1966	Nov. 1969	A	No	4
42	M	70	Sep. 1966	Sep. 1967	D	Not†	2
43	M	47	Sep. 1966	Dec. 1967	D	Yes	2
44	M	67	Oct. 1966	Apr. 1968	D	Not†	2
45	F	58	Jan. 1967	Aug. 1969	A	No	3
46	M	75	Jan. 1967	Oct. 1969	A	No	3
47	M	40	Apr. 1967	Jul. 1969	A	No	3
48	F	35	Apr. 1967	Jul. 1969	A	Yes	3
49	F	49	May 1967	Dec. 1968	D	Yes	2
50	F	21	Jun. 1967	Mar. 1969	A	No	2

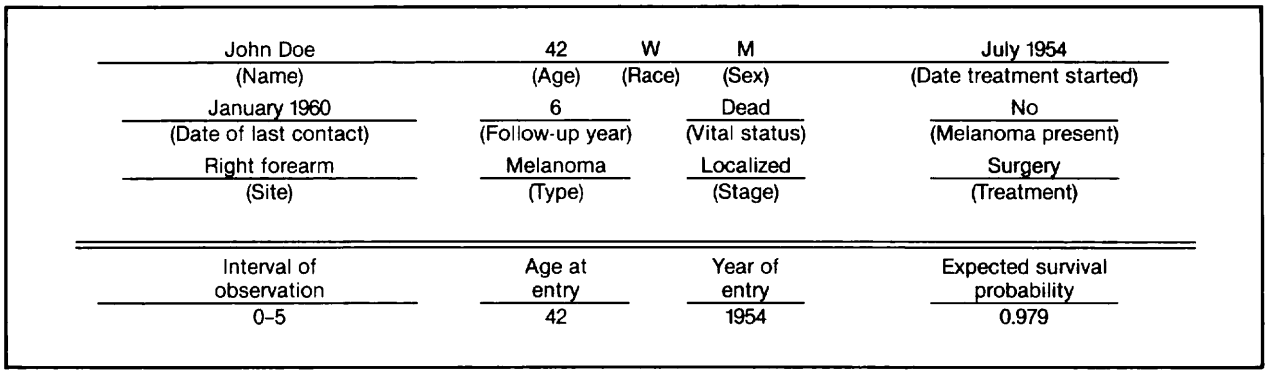
*A, alive; D, dead
†Died of intercurrent disease

information on the survival pattern, that is, the manner in which the patient group was depleted during the total period of observation.

The procedures described here are designed for the individual investigator who wants to analyze carefully the survival experience of a small series of patients—in this illustration, 50 patients. However, the same underlying methodology is used in analyzing large series with electronic computers.

Patient Data Card. To facilitate sorting and counting, it is advisable to prepare a data card on each patient, such as the one shown in Figure 2-1. The upper part (above the double line) provides the following items of basic descriptive information:

1. Name: a case number, in addition to the name, may be useful for identification.
2. Age: completed years of age at time of initiation of treatment
3. Race and sex
4. Dates of first treatment and of last contact: month and year
5. The interval of last observation (designated *fol-*



John Doe	42	W	M	July 1954
(Name)	(Age)	(Race)	(Sex)	(Date treatment started)
January 1960	6		Dead	No
(Date of last contact)	(Follow-up year)		(Vital status)	(Melanoma present)
Right forearm	Melanoma		Localized	Surgery
(Site)	(Type)		(Stage)	(Treatment)

Interval of observation	Age at entry	Year of entry	Expected survival probability
0–5	42	1954	0.979

Fig. 2-1. Data card: patient 2, Table 2-1.

low-up year on card) is the interval during which an event occurred, either death (or other appropriate response such as recurrence) or withdrawal from observation. The interval of last observation is the number of completed entire intervals of follow-up plus 1; for example, 5 years 6 months = 5 completed years, which implies an event occurring in the sixth year. Patients followed for 5 years, up to but not including the sixth year, have a follow-up interval of last observation of 6 years.

6. Vital status and presence of disease: information on presence or absence of cancer at time of death is highly desirable.
7. Diagnostic: site of the tumor, histologic type, and stage of disease
8. Treatment: brief summary

Observed Survival Rate. The life-table method for calculating a survival rate, using all the follow-up information available on the 50 patients under study, is illustrated in Table 2-2. There are six steps necessary in preparing such a table:

1. The patient data cards are tallied for vital status and follow-up year of last observation (columns 3 and 4). The sum of the entries in columns 3 and 4 must equal the total number of patients. Note that the 17 patients alive at the beginning of the last interval of observation in column 2 (6 years and over) were also entered in column 4 (number last seen alive during year).
2. The number of patients alive at the beginning of each year is entered in column 2 and is obtained by successive subtraction. Thus, of 50 patients alive at start of treatment, that is, at the beginning of the first year of observation, 9 died during the first year and 41 were alive at the beginning of the second year.
3. The "effective number exposed to risk of dying" (column 5) is based on the assumption that patients last seen alive during any year of follow-up were, on the average, observed for one half of that year. Thus, for the third year the "effective number" is $34 - (\frac{1}{2} \times 4) = 32.0$, and for the fourth year it is $28 - (\frac{1}{2} \times 5) = 25.5$.
4. The proportion dying during any year (column 6) is found by dividing the entry in column 3 by the entry in column 5. Thus, for the first year, the proportion dying is $9 \div 50.0 = 0.180$ and for the second year it is $6 \div 40.5 = 0.148$.
5. The proportion surviving the year (column 7), that is, the observed annual survival rate, is obtained by subtracting the proportion dying (column 6) from 1 (1.000).
6. The proportion surviving from first treatment to the end of each year (column 8), that is, the observed cumulative survival rate, is the product

Table 2-2. Calculation of Observed Survival Rate by the Actuarial (Life-Table) Method

YEAR OF LAST OBSERVATION (1)	NO. ALIVE AT BEGINNING OF YEAR (2)	NO. DYING DURING YEAR (3)	NO. LAST SEEN ALIVE DURING YEAR (4)	EFFECTIVE NO. EXPOSED TO RISK OF DYING (5)	PROPORTION DYING DURING YEAR (6)	PROPORTION SURVIVING YEAR (7)	PROPORTION SURVIVING FROM FIRST TREATMENT TO END OF YEAR (8)
1	50	9	0	50.0	0.180	0.820	0.820
2	41	6	1	40.5	0.148	0.852	0.699
3	34	2	4	32.0	0.063	0.937	0.655
4	28	1	5	25.5	0.039	0.961	0.629
5	22	2	3	20.5	0.098	0.902	0.567
⩾6	17	—	17	—	—	—	—
Total		20	30				

of the annual survival rates for the given year and all preceding years. For example, for the fifth year the proportion 0.567 is the product of all entries in column 7 from the first through the fifth years.

The 5-year survival rate calculated by the life-table method is 0.567, or 57%. In this instance, the calculation obtained by using the information available on all 50 patients agrees with the rate based on the 30 patients eligible for inclusion in the calculation by the direct method. Such close agreement by the two methods usually does not occur when some patients have to be excluded from the calculation of a survival rate by the direct method. In such instances, the life-table method is more reliable because it is based on more information.

One advantage of the life-table method is that it provides information about changes in the risk of dying in successive intervals of observation. Thus, we see from column 6 that the proportion of patients dying in each of the first 4 years after treatment decreased from 18% in the first year to 4% in the fourth. (The increase to 10% in the fifth year may be due to chance, since we are dealing here with small numbers—only 22 patients were alive at the beginning of the fifth year.)

The cumulative rates in column 8 may be used to plot a survival curve, providing a pictorial description of the survival pattern as shown in Figure 2-2. In Figure 2-3, the survival pattern for patients with

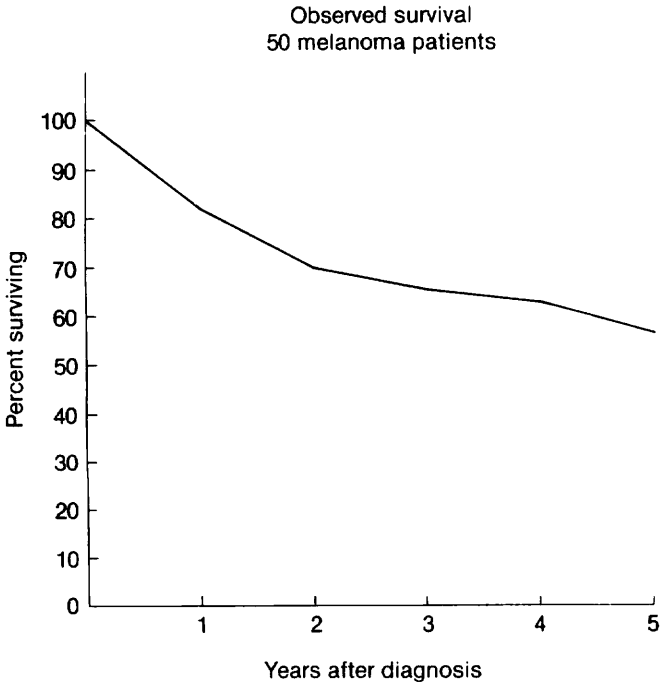


Fig. 2-2. Survival curve for 50 white patients with melanoma of the skin

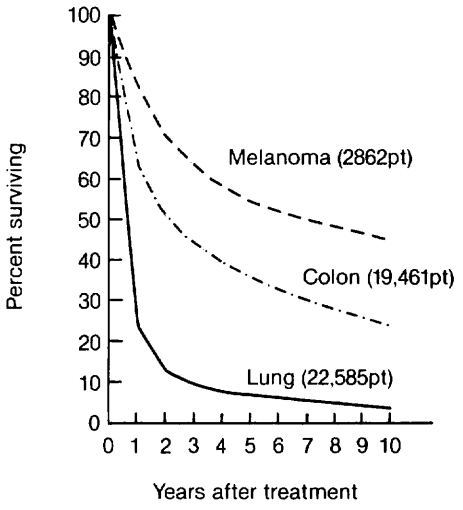


Fig. 2-3. Survival curves for patients with melanoma, colon cancer, and lung cancer: arithmetic scale. (Data from End-Results Group: End Results in Cancer, Report No. 4, DHEW Publication NIH 73-272. Bethesda, MD, National Cancer Institute, 1972)

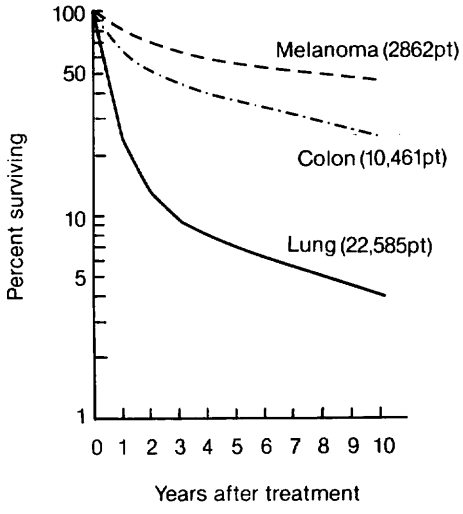


Fig. 2-4. Survival curves for patients with melanoma, colon cancer, and lung cancer: logarithmic scale. (Data from End-Results Group: End Results in Cancer, Report No. 4, DHEW Publication NIH 73-272. Bethesda, MD, National Cancer Institute, 1972)

melanoma of the skin (based on a large series) is compared with the patterns for cancers of the colon and of the lung for a 10-year period of observation.

The same set of survival rates was plotted in Figure 2-4 using a logarithmic scale, which provides a pictorial representation of changes in the rate at which patients are dying—a steep slope indicates a high rate, a shallow slope indicates a low rate. For each disease group, the death rate slowed appreciably

Table 2-3. Calculation of Adjusted Survival Rate

YEAR OF LAST OBSERVATION (1)	NO. ALIVE AT BEGINNING OF YEAR (2)	NO. DYING DURING YEAR		NO. LAST SEEN ALIVE DURING YEAR (4)	EFFECTIVE NO. EXPOSED TO RISK OF DYING (5)	PROPORTION DYING DURING YEAR (6)	PROPORTION SURVIVING TO END OF YEAR (7)	CUMULATIVE PROPORTION SURVIVING (8)
		WITH DISEASE (3a)	WITHOUT DISEASE (3b)					
1	50	8	1	0	49.5	0.162	0.838	0.838
2	41	4	2	1	39.5	0.101	0.899	0.754
3	34	2	0	4	32.0	0.063	0.937	0.706
4	28	1	0	5	25.5	0.039	0.961	0.679
5	22	2	0	3	20.5	0.098	0.902	0.613
⩾6	17	—	—	17	—	—	—	—
Total		17	3	30				

after the third year; the slope of each curve becomes shallower. However, it is clear from Figure 2-4 that patients with lung cancer were dying at a greater rate from the third through the tenth years than patients with cancer of the colon or with melanoma. In contrast, examination of Figure 2-3 might lead one to the erroneous conclusion that beyond the third year, lung cancer patients died at a lower rate. This is because Figure 2-3 portrays *absolute* changes, while Figure 2-4 provides a true picture of *relative* changes.

Adjusted Survival Rate. The *observed* survival rate described above accounts for all deaths, regardless of cause. While this is a true reflection of total mortality in the patient group, we are frequently interested in describing mortality attributable to the disease under study. Examination of Table 2-1 reveals that in four instances melanoma was not present at time of death (patients 2, 13, 42, and 44). Three of these deaths occurred within the first 5 years of follow-up and thus influenced the 5-year survival rate calculated in Table 2-2.

Whenever reliable information on cause of death is available, an adjustment can be made for deaths due to causes other than the disease under study. The procedure is shown in Table 2-3. Observed deaths are recorded as "with disease" (column 3a) or "without disease" (column 3b). Patients who died "without disease" are treated in the same manner as patients "last seen alive during year" (column 4); that is, both groups are withdrawn from the risk of dying from melanoma. Thus, the "effective number exposed to risk of dying" (from melanoma) in the second year of observation is equal to $41 - (\frac{1}{2}[2 + 1]) = 39.5$.

The 5-year *adjusted* survival rate is 61% compared to an *observed* rate of 57%. The adjusted rate indicates that 61% of patients with melanoma escaped the risk of death from the disease within 5 years of treatment.

Use of the adjusted rate is particularly important in comparing patient groups that may differ with respect to factors such as sex, age, race, and socioeconomic status. Of the 50 patients listed in Table 2-1, 24 are males and 26 females. The observed survival curves are plotted in the upper part of Figure 2-5. There is a large gap between the curves for the two sexes. However, 3 of the 12 males who died during the first 5 years of observation had no evidence of melanoma at time of death. In contrast, melanoma was present at time of death in all eight females who died. The effect of the adjustment for cause of death is shown in the lower portion of Figure 2-5. The survival curve for males is still below the curve for females, but the gap has been narrowed. The 5-year adjusted survival rate is 58% for males and 65% for females. The corresponding observed rates are 48% and 65%, a much larger difference.

Relative Survival Rate. Information on cause of death is sometimes unavailable or unreliable. Under such circumstances, it is not possible to compute an adjusted survival rate. However, it is possible to account for differences among patient groups in *normal mortality expectation*, that is, differences in the risk of dying from causes other than the disease

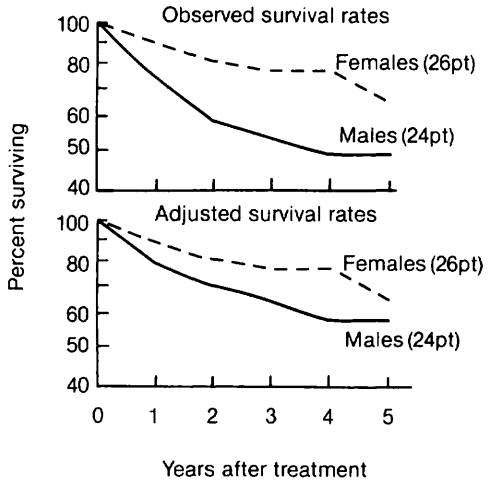


Fig. 2-5. Comparison of survival curves (logarithmic scale) for males and females with melanoma: observed and adjusted survival rates

under study. This can be done by means of the relative survival rate, which is the ratio of the observed survival rate to the expected rate for a group of people in the general population similar to the patient group with respect to race, sex, age, and calendar period of observation.

Table 2-4 provides 5-year "normal" survival probabilities for white males and females in the United States, based on mortality experience in calendar years 1950, 1955, 1960, 1965, 1970, and 1975. The appropriate probability, depending on the sex and age of the patient and the calendar year of entry to observation, is taken from this table and entered in the lower portion of the patient data card (Fig. 2-1). Thus, for example, for patient 2 (Table 2-1), who is a 42-year-old man with a 1954 date of entry, the 5-year expected survival probability is 0.979. For patient 17, a 31-year-old woman who entered observation in 1961, the expected probability is 0.995. Thus, for the hypothetical group of patients in Table 2-1, the average expected 5-year survival probability is the sum of the individual probabilities (46.257) divided by the number of patients (50) and equals 0.92. The ratio of the observed (57%) to the expected (92%) survival rate is 62%. This is the relative rate and in this instance it is almost identical with the adjusted rate.

Although in this illustration 5-year results were used to depict the relative survival rate calculation, it is conventional to calculate relative survival rates for each interval and cumulatively for successive follow-up intervals. For the more detailed analysis, one must consult more extensive expected rate tables and more explicit methodology (see bibliography entry 6).

In Figure 2-6, comparison is made between the

Table 2-4. Five-Year Survival Probabilities for U.S. Whites: 1950, 1955, 1960, 1965, 1970, and 1975

AGE IN YEARS (INCLUSIVE RANGE)	1950 (1948-1952)	1955 (1953-1957)	1960 (1958-1962)	1965 (1963-1967)	1970 (1968-1972)	1975 (1973-1977)
Male						
<1	0.964	0.969	0.970	0.972	0.977	0.981
1 and 2	0.995	0.996	0.996	0.996	0.996	0.997
5 (3-7)	0.997	0.997	0.998	0.998	0.998	0.998
10 (8-12)	0.997	0.997	0.997	0.998	0.998	0.998
15 (13-17)	0.993	0.994	0.994	0.994	0.993	0.993
20 (18-22)	0.991	0.991	0.992	0.991	0.990	0.991
25 (23-27)	0.992	0.992	0.992	0.992	0.992	0.992
30 (28-32)	0.991	0.991	0.991	0.991	0.991	0.992
35 (33-37)	0.986	0.987	0.988	0.987	0.987	0.989
40 (38-42)	0.978	0.979	0.980	0.980	0.979	0.982
45 (43-47)	0.963	0.965	0.966	0.966	0.967	0.970
50 (48-52)	0.942	0.944	0.943	0.944	0.947	0.952
55 (53-57)	0.912	0.916	0.915	0.913	0.915	0.926
60 (58-62)	0.869	0.873	0.872	0.873	0.873	0.884
65 (63-67)	0.814	0.815	0.815	0.813	0.816	0.834
70 (68-72)	0.741	0.746	0.745	0.741	0.745	0.759
75 (73-77)	0.633	0.642	0.650	0.649	0.642	0.658
80 (78-82)	0.499	0.504	0.509	0.520	0.523	0.547
⩾85	0.350	0.349	0.349	0.350	0.379	0.421
Female						
<1	0.972	0.976	0.977	0.979	0.982	0.985
1 and 2	0.996	0.997	0.997	0.997	0.997	0.997
5 (3-7)	0.998	0.998	0.998	0.998	0.998	0.999
10 (8-12)	0.998	0.998	0.999	0.999	0.999	0.999
15 (13-17)	0.997	0.997	0.998	0.998	0.997	0.997
20 (18-22)	0.996	0.997	0.997	0.997	0.997	0.997
25 (23-27)	0.996	0.996	0.996	0.997	0.996	0.997
30 (28-32)	0.994	0.995	0.995	0.995	0.995	0.996
35 (33-37)	0.991	0.992	0.993	0.993	0.993	0.994
40 (38-42)	0.987	0.988	0.988	0.988	0.988	0.990
45 (43-47)	0.980	0.982	0.982	0.982	0.982	0.984
50 (48-52)	0.969	0.972	0.972	0.972	0.973	0.975
55 (53-57)	0.953	0.959	0.960	0.959	0.960	0.963
60 (58-62)	0.925	0.934	0.937	0.939	0.941	0.944
65 (63-67)	0.883	0.890	0.900	0.901	0.908	0.920
70 (68-72)	0.816	0.832	0.841	0.846	0.854	0.869
75 (73-77)	0.708	0.727	0.746	0.754	0.761	0.784
80 (78-82)	0.558	0.580	0.592	0.611	0.633	0.672
⩾85	0.406	0.394	0.400	0.405	0.472	0.512

Source: National Center for Health Statistics

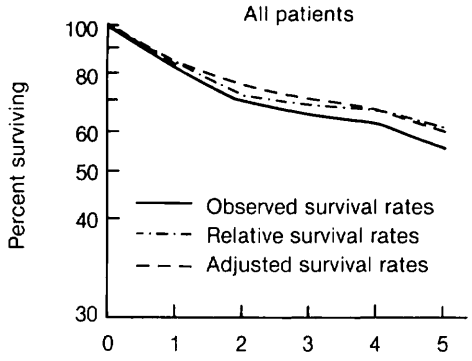


Fig. 2-6. Comparison of survival curves based on observed, adjusted, and relative rates (logarithmic scale)

survival curves based on the observed, adjusted, and relative rates. It can be seen that the values along the adjusted and relative survival curves are not always nearly identical. In practice, if the series is not too small and the patients are roughly representative of the population of the United States (taking race, sex, and age into account), the relative survival rate provides a useful estimate of the probability of escaping the risk of dying from the specific disease under study. However, if reliable information on cause of death is available, it is preferable to use the adjusted rate. This is particularly true if the series is small or if the patients are drawn largely from a particular socioeconomic segment of the population.

In reporting on patient survival, the exact method used in calculating the rates must be specified. The different types of rates described above are all useful, but rates computed by different methods are not directly comparable with each other. Thus, in comparing the survival of different patient groups, rates must be computed by the same method.

STANDARD ERROR OF A SURVIVAL RATE

A survival rate describes the experience of the specific group of patients from which it is computed. These results are frequently used to generalize to a larger population or universe. The existence of universal values is postulated and these values are estimated from the group under study, which thus represents a sample from the larger population. If a survival rate were calculated from a second sample taken from the same universe, it is unlikely that the results would be exactly the same. The difference between the two results is called the *sampling variation* (chance variation or sampling error). The *standard error* is a measure of the extent to which sampling variation influences the computed survival rate. In repeated observations under the same conditions, the true or population survival rate will lie within the range of two standard errors on either side of the computed rate about 95 times in 100. This range is called the *95% confidence interval.*

When the observed survival rate has been computed by the direct method, the standard error is computed from the formula

$$\sqrt{\frac{p\,(1-p)}{n}}$$

where "p" is the survival rate and "n" is the number of patients exposed to risk of death. In the illustration of the direct method, a 5-year survival rate of 57% was obtained based on the experience of 30 patients ($17 \div 30 = 0.567$). Thus, the standard error is equal to 0.090 (square root of $[0.567 \times 0.433 \div 30]$). To obtain the 95% confidence interval, twice the standard error (18%) is subtracted from and added to the survival rate. This means that the chances are about 95 in 100 that the true 5-year rate is between 39% and 75% for our example.

Standard Error of the Actuarial Survival Rate. In order to calculate the standard error of the 5-year survival rate when the actuarial method is used (see bibliography entries 4, 12, 14), two columns of figures may be added to Table 2-2 as shown in Table 2-5. The first additional column (column 9) is obtained by subtracting the values in column 3 from the values in column 5 of Table 2-2. The last column needed (column 10) is obtained by dividing the entries in column 6 by the corresponding figures in column 9. The sum of the figures in column 10 is also entered into the table and in this example equals 0.0177.

The standard error of the 5-year survival rate by the actuarial method is the calculated 5-year survival rate multiplied by the square root of the total of the entries in column 10 of Table 2-5, that is, $0.567\ \sqrt{0.0177} = 0.075$. The approximate 95% confidence interval for the population 5-year survival rate is found, as shown earlier for the direct method, by adding and subtracting two times the standard error to and from the 5-year survival rate that has been calculated, that is, 0.567 plus and minus (2×0.075), which gives an interval from 0.42 to 0.72.

If the above computations seem to be too involved, an approximation to the standard error of the actuarial survival rate may be quickly obtained from published tables prepared by Ederer (see bibliography entry 5).

It is noteworthy that the standard error of the survival rate obtained by the actuarial method is smaller than the standard error of the survival rate calculated by the direct method (0.075 *vs* 0.090). This difference reflects the advantage in terms of statistical reliability of using all available information, that is,

Table 2-5. Calculation of Standard Error of Survival Rate by Actuarial (Life-Table) Method

YEAR OF LAST OBSERVATION (1)	NO. ALIVE AT BEGINNING OF YEAR (2)	NO. DYING DURING YEAR (3)	NO. LAST SEEN ALIVE DURING YEAR (4)	EFFECTIVE NO. EXPOSED TO RISK OF DYING (5)	PROPORTION DYING DURING YEAR (6)	PROPORTION SURVIVING YEAR (7)	PROPORTION SURVIVING FROM FIRST TREATMENT TO END OF YEAR (8)	ENTRY (5) MINUS ENTRY (3) (9)	ENTRY (6) DIVIDED BY ENTRY (9) (10)
1	50	9	0	50.0	0.180	0.820	0.820	41.0	0.0044
2	41	6	1	40.5	0.148	0.852	0.699	34.5	0.0043
3	34	2	4	32.0	0.063	0.937	0.655	30.0	0.0021
4	28	1	5	25.5	0.039	0.961	0.629	24.5	0.0016
5	22	2	3	20.5	0.098	0.902	0.567	18.5	0.0053
⩾6	17	—	17	—	—	—	—	—	—
Total		20	30						0.0177

Standard error of 5-year survival rate = 5-year survival rate × $\sqrt{\text{total of column (10)}}$
$= 0.567 \times \sqrt{0.0177} = 0.567 \times 0.1330 = 0.075$

information on patients under observation for less than 5 years. The issue is discussed in detail by Cutler (bibliography entry 4).

Standard Error of Relative Survival Rate. The standard error of the relative survival rate is easily obtained by dividing the standard error of the observed survival rate (obtained by either the direct or actuarial method) by the expected survival rate. Thus, from the actuarial method the 5-year survival rate is 57% and the expected survival rate is 92%, with a resulting relative survival rate of 62%. The standard error of the observed survival rate is 0.075.

In this example the standard error of the 5-year relative survival rate is as follows:

$$\frac{\text{Standard error of observed rate}}{\text{Expected survival rate}} = \frac{0.075}{0.920} = 0.082$$

The 95% confidence limits for the 5-year relative survival rate are, therefore, as shown below:

$$0.62 = 2(.08) = 0.46, 0.78.$$

Comparison of Survival Rates in Two Patient Groups. In comparing survival rates of two patient groups, the statistical significance of the observed difference is of interest. The essential question is: What is the probability that the observed difference may have occurred by chance? The standard error of the survival rate provides a simple means for appraising this question. If the 95% confidence intervals of two survival rates do not overlap, the observed difference would be customarily considered as statistically significant, that is, unlikely to be due to chance.

Standard statistical tests describe the z-test, which provides a numeric estimate of the probability that a difference as large as that observed would have occurred if only chance were operating. The statistic z is calculated by the following formula:

$$z = \frac{|p_1 - p_2|}{\sqrt{(SE_1)^2 + (SE_2)^2}}$$

in which

1. p_1 is the survival rate for group 1.
2. p_2 is the survival rate for group 2.
3. $|p_1 - p_2|$ is the *absolute* value of the difference (*i.e.*, the *magnitude* of the difference, whether positive or negative).
4. SE_1 is the standard error of p_1.
5. SE_2 is the standard error of p_2.

If $z \geqslant 1.96$, the probability that a difference as large as that observed occurred by chance is $\leqslant 5\%$. If $z \geqslant 2.56$, the probability is $\leqslant 1\%$. It is conventional in most (but not all) applications to regard as statistically significant a difference that would occur by chance with a probability of 5% or less. For example, let us apply the z-test to the difference in observed 5-year survival rates by the actuarial method for the 24 males and 26 females among the 50 melanoma patients (*i.e.*, let us test whether there is a statistically significant difference in survival of the males with melanoma compared with the females).

Designate the 5-year survival rate for males by p_1 and for females by p_2. We find $p_1 = 0.485$ and $p_2 = 0.646$. Employing the method shown in Table 2-5, $SE_1 = 0.105$ and $SE_2 = 0.105$.

Then,

$$z = \frac{|0.485 - 0.646|}{\sqrt{0.105^2 + 0.105^2}} = \frac{0.161}{0.148} = 1.09$$

The calculated z value is smaller than 1.96 and therefore not statistically significant at the 5% level. This result indicates that for a study of this size (24 males and 26 females) the difference in p's (0.485 *vs* 0.646) is not large enough for us to reject chance or sampling variation as the cause.

In a study with more patients, the same size difference in survival rates as seen here would be less likely to be due to chance and might be statistically significant (*i.e.*, z might equal or exceed 1.96). In order for this to come about, the value of the denominator in the equation for z would have to decrease in value. The denominator, $\sqrt{(SE_1)^2 + (SE_2)^2}$, is called the *standard error of the difference in rates* and does tend to become smaller as study size increases. It should also be noted that superior survival of female patients with melanoma compared with males has been observed in large series of patients with resultant significant z values.

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PART II

STAGING OF CANCER AT SPECIFIC ANATOMIC SITES

HEAD AND NECK SITES

3

Lip and Oral Cavity

Cancers of the head and neck may arise on all lining membranes of the upper aerodigestive tract. The "T" classifications indicating the extent of the primary tumor are generally similar but differ in specific details for each site because of anatomic considerations. The "N" classification for cervical lymph node metastasis is uniform for all sites. The staging systems presented in this section are all clinical-diagnostic staging, based on the best possible estimate of the extent of disease before treatment. Although surgical-evaluative classifications and pathologic classifications are possible, they are of less practical importance in the management of these tumors. However, when surgical treatment is carried out, cancer of the head and neck can be staged during these periods of management using all information available.

This section presents the staging classification for four major head and neck sites: the oral cavity, the pharynx (nasopharynx, oropharynx, hypopharynx), the larynx, and the paranasal sinuses.

ORAL CAVITY

Anatomy (International Classification of Diseases for Oncology—ICD-O 140-145)

Primary Site. The oral cavity extends from the skin-vermilion junction of the lips to the junction of the hard and soft palate above and to the line of circumvallate papillae below and is divided into the following specific areas:

Lip (ICD-O 140). The lip begins at the junction of the vermilion border with the skin and includes only the vermilion surface or that portion of the lip which comes into contact with the opposing lip. It is well defined into an upper and lower lip joined at the commissures of the mouth.

Buccal Mucosa (ICD-O 140). This includes all the membrane lining of the inner surface of the cheeks and lips, from the line of contact of the opposing lips to the line of attachment of mucosa of the alveolar ridge (upper and lower) and pterygomandibular raphe.

Lower Alveolar Ridge (ICD-O 143). This ridge includes the alveolar process of the mandible and its covering mucosa, which extends from the line of attachment of mucosa in the buccal gutter to the line of free mucosa of the floor of the mouth. Posteriorly it extends to the ascending ramus of the mandible.

Upper Alveolar Ridge (ICD-O 143). The upper ridge is the alveolar process of the maxilla and its covering mucosa, which extends from the line of attachment of mucosa in the upper gingival buccal gutter to the junction of the hard palate. Its posterior margin is the upper end of the pterygopalatine arch.

Retromolar Gingiva (Retromolar Trigone) (ICD-O 145). This is the attached mucosa overlying the ascending ramus of the mandible from the level of the posterior surface of the last molar tooth to the apex superiorly, adjacent to the tuberosity of the maxilla.

Floor of the Mouth (ICD-O 144). This is a semilunar space over the mylohyoid and hyoglossus muscles, extending from the inner surface of the lower alveolar ridge to the undersurface of the tongue. Its posterior boundary is the base of the anterior pillar of the tonsil. It is divided into two sides by the frenulum of the tongue and contains the ostia of the submaxillary and sublingual salivary glands.

Hard Palate (ICD-O 145). This is the semilunar area between the upper alveolar ridge and the mucous membrane covering the palatine process of the maxillary palatine bones. It extends from the inner surface of the superior alveolar ridge to the posterior edge of the palatine bone.

Anterior Two Thirds of the Tongue (Oral Tongue) (ICD-O 144). This is a freely mobile portion of the tongue that extends anteriorly from the line of circumvallate papillae to the undersurface of the tongue at the junction of the floor of the mouth. It is composed of four areas: the tip, the lateral borders, the dorsum, and the undersurface (nonvillous surface of the tongue). The undersurface of the tongue is considered as a separate category by the World Health Organization (WHO) (ICD-O 141.3).

Nodal Stations. The main routes of drainage are into the first station nodes, which are the jugulodigastric, jugulo-omohyoid, upper deep cervical, lower deep cervical, and submaxillary and submental lymph nodes. Some primary sites drain bilaterally. Second station nodes include parotid lymph nodes (juxtaposition nodes).

Metastatic Sites. Distant spread to the lungs is common; skeletal or hepatic metastases occur less often. Mediastinal lymph node metastases are considered distant metastases.

Staging Procedures

A variety of procedures and special studies may be employed in the process of staging a given tumor. Both the clinical usefulness and cost efficiency must be considered. The following minimum requirements are made for staging a cancer of the oral cavity:

Essential for staging

1. Complete physical examination of the head and neck including indirect laryngoscopy and nasopharyngoscopy
2. Biopsy of primary tumor
3. Chest roentgenogram
4. Panorex films or other x-ray films for tumors overlying the jaws
5. Roentgenograms of paranasal sinuses for tumors overlying the palate

Possibly useful for staging or patient management

1. Multichemistry screen
2. Staining of surface mucosa with toluidine blue
3. Performance status (Karnofsky or ECOG scale)

Possibly useful for future staging systems or research studies

1. Panendoscopy (direct laryngoscopy, bronchoscopy, esophagoscopy)
2. Studies of immune competence

RULES FOR CLASSIFICATION

Clinical-Diagnostic Staging. The assessment of the primary tumor is based upon inspection and palpation of the oral cavity and neck. Additional studies may include plain, tomographic, and contrast roentgenograms, particularly evaluating bone invasion of the mandible or upper alveoli. Examinations for distant metastases include chest film, blood chemistries, blood count, and other routine studies as indicated. The tumor must be confirmed histologically and any other pathologic data obtained on biopsy may be included.

Postsurgical Resection-Pathologic Staging. Complete resection of the primary site, radical nodal dissections, and pathologic examination of the resected specimens allow the use of this designation. Specimens that are resected after radiation or chemotherapy need to be especially noted.

Surgical-Evaluative Staging. Confirmation of the extent of disease is made by biopsy of suspected mucosal or submucosal spread, aspiration, or open biopsy of suspicious nodes. Biopsy of suspected distant metastasis is desirable but not required. This time period would be used infrequently.

Retreatment Staging. Utilization of available procedures noted above is required, particularly confirmation by biopsy, since previous treatment by surgery or irradiation leads to scarring and induration. A reevaluation for distant metastases is important, as are T and N classifications. This time period should be used after a disease-free interval and when further definitive treatment is planned.

TNM Classification

Primary Tumor (T)

- TX Minimum requirements to assess the primary tumor cannot be met.
- T0 No evidence of primary tumor
- Tis Carcinoma *in situ*
- T1 Greatest diameter of primary tumor 2 cm or less
- T2 Greatest diameter of primary tumor more than 2 cm but not more than 4 cm
- T3 Greatest diameter of primary tumor more than 4 cm
- T4 Massive tumor more than 4 cm in diameter with deep invasion to involve antrum, pterygoid muscles, base of tongue, skin of neck

Nodal Involvement (N)

Cervical Node Classification. The following regional node classification is applicable to all squamous cell carcinoma of the upper aerodigestive tract. In clinical evaluation, the actual size of the nodal mass should be measured and allowance should be made for intervening soft tissues. It is recognized that most masses over 3 cm in diame

- N2b Multiple clinically positive homolateral nodes, none more than 6 cm in diameter
- N3 Massive homolateral node(s), bilateral nodes, or contralateral node(s)
- N3a Clinically positive homolateral node(s), one more than 6 cm in diameter
- N3b Bilateral clinically positive nodes (in this situation, each side of the neck should be staged separately; *i.e.*, N3b: right, N2a; left, N1)
- N3c Contralateral clinically positive node(s) only

Distant Metastasis (M)

- MX Minimum requirements to assess the presence of distant metastasis cannot be met.
- M0 No evidence of distant metastasis
- M1 Distant metastasis present
  Specify _____

Specify sites according to the following notations:

Pulmonary	PUL
Osseous	OSS
Hepatic	HEP
Brain	BRA
Lymph nodes	LYM
Bone marrow	MAR
Pleura	PLE
Skin	SKI
Eye	EYE
Other	OTH

Postsurgical Treatment Residual Tumor (R)

Does not enter into staging tumor but may be a factor in deciding management

- R0 No residual tumor
- R1 Microscopic residual tumor
- R2 oscopic residual tumor
  ify _____

rouping

T1, N0, M0
T2, N0, M0
T3, N0, M0
T1, T2, T3; N1, M0
T4, N0 or N1, M0
Any T, N2 or N3, M0
Any T, any N, M1

hology

inant cancer is squamous cell carcinoma; iagnosis is required to utilize this classi- mor grading is recommended using ssification. Other tumors of glandular odontogenic apparatus, lymphoid tissue, soft tissue, and bone and cartilage origin require special consideration and are not to be included. Reference to the WHO nomenclature is recommended. Although the grade of the tumor does not enter into staging of the tumor, it should be recorded.

Tumor Grade (G)

G1	Well differentiated
G2	Moderately well differentiated
G3-G4	Poorly to very poorly differentiated

Use whichever indicator is most appropriate (term or G + number)

Performance Status of Host (H)

Performance status of the host should be recorded because this information at times is pertinent to the treatment of the patient.

AJCC	PERFORMANCE	ECOG SCALE	KARNOFSKY SCALE (%)
H0	Normal activity	0	90-100
H1	Symptomatic but ambulatory; cares for self	1	70-80
H2	Ambulatory more than 50% of time; occasionally needs assistance	2	50-60
H3	Ambulatory 50% or less of time; nursing care needed	3	30-40
H4	Bedridden; may need hospitalization	4	10-20

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Data Form for Cancer Staging

Patient identification
Name _____
Address _____
Hospital or clinic number _____
Age _____ Sex _____ Race _____

Institutional identification
Hospital or clinic _____
Address _____

Oncology Record

Anatomic site of cancer _____

Histologic type† _____ Grade (G) _____

Chronology of classification* [ ] Clinical-diagnostic (cTNM) [ ] Surgical-evaluative (sTNM)
[ ] Postsurgical resection–pathologic (pTNM)
[ ] Retreatment (rTNM) [ ] Autopsy (aTNM)

Date of classification _____

Definitions for All Time Periods

Primary Tumor (T)

[ ] TX Minimum requirements to assess the primary tumor cannot be met.
[ ] T0 No evidence of primary tumor
[ ] Tis Carcinoma *in situ*
[ ] T1 Greatest diameter of primary tumor 2 cm or less
[ ] T2 Greatest diameter of primary tumor more than 2 cm but not more than 4 cm
[ ] T3 Greatest diameter of primary tumor more than 4 cm
[ ] T4 Massive tumor more than 4 cm in diameter with deep invasion to involve antrum, pterygoid muscles, base of tongue, skin of neck

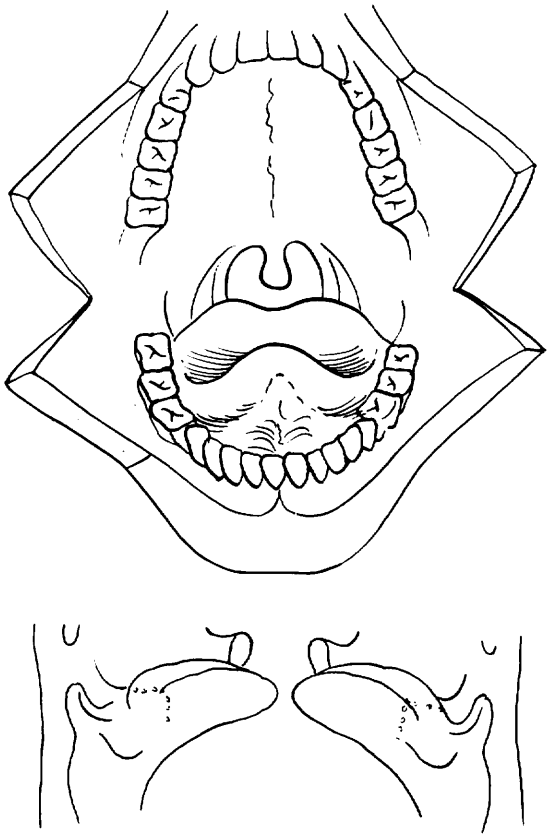
Lymph Nodes (N)

Same definitions to be used if postsurgical treatment–pathologic staging is used:

[ ] NX Minimum requirements to assess the regional nodes cannot be met.
[ ] N0 No clinically positive node
[ ] N1 Single clinically positive homolateral node 3 cm or less in diameter
[ ] N2 Single clinically positive homolateral node more than 3 but not more than 6 cm in diameter or multiple clinically positive homolateral nodes, none more than 6 cm in diameter
  [ ] N2a Single clinically positive homolateral node more than 3 cm but not more than 6 cm in diameter
  [ ] N2b Multiple clinically positive homolateral nodes, none more than 6 cm in diameter
[ ] N3 Massive homolateral node(s), bilateral nodes, or contralateral node(s)
  [ ] N3a Clinically positive homolateral node(s), one more than 6 cm in diameter
  [ ] N3b Bilateral clinically positive nodes (in this situation, each side of the neck should be staged separately; *i. e.*, N3b: right, N2a; left, N1)
  [ ] N3c Contralateral clinically positive node(s) only

Distant Metastasis (M)

[ ] MX Minimum requirements to assess the presence of distant metastasis
[ ] M0 No (known) distant metastasis
[ ] M1 Distant metastasis present
Specify _____



Tumor size: _____ cm

Location of Tumor

[ ] Lips: Upper
Lower
[ ] Buccal mucosa
[ ] Floor of mouth
[ ] Oral tongue
[ ] Hard palate
[ ] Gingivae: Upper
Lower
Retromolar trigone

Examination by _____ M.D.
Date _____

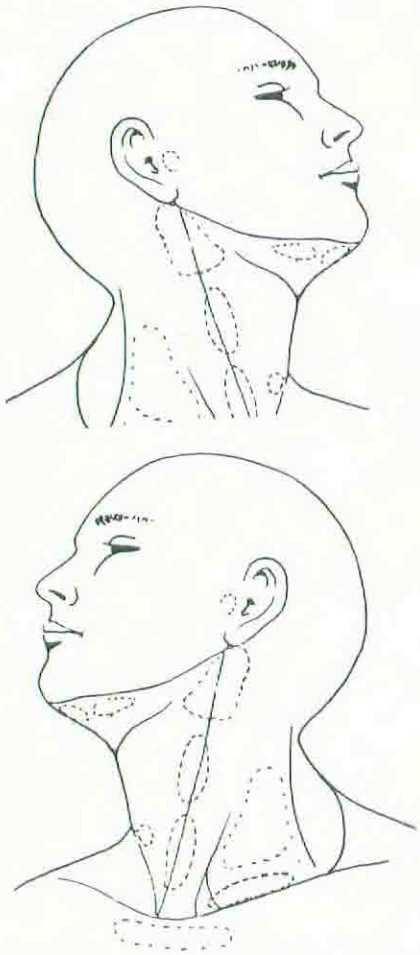
*Use a separate form each time a case is staged.
†See reverse side for additional information.

Characteristics of Tumor

[ ] Exophytic
[ ] Superficial
[ ] Moderately infiltrating
[ ] Deeply infiltrating
[ ] Ulcerated
[ ] Extends to or overlies bone
[ ] Gross erosion of bone
[ ] Radiographic destruction of bone

Involvement of Neighboring Regions

[ ] Tonsillar pillar or soft palate
[ ] Nasal cavity or antrum
[ ] Nasopharynx
[ ] Pterygoid muscles
[ ] Soft tissues or skin of neck



Indicate on diagram primary tumor and regional nodes involved.

Stage Grouping

[ ]	Stage I	T1, N0, M0
[ ]	Stage II	T2, N0, M0
[ ]	Stage III	T3, N0, M0 T1, T2, T3; N1, M0
[ ]	Stage IV	T4, N0, N1; M0 Any T, N2, N3; M0 Any T, any N, M1

Staging Procedures

A variety of procedures and special studies may be employed in the process of staging a given tumor. Both the clinical usefulness and cost efficiency must be considered. The following suggestions are made for staging a cancer of the oral cavity.

Essential for staging

1. Complete physical examination of the head and neck including indirect laryngoscopy and nasopharyngoscopy
2. Biopsy of primary tumor
3. Chest roentgenogram
4. Panorex films or other x-ray films for tumors overlying the jaws
5. Roentgenograms of paranasal sinuses for tumors overlying the palate

May be useful for staging or patient management

1. Multichemistry screen
2. Staining of surface mucosa with toluidine blue
3. Performance status (Karnofsky or ECOG scale)

May be useful for future staging systems or research studies

1. Panendoscopy (direct laryngoscopy, bronchoscopy, esophagoscopy)
2. Studies of immune competence

Histologic Type of Cancer

Predominant cancer is squamous cell carcinoma.

Histologic Grade

[ ]	G1	Well differentiated
[ ]	G2	Moderately well differentiated
[ ]	G3–G4	Poorly to very poorly differentiated

Postsurgical Resection–Pathologic Residual Tumor (R)

This does not enter into staging but may be a factor in deciding further treatment.

[ ]	R0	No residual tumor
[ ]	R1	Microscopic residual tumor
[ ]	R2	Macroscopic residual tumor

Specify _____

Performance Status of Host (H)

Several systems for recording a patient's activity and symptoms are in use and are more or less equivalent, as follows:

	AJCC	Performance	ECOG Scale	Karnofsky Scale (%)
[ ]	H0	Normal activity	0	90–100
[ ]	H1	Symptomatic but ambulatory; cares for self	1	70–80
[ ]	H2	Ambulatory more than 50% of time; occasionally needs assistance	2	50–60
[ ]	H3	Ambulatory 50% or less of time; nursing care needed	3	30–40
[ ]	H4	Bedridden; may need hospitalization	4	10–20

4

Pharynx

OROPHARYNX (ICD-O 146), NASOPHARYNX (ICD-O 147), and HYPOPHARYNX (ICD-O 148)

Anatomy

Primary Site. The pharynx is divided into three regions: oropharynx, nasopharynx, and hypopharynx.

Oropharynx. The oropharynx extends from the plane of the hard palate superiorly to the plane of the hyoid bone inferiorly and is continuous with the oral cavity. The faucial arch includes both the surfaces of the entire soft palate and the uvula, the anterior border and base of the anterior tonsillar pillar, and the line of the circumvallate papillae. The base of the tongue extends from the line of the circumvallate papillae to the junction with the base of the epiglottis (the vallecula) and includes the pharyngoepiglottic and glossoepiglottic folds. The lateral wall of the oropharynx is comprised largely of the tonsil and tonsillar fossae. The posterior tonsillar pillar, the narrow lateral wall, and the posterior wall make up the pharyngeal wall.

Nasopharynx. The anterior limit of the nasopharynx is the choana, through which it is continuous with the nasal cavity. Its roof is attached to the base of the skull and slopes downward to become continuous with the posterior pharyngeal wall. The lateral wall is composed of the torus tubarius, the eustachian tube orifice, and that portion of the mucosa of the fossa of Rosenmueller extending up to its apex and junction with the roof. The inferior limit of the nasopharynx is level with the plane of the hard palate.

Hypopharynx. The hypopharynx extends from the plane of the hyoid bone superiorly to the plane of the lower border of the cricoid cartilage inferiorly. It is made up of three distinct regions: the piriform sinus, the posterior surface of the larynx (the postcricoid area), and the lower posterior pharyngeal wall.

Each region is subdivided into sites that are summarized as follows:

Oropharynx (146)

1. Anterior wall (glosso-epiglottic area)—tongue posterior to the vallate papillae; base of tongue or posterior third (141.0)

2. Lateral wall
   a. Tonsil (146.0)
   b. Tonsillar fossa (146.1) and faucial pillars (146.2)
   c. Glossotonsillar sulci
3. Posterior wall
4. Superior wall
   a. Inferior surface of soft palate (146.3)
   b. Uvula (146.4)

Nasopharynx (147)

1. Posterosuperior wall, extends from the level of the junction of the hard and soft palates to the base of the skull (147.0, 147.1).
2. Lateral wall, includes the fossa of Rosenmueller (147.2).
3. Inferior wall, consists of the superior surface of the soft palate (147.3).

Note: The margin of the choanal orifices including the posterior margin of the nasal septum is included with the nasal fossa.

Hypopharynx (148)

1. Pharyngo-esophageal junction (postcricoid area) extends from the level of the arytenoid cartilages and connecting folds to the inferior border of the cricoid cartilage (148.0).
2. Piriform sinus extends from the pharyngo-epiglottic fold to the upper end of the esophagus (148.1). It is bounded laterally by the thyroid cartilage and medially by the surface of the arytenoepiglottic fold (148.2) and the arytenoid and cricoid cartilages.
3. Posterior pharyngeal wall extends from the level of the floor of the vallecula to the level of the cricoarytenoid joints (148.3).

Nodal Stations. The main routes of drainage are into the first station nodes—jugulodigastric, jugulo-omohyoid, upper deep cervical, lower deep cervical, and submaxillary and submental lymph nodes. Some primary sites drain bilaterally. There are additional first station nodes that include retropharyngeal and parapharyngeal lymph nodes. Second station nodes include parotid nodes.

Metastatic Sites. Distant spread to lungs is common. Skeletal and other distant metastases occur less often. Mediastinal lymph node metastases are considered distant metastases.

Staging Procedures

A variety of procedures and special studies may be employed in the process of staging a given tumor. Both the clinical usefulness and cost efficiency must be considered. The following suggestions are made for staging a cancer of the pharynx:

Essential for staging

1. Complete physical examination of the head and neck, including indirect laryngoscopy and nasopharyngoscopy
2. Biopsy of primary tumor
3. Chest roentgenogram
4. Roentgenograms of skull (nasopharynx)
5. Direct examination of oropharynx and hypopharynx

Possibly useful for staging or patient management

1. Multichemistry screen
2. Soft tissue roentgenograms of neck; computed tomography (CT) scans
3. Barium swallow
4. Performance status (Karnofsky or ECOG scale)

Possibly useful for future staging systems or research studies

1. Panendoscopy (direct laryngoscopy, bronchoscopy, esophagoscopy)
2. Studies of immune competence
3. Assay of antibodies to Epstein-Barr viral capsid antigen (nasopharynx)

Rules for Classification

Clinical-Diagnostic Staging. The assessment of the pharynx is based primarily upon inspection by indirect mirror examination and direct endoscopy. Palpation of sites (when feasible) and neck nodes is essential. Neurologic evaluation of all cranial nerves is required. Additional studies include plain, tomographic, and contrast roentgenograms of the pharynx according to the site of interest. Examinations for distant metastases include chest film, blood chemistries, blood count, and other routine studies as indicated. The tumor must be confirmed histologically, and any other pathologic data obtained on biopsy may be included.

Postsurgical Resection-Pathologic Staging. Complete resection of primary sites and radical nodal dissections and pathologic examination of the resected specimen allow for the use of this designation. Specimens that are resected after radiation or chemotherapy need to be noted especially.

Surgical-Evaluative Staging. Confirmation of the extent of disease by biopsy of suspected mucosal or submucosal spread, aspirations or open biopsy of suspicious nodes, and biopsy of suspected distant metastases is desirable, but not required. This time period would be used infrequently.

Retreatment Staging. Utilization of available procedures noted above is required, particularly con-

firmation by biopsy, because previous treatment by surgery or irradiation leads to scarring and induration. A reevaluation for distant metastases is important, as well as T and N classifications. This time period should be used after a disease-free interval and when further definitive treatment is planned.

TNM Classification

Primary Tumor (T)

TX Minimum requirements to assess the primary tumor cannot be met.
T0 No evidence of primary tumor

Oropharynx

Tis Carcinoma *in situ*
T1 Tumor 2 cm or less in greatest diameter
T2 Tumor more than 2 cm but not more than 4 cm in greatest diameter
T3 Tumor more than 4 cm in greatest diameter
T4 Massive tumor more than 4 cm in diameter with invasion of bone, soft tissues of neck, or root (deep musculature) of tongue

Nasopharynx

Tis Carcinoma *in situ*
T1 Tumor confined to one site of nasopharynx or no tumor visible (positive biopsy only)
T2 Tumor involving two sites (both posterosuperior and lateral walls)
T3 Extension of tumor into nasal cavity or oropharynx
T4 Tumor invasion of skull, cranial nerve involvement, or both

Hypopharynx

Tis Carcinoma *in situ*
T1 Tumor confined to one site
T2 Extension of tumor to adjacent region or site without fixation of hemilarynx
T3 Extension of tumor to adjacent region or site with fixation of hemilarynx
T4 Massive tumor invading bone or soft tissues of neck

Nodal Involvement (N)

Cervical Node Classification. The following regional node classification is applicable to all squamous cell carcinoma of the upper aerodigestive tract. In clinical evaluation, the actual size of the nodal mass should be measured and allowance should be made for intervening soft tissues. It is recognized that most masses over 3 cm in diameter are not single nodes but are confluent nodes or tumor in soft tissues of the neck. There are three stages of clinically positive nodes: N1, N2, and N3. The use of subgroups a, b, and c is not required but is recommended. Midline nodes are considered homolateral nodes.

NX Minimum requirements to assess the regional nodes cannot be met.
N0 No clinically positive node
N1 Single clinically positive homolateral node 3 cm or less in diameter
N2 Single clinically positive homolateral node more than 3 cm but not more than 6 cm in diameter, or multiple clinically positive homolateral nodes, none more than 6 cm in diameter
N2a Single clinically positive homolateral node more than 3 cm but not more than 6 cm in diameter
N2b Multiple clinically positive homolateral nodes, none more than 6 cm in diameter
N3 Massive homolateral node(s), bilateral nodes, or contralateral node(s)
N3a Clinically positive homolateral node(s), one more then 6 cm in diameter
N3b Bilateral clinically positive nodes (in this situation, each side of the neck should be staged separately; *i.e.*, N3b: right, N2a; left, N1)
N3c Contralateral clinically positive node(s) only

Distant Metastasis (M)

MX Minimum requirements to assess the presence of distant metastasis cannot be met.
M0 No evidence of metastasis
M1 Distant metastasis present
Specify _____

Specify sites according to the following notations:

Pulmonary	PUL
Osseous	OSS
Hepatic	HEP
Brain	BRA
Lymph nodes	LYM
Bone marrow	MAR
Pleura	PLE
Skin	SKI
Eye	EYE
Other	OTH

Postsurgical Treatment Residual Tumor (R)

R0 No residual tumor
R1 Microscopic residual tumor
R2 Macroscopic residual tumor
Specify _____

Stage Grouping

Stage I T1, N0, M0

Stage II	T2, N0, M0
Stage III	T3, N0, M0
	T1 or T2 or T3, N1, M0
Stage IV	T4, N0 or N1, M0
	Any T, N2 or N3, M0
	Any T, any N, M1

Histopathology

The predominant cancer is squamous cell carcinoma; pathologic diagnosis is required to utilize this classification. Tumor grading is recommended using Broders' classification. Other tumors of glandular epithelium, odontogenic apparatus origin, lymphoid tissue, soft tissue, and bone and cartilage origin require special consideration and are not to be included. Reference to the WHO nomenclature is recommended.

Tumor Grade (G)

G1	Well differentiated
G2	Moderately well differentiated
G3-G4	Poorly to very poorly differentiated

Use whichever indicator is most appropriate (term or G + number).

Performance Status of Host (H)

Performance status of the host should be recorded because this information at times is pertinent to the treatment of the patient.

AJCC	PERFORMANCE	ECOG SCALE	KARNOFSKY SCALE (%)
H0	Normal activity	0	90-100
H1	Symptomatic but ambulatory; cares for self	1	70-80
H2	Ambulatory more than 50% of time; occasionally needs assistance	2	50-60
H3	Ambulatory 50% or less of time; nursing care needed	3	30-40
H4	Bedridden; may need hospitalization	4	10-20

BIBLIOGRAPHY

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2. Futrell JW, Bennett SH, Hoye RC et al: Predicting survival in cancer of the larynx or hypopharynx. Am J Surg 122:451-457, 1971
3. Jesse RH, Sugarbaker EV: Squamous cell carcinoma of the oral pharynx: Why we fail. Am J Surg 132:435-439, 1976

Data Form for Cancer Staging

Patient identification
Name _____
Address _____
Hospital or clinic number _____
Age _____ Sex _____ Race _____

Institutional identification
Hospital or clinic _____
Address _____

Oncology Record

Anatomic site of cancer _____
Chronology of classification* [ ] Clinical-diagnostic (cTNM) [ ] Surgical-evaluative (sTNM)
Date of classification _____

Histologic type† _____ Grade (G) _____
[ ] Postsurgical resection–pathologic (pTNM)
[ ] Retreatment (rTNM) [ ] Autopsy (aTNM)

Definitions: TNM Classification

Primary Tumor (T)

[ ] TX Minimum requirements to assess the primary tumor cannot be met.
[ ] T0 No evidence of primary tumor

Oropharynx

[ ] Tis Carcinoma *in situ*
[ ] T1 Tumor 2 cm or less in greatest diameter
[ ] T2 Tumor more than 2 cm but not more than 4 cm in greatest diameter
[ ] T3 Tumor more than 4 cm in greatest diameter
[ ] T4 Massive tumor more than 4 cm in diameter with invasion of bone, soft tissues of neck, or root (deep musculature) of tongue

Nasopharynx

[ ] Tis Carcinoma *in situ*
[ ] T1 Tumor confined to one side of nasopharynx or no tumor visible (positive biopsy only)
[ ] T2 Tumor involving two sites (both posterosuperior and lateral walls)
[ ] T3 Extension of tumor into nasal cavity or oropharynx
[ ] T4 Tumor invasion of skull, cranial nerve involvement, or both

Hypopharynx

[ ] Tis Carcinoma *in situ*
[ ] T1 Tumor confined to one site
[ ] T2 Extension of tumor to adjacent region or site without fixation of hemilarynx
[ ] T3 Extension of tumor to adjacent region or site with fixation of hemilarynx
[ ] T4 Massive tumor invading bone or soft tissues of neck

Nodal Involvement (N)

[ ] NX Minimum requirements to assess regional nodes cannot be met.
[ ] N0 No clinically positive node
[ ] N1 Single clinically positive homolateral node 3 cm or less in diameter
[ ] N2 Single clinically positive homolateral node more than 3 but not more than 6 cm in diameter or multiple clinically positive homolateral nodes, none more than 6 cm in diameter
  [ ] N2a Single clinically positive homolateral node more than 3 cm but not more than 6 cm in diameter
  [ ] N2b Multiple clinically positive homolateral nodes, none more than 6 cm in diameter
[ ] N3 Massive homolateral node(s), bilateral nodes, or contralateral node(s).
  [ ] N3a Clinically positive homolateral node(s), one more than 6 cm in diameter
  [ ] N3b Bilateral clinically positive nodes (in this situation, each side of the neck should be staged separately; *i.e.*, N3b: right, N2a; left, N1)
  [ ] N3c Contralateral clinically positive node(s) only

Distant Metastasis (M)

[ ] MX Minimum requirements to assess the presence of distant metastasis cannot be met.
[ ] M0 No (known) distant metastasis
[ ] M1 Distant metastasis present
Specify _____

Location of Tumor

Oropharynx

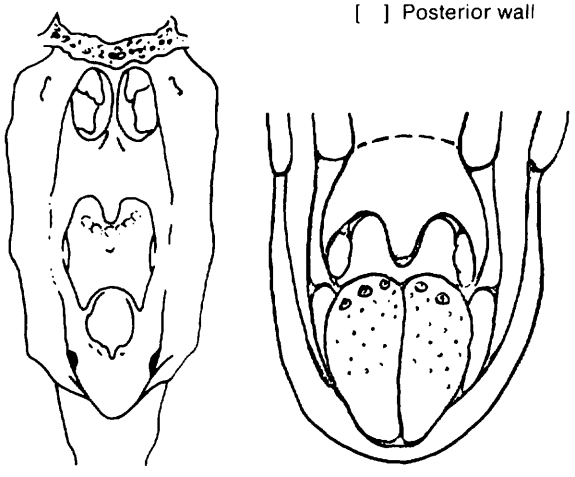
[ ] Faucial arch
[ ] Tonsillar fossa, tonsil
[ ] Base of tongue
[ ] Pharyngeal wall

Nasopharynx

[ ] Posterosuperior wall
[ ] Lateral wall

Hypopharynx

[ ] Piriform fossa
[ ] Postcricoid area
[ ] Posterior wall



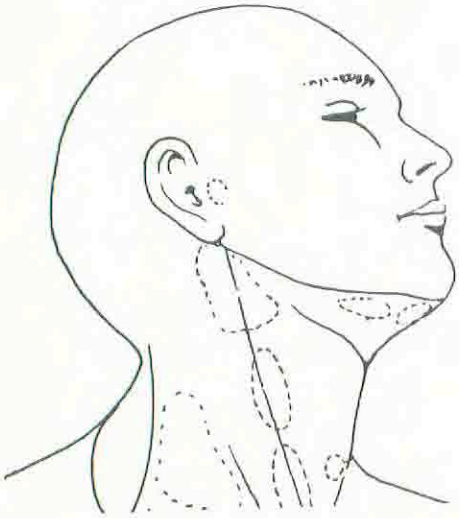
Size of primary tumor: _____ cm

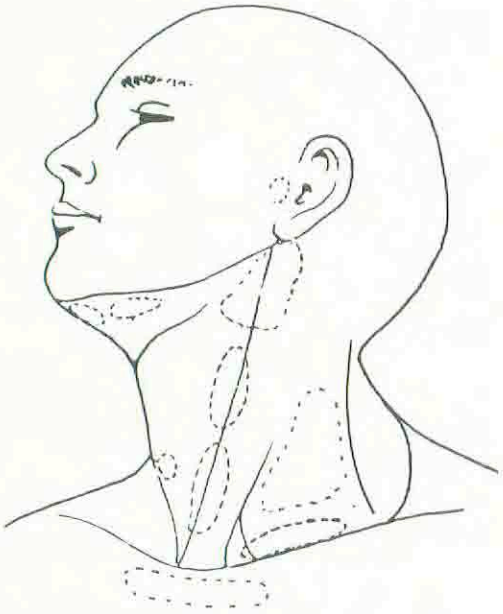
Examination by _____ M.D.
Date _____

*Use a separate form each time a case is staged.
†See reverse side for additional information.

Characteristics of Tumor (check one)

[ ] Superficial
[ ] Exophytic
[ ] Moderate infiltration
[ ] Deep infiltration





Regional lymph nodes; illustrate if metastatic.

Stage Grouping

[ ] Stage I	T1, N0, M0
[ ] Stage II	T2, N0, M0
[ ] Stage III	T3, N0, M0
	T1, T2, T3; N1, M0
[ ] Stage IV	T4, N0, N1; M0
	Any T, N2, N3; M0
	Any T, any N, M1

Staging Procedures

A variety of procedures and special studies may be employed in the process of staging a given tumor. Both the clinical usefulness and cost efficiency must be considered. The following suggestions are made for staging a cancer of the pharynx:

Essential for staging

1. Complete physical examination of the head and neck, including indirect laryngoscopy and nasopharyngoscopy
2. Biopsy of primary tumor
3. Chest roentgenogram
4. Roentgenograms of skull (nasopharynx)
5. Direct examination of oropharynx and hypopharynx

May be useful for staging or patient management

1. Multichemistry screen
2. Soft tissue roentgenograms of neck; CT scans
3. Barium swallow
4. Performance status (Karnofsky or ECOG scale)

May be useful for future staging systems or research studies

1. Panendoscopy (direct laryngoscopy, bronchoscopy, esophagoscopy)
2. Studies of immune competence
3. Assay of antibodies to Epstein–Barr viral capsid antigen (nasopharynx)

Histologic Type of Cancer

Predominant cancer is squamous cell carcinoma.

Histologic Grade

[ ] G1	Well differentiated
[ ] G2	Moderately well differentiated
[ ] G3–G4	Poorly to very poorly differentiated

Postsurgical Resection–Pathologic Residual Tumor (R)

Does not enter into staging but may be a factor in deciding further treatment

[ ] R0 No residual tumor
[ ] R1 Microscopic residual tumor
[ ] R2 Macroscopic residual tumor
Specify _____

Performance Status of Host (H)

Several systems for recording a patient's activity and symptoms are in use and are more or less equivalent as follows:

AJCC	*Performance*	*ECOG Scale*	*Karnofsky Scale (%)*
[ ] H0	Normal activity	0	90–100
[ ] H1	Symptomatic but ambulatory; cares for self	1	70–80
[ ] H2	Ambulatory more than 50% of time; occasionally needs assistance	2	50–60
[ ] H3	Ambulatory 50% or less of time; nursing care needed	3	30–40
[ ] H4	Bedridden; may need hospitalization	4	10–20

5

Larynx

ANATOMY (ICD-O 161)

Primary Site. The following anatomic definition of larynx allows classification of carcinomas arising in the encompassed mucous membranes but excludes cancers arising on the lateral or posterior pharyngeal wall, piriform fossa, postcricoid area, and the vallecula or base of tongue.

The anterior limit of the larynx is composed of the anterior or lingual surface of the suprahyoid epiglottis, the thyrohyoid membrane, the anterior commissure, and the anterior wall of the subglottic region, which is composed of the thyroid cartilage, the cricothyroid membrane, and the anterior arch of the cricoid cartilage.

The posterior and lateral limits include the arytenoepiglottic folds, the arytenoid region, the interarytenoid space, and the posterior surface of the subglottic space, represented by the mucous membrane covering the cricoid cartilage.

The superolateral limits are composed of the tip and the lateral borders of the epiglottis.

The inferior limits are made up of the plane passing through the inferior edge of the cricoid cartilage.

For purposes of this clinical-stage classification, the larynx is divided into three regions: supraglottis, glottis, and subglottis. The *supraglottis* is composed of the epiglottis (both its lingual and laryngeal aspects), arytenoepiglottic folds, arytenoids, and ventricular bands (false cords). The inferior boundary of the supraglottis is a horizontal plane passing through the apex of the ventricle. The *glottis* is composed of the true vocal cords, including the anterior and posterior commissures. The lower boundary is the horizontal plane 1 cm below the apex of the ventricle. The *subglottis* is the region extending from the lower boundary of the glottis to the lower margin of the cricoid cartilage.

The division of the larynx is summarized in the following table:

REGION	SITE
Supraglottis	Ventricular bands (false cords) Arytenoids Epiglottis (both lingual and laryngeal aspects) Suprahyoid epiglottis Infrahyoid epiglottis Arytenoepiglottic folds
Glottis	True vocal cords including anterior and posterior commissures
Subglottis	Subglottis

Nodal Stations. The first station nodes include jugulodigastric, jugulo-omohyoid, paratracheal, and deep cervical nodes.

Metastatic Sites. Distant spread to lungs is common. Skeletal and other distant metastases occur less often. Mediastinal lymph node metastases are considered distant metastases.

STAGING PROCEDURES

A variety of procedures and special studies may be employed in the process of staging a given tumor. Both clinical usefulness and cost efficiency must be considered. The following suggestions are made for staging a cancer of the larynx:

Essential for staging

1. Complete physical examination of the head and neck, including indirect laryngoscopy and nasopharyngoscopy
2. Direct laryngoscopy and biopsy of primary tumor
3. Chest x-ray film

Possibly useful for staging or patient management

1. Multichemistry screen
2. Laryngeal tomograms
3. Soft-tissue films of the neck, CT scans
4. Performance status (Karnofsky or ECOG scale)

Possibly useful for future staging systems or research studies

1. Bronchoscopy, esophagoscopy
2. Studies of immune competence

RULES FOR CLASSIFICATION

Clinical-Diagnostic Staging. The assessment of the larynx is accomplished primarily by inspection using indirect mirror examination and direct laryngoscopy. Additional studies include plain films of soft tissue, tomograms, contrast roentgenograms (*e.g.*, laryngograms), and barium studies of the pharynx according to suspected extension and spread. Nodal stations are examined by careful palpation. Examinations for distant metastases include chest film, blood chemistries, blood count, and other routine studies as indicated.

Surgical-Evaluative Staging. Confirmation of the extent of disease by biopsy of suspected mucosal or submucosal spread, aspirations or open biopsy of suspicious nodes, and biopsy of suspected distant metastases is desirable but not required.

Postsurgical Resection-Pathologic Staging. Complete resection of primary sites and radical nodal dissections allow the use of this designation. Specimens that are resected after radiation or chemotherapy need to be noted especially.

Retreatment Staging. Utilization of available procedures noted above is required, particularly confirmation by biopsy, because previous treatment by surgery or irradiation leads to scarring and induration. A reevaluation for distant metastases is important, as well as T and N classifications.

TNM CLASSIFICATION

Primary Tumor (T)

TX Minimum requirements to assess the primary tumor cannot be met.
T0 No evidence of primary tumor

Supraglottis

Tis Carcinoma *in situ*
T1 Tumor confined to region of origin with normal mobility
T2 Tumor involving adjacent supraglottic site(s) or glottis without fixation
T3 Tumor limited to larynx with fixation or extension to involve postcricoid area, medial wall of piriform sinus, or preepiglottic space
T4 Massive tumor extending beyond the larynx to involve oropharynx, soft tissues of neck, or destruction of thyroid cartilage

Glottis

Tis Carcinoma *in situ*
T1 Tumor confined to vocal cord(s) with normal mobility (includes involvement of anterior or posterior commissures)
T2 Supraglottic or subglottic extension of tumor with normal or impaired cord mobility, or both
T3 Tumor confined to the larynx with cord fixation
T4 Massive tumor with thyroid cartilage destruction or extension beyond the confines of the larynx, or both

Subglottis

Tis Carcinoma *in situ*
T1 Tumor confined to the subglottic region
T2 Tumor extension to vocal cords with normal or impaired cord mobility
T3 Tumor confined to larynx with cord fixation
T4 Massive tumor with cartilage destruction or extension beyond the confines of the larynx, or both

Nodal Involvement (N)

Cervical Node Classification. The following regional node classification is applicable to all squamous cell carcinoma of the upper aerodigestive tract. In clinical evaluation, the actual size of the nodal mass should be measured and allowance should be made for intervening soft tissues. It is recognized that most masses over 3 cm in diameter are not single nodes but are confluent nodes or tumor in soft tissues of the neck. There are three stages of clinically positive nodes: N1, N2, and N3. The use of subgroups a, b, and c is not required, but is recommended. Midline nodes are considered homolateral nodes.

NX Minimum requirements to assess the regional node cannot be met.
N0 No clinically positive node
N1 Single clinically positive homolateral node 3 cm or less in diameter
N2 Single clinically positive homolateral node more than 3 cm but not more than 6 cm in diameter or multiple clinically positive homolateral nodes, none more than 6 cm in diameter
N2a Single clinically positive homolateral node more than 3 cm but not more than 6 cm in diameter
N2b Multiple clinically positive homolateral nodes, none more than 6 cm in diameter
N3 Massive homolateral node(s), bilateral nodes, or contralateral node(s)
N3a Clinically positive homolateral node(s), one more than 6 cm in diameter
N3b Bilateral clinically positive nodes (in this situation, each side of the neck should be staged separately; *i.e.*, N3b: right, N2a; left, N1)
N3c Contralateral clinically positive node(s) only

Distant Metastasis (M)

MX Minimum requirements to assess the presence of distant metastasis cannot be met.
M0 No (known) distant metastasis
M1 Distant metastasis present
Specify _____

Specify sites according to the following notations:

Pulmonary	PUL
Osseous	OSS
Hepatic	HEP
Brain	BRA
Lymph nodes	LYM
Bone marrow	MAR
Pleura	PLE
Skin	SKI
Eye	EYE
Other	OTH

STAGE GROUPING

Stage I	T1, N0, M0
Stage II	T2, N0, M0
Stage III	T3, N0, M0
	T1 or T2 or T3, N1, M0
Stage IV	T4, N0 or N1, M0
	Any T, N2 or N3, M0
	Any T, any N, M1

HISTOPATHOLOGY

The predominant cancer is squamous cell carcinoma; pathologic diagnosis is required to utilize this classification. Tumor grading is recommended using Broders' classification. Other tumors of glandular epithelium, odontogenic apparatus origin, lymphoid tissue, soft tissue, and bone and cartilage origin require special consideration and are not to be included. Reference to the WHO nomenclature is recommended.

Tumor Grade (G)

G1 Well differentiated
G2 Moderately well differentiated
G3-G4 Poorly to very poorly differentiated

Use whichever indicator is most appropriate (term or G + number)

POSTSURGICAL TREATMENT RESIDUAL TUMOR (R)

This does not enter into staging of the tumor but may be a factor in deciding management.

R0 No residual tumor
R1 Microscopic residual tumor
R2 Macroscopic residual tumor
Specify _____

PERFORMANCE STATUS OF HOST (H)

Performance status of the host should be recorded because this information at times is pertinent to the treatment of the patient.

AJCC	PERFORMANCE	ECOG SCALE	KARNOFSKY SCALE (%)
H0	Normal activity	0	90-100
H1	Symptomatic but ambulatory; cares for self	1	70-80
H2	Ambulatory more than 50% of time; occasionally needs assistance	2	50-60
H3	Ambulatory 50% or less of time; nursing care needed	3	30-40
H4	Bedridden; may need hospitalization	4	10-20

DATA FORM

The data form for staging of cancer of the larynx, in addition to permitting recording of the extent of the cancer, also indicates the examinations necessary for staging and what examinations and data are necessary for each time period of staging.

BIBLIOGRAPHY

1. Flynn MB, Jesse RH, Lindberg RT: Surgery and irradiation in the treatment of squamous cell cancer of the supraglottic larynx. Am J Surg 124:477-481, 1972
2. Futrell JW, Bennett SH, Hoye RC et al: Predicting survival in cancer of the larynx or hypopharynx. Am J Surg 122:451-457, 1971
3. Harris HS, Watson FR, Spratt JS Jr: Carcinoma of the larynx. Am J Surg 118:676-684, 1969
4. Powell RW, Redd BL, Wilkins SA: An evaluation of treatment of cancer of the larynx. Am J Surg 110:635-643, 1965
5. Shah JP, Tollefsen HR: Epidermoid carcinoma of the supraglottic larynx: Role of neck dissection in initial surgical treatment. Am J Surg 128:494-499, 1974
6. Wang CC, Schultz MD, Miller D: Combined radiation therapy and surgery for carcinoma of the supraglottis and pyriform sinus. Am J Surg 124:551-544, 1972

Data Form for Cancer Staging

Patient identification
Name _____
Address _____
Hospital or clinic number _____
Age _____ Sex _____ Race _____

Institutional identification
Hospital or clinic _____
Address _____

Oncology Record

Anatomic site of cancer _____
Chronology of classification* [ ] Clinical-diagnostic (cTNM) [ ] Surgical-evaluative (sTNM)
Date of classification _____

Histologic type† _____ Grade (G) _____
[ ] Postsurgical resection–pathologic (pTNM)
[ ] Retreatment (rTNM) [ ] Autopsy (aTNM)

Definitions: TNM Classification

Primary Tumor (T)

[ ] TX Minimum requirements to assess the primary tumor cannot be met.
[ ] T0 No evidence of primary tumor

Supraglottis

[ ] Tis Carcinoma *in situ*
[ ] T1 Tumor confined to site of origin with normal mobility
[ ] T2 Tumor involves adjacent supraglottic site(s) or glottis without fixation
[ ] T3 Tumor limited to larynx with fixation or extension to involve postcricoid area, medial wall of piriform sinus, or preepiglottic space
[ ] T4 Massive tumor extending beyond the larynx to involve oropharynx, soft tissues of neck, or destruction of thyroid cartilage

Glottis

[ ] Tis Carcinoma *in situ*
[ ] T1 Tumor confined to vocal cord(s) with normal mobility (including involvement of anterior or posterior commissures)
[ ] T2 Supraglottic or subglottic extension of tumor with normal or impaired cord mobility
[ ] T3 Tumor confined to the larynx with cord fixation
[ ] T4 Massive tumor with thyroid cartilage destruction or extension beyond the confines of the larynx, or both

Subglottis

[ ] Tis Carcinoma *in situ*
[ ] T1 Tumor confined to the subglottic region
[ ] T2 Tumor extension to vocal cords with normal or impaired cord mobility
[ ] T3 Tumor confined to larynx with cord fixation
[ ] T4 Massive tumor with cartilage destruction or extension beyond the confines of the larynx, or both

Nodal Involvement (N)

[ ] NX Minimum requirements to assess the regional nodes cannot be met.
[ ] N0 No clinically positive nodes
[ ] N1 Single clinically positive homolateral node 3 cm or less in diameter
[ ] N2 Single clinically positive homolateral node more than 3 but not more than 6 cm in diameter or multiple clinically positive homolateral nodes, none more than 6 cm in diameter
[ ] N2a Single clinically positive homolateral node more than 3 cm but not more than 6 cm in diameter
[ ] N2b Multiple clinically positive homolateral nodes, none more than 6 cm in diameter
[ ] N3 Massive homolateral node(s), bilateral nodes, or contralateral node(s)
[ ] N3a Clinically positive homolateral node(s), one more than 6 cm in diameter
[ ] N3b Bilateral clinically positive nodes (in this situation, each side of the neck should be staged separately; *i.e.*, N3b: right, N2a; left, N1)
[ ] N3c Contralateral clinically positive node(s) only

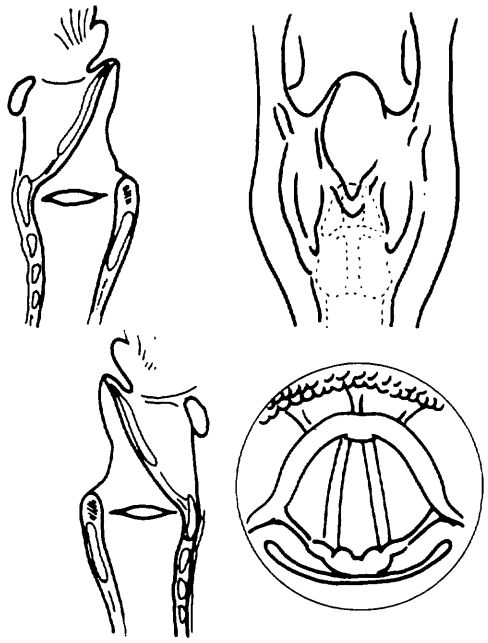
Distant Metastasis (M)

[ ] MX Minimum requirements to assess the presence of distant metastasis cannot be met.
[ ] M0 No (known) distant metastasis
[ ] M1 Distant metastasis present
Specify _____

Location of Tumor

Supraglottis

[ ] Ventricular band
[ ] Arytenoid
[ ] Suprahyoid epiglottis
[ ] Infrahyoid epiglottis
[ ] Arytenoepiglottic fold



Examination by _____ M.D.
Date _____

*Use a separate form each time a case is staged.
†See reverse side for additional information.

Glottis

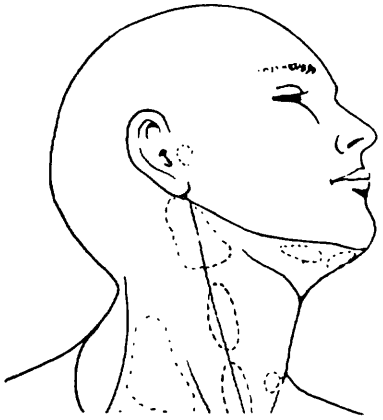
[ ] Vocal cords (including commissures)

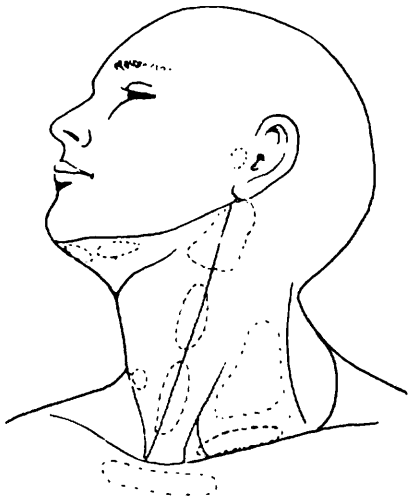
Subglottis

Characteristics of Tumor

[ ] Superficial
[ ] Exophytic
[ ] Moderate infiltration
[ ] Deep infiltration
[ ] Impaired cord mobility
[ ] Cord fixation
[ ] Cartilage destruction
[ ] Tumor confined to larynx

[ ] Tumor extension to the following:
- [ ] Base of tongue
- [ ] Piriform sinus
- [ ] Postcricoid region
- [ ] Preepiglottic space
- [ ] Trachea
- [ ] Soft tissue or skin of neck





Indicate on diagram primary tumor and regional nodes involved.

Stage Grouping

[ ]	Stage I	T1, N0, M0
[ ]	Stage II	T2, N0, M0
[ ]	Stage III	T3, N0, M0
		T1, T2, T3; N1, M0
[ ]	Stage IV	T4, N0, N1; M0
		Any T, N2, N3; M0
		Any T, any N, M1

Staging Procedures

A variety of procedures and special studies may be employed in the process of staging a given tumor. Both the clinical usefulness and cost efficiency must be considered. The following suggestions are made for staging a cancer of the larynx:

Essential for staging

1. Complete physical examination of the head and neck including indirect laryngoscopy and nasopharyngoscopy
2. Biopsy of primary tumor
3. Chest roentgenogram
4. Roentgenograms of skull (nasopharynx)
5. Direct examination of hypopharynx

May be useful for staging or patient management

1. Multichemistry screen
2. Soft-tissue roentgenograms of neck, CT scans
3. Barium swallow
4. Performance status (Karnofsky or ECOG scale)

May be useful for future staging systems or research studies

1. Panendoscopy (direct laryngoscopy, bronchoscopy, esophagoscopy)
2. Studies of immune competence
3. Assay of antibodies to Epstein-Barr viral capsid antigen (nasopharynx)

Histologic Type of Cancer

The predominant cancer is squamous cell carcinoma.

Histologic Grade

[ ]	G1	Well differentiated
[ ]	G2	Moderately well differentiated
[ ]	G3–G4	Poorly to very poorly differentiated

Postsurgical Resection–Pathologic Residual Tumor (R)

Does not enter into the staging but may be a factor in deciding further treatment

[ ]	R0	No residual tumor
[ ]	R1	Microscopic residual tumor
[ ]	R2	Macroscopic residual tumor
		Specify _____

Performance Status of Host (H)

Several systems for recording a patient's activity and symptoms are in use and are more or less equivalent as follows:

	AJCC	*Performance*	*ECOG Scale*	*Karnofsky Scale (%)*
[ ]	H0	Normal activity	0	90–100
[ ]	H1	Symptomatic but ambulatory; cares for self	1	70–80
[ ]	H2	Ambulatory more than 50% of time; occasionally needs assistance	2	50–60
[ ]	H3	Ambulatory 50% or less of time; nursing care needed	3	30–40
[ ]	H4	Bedridden; may need hospitalization	4	10–20

6

Paranasal Sinuses

ANATOMY (ICD-O 160.9)

Primary Site. Cancer of the maxillary sinus is the most common of the paranasal sinus cancers; it is the only site to which the following classification applies. The ethmoid sinuses and nasal cavity may ultimately be defined similarly with further study. Tumors of the sphenoid and frontal sinuses are so rare as not to warrant staging.

Ohngren's line, a theoretic plane joining the medial canthus of the eye with the angle of the mandible, may be used to divide the maxillary antrum into the anteroinferior portion (the infrastructure) and the superoposterior portion (the suprastructure).

Nodal Stations. The major lymphatic drainage of the maxillary antrum is through the lateral and inferior collecting trunks to first station submaxillary, parotid, and jugulodigastric nodes and through the superoposterior trunk to retropharyngeal and deep cervical nodes.

Metastatic Sites. Distant spread to lungs is most common; occasionally there is spread to bone and remote lymph nodes.

STAGING PROCEDURES

A variety of procedures and special studies may be employed in the process of staging a given tumor. Both the clinical usefulness and cost efficiency must be considered. The following suggestions are made for staging a cancer of the paranasal sinuses:

Essential for staging

1. Complete physical examination of the head and neck including indirect laryngoscopy and nasopharyngoscopy
2. Biopsy of the primary tumor (antrotomy if necessary)
3. Chest roentgenogram
4. Roentgenograms of paranasal sinuses

Possibly useful for staging or patient management

1. Multichemistry screen
2. Roentgenograms of base of skull, CT scans
3. Performance status (Karnofsky or ECOG scale)

Possibly useful for future staging systems or research studies

1. Panendoscopy (direct laryngoscopy, bronchoscopy, esophagoscopy)
2. Studies of immune competence

RULES FOR CLASSIFICATION

Clinical-Diagnostic Staging. The assessment of primary maxillary antrum tumors is based upon inspection, palpation, including examination of the orbit, nasal and oral cavities, and nasopharynx, and neurologic evaluation of the cranial nerves. Radiographic studies include plain films and tomograms for evaluation of bone destruction. Neck nodes are assessed by palpation. Examinations for distant metastases include chest film, blood chemistries, blood count, and other routine studies as indicated.

Surgical-Evaluative Staging. Confirmation of the extent of disease by biopsy of suspected mucosal or submucosal spread, aspirations or open biopsy of suspicious nodes, and biopsy of suspected distant metastases is desirable but not required.

Postsurgical Resection-Pathologic Staging. Complete resection of primary sites and radical nodal dissections allow the use of this designation. Specimens that are resected after radiation or chemotherapy need to be noted especially.

Retreatment Staging. Utilization of available procedures noted above is required, particularly confirmation by biopsy, because previous treatment by surgery or irradiation leads to scarring and induration. A reevaluation for distant metastases is important, as well as T and N classifications.

TNM CLASSIFICATION

Primary Tumor (T)

- TX Minimum requirements to assess the primary tumor cannot be met.
- T0 No evidence of primary tumor
- T1 Tumor confined to the antral mucosa of the infrastructure with no bone erosion or destruction
- T2 Tumor confined to the suprastructure mucosa without bone destruction or to the infrastructure, with destruction of medial or inferior bony walls only
- T3 More extensive tumor invading skin of cheek, orbit, anterior ethmoid sinuses, or pterygoid muscle
- T4 Massive tumor with invasion of cribriform plate, posterior ethmoids, sphenoid, nasopharynx, pterygoid plates, or base of skull

Nodal Involvement (N)

Cervical Node Classification. The following regional node classification is applicable to all squamous cell carcinoma of the upper aerodigestive tract. In clinical evaluation, the actual size of the nodal mass should be measured and allowance should be made for intervening soft tissues. It is recognized that most masses over 3 cm in diameter are not single nodes but are confluent nodes or tumor in soft tissues of the neck. There are three stages of clinically positive nodes: N1, N2, and N3. The use of subgroups a, b, and c is not required but is recommended. Midline nodes are considered homolateral nodes.

- NX Minimum requirements to assess the regional nodes cannot be met.
- N0 No clinically positive node
- N1 Single clinically positive homolateral node 3 cm or less in diameter
- N2 Single clinically positive homolateral node more than 3 cm but not more than 6 cm in diameter or multiple clinically positive homolateral nodes, none more than 6 cm in diameter
  - N2a Single clinically positive homolateral node, more than 3 cm but not more than 6 cm in diameter
  - N2b Multiple clinically positive homolateral nodes, none more than 6 cm in diameter
- N3 Massive homolateral node(s), bilateral nodes, or contralateral node(s)
  - N3a Clinically positive homolateral node(s), one more than 6 cm in diameter
  - N3b Bilateral clinically positive nodes (in this situation, each side of the neck should be staged separately; *i.e.*, N3b: right, N2a; left, N1)
  - N3c Contralateral clinically positive node(s) only

Distant Metastasis (M)

- MX Minimum requirements to assess the presence of distant metastasis cannot be met.
- M0 No evidence of distant metastasis
- M1 Distant metastasis present
  Specify _____

Specify sites according to the following notations:

Pulmonary	PUL
Osseous	OSS
Hepatic	HEP
Brain	BRA
Lymph nodes	LYM
Bone marrow	MAR
Pleura	PLE
Skin	SKI
Eye	EYE
Other	OTH

POSTSURGICAL TREATMENT RESIDUAL TUMOR (R)

R0 No residual tumor
R1 Microscopic residual tumor
R2 Macroscopic residual tumor
Specify _____

STAGE GROUPING

Stage I	T1, N0, M0
Stage II	T2, N0, M0
Stage III	T3, N0, M0
	T1, T2, T3; N1, M0
Stage IV	T4, N0 or N1, M0
	Any T, N2 or N3, M0
	Any T, any N, M1

HISTOPATHOLOGY

The predominant cancer is squamous cell carcinoma; pathologic diagnosis is required to utilize this classification. Tumor grading is recommended using Broders' classification. Other tumors of glandular epithelium, odontogenic apparatus, lymphoid tissue, soft tissue, and bone and cartilage origin require special consideration and are not to be included. Reference to the WHO nomenclature is recommended.

Tumor Grade (G)

G1 Well differentiated
G2 Moderately well differentiated
G3-G4 Poorly to very poorly differentiated

Use whichever indicator is most appropriate (term or G + number)

Performance Status of Host (H)

Performance status of the host should be recorded because this information at times is pertinent to the treatment of the patient.

AJCC	PERFORMANCE	ECOG SCALE	KARNOFSKY SCALE (%)
H0	Normal activity	0	90-100
H1	Symptomatic but ambulatory; cares for self	1	70-80
H2	Ambulatory more than 50% of time; occasionally needs assistance	2	50-60
H3	Ambulatory 50% or less of time; nursing care needed	3	30-40
H4	Bedridden; may need hospitalization	4	10-20

DATA FORM

The data form for staging of cancer of the paranasal sinuses, in addition to permitting recording of the extent of the cancer, also indicates the examinations necessary for staging and what examinations and data are necessary for each time period of staging.

BIBLIOGRAPHY

1. Goepfert H, Jesse RH, Lindberg RD: Arterial infusion and radiation therapy in the treatment of advanced cancer of the nasal cavity and perinasal sinuses. Am J Surg 126:464-468, 1973
2. Jesse RH: Preoperative versus postoperative radiation in the treatment of squamous carcinoma of the perinasal sinuses. Am J Surg 110:552-556, 1965
3. Sisson GA, Johnson NE, Ammiri CS: Cancer of the maxillary sinus: Clinical classification and management. Ann Otol Rhinol Laryngol 72:1050-1059, 1963

Data Form for Cancer Staging

Patient identification
Name _____
Address _____
Hospital or clinic number _____
Age _____ Sex _____ Race _____

Institutional identification
Hospital or clinic _____
Address _____

Oncology Record

Anatomic site of cancer _____
Chronology of classification* [ ] Clinical-diagnostic (cTNM)
[ ] Surgical-evaluative (sTNM)
Date of classification _____

Histologic type† _____ Grade (G) _____
[ ] Postsurgical resection–pathologic (pTNM)
[ ] Retreatment (rTNM) [ ] Autopsy (aTNM)

Definitions: TNM Classification

Primary Tumor (T)

[ ] TX Minimum requirements to assess the primary tumor cannot be met.
[ ] T0 No evidence of primary tumor
[ ] Tis Carcinoma *in situ*
[ ] T1 Tumor confined to the antral mucosa of the infrastructure with no bone erosion or destruction
[ ] T2 Tumor confined to the suprastructure mucosa without bone destruction, or to the infrastructure with destruction of medial or inferior bony walls only
[ ] T3 More extensive tumor invading skin of cheek, orbit, anterior ethmoid sinuses, or pterygoid muscle
[ ] T4 Massive tumor with invasion of cribriform plate, posterior ethmoids, sphenoid, nasopharynx, pterygoid plates, or base of skull

Nodal Involvement (N)

[ ] NX Minimum requirements to assess the regional nodes cannot be met.
[ ] N0 No clinically positive nodes
[ ] N1 Single clinically positive homolateral node 3 cm or less in diameter
[ ] N2 Single clinically positive homolateral node more than 3 cm but not more than 6 cm in diameter or multiple clinically positive homolateral nodes, none more than 6 cm in diameter
  [ ] N2a Single clinically positive homolateral node more than 3 cm but not more than 6 cm in diameter
  [ ] N2b Multiple clinically positive homolateral nodes, none more than 6 cm in diameter
[ ] N3 Massive homolateral node(s), bilateral nodes, or contralateral node(s)
  [ ] N3a Clinically positive homolateral node(s), one more than 6 cm in diameter
  [ ] N3b Bilateral clinically positive nodes (in this situation, each side of the neck should be staged separately; *i.e.*, N3b: right, N2a; left, N1)
  [ ] N3c Contralateral clinically positive node(s) only

Distant Metastasis (M)

[ ] MX Minimum requirements to assess the presence of distant metastasis cannot be met.
[ ] M0 No (known) distant metastasis
[ ] M1 Distant metastasis present
Specify _____

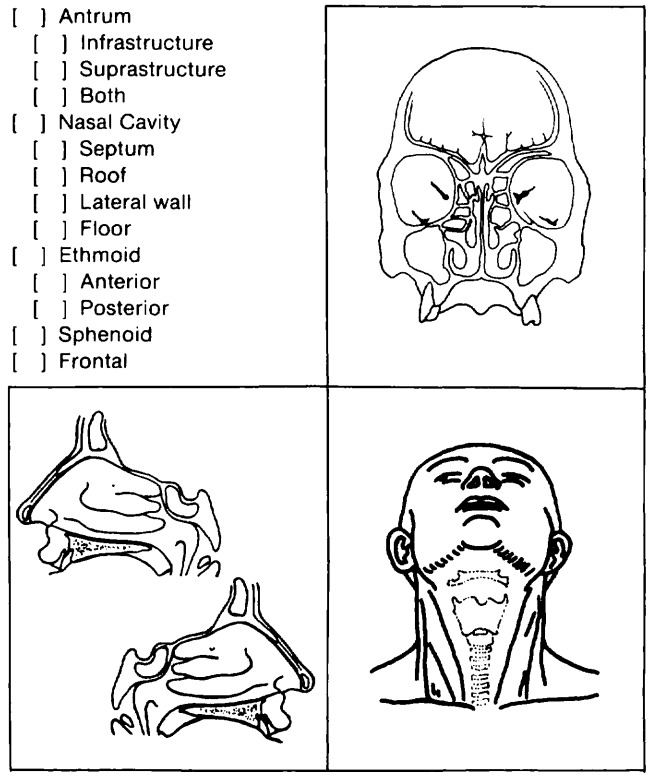
*Use a separate form each time a case is staged.
†See reverse side for additional information.

Site-Specific Information

Status before treatment anywhere is noted here.

Location of Tumor

[ ] Antrum
  [ ] Infrastructure
  [ ] Suprastructure
  [ ] Both
[ ] Nasal Cavity
  [ ] Septum
  [ ] Roof
  [ ] Lateral wall
  [ ] Floor
[ ] Ethmoid
  [ ] Anterior
  [ ] Posterior
[ ] Sphenoid
[ ] Frontal



Indicate on diagram primary tumor and regional nodes involved.

Characteristics of Tumor

[ ] Radiographic destruction of bone
[ ] Invasion of adjacent areas
  [ ] Skin [ ] Orbit
  [ ] Palate [ ] Base of skull
  [ ] Nasopharynx [ ] Pterygoid muscles
  [ ] Cribriform plate [ ] Pterygoid bone

Examination by _____ M.D.
Date _____

Stage Grouping

[ ]	Stage I	T1, N0, M0
[ ]	Stage II	T2, N0, M0
[ ]	Stage III	T3, N0, M0
		T1, T2, T3, N1, M0
[ ]	Stage IV	T4, N0, N1, M0
		Any T, N2, N3, M0
		Any T, any N, M1

Staging Procedures

A variety of procedures and special studies may be employed in the process of staging a given tumor. Both the clinical usefulness and cost efficiency must be considered. The following suggestions are made for staging a cancer of the pharynx.

Essential for staging

1. Complete physical examination of the head and neck including indirect laryngoscopy and nasopharyngoscopy
2. Biopsy of primary tumor
3. Chest roentgenogram
4. Roentgenograms of skull (nasopharynx)
5. Direct examination of hypopharynx

May be useful for staging or patient management

1. Multichemistry screen
2. Soft-tissue roentgenograms of neck; CT scans
3. Barium swallow
4. Performance status (Karnofsky or ECOG scale)

May be useful for future staging systems or research studies

1. Panendoscopy (direct laryngoscopy, bronchoscopy, esophagoscopy)
2. Studies of immune competence
3. Assay of antibodies to Epstein–Barr viral capsid antigen (nasopharynx)

Histologic Type of Cancer

Predominant cancer is squamous cell or undifferentiated carcinoma. Adenocarcinoma and other cellular types also occur.

Histologic Grade

[ ]	G1	Well differentiated
[ ]	G2	Moderately well differentiated
[ ]	G3–G4	Poorly to very poorly differentiated

Postsurgical Resection–Pathologic Residual Tumor (R)

Does not enter into the staging but may be a factor in deciding further treatment.

[ ]	R0	No residual tumor
[ ]	R1	Microscopic residual tumor
[ ]	R2	Macroscopic residual tumor
		Specify _____

Performance Status of Host (H)

Several systems for recording a patient's activity and symptoms are in use and are more or less equivalent as follows:

	AJCC	*Performance*	*ECOG Scale*	*Karnofsky Scale (%)*
[ ]	H0	Normal activity	0	90–100
[ ]	H1	Symptomatic but ambulatory; cares for self	1	70–80
[ ]	H2	Ambulatory more than 50% of time; occasionally needs assistance	2	50–60
[ ]	H3	Ambulatory 50% or less of time; nursing care needed	3	30–40
[ ]	H4	Bedridden; may need hospitalization	4	10–20

7

Salivary Glands

This staging system is based on an extensive retrospective study of malignant tumors of the major salivary glands collected from eleven participating U.S. and Canadian institutions. Computer analysis of the data revealed that numerous factors affected patient survival, including the histologic diagnosis, cellular differentiation of the tumor, its site, size, degree of fixation, or local extension and nerve involvement. The status of regional lymph nodes and of distant metastases were also of major significance. The classification here proposed involves only four clinical variables: tumor size, local extension of the tumor, the palpability and suspicion of nodes, and the presence or absence of distant metastasis. It offers a simple but effective and accurate method of evaluating the stage of salivary gland cancer.

ANATOMY (ICD-O 142)

Primary Site. The major salivary glands include the parotid, submaxillary, and sublingual glands. Tumors arising in minor salivary glands (mucus-secreting glands in the lining membrane of the upper aerodigestive tract) are not included in this staging system.

Nodal Stations. The first station nodes are immediately adjacent to the salivary glands and include parotid, submaxillary, and submental lymph nodes. The first station also includes the deep cervical lymph nodes.

STAGING PROCEDURES

A variety of procedures and special studies may be employed in the process of staging a given tumor. Both the clinical usefulness and cost efficiency must be considered. The following suggestions are made for staging a cancer of the salivary glands:

Essential for staging

1. Complete physical examination of the head and neck
2. Pathologic study of surgically removed specimen
3. Known residual tumor if present after resection of tumor
4. Chest roentgenogram

Possibly useful for staging or patient management

1. Multichemistry screen
2. Parotid or submaxillary sialogram
3. Roentgenograms of mandible and CT scans
4. Radioactive technetium scan
5. Performance status (Karnofsky or ECOG scale)

Possibly useful for future staging systems or research studies

Studies of immune competence

RULES FOR CLASSIFICATION

Clinical-Diagnostic Staging. The assessment of primary tumor includes inspection and palpation and neurologic evaluation of the seventh cranial or other nerves. Radiologic studies may include films of the mandible and possibly sialograms.

Surgical-Evaluative Staging. This should be based on all clinical data including that obtained on surgical exploration of the salivary gland and the nodal areas but not the pathologic data obtained on the resected specimen if a definitive resection of the cancer is carried out.

Postsurgical Resection-Pathologic Staging. The surgical pathology report and all other available data should be used to assign a pathologic classification to those patients who have a resection of the cancer.

Retreatment Staging. After a cancer has once been treated definitively with a disease-free interval and recurs, the recurrence can be reclassified using all available information; the patient should again be staged using procedures noted for clinical-diagnostic and surgical-evaluative classifications.

TNM CLASSIFICATION

Primary Tumor (T)

TX Minimum requirements to assess the primary tumor cannot be met.
T0 No evidence of primary tumor
T1 Tumor 2.0 cm or less in greatest diameter without significant local extension*
T2 Tumor more than 2.0 cm but not more than 4.0 cm in greatest diameter without significant local extension
T3 Tumor more than 4.0 cm but not more than 6.0 cm in greatest diameter without significant local extension
T4a Tumor over 6.0 cm in greatest diameter without significant local extension
T4b Tumor of any size with significant local extension*

*Significant local extension is defined as evidence of tumor involvement of skin, soft tissues, bone, or the lingual or facial nerves.

Nodal Involvement (N)

NX Minimum requirements to assess the regional nodes cannot be met.
N0 No evidence of regional lymph node involvement
N1 Evidence of regional lymph node involvement

Distant Metastasis (M)

MX Minimum requirements to assess the presence of distant metastasis cannot be met.
M0 No (known) distant metastasis
M1 Distant metastasis present
Specify _____

Specify sites according to the following notations:

Pulmonary	PUL
Osseous	OSS
Hepatic	HEP
Brain	BRA
Lymph nodes	LYM
Bone marrow	MAR
Pleura	PLE
Skin	SKI
Eye	EYE
Other	OTH

POSTSURGICAL TREATMENT RESIDUAL TUMOR (R)

R0 No residual tumor
R1 Microscopic residual tumor
R2 Macroscopic residual tumor
Specify _____

STAGE GROUPING

Stage I	T1, N0, M0
	T2, N0, M0
Stage II	T3, N0, M0
Stage III	T1, T2; N1, M0
	T4a, T4b; N0, M0
Stage IV	T3, N1, M0
	T4a, T4b; N1, M0
	Any T, any N, M1

HISTOPATHOLOGY

The histologic classification recommended is a modification of the WHO classification of salivary gland tumors. The major malignant varieties include the following:

Acinic cell carcinoma
Adenoid cystic carcinoma (cylindroma)
Adenocarcinoma
Squamous cell carcinoma
Carcinoma in pleomorphic adenoma (malignant mixed tumor)

Mucoepidermoid carcinoma
  Well differentiated (low grade)
  Poorly differentiated (high grade)
Other

PERFORMANCE STATUS OF HOST (H)

Performance status of the host should be recorded because this information at times is pertinent to the treatment of the patient.

AJCC	PERFORMANCE	ECOG SCALE	KARNOFSKY SCALE (%)
H0	Normal activity	0	90-100
H1	Symptomatic but ambulatory; cares for self	1	70-80
H2	Ambulatory more than 50% of time; occasionally needs assistance	2	50-60
H3	Ambulatory 50% or less of time; nursing care needed	3	30-40
H4	Bedridden; may need hospitalization	4	10-20

Tumor Grade (G)

G1 Well differentiated
G2 Moderately well differentiated
G3-G4 Poorly to very poorly differentiated

Use whichever indicator is most appropriate (term or G + number)

DATA FORM

The data form for staging of cancer of the salivary glands, in addition to permitting recording of the extent of the cancer, also indicates the examinations necessary for staging and what examinations and data are necessary for each time period of staging.

Data Form for Cancer Staging

Patient identification
Name _____
Address _____
Hospital or clinic number _____
Age _____ Sex _____ Race _____

Institutional identification
Hospital or clinic _____
Address _____

Oncology Record

Anatomic site of cancer _____
Chronology of classification* [ ] Clinical-diagnostic (cTNM)
[ ] Surgical-evaluative (sTNM)
Date of classification _____

Histologic type† _____ Grade (G) _____
[ ] Postsurgical resection–pathologic (pTNM)
[ ] Retreatment (rTNM) [ ] Autopsy (aTNM)

Definitions: TNM Classification

Primary Tumor (T)

[ ] TX Minimum requirements to assess the primary tumor cannot be met.
[ ] T0 No evidence of primary tumor
[ ] Tis Carcinoma *in situ*
[ ] T1 Tumor 2 cm or less in greatest diameter without significant local extension
[ ] T2 Tumor more than 2 cm but not more than 4 cm in greatest diameter without significant local extension
[ ] T3 Tumor more than 4 cm but not more than 6 cm in greatest diameter without significant local extension
[ ] T4a Tumor more than 6 cm in greatest diameter without significant local extension
[ ] T4b Any size tumor with significant local extension

Note: Significant local extension is defined as evidence of tumor involvement of skin, soft tissues, bone, or the lingual or facial nerves.

Nodal Involvement (N)

[ ] NX Minimum requirements to assess the regional nodes cannot be met.
[ ] N0 No evidence of regional lymph node involvement
[ ] N1 Evidence of regional lymph node involvement

Distant Metastasis (M)

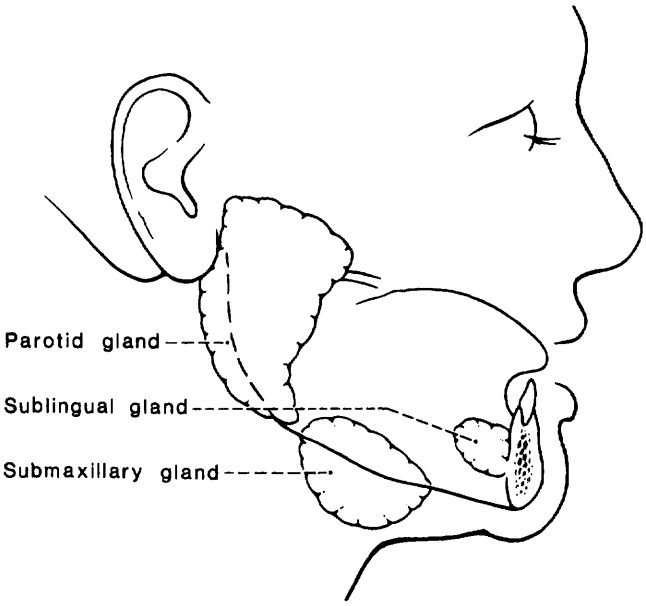
[ ] MX Minimum requirements to assess the presence of distant metastasis cannot be met.
[ ] M0 No (known) metastasis
[ ] M1 Distant metastasis present
Specify _____

Site-Specific Information—Salivary Glands; Location of Tumor

[ ] Parotid
[ ] Submaxillary
[ ] Sublingual
[ ] Side
[ ] Right
[ ] Left
[ ] Bilateral

Size of Tumor

Largest diameter _____ cm



Indicate on diagram primary tumor and regional nodes involved.

Characteristics of Tumor

[ ] Mobile
[ ] Limited mobility
[ ] Fixed
[ ] Hard
[ ] Soft
[ ] Cystic
[ ] Adjacent tissues involved. No. _____
Specify _____

Nerve involvement
[ ] None
[ ] Facial
[ ] Hypoglossal
[ ] Lingual
[ ] Vagus
[ ] Other _____
[ ] Partial paralysis
[ ] Complete paralysis

Examination by _____ M.D.
Date _____

*Use a separate form each time a case is staged.
†See reverse side for additional information.

Stage Grouping

[ ]	Stage I	T1, N0, M0
[ ]	Stage II	T2, N0, M0
[ ]	Stage III	T3, N0, M0
		T1, T2, T3, N1, M0
[ ]	Stage IV	T4, N0, N1, M0
		Any T, N2, N3, M0
		Any T, any N, M1

Staging Procedures

A variety of procedures and special studies may be employed in the process of staging a given tumor. Both the clinical usefulness and cost efficiency must be considered. The following suggestions are made for staging a cancer of the salivary glands:

Essential for staging

1. Complete physical examination of the head and neck including indirect laryngoscopy and nasopharyngoscopy
2. Biopsy of primary tumor
3. Chest roentgenogram
4. Roentgenograms of skull (nasopharynx)
5. Direct examination of hypopharynx

May be useful for staging or patient management

1. Multichemistry screen
2. Soft-tissue roentgenograms of neck; CT scans
3. Barium swallow
4. Performance status (Karnofsky or ECOG scale)

May be useful for future staging systems or research studies

1. Panendoscopy (direct laryngoscopy, bronchoscopy, esophagoscopy)
2. Studies of immune competence
3. Assay of antibodies to Epstein–Barr viral capsid antigen (nasopharynx)

Histologic Type of Cancer

[ ] Mucoepidermoid carcinoma
[ ] Adenoid cystic carcinoma
[ ] Squamous cell carcinoma
[ ] Acinic cell carcinoma
[ ] Malignant mixed tumor

Histologic Grade

[ ]	G1	Well differentiated
[ ]	G2	Moderately well differentiated
[ ]	G3–G4	Poorly to very poorly differentiated

Postsurgical Resection–Pathologic Residual Tumor (R)

Does not enter into staging but may be a factor in deciding further treatment

[ ]	R0	No residual tumor
[ ]	R1	Microscopic residual tumor
[ ]	R2	Macroscopic residual tumor
		Specify _____

Performance Status of Host (H)

Several systems for recording a patient's activity and symptoms are in use and are more or less equivalent as follows:

AJCC	*Performance*	*ECOG Scale*	*Karnofsky Scale (%)*
[ ] H0	Normal activity	0	90–100
[ ] H1	Symptomatic but ambulatory; cares for self	1	70–80
[ ] H2	Ambulatory more than 50% of time; occasionally needs assistance	2	50–60
[ ] H3	Ambulatory 50% or less of time; nursing care needed	3	30–40
[ ] H4	Bedridden; may need hospitalization	4	10–20

8

Thyroid Gland

The following staging system for cancer of the thyroid gland was developed after an analysis of more than 1000 case protocols. Although staging for cancers in other head and neck sites is based entirely on the anatomic extent of disease, it is not possible to follow this pattern for the unique group of malignant tumors that arise in the thyroid. Both the histologic diagnosis and the age of the patient are of such importance in the behavior and prognosis of thyroid cancer that these factors have to be accounted for in any staging system.

ANATOMY (ICD-O 193)

Primary site. The thyroid gland ordinarily is composed of a right and a left lobe lying adjacent and lateral to the upper trachea and esophagus. An isthmus connects the two lobes and in some cases a pyramidal lobe is present extending upward anterior to the thyroid cartilage.

Nodal Stations. Lymphatic drainage from the thyroid gland is in several directions: to the tracheoesophageal nodes bilaterally, to upper anterior mediastinal nodes, to the delphian node overlying the thyroid cartilage, to nodes of the jugular chain bilaterally, and toward the base of the skull to retropharyngeal nodes.

Metastatic Sites. Distant spread occurs by contiguous lymphatic or hematogenous routes, for example, to lungs and bones, but many other sites may be involved.

STAGING PROCEDURES

A variety of procedures and special studies may be employed in the process of staging a given tumor. Both the clinical usefulness and cost efficiency must be considered. The following suggestions are made for staging a cancer of the thyroid:

Essential for staging

1. Complete physical examination of the head and neck including indirect laryngoscopy
2. Chest roentgenograms, AP and lateral views
3. Pathologic study of surgically removed specimen
4. Known residual tumor if present after resection of tumor

Possibly useful for staging or patient management

1. Multichemistry screen
2. Radioactive thyroid scan
3. Serum calcitonin determination
4. Ultrasound examination
5. Soft-tissue films of the neck, CT scans
6. Bone scans
7. Performance status (Karnofsky or ECOG scale)

Possibly useful for future staging systems or research studies

1. Studies of immune competence
2. Thyroid function tests

RULES FOR CLASSIFICATION

(See introductory paragraphs on General Rules for the Staging of Cancer). Both clinical-diagnostic staging (cTNM) and surgical-evaluative staging (sTNM) may be used as a basis for staging thyroid cancer. However, postsurgical resection-pathologic staging (pTNM) furnishes the greatest amount of evaluative evidence and proves most useful.

TNM CLASSIFICATION

Primary Tumor (T)

TX Minimum requirements to assess the primary tumor cannot be met.
T0 No evidence of primary tumor
Tis Carcinoma *in situ*
T1 Greatest diameter of primary tumor 3 cm or less
T2 Greatest diameter of primary tumor more than 3 cm
T3 Multiple intraglandular foci of primary tumor
T4 Fixation of primary tumor, direct invasion through thyroid capsule

Nodal Involvement (N)

NX Minimum requirements to assess the regional nodes cannot be met.
N0 No clinically or histologically positive node(s)
N1 Clinically positive or histologically positive node(s)

Distant Metastasis (M)

MX Minimum requirements to assess the presence of distant metastasis cannot be met.
M0 No (known) distant metastasis
M1 Distant metastasis present
Specify _____

Specify sites according to the following notations:

Pulmonary	PUL	Bone marrow	MAR
Osseous	OSS	Pleura	PLE
Hepatic	HEP	Skin	SKI
Brain	BRA	Eye	EYE
Lymph nodes	LYM	Other	OTH

HISTOPATHOLOGY

The World Health Organization (WHO) classification of thyroid cancer should be used, including at least the four major types:

Papillary carcinoma (with or without follicular foci)
Follicular carcinoma (extent of invasion of tumor capsule should be noted)
Medullary carcinoma
Undifferentiated (anaplastic) carcinoma
Unclassified malignant tumor

TUMOR GRADE (G)

G1 Well differentiated
G2 Moderately well differentiated
G3-G4 Poorly to very poorly differentiated

Use whichever indicator is most appropriate (term or G + number)

STAGE GROUPING

Two different stage groupings are required due to the role played by the patient's age in the behavior of the tumor. The 10-year relative survival rates observed are indicated for each stage (see Stage Grouping, Table 8-1).

Table 8-1. Stage Grouping

CANCER TYPE	UNDER 45 YEARS	45 YEARS AND OVER
Papillary		
Stage I	Any T, any N, M0	Any T, N0, M0 T1, N1, M0
Stage II	Any T, any N, M1	T2-4, N1, M0
Stage III	None *	None
Stage IV	None	Any T, any N, M1
Follicular		
Stage I	Any T, any N, M0	T1, N0, M0
Stage II	Any T, any N, M1	T2-4, N0, M0
Stage III	None	Any T, N1, M0
Stage IV	None	Any T, any N, M1
Medullary		
Stage I	None	None
Stage II	Any T, any N, M0	None
Stage III	None	Any T, any N, M0
Stage IV	Any T, any N, M1	Any T, any N, M1
Undifferentiated		
Stage I	None	None
Stage II	None	None
Stage III	None	None
Stage IV	Any T, any N, any M	Any T, any N, any M

* "None" is used to indicate that cases are assigned to other defined stages.

POSTSURGICAL RESECTION RESIDUAL TUMOR (R)

This does not enter into staging of the tumor but may be a factor in deciding further treatment.

R0 No residual tumor
R1 Microscopic residual tumor
R2 Macroscopic residual tumor
Specify _____

PERFORMANCE STATUS OF HOST (H)

Performance status of the host should be recorded because this information at times is pertinent to the treatment of the patient.

AJCC	PERFORMANCE	ECOG SCALE	KARNOFSKY SCALE (%)
H0	Normal activity	0	90-100
H1	Symptomatic but ambulatory; cares for self	1	70-80
H2	Ambulatory more than 50% of time; occasionally needs assistance	2	50-60
H3	Ambulatory 50% or less of time; nursing care needed	3	30-40
H4	Bedridden; may need hospitalization	4	10-20

DATA FORM

The data form for staging of cancer of the thyroid, in addition to permitting the recording of the extent of the cancer, also indicates the examinations necessary for staging and those examinations and data necessary for each time period of staging.

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Data Form for Cancer Staging

Patient identification
Name _____
Address _____
Hospital or clinic number _____
Age _____ Sex _____ Race _____

Institutional identification
Hospital or clinic _____
Address _____

Oncology Record

Anatomic site of cancer _____
Chronology of classification* [ ] Clinical-diagnostic (cTNM) [ ] Surgical-evaluative (sTNM)
Date of classification _____

Histologic type _____ Grade (G) _____
[ ] Postsurgical resection–pathologic (pTNM)
[ ] Retreatment (rTNM) [ ] Autopsy (aTNM)

Definitions: TNM Classification

Primary Tumor (T)

[ ] TX Minimum requirements to assess the primary tumor cannot be met.
[ ] T0 No evidence of primary tumor
[ ] Tis Carcinoma *in situ*
[ ] T1 Greatest diameter of primary tumor 3 cm or less
[ ] T2 Greatest diameter of primary tumor more than 3 cm
[ ] T3 Multiple intraglandular foci of primary tumor
[ ] T4 Fixation of primary tumor; direct invasion through thyroid capsule

Nodal Involvement (N)

[ ] NX Minimum requirements to assess the regional nodes cannot be met.
[ ] N0 No clinically or histologically positive node(s)
[ ] N1 Clinically positive or histologically positive node(s)

Distant Metastasis (M)

[ ] MX Minimum requirements to assess the presence of distant metastasis cannot be met.
[ ] M0 No (known) distant metastasis
[ ] M1 Distant metastasis present
Specify _____

Stage Grouping

Cancer Type	*Under 45 Years*	*45 Years and Over*
Papillary		
[ ] Stage I	Any T, any N, M0	Any T, N0, M0; T1, N1, M0
[ ] Stage II	Any T, any N, M1	T2–4, N1, M0
[ ] Stage III	None	None
[ ] Stage IV	None	Any T, any N, M1
Follicular		
[ ] Stage I	Any T, any N, M0	T1, N0, M0
[ ] Stage II	Any T, any N, M1	T2–4, N0, M0
[ ] Stage III	None	Any T, N1, M0
[ ] Stage IV	None	Any T, any N, M1
Medullary		
[ ] Stage I	None	None
[ ] Stage II	Any T, any N, M0	None
[ ] Stage III	None	Any T, any N, M0
[ ] Stage IV	Any T, any N, M1	Any T, any N, M1
Undifferentiated		
[ ] Stage I	None	None
[ ] Stage II	None	None
[ ] Stage III	None	None
[ ] Stage IV	Any T, any N, any M	Any T, any N, any M

*Use a separate form each time a case is staged.

Staging Procedures

A variety of procedures and special studies may be employed in the process of staging a given tumor. Both the clinical usefulness and cost efficiency must be considered. The following suggestions are made for staging a cancer of the thyroid:

Essential for staging

1. Complete physical examination of the head and neck including indirect laryngoscopy and nasopharyngoscopy
2. Biopsy of primary tumor
3. Chest roentgenogram
4. Roentgenograms of skull (nasopharynx)
5. Direct examination of hypopharynx

May be useful for staging or patient management

1. Multichemistry screen
2. Soft-tissue roentgenograms of neck; CT scans
3. Barium swallow
4. Performance status (Karnofsky or ECOG scale)

May be useful for future staging systems or research studies

1. Panendoscopy (direct laryngoscopy, bronchoscopy, esophagoscopy)
2. Studies of immune competence
3. Assay of antibodies to Epstein–Barr viral capsid antigen (nasopharynx)

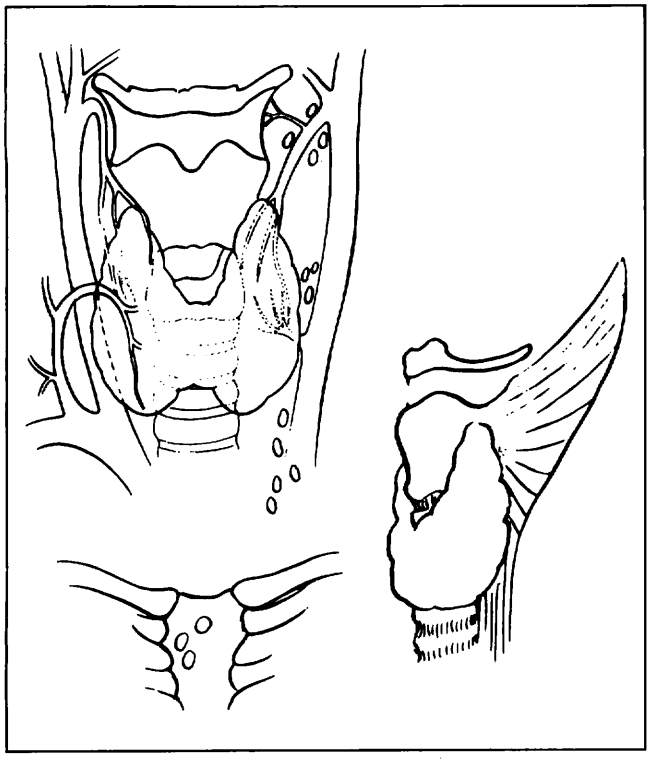
Histologic Type of Cancer

[ ] Papillary (with or without follicular foci)
[ ] Follicular
[ ] Medullary
[ ] Undifferentiated
[ ] Unclassified

Histologic Grade

[ ] G1 Well differentiated
[ ] G2 Moderately well differentiated
[ ] G3–G4 Poorly to very poorly differentiated

Examination by _____ M.D.
Date _____



Tumor size: _____ cm (greatest diameter)

Check site of nodal involvement:
- Cervical unilateral _____
- Cervical bilateral _____
- Delphian _____
- Mediastinal _____

Indicate on diagram primary tumor and regional nodes involved.

Postsurgical Resection–Pathologic Residual Tumor (R)

Does not enter into staging but may be a factor when deciding further treatment

[ ] R0 No residual tumor
[ ] R1 Microscopic residual tumor
[ ] R2 Macroscopic residual tumor
Specify _____

Performance Status of Host (H)

Several systems for recording a patient's activity and symptoms are in use and are more or less equivalent as follows:

AJCC	*Performance*	*ECOG Scale*	*Karnofsky Scale (%)*
[ ] H0	Normal activity	0	90–100
[ ] H1	Symptomatic but ambulatory; cares for self	1	70–80
[ ] H2	Ambulatory more than 50% of time; occasionally needs assistance	2	50–60
[ ] H3	Ambulatory 50% or less of time; nursing care needed	3	30–40
[ ] H4	Bedridden; may need hospitalization	4	10–20

Site-Specific Information

Thyroid History

History of previous irradiation to head & neck area
Yes _____ No _____
Other endocrine disease present
Yes _____ No _____
Family history of thyroid cancer
Yes _____ No _____
Family history of endocrine tumors
Yes _____ No _____

Primary Tumor

Location:
Right _____ Left _____ Midline _____
Size:
Largest diameter _____ cm
Characteristics:
Single _____ Multiple _____ Bilateral _____
Fixation (extension through thyroid capsule)
Yes _____ Massive _____ No _____
Neurologic involvement
Yes _____ No _____
Blood vessel invasion
Yes _____ No _____
Radioactive scan done
Yes _____ (Type) _____ No _____
Cold _____ Hot _____ Neither _____

9

Esophagus

ANATOMY (ICD-O 150)

Primary Site. For purposes of classification, staging, and reporting of cancer of the esophagus, the esophagus is considered as consisting of three principal regions. These regions are to be classified and reported separately. The *cervical esophagus* extends from the pharyngeal-esophageal junction (the cricopharyngeal sphincter) down to the level of the thoracic inlet, about 18 cm from the upper incisor teeth (approximately the upper one third of the esophagus). The *upper and midthoracic esophagus* extends from the thoracic inlet to a point 10 cm above the esophagogastric junction, which is usually at the level of the lower border of the eighth thoracic vertebra and about 31 cm from the upper incisor teeth (approximately the middle one third of the esophagus). The *lower thoracic esophagus* extends from a point 10 cm above the esophagogastric junction to the cardiac orifice of the stomach, which is about 40 cm from the upper incisor teeth (approximately the lower one third of the esophagus).

Nodal Stations. The regional lymph nodes for the cervical esophagus are the cervical or supraclavicular nodes, or both. For the thoracic esophagus, the regional nodes are the adjacent mediastinal lymph nodes. Involvement of more distant nodes is considered distant metastasis.

Metastatic Sites. The liver, lungs, and adrenals are the most common sites of distant metastases in other organs. Remote metastasis from carcinoma of the esophagus, although ultimately fatal, often carries a better intermediate prognosis than when the primary lesion has extended outside the esophagus—the latter a condition that is rapidly fatal.

RULES FOR CLASSIFICATION

Clinical-Diagnostic Staging. This classification is based on the anatomic extent of cancer that can be detected by examination before any treatment. Such an examination may include a medical history, physical examination, routine and special roentgenograms, endoscopic examinations including mediastinoscopy, mediastinotomy, thoracentesis, or thoracoscopy,

and other special examinations, including those used to demonstrate the presence of distant metastasis. Clinical assessment of regional lymph nodes for thoracic esophageal segments is not ordinarily possible. Thus, this classification is only appropriate for the cervical esophagus.

Surgical-Evaluative Staging. Patients on whom evaluative procedures are performed, such as exploratory thoracotomy (including biopsy), are included in this classification. The surgical-evaluative classification should be based on all data obtained for the clinical classification and information derived from exploratory surgery, including biopsy of mediastinal and abdominal nodes but not including information obtained by gross and histologic examination of therapeutically resected specimens.

Postsurgical Resection-Pathologic Staging. Esophageal cancer patients having similar therapeutic resections may be classified in a postsurgical treatment classification. This classification should be based on all data described in the clinical-diagnostic and surgical-evaluative classifications, as well as on that information derived from complete histologic examination of resected specimens.

Retreatment Staging. In the course of follow-up examinations, a patient may manifest evidence of progressive disease indicating treatment failure. Before initiating further treatment, the extent of tumor should be reassessed carefully, using all available information, and the patient should again be staged under the retreatment classification.

Autopsy Staging. In case of death of an esophageal cancer patient, the extent of the cancer, if any is found at autopsy, may be recorded by the TNM system; an autopsy stage may be reported, which is used only when the cancer is first diagnosed at autopsy.

TNM CLASSIFICATION

Primary Tumor (T)

For all three segments of the esophagus

- TX Minimum requirements to assess the primary tumor cannot be met.
- T0 No evidence of primary tumor
- Tis Carcinoma *in situ*
- T1 A tumor that involves 5 cm or less of esophageal length, that produces no obstruction,* and that has no circumferential involvement and no extraesophageal spread†
- T2 A tumor that involves more than 5 cm of esophageal length without extraesophageal spread† or a tumor of any size that produces obstruction* or that involves the entire circumference but without extraesophageal spread
- T3 Any tumor with evidence of extraesophageal spread†

*Roentgenographic evidence of significant impediment to the passage of liquid contrast material past the tumor or endoscopic evidence of esophageal obstruction

Nodal Involvement (N)

Cervical esophagus. The regional lymph nodes in the cervical esophagus are the cervical and supraclavicular nodes.

- NX Minimum requirements to assess the regional nodes cannot be met.
- N0 No clinically palpable nodes
- N1 Movable, unilateral, palpable nodes
- N2 Movable, bilateral, palpable nodes
- N3 Fixed nodes

Thoracic esophagus. NX (clinical evaluation): Regional lymph nodes for the upper, midthoracic, and lower thoracic esophagus that are not ordinarily accessible for clinical evaluation

Distant Metastasis (M)

- MX Minimum requirements to assess the presence of distant metastasis cannot be met.
- M0 No evidence of distant metastasis‡
- M1 Distant metastasis present
  Specify _____

Specify sites according to the following notations:

Pulmonary	PUL
Osseous	OSS
Hepatic	HEP
Brain	BRA
Lymph nodes	LYM
Bone marrow	MAR
Pleura	PLE
Skin	SKI
Eye	EYE
Other	OTH

†Extension of cancer outside the esophagus is seen by clinical, roentgenographic, or endoscopic evidence of any of the following:
Recurrent laryngeal, phrenic, or sympathetic nerve involvement
Fistula formation
Involvement of the tracheal or bronchial tree
Vena cava or azygos vein obstruction
Malignant effusion: mediastinal widening itself is not evidence of extraesophageal spread.

‡In the cervical esophagus, any lymph node involvement other than that of cervical or supraclavicular lymph nodes is considered distant metastasis. For the thoracic esophagus any cervical, supraclavicular, scalene, or abdominal lymph nodes are considered distant metastasis sites.

DEFINITIONS FOR POSTSURGICAL RESECTION CLASSIFICATION (pTNM)

Primary Tumor (T)

TX Minimum requirements to assess the primary tumor cannot be met.
Tis Preinvasive carcinoma (carcinoma *in situ*)
T0 No evidence of tumor found on histologic examination of specimen
T1 Tumor with invasion of the mucosa or submucosa but not the muscle coat
T2 Tumor with invasion of the muscle coat
T3 Tumor with invasion beyond the muscle coat or with gross invasion of contiguous structures
pT3a Tumor with invasion beyond the muscle coat
pT3b Tumor with gross invasion of contiguous structures

Regional Lymph Nodes (N)

NX Minimum requirements to assess the regional nodes cannot be met.
N0 Regional nodes not involved
N1 Unilateral regional nodes involved
N2 Bilateral regional nodes involved
N3 Extensive multiple regional nodes involved

The pN categories correspond to N categories

Distant Metastasis (M)

MX Minimum requirements to assess the presence of distant metastasis cannot be met.
M0 No distant metastasis
M1 Distant metastatic involvement

Postsurgical Treatment Residual Tumor (R)

R0 No residual tumor
R1 Microscopic residual tumor
R2 Macroscopic residual tumor

STAGE GROUPING*

The various TNM classifications can be gathered together to represent four groups of patients: (1) those patients having an excellent prognosis (83% 5-yr survival); (2) those patients having only a fair outcome (46% 5-yr survival); (3) those patients with progressive disease and a poor outlook (26% survival); and (4) those patients with distant spread (only 7% surviving at 5 yr) (see bibliographic reference 2).

*The cervical regional lymph nodes are accessible to clinical evaluation when the primary tumor is in the cervical esophagus, so these lesions can be staged on a clinical-diagnostic basis. This is not true for other segments of the cervical esophagus. If surgical resection has been carried out, all tumors in all segments of the esophagus can be staged on a postsurgical resection-pathologic basis.

Clinical-diagnostic classification for cervical esophagus

Stage 0	Tis, N0, M0
Stage I	T1, N0, M0
Stage II	T1, N1, N2; M0
	T2, N0-N2; M0
Stage III	T3, any N, M0
	Any T, N3, M0
Stage IV	Any T, any N, M1

Postsurgical resection-pathologic classification of all segments

Stage I	T1, N0, M0
Stage II	T2, N0, M0
Stage III	T3, N0, M0
	Any T, N1-N3; M0
Stage IV	Any T, any N, M1

HISTOPATHOLOGY

Approximately 98% of esophageal cancers are squamous cell carcinomas and approximately 2% are adenocarcinomas. Rarely do various sarcomas and melanomas occur.

TUMOR GRADE (G)

G1 Well differentiated
G2 Moderately well differentiated
G3-G4 Poorly to very poorly differentiated

Use whichever indicator is most appropriate (term or G + number).

PERFORMANCE STATUS OF HOST (H)

Several systems for recording a patient's activity and symptoms are in use and are more or less equivalent as follows:

AJCC	PERFORMANCE	ECOG SCALE	KARNOFSKY SCALE (%)
H0	Normal activity	0	90-100
H1	Symptomatic but ambulatory; cares for self	1	70-80
H2	Ambulatory more than 50% of time; occasionally needs assistance	2	50-60
H3	Ambulatory 50% or less of time; nursing care needed	3	30-40
H4	Bedridden; may need hospitalization	4	10-20

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Data Form for Cancer Staging

Patient identification
Name _____
Address _____
Hospital or clinic number _____
Age _____ Sex _____ Race _____

Institutional identification
Hospital or clinic _____
Address _____

Oncology Record

Anatomic site of cancer _____
Chronology of classification* [ ] Clinical-diagnostic (cTNM)
[ ] Surgical-evaluative (sTNM)
Date of classification _____

Histologic type† _____ Grade (G) _____
[ ] Postsurgical resection–pathologic (pTNM)
[ ] Retreatment (rTNM) [ ] Autopsy (aTNM)

Definitions: TNM Clinical-Diagnostic Classification for Cervical Esophagus Only

Further definitions for postsurgical resection–pathologic classification on reverse side apply to all segments.

Primary Tumor (T)

[ ] T0 No demonstrable tumor in the esophagus
[ ] Tis Carcinoma *in situ*
[ ] T1 A tumor that involves 5 cm or less of esophageal length, that produces no obstruction, and that has no circumferential involvement and no extraesophageal spread†
[ ] T2 A tumor that involves more than 5 cm of esophageal length without extraesophageal spread or a tumor of any size that produces obstruction or that involves the entire circumference but without extraesophageal spread
[ ] T3 Any tumor with evidence of extraesophageal spread

Nodal Involvement (N)

Cervical Esophagus

The regional lymph nodes in the cervical esophagus are the cervical and supraclavicular nodes.

Thoracic Esophagus

Regional lymph nodes for the upper, midthoracic, and lower thoracic esophagus are not ordinarily accessible for clinical evaluation.

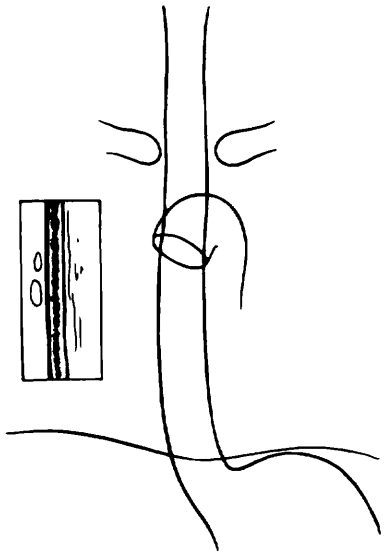
[ ] NX Minimum requirements to assess the regional nodes cannot be met.
[ ] N0 No clinically palpable nodes
[ ] N1 Movable, unilateral, palpable nodes
[ ] N2 Movable, bilateral, palpable nodes
[ ] N3 Fixed nodes

Distant Metastasis (M)

[ ] MX Minimum requirements to assess the presence of distant metastasis cannot be met.
[ ] M0 No (known) distant metastasis*
[ ] M1 Distant metastasis present
Specify _____

Site-Specific Information

See reverse side.



Length of tumor: _____ cm

Indicate on diagram primary tumor and regional nodes involved.

Stage Grouping

Clinical-diagnostic classification for cervical esophagus

[ ] Stage 0 Tis, N0, M0
[ ] Stage I T1, N0, M0
[ ] Stage II T1, N1, N2; M0
T2, N0–N2; M0
[ ] Stage III T3, any N, M0
Any T, N3, M0
[ ] Stage IV Any T, any N, M1

Postsurgical resection–pathologic classification

[ ] Stage I T1, N0, M0
[ ] Stage II T2, N0, M0
[ ] Stage III T3, N0, M0
Any T, N1–N3, M0
[ ] Stage IV Any T, any N, M1

Examination by _____ M.D.
Date _____

*Use a separate form each time a case is staged.
†See reverse side for additional information.

Site-Specific Information

Esophagus Location

[ ] Cervical
[ ] Supraclavicular
[ ] Abdominal

Distance From Incisors

[ ] Cervical 18 cm
[ ] Upper thoracic 18–30 cm
[ ] Lower thoracic 30 cm

Histology

Squamous cell epithelioma _____
Other _____
Length of tumor _____ cm

[ ] Encircles esophagus
[ ] Evidence of obstruction
[ ] Extraesophageal extension
  [ ] Nerve involvement
  [ ] Tracheobronchial tree
  [ ] Caval obstruction
  [ ] Pleural effusion
  [ ] Mediastinal widening (not necessarily evidence of extra-esophageal spread)

Lymph Nodes

[ ] Palpable
[ ] Bilateral
[ ] Fixed
Number _____
Size of largest node _____ cm^2

Definitions for Postsurgical Resection–Pathologic Classification

Primary Tumor (T)

[ ] TX Minimum requirements to assess the primary tumor cannot be met.
[ ] Tis Preinvasive carcinoma (carcinoma *in situ*)
[ ] T0 No evidence of tumor found on histologic examination of specimen
[ ] T1 Tumor with invasion of the mucosa or submucosa but not the muscle coat
[ ] T2 Tumor with invasion of the muscle coat
[ ] T3 Tumor with invasion beyond the muscle coat *or* with gross invasion of contiguous structures
  [ ] T3a Tumor with invasion beyond the muscle coat
  [ ] T3b Tumor with gross invasion of contiguous structures

Regional Lymph Nodes (N)

[ ] NX Minimum requirements to assess the regional nodes cannot be met.
[ ] N0 Regional nodes not involved
[ ] N1 Unilateral regional nodes involved
[ ] N2 Bilateral regional nodes involved
[ ] N3 Extensive multiple regional nodes involved

Distant Metastasis (M)

[ ] MX Minimum requirements to assess the presence of distant metastasis cannot be met.
[ ] M0 No (known) distant metastasis
[ ] M1 Distant metastasis present
Specify _____

Histologic Type of Cancer

Approximately 98% of esophageal cancers are squamous cell carcinomas and approximately 2% are adenocarcinomas. Rarely do various sarcomas and melanomas occur.

Tumor Grade (G)

[ ] G1 Well differentiated
[ ] G2 Moderately well differentiated
[ ] G3–G4 Poorly to very poorly differentiated

Use whichever indicator is most appropriate (term or G + number).

Postsurgical Resection Residual Tumor (R)

Does not enter into staging tumor but may be a factor in deciding management

[ ] R0 No residual tumor
[ ] R1 Microscopic residual tumor
[ ] R2 Macroscopic residual tumor
Specify _____

Performance Status of Host (H)

Performance status of the host should be recorded because this information at times is pertinent to the treatment of the patient.

AJCC	*Performance*	*ECOG Scale*	*Karnofsky Scale (%)*
[ ] H0	Normal activity	0	90–100
[ ] H1	Symptomatic but ambulatory; cares for self	1	70–80
[ ] H2	Ambulatory more than 50% of time; occasionally needs assistance	2	50–60
[ ] H3	Ambulatory 50% or less of time; nursing care needed	3	30–40
[ ] H4	Bedridden; may need hospitalization	4	10–20

10

Stomach

ANATOMY (ICD-O 151)

The stage classification for carcinoma of the stomach as an aid in selecting treatment is based on the clinical extent of the disease as demonstrated by clinical examination and by roentgenographic and endoscopic studies. A staging classification for end-results reporting is based on the extent of disease at the time of surgical exploration of the abdomen, histopathologic study of the excised surgical specimen, or clinical examination (in advanced disease).

Only those cases that have histologically proven primary carcinoma or histologically proven metastasis with clinical evidence of a primary tumor in the stomach are to be included in this classification.

The prognosis of carcinoma of the stomach depends on the degree of penetration of the stomach wall by the primary lesion. Size or location of the primary tumor is of less significance. The histologic classification of carcinoma of the stomach is not helpful in assessing prognosis.

The clinical classification defines the extent of disease in terms of three components: (1) the primary tumor, designated by the letter T and expressed in terms of the degree of penetration by the cancer through the stomach wall; (2) the regional lymph nodes, designated by the letter N, which are the intra-abdominal subdiaphragmatic nodes; and (3) distant metastasis, designated by the letter M.

For clinical-diagnostic classification, the primary tumor is always designated by the letter cT and for postsurgical treatment-pathologic classification, by the letters pT. The description of the primary lesion is similar for the clinical-diagnostic and postsurgical treatment-pathologic classifications.

Primary Site. The stomach is the first part of the abdominal alimentary tract. Its first portion is the esophagogastric junction, which is immediately below the diaphragm. The pylorus is the part of the stomach through which the stomach contents empty into the duodenum, the first segment of the intestine. The upper portion of the stomach is the fundus and the lower part is the antrum. The shorter right border is the lesser curvature and that

on the left is the greater curvature. The wall of the stomach comprises three tissue layers: an inner mucosal layer, a smooth muscular layer (circular, oblique, and longitudinal), and an outer serosal or visceral peritoneal surface.

Nodal Stations. The major lymphatic collecting trunks are parallel with the left gastric artery, the splenic artery, and the hepatic artery. The major first station nodes are the lesser curvature, left gastropancreatic, juxtacardiac, gastroduodenal, gastropyloric, suprapyloric, pancreatoduodenal, celiac, splenic, and hepatic lymph nodes. The second station nodes include the para-aortic nodes.

Metastatic Sites. Distant spread to liver, bone, supraclavicular lymph nodes, and lung is common, but widespread visceral involvement occurs.

RULES FOR CLASSIFICATION

Clinical-Diagnostic Staging. The clinical assessment of the primary tumor includes medical history, physical examination, radiological examinations, and related imaging techniques (radionuclide scans, ultrasound, NMR, etc.), endoscopy, and laparoscopy. The cancer must be confirmed by cytology or biopsy.

Surgical-Evaluative Staging. All information obtained on surgical exploration is used along with clinical data when resection is not carried out.

Postgastrectomy Resection-Pathologic Staging. Partial and total gastric resection specimens, including all macroscopic tumor and regional nodes, provide for the use of this staging designation.

TNM CLASSIFICATION

Primary Tumor (T)

The principal factor is the degree of penetration of the stomach wall by carcinoma.

- TX Minimum requirements to assess the primary tumor cannot be met.
- T0 No evidence of primary tumor
- Tis Tumor limited to mucosa without penetration into the lamina propria
- T1 Tumor limited to mucosa or mucosa and submucosa regardless of its extent (or location)
- T2 Tumor involves the mucosa and the submucosa (including the muscularis propria), and extends to or into the serosa but does not penetrate through the serosa.
- T3 Tumor penetrates through the serosa without invading contiguous structures.
- T4a Tumor penetrates through the serosa and involves immediately adjacent tissues such as lesser omentum, perigastric fat, regional ligaments, greater omentum, transverse colon, spleen, esophagus, or duodenum by way of intraluminal extension.
- T4b Tumor penetrates through the serosa and involves the liver, diaphragm, pancreas, abdominal wall, adrenal glands, kidney, retroperitoneum, small intestine or esophagus, or duodenum by way of serosa.

Nodal Involvement (N)

The regional lymph nodes are the intra-abdominal subdiaphragmatic nodes.

- NX Minimum requirements to assess the regional nodes cannot be met.
- N0 No metastases to regional lymph nodes
- N1 Involvement of perigastric lymph nodes within 3 cm of the primary tumor along the lesser or greater curvature
- N2 Involvement of the regional lymph nodes more than 3 cm from the primary tumor, that are removed or removable at operation, including those located along the left gastric, splenic, celiac, and common hepatic arteries
- N3 Involvement of other intra-abdominal lymph nodes such as the para-aortic, hepatoduodenal, retropancreatic, and mesenteric nodes

Distant Metastasis (M)

- MX Minimum requirements to assess the presence of distant metastasis cannot be met.
- M0 No (known) distant metastasis
- M1 Distant metastasis present
  Specify _____

Specify sites according to the following notations:

Peritoneal	PER
Pulmonary	PUL
Osseous	OSS
Hepatic	HEP
Brain	BRA
Lymph nodes (above diaphragm or nonabdominal)	LYM
Bone marrow	MAR
Pleura	PLE
Skin	SKI
Eye	EYE
Other	OTH

STAGE GROUPING

Staging solely on clinical-diagnostic measures is not completely satisfactory. For this reason staging can be done on clinical-diagnostic and pathologic infor-

mation as c-pTNM or as surgical-evaluative, sTNM, or, if resection has been carried out, as pTNM.

Stage Grouping of Carcinoma of the Stomach

Stage 0	Tis, N0, M0
Stage I	T1, N0, M0
Stage II	T2, T3; N0, M0
Stage III	T1-T3; N1, N2; M0
	T4a, N0-N2; M0
Stage IV	T1-T3; N3, M0
	T4b, any N, M0
	Any T, any N, M1

HISTOPATHOLOGY

The staging recommendations relate only to adenocarcinoma and not to other types such as lymphoma or sarcomas. Adenocarcinomas should be divided into the following subtypes:

1. Intestinal
2. Diffuse
3. Mixed

Tumor Grade (G)

G1	Well differentiated
G2	Moderately well differentiated
G3-G4	Poorly to very poorly differentiated

Use whichever indicator is most appropriate (term or G + number).

POSTGASTRECTOMY RESIDUAL TUMOR (R)

This does not enter into staging tumor but may be a factor in deciding management.

R0	No residual tumor
R1	Microscopic residual tumor
R2	Macroscopic residual tumor
	Specify _____

PERFORMANCE STATUS OF HOST (H)

Performance status of the host should be recorded because this information at times is pertinent to the treatment of the patient.

AJCC	PERFORMANCE	ECOG SCALE	KARNOFSKY SCALE (%)
H0	Normal activity	0	90-100
H1	Symptomatic but ambulatory; cares for self	1	70-80
H2	Ambulatory more than 50% of time; occasionally needs assistance	2	50-60
H3	Ambulatory 50% or less of time; nursing care needed	3	30-40
H4	Bedridden; may need hospitalization	4	10-20

DATA FORM

The data form for staging of cancer of the stomach, in addition to permitting recording of the extent of the cancer, also indicates the examinations necessary for staging and the examinations and data necessary for each time period of staging.

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Data Form for Cancer Staging

Patient identification
Name _____
Address _____
Hospital or clinic number _____
Age _____ Sex _____ Race _____

Institutional identification
Hospital or clinic _____
Address _____

Oncology Record

Anatomic site of cancer _____
Chronology of classification* [ ] Clinical-diagnostic (cTNM)
[ ] Surgical-evaluative (sTNM)
Date of classification _____

Histologic type† _____ Grade (G) _____
[ ] Postsurgical resection–pathologic (pTNM)
[ ] Retreatment (rTNM) [ ] Autopsy (aTNM)

Definitions: TNM Classification

Primary Tumor (T)

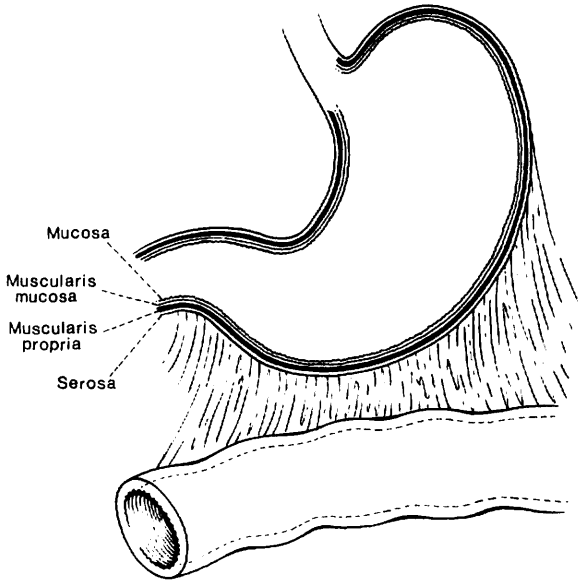
[ ] TX Minimum requirements to assess the primary tumor cannot be met.
[ ] T0 No evidence of primary tumor
[ ] Tis Carcinoma *in situ*
[ ] T1 Tumor limited to mucosa and submucosa regardless of its extent or location
[ ] T2 Tumor involves the mucosa, the submucosa (including the muscularis propria), and extends to or into the serosa, but does not penetrate through the serosa.
[ ] T3 Tumor penetrates through the serosa without invading contiguous structures.
[ ] T4a Tumor penetrates through the serosa and involves immediately adjacent tissues such as lesser omentum, perigastric fat, regional ligaments, greater omentum, transverse colon, spleen, esophagus, or duodenum by way of intraluminal extension.
[ ] T4b Tumor penetrates through the serosa and involves the liver, diaphragm, pancreas, abdominal wall, adrenal glands, kidney, retroperitoneum, small intestine or esophagus, or duodenum by way of serosa.

Nodal Involvement (N)

[ ] NX Minimum requirements to assess the regional nodes cannot be met.
[ ] N0 No metastases to regional lymph nodes
[ ] N1 Involvement of perigastric lymph nodes within 3 cm of the primary tumor along the lesser or greater curvature
[ ] N2 Involvement of the regional lymph nodes more than 3 cm from the primary tumor that are removed or removable at operation, including those located along the left gastric, splenic, celiac, and common hepatic arteries
[ ] N3 Involvement of other intra-abdominal lymph nodes which are not removable at operation, such as the para-aortic, hepatoduodenal, retropancreatic, and mesenteric nodes

Distant Metastasis (M)

[ ] MX Minimum requirements to assess the presence of distant metastasis cannot be met.
[ ] M0 No (known) distant metastasis
[ ] M1 Distant metastasis present
Specify _____



Indicate on diagram primary tumor and regional nodes involved.

Primary Tumor

Site _____
Size _____
Depth of penetration _____
Layers involved _____

Method(s) of Determination

_____
_____

Nodes

Negative _____
Positive _____
Groups involved _____

Examination by _____ M.D.
Date _____

*Use a separate form each time a case is staged.
†See reverse side for additional information.

Stage Grouping

[ ]	Stage 0	Tis, N0, M0
[ ]	Stage I	T1, N0, M0
[ ]	Stage II	T2 or T3; N0, M0
[ ]	Stage III	T1–T3; N1, N2; M0
		T4a, N0–N2; M0
[ ]	Stage IV	T1–T3; N3, M0
		T4b, any N, M0
		Any T, any N, M1

Clinical-Diagnostic Stage

The clinical assessment of the primary tumor includes medical history, physical examination, routine and special roentgenograms (*e.g.*, fluoroscopy, barium studies), endoscopy, laparoscopy, ultrasound, and computerized tomography. The cancer must be confirmed by biopsy. As newer techniques are improved and gain wider use, clinical staging can be more reliable.

Postgastrectomy–Pathologic Stage

Partially and completely resected stomach specimens and regional nodes provide for the use of this staging designation.

Surgical-Evaluative Stage

All information obtained on surgical exploration is used along with clinical-diagnostic data when resection is not carried out.

Histopathology

Predominant cancer is adenocarcinoma.

[ ] Intestinal type
[ ] Diffuse type
[ ] Mixed type

Histologic Grade

[ ]	G1	Well differentiated
[ ]	G2	Moderately well differentiated
[ ]	G3–G4	Poorly to very poorly differentiated

Residual Tumor (R)

[ ]	R0	No residual tumor
[ ]	R1	Microscopic residual tumor
[ ]	R2	Macroscopic residual tumor
		Specify _____

Performance Status of Host (H)

Performance status of the host should be recorded because this information at times is pertinent to the treatment of the patient.

AJCC		*Performance*	*ECOG Scale*	*Karnofsky Scale (%)*
[ ]	H0	Normal activity	0	90–100
[ ]	H1	Symptomatic but ambulatory; cares for self	1	70–80
[ ]	H2	Ambulatory more than 50% of time; occasionally needs assistance	2	50–60
[ ]	H3	Ambulatory 50% or less of time; nursing care needed	3	30–40
[ ]	H4	Bedridden; may need hospitalization	4	10–20

11

Colon and Rectum

In retrospective studies, inadequacies of the clinical data prohibited the development of meaningful clinical staging (cTNM) for either site individually. Generally, however, the data were sufficiently reliable and consistent when based on postsurgical treatment-pathologic information to permit development of a staging system for those cases in which histopathologic examination of therapeutically resected specimens was done (pTNM). In both sites, analysis of the postsurgical treatment data suggested that prognosis was related to the depth of penetration of the tumor, regional lymph node involvement, presence or absence of distant metastases, and complications, such as the presence of fistula. A comparison of survival data for the colon with that of the rectum based on penetration (pT), lymph node status (N), and distant metastases (M) showed such a similarity that it suggested the practicality of developing from the retrospective data one set of pTNM categories for postsurgical treatment evaluation and one set of stage grouping definitions. However, in any analysis of postsurgical treatment evaluation and stage groupings, the two sites should be kept separate.

It may well be that, as various biologic markers relevant to host resistance become identified, factors in addition to those of anatomic extent will become important in the classification and staging of cancer of the colon and of the rectum.

ANATOMY (ICD-O 153 and 154)

Primary Site. The large intestine (or colon) extends from the terminal ileum to the anal canal, although for simplicity it may be divided into three subdivisions exclusive of the rectum: right, middle, and left. Still more simply, the large intestine may be divided into the intraperitoneal colon and the rectum (distal 10 cm). All intraperitoneal colonic lesions are treated similarly. The rectal lesions are handled quite differently; some have a somewhat worse prognosis. However, the conventional, more minute subdivisions are described briefly, inasmuch as they may be of relevance in prospective studies concerned with carcinogenesis, classification, staging, and reporting of cancer of the colorectum.

The junction of the ileum and cecum is marked by the ileocecal valve, which is an anteroposterior slit formed by the partial invagination of the distal end of the ileum into the cecum.

The cecum is a large pouch that constitutes the proximal segment of the large intestine, measures about 6 cm by 9 cm, and is invested completely by the peritoneum. The vermiform appendix arises from the medial and posterior aspect of the cecum below the ileocecal junction. The appendix, therefore, may lie in any axis of a circle, the center of the circle being represented by the cecal attachment. The ascending colon is 15 cm to 20 cm long and is ordinarily retroperitoneal.

Lying at the undersurface of the right lobe of the liver and close to the duodenum and the right kidney, the hepatic flexure presents a difficult problem of differential diagnosis, and cancer at this site may invade these organs relatively early.

The transverse colon lies in a more anterior position than do other portions of the colon, so tumors here should be more readily palpable. It is supported by the transverse mesocolon, which in turn is attached to the pancreas. Anteriorly, its serosa is contiguous with the gastrocolic ligament, which is attached to the stomach.

The splenic flexure lies at a higher level and is more fixed than the hepatic flexure; it is intimately related to the spleen, the tail of the pancreas, and the left kidney. The descending colon, 10 cm to 15 cm long, is only partially invested by peritoneum, the posterior portion being in a retroperitoneal position.

The sigmoid loop extends from the medial border on the left psoas major muscle to the beginning of the rectum. It is suspended by its mesocolon (the sigmoid mesocolon), which is variable in length. When the mesocolon is excessively long, the resulting "redundant" sigmoid may come to lie in the right lower quadrant of the abdomen.

The rectum, about 12 cm long, extends from a point opposite the third sacral vertebra down to the apex of the prostate in the male and to the apex of the perineal body in the female, that is, to a point 4 cm anterior to the tip of the coccyx. (Arbitrarily, it may be defined as the distal 10 cm of the large intestine, as measured by preoperative sigmoidoscopy from the anal verge.) From the anal mucocutaneous junction, it extends approximately 10 cm to 12 cm. The rectosigmoid area is considered as being 10 cm to 15 cm from the anal mucocutaneous junction. In this retrospective study, all rectosigmoid cases have been grouped with those of the rectum. The rectum has no epiploic appendages, no haustrations, and no taeniae. It is covered by peritoneum in front and on both sides in its upper third and on the anterior wall only in its middle third; there is no peritoneal covering in the lower third. In the lower rectum, the mucosa is thrown into longitudinal folds known as the rectal columns or the columns of Morgagni. Between them, just above the white line of Hilton, are the anal pits or sinuses.

About 4 cm long, the anal canal courses downward and backward from the apex of the prostate or the perineal body. The anocutaneous line, or white line of Hilton, at the base of the rectal columns marks the site of the original anal membrane that separated the entodermal gut from the ectodermal proctoderm.

Nodal Stations. Whenever possible, the status of the principal lymph nodes at the base of the mesocolon should be recorded, namely those proximal to the origins of the ileocolic, right colic, middle colic, and inferior mesenteric arteries. As will be noted in the definitions under N and for stage, involvement of the principal (para-aortic) lymph nodes, in contrast to involvement of intervening nodes, constitutes distant metastasis. Intervening, or regional, nodes are as follows: *intermediate* (along the course of the major vessels supplying the colon), *paracolic* (following the vascular arcades of Drummond's marginal artery), and *epicolic* (in close proximity to the colon, being found along the mesocolic border of the colon and often in the epiploic appendages).

Although the flow of lymph usually traverses each group of nodes from the epiploic to the principal nodes, occasionally it flows directly to the intermediate or even to the principal nodes, bypassing those that intervene. (Increasing use of the "no-touch" isolation technique in resecting colonic lesions has been thought by some to minimize the degree to which lymph node involvement (N) can be assessed as a component of the surgical-evaluative classification. However, nodes can be evaluated after the vascular supply has been ligated, even with the no-touch technique.)

Listed below are the regional lymph nodes for each colorectal segment:

SEGMENT	REGIONAL LYMPH NODES
Cecum	Anterior cecal; posterior cecal; ileocolic
Ascending colon	Ileocolic; right colic; middle colic
Hepatic flexure	Right colic; middle colic
Transverse colon	Middle colic
Splenic flexure, Descending colon, Sigmoid colon	Left colic; inferior mesenteric
Rectosigmoid	Perirectal; left colic; sigmoid mesenteric; inferior mesenteric

SEGMENT	REGIONAL LYMPH NODES
Rectum	Perirectal; left colic; sigmoid mesenteric; inferior mesenteric; internal iliac (hypogastric); lateral sacral; common iliac; sacral promontory (Gerota)

Note: Lymph nodes between origins of the inferior and superior mesenteric arteries are nonresectable, for example, superior mesenteric lymph nodes. Therefore, although regional in the classic anatomic sense, they are designated "distant" for purposes of clinical stage classification. (Colonic resections are distal to the superior mesenteric artery and its contiguous nodes.) Similarly, lymph flow from the lower rectum may be to regional lymph nodes (*i.e.*, internal iliac [hypogastric], common iliac, lateral sacral, or sacral promontory), which are not resected at the time of an abdominoperineal resection but may be resected as a separate procedure.

In summary, regional lymph nodes are to be distinguished from juxtaregional. In the colon, the regional lymph nodes are the pericolic nodes and the nodes located along the ileocolic, right colic, middle colic, and inferior mesenteric arteries. The juxtaregional lymph nodes are the periaortic and other subdiaphragmatic intra-abdominal nodes. In the rectum, the regional nodes are the perirectal nodes and the nodes distal to the origin of the inferior mesenteric artery. The juxtaregional nodes are the para-aortic and other subdiaphragmatic intra-abdominal nodes.

RULES FOR CLASSIFICATION

Clinical-Diagnostic Staging. Clinical assessment includes medical history, physical examination, routine and special roentgenograms (including barium enema and fluoroscopy), sigmoidoscopy, colonoscopy (with biopsy of lesions above the level of the sigmoid colon), fiberoptics (with biopsy when possible), cytologic examination of colon washings, laboratory examinations (*e.g.*, occult blood determination in the stool), carcinoembryonic antigen (CEA) assay, and special examinations used to demonstrate the presence of extracolonic metastasis (*e.g.*, chest films, blood counts, liver chemistries).

Surgical-Evaluative Staging. Surgical-evaluative assessment should include all the data that would be obtained for clinical classification, as well as the information obtained at the time of exploratory laparotomy, including biopsy but not including information obtained by complete histopathologic examination of a therapeutically resected specimen.

Postsurgical Resection-Pathologic Staging. This classification describes the known extent of the colorectal carcinoma after complete examination of the resected specimen. Important determinants of survival in the pTNM classification are the depth of tumor penetration, involvement of regional lymph nodes, and presence of distant metastasis. Other anatomic factors associated with survival are local intravascular invasion (venous or lymphatic) and grade.

TNM CLASSIFICATION

The definitions of TNM categories for carcinoma of the colon and rectum follow. Each case must be assigned the highest category of T, N, and M that describes the full extent of disease in that case.

Primary Tumor (T)

- TX Minimum requirements to assess the primary tumor cannot be met.
- T0 No evidence of primary tumor
- Tis Carcinoma *in situ* (no invasion of lamina propria)
- T1 Tumor confined to the mucosa or submucosa (*e.g.*, carcinoma *de novo* or carcinomatous adenoma, either polypoid or papillary/villous)
- T2 Tumor limited to wall of colon or rectum but not beyond—*viz.*, invasion into muscularis propria or subserosa (colon and proximal rectum) and into muscularis propria but not beyond (distal rectum)
- T2a Tumor extending into muscularis propria but not penetrating through it
- T2b Tumor extending through the wall with complete penetration of the muscularis propria
- T3 Tumor invades all layers of bowel wall including serosa (colorectal) with or without extension to adjacent or contiguous tissues. Fistula may or may not be present.
- T4 Tumor has spread by direct extension beyond contiguous tissue or the immediately adjacent organs.
- T Multiple primary carcinoma. The greatest extent of the tumor is indicated as usual by a suffix as described above, and the number of multiple tumors is indicated by a parenthetic numerical prefix

Regional Nodal Involvement (N)

- NX Minimum requirements to assess the regional nodes cannot be met.
- N0 Nodes not involved
- N1 One to three involved regional nodes adjacent to primary lesion
- N2 Regional nodes involved extending to line of resection or ligature of blood vessels

N3 Nodes contain metastasis, location not identified. Specify number examined; number involved. (Case cannot be properly staged.)

Distant Metastasis (M)

MX Minimum requirements to assess the presence of distant metastasis cannot be met.
M0 No (known) distant metastasis
M1 Distant metastasis present (including extra-abdominal nodes; intra-abdominal nodes proximal to mesocolon and inferior mesenteric artery (juxtaregional); peritoneal implants, liver, lungs, and bones).
Specify _____

Specify sites according to the following notations:

Pulmonary	PUL	Bone marrow	MAR
Osseous	OSS	Pleura	PLE
Hepatic	HEP	Skin	SKI
Brain	BRA	Eye	EYE
Lymph nodes	LYM	Other	OTH

Add + to the abbreviated notation to indicate that the pathology (p) is proved.

POSTSURGICAL RESECTION RESIDUAL TUMOR (R)

R0 No residual tumor
R1 Microscopic residual tumor
R2 Macroscopic residual tumor
Specify _____

STAGE GROUPING

Stage 0

Tis, N0, M0
Carcinoma *in situ*

Stage I

Stage IA: T1, N0, M0
Tumor confined to mucosa or submucosa
Stage IB: T2, N0, M0
Tumor involves muscularis propria but not beyond.

Stage II

T3, N0, M0
Tumor involves all layers of bowel wall with or without invasion of immediately adjacent structures.

Stage III

Any T, N1-N3; M0
Any degree of bowel wall invasion with regional node metastasis
T4, N0, M0
Tumor extends beyond the contiguous tissue or immediately adjacent organs with no regional node metastasis (see bibliography reference 2).

Stage IV

Any T, any N, M1
Any degree of invasion of bowel wall with or without metastasis to regional lymph nodes but with evidence of distant metastasis

HISTOPATHOLOGY

The predominant cancer is adenocarcinoma; pathologic diagnosis is required for this classification. Tumor grading is recommended. Reference to WHO nomenclature is advised. Other determinants of probable importance to be evaluated in prospective studies of postsurgical treatment assessment are tumor margin circumscription, histopathologic differentiation (*e.g.*, nuclear grade, growth pattern, and mucin production), and host-cellular reaction (lymphocyte and plasma cell infiltration in and about the tumor as well as in contiguous tissues). It is essential that in each case the specific histologic type and the presence or absence of intravasal permeation (lymphatic, venous, or both) be recorded routinely.

TUMOR GRADE (G)

GX Grade or differentiation not determined, not stated, or not applicable
G1 Well differentiated
G2 Moderately well differentiated
G3 Poorly differentiated
G4 Undifferentiated

Note: The Dukes classification for cancer of the rectum and subsequently, with modifications, for cancer of the colon, has been widely in use. For that reason a grid is presented before the data form to show the comparisons.

PERFORMANCE STATUS OF HOST (H)

Performance status of the host should be recorded because this information at times is pertinent to the treatment of the patient.

AJCC	PERFORMANCE	ECOG SCALE	KARNOFSKY SCALE (%)
H0	Normal activity	0	90-100
H1	Symptomatic but ambulatory; cares for self	1	70-80
H2	Ambulatory more than 50% of time; occasionally needs assistance	2	50-60
H3	Ambulatory 50% or less of time; nursing care needed	3	30-40
H4	Bedridden; may need hospitalization	4	10-20

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CARCINOMA OF THE COLORECTUM

Stage Classification and Stage Grouping (AJCC, UICC, Dukes, Astler-Coller)

AJCC 1982	*UICC 1978 (3rd ed)*	*Dukes (1932, 1935)**	*Astler-Coller†*
Stage 0 Carcinoma *in situ* Tis N0 M0	*Stage 0* Tis, N0, M0		*Stage 0* 0
Stage I IA Tumor confined to mucosa or submucosa T1, N0, M0	*Stage I* 1A	*A*	*Stage I*
IB Tumor involves muscularis propria but not beyond T2, N0, M0	T1, N0, M0 1B T2, N0, M0	A A	A B1
Stage II Involvement of all layers of bowel wall with or without invasion of immediately adjacent structures T3, N0, M0	*Stage II* T3, T4, N0, M0 (T3a with fistula) (T3b without fistula)	*B*	*Stage II* B2
Stage III Any degree of bowel wall with regional node metastasis Any T, N1-N3; M0 Extends beyond contiguous tissue or immediately adjacent organs with no regional lymph node metastasis T4, N0, M0	*Stage III* Any T, N1, M0	*C* (1932) C1 (1935) C2 (1935)	*Stage III* C1 C2
Stage IV Any invasion of bowel wall with or without regional lymph node metastasis but with evidence of distant metastasis Any T, any N, M1	*Stage IV* Any T, any N, M1	*Type 4* (so-called D)	*Stage IV* D

*Dukes: A = Limited to bowel wall; B = Spread to extramural tissue; C = Involvement of regional nodes (C1: Near primary lesion; C2: Proximal node involved at point of ligation); Type 4 (so-called D) = Distant metastasis

†Astler-Coller: A = Limited to mucosa; B1 = Same as AJCC Stage IB (T2a); B2 = Same as AJCC Stage IB (T2b); C1 = Limited to wall with involved nodes; C2 = Through all layers of wall with involved nodes

Data Form for Cancer Staging

Patient identification
Name _____
Address _____
Hospital or clinic number _____
Age _____ Sex _____ Race _____

Institutional identification
Hospital or clinic _____
Address _____

Oncology Record

Anatomic site of cancer _____
Chronology of classification* [ ] Clinical-diagnostic (cTNM)
[ ] Surgical-evaluative (sTNM)
Date of classification _____

Histologic type† _____ Grade (G) _____
[ ] Postsurgical resection–pathologic (pTNM)
[ ] Retreatment (rTNM) [ ] Autopsy (aTNM)

Definitions: TNM Classification

Primary Tumor (T)

[ ] TX Minimum requirements to assess the primary tumor cannot be met.
[ ] T0 No evidence of primary tumor
[ ] Tis Carcinoma *in situ*
[ ] T1 Tumor confined to mucosa or submucosa
[ ] T2 Tumor limited to bowel wall but not beyond
  [ ] T2a Partial invasion of muscularis propria
  [ ] T2b Complete invasion of muscularis propria
[ ] T3 Tumor invasion of all layers of bowel wall with or without invasion of adjacent or contiguous tissues; fistula may or may not be present.
[ ] T4 Tumor spread by direct extension beyond contiguous tissue or the immediately adjacent organs
[ ] T Multiple primary carcinoma; classify most extensive tumors. (Indicate number in brackets.)

Nodal Involvement (N)

[ ] NX Minimum requirements to assess the regional nodes cannot be met.
[ ] N0 Nodes not involved
[ ] N1 One to three involved regional nodes adjacent to primary lesion [ ]
[ ] N2 Regional nodes involved extending to line of resection or ligature of blood vessels [ ]
[ ] N3 Nodes contain metastasis, location not identified. Specific number examined [ ]; number involved [ ]

Distant Metastasis (M)

[ ] MX Minimum requirements to assess the presence of distant metastasis cannot be met.
[ ] M0 No (known) distant metastasis
[ ] M1 Evidence of distant metastasis
Specify _____

Stage Grouping

[ ]	Stage 0	Tis, N0, M0
[ ]	Stage I	
	IA	T1, N0, M0
	IB	T2, N0, M0
[ ]	Stage II	T3, N0, M0
[ ]	Stage III	Any T, N1–N3, M0
		T4, N0, M0
[ ]	Stage IV	Any T, any N, M1

*Use a separate form each time a case is staged.
†See reverse side for additional information.

Site-Specific Information

History
Symptoms _____
Duration _____
Physical examination
Rectal _____
Abdominal palpation _____
Proctosigmoidoscopy _____
Fiberoptic colonoscopy _____
Laparoscopy _____
Liver edge palpable Yes _____ No _____
Roentgenographic Studies
Type _____
Findings _____
Site or level _____
Laboratory studies
Hb _____
CEA (serum) _____ ng
Other markers (Specify) _____
Fecal occult blood smear [ ] Positive
[ ] Negative
[ ] Not done
Cytology [ ] Positive
[ ] Negative
[ ] Not done
Pathologic findings
Primary tumor Biopsy [ ] Resected tumor [ ]
Site (note diagrams):
Indicate by numeral _____
Size greatest diameter _____
Gross characteristics _____
Depth of penetration of bowel wall _____
Blood vessel invasion: Venous _____
Arterial _____
Not stated _____
Additional tissues involved: Adjacent _____
Distant _____
Complications: Fistula _____ Other _____
Other neoplasms: Number [ ] Location _____
Type _____
Nodal involvement
Cannot assess _____
None _____
Regional _____ (Specify _____)
Distant _____ (Number _____ Proved _____)
Metastasis
None _____ Yes _____ Specify _____
Proved _____ Histologically confirmed Yes _____
No _____

Examination by _____ M.D.
Date _____

Histologic Type of Cancer

The predominant cancer is adenocarcinoma (98%).

Histologic Grade

[ ] G1 Well differentiated
[ ] G2 Moderately well differentiated
[ ] G3–G4 Poorly to very poorly differentiated

Postsurgical Resection–Pathologic Residual Tumor (R)

[ ] R0 No residual tumor
[ ] R1 Microscopic residual tumor
[ ] R2 Macroscopic residual tumor
Specify _____

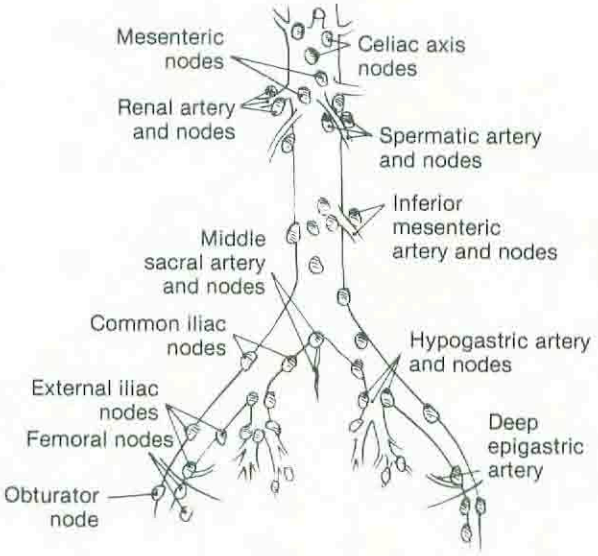
Performance Status of Host (H)

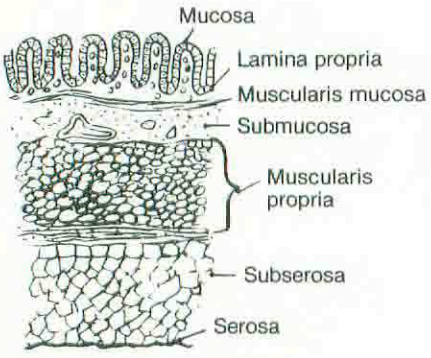
Several systems for recording a patient's activity and symptoms are in use and are more or less equivalent as follows:

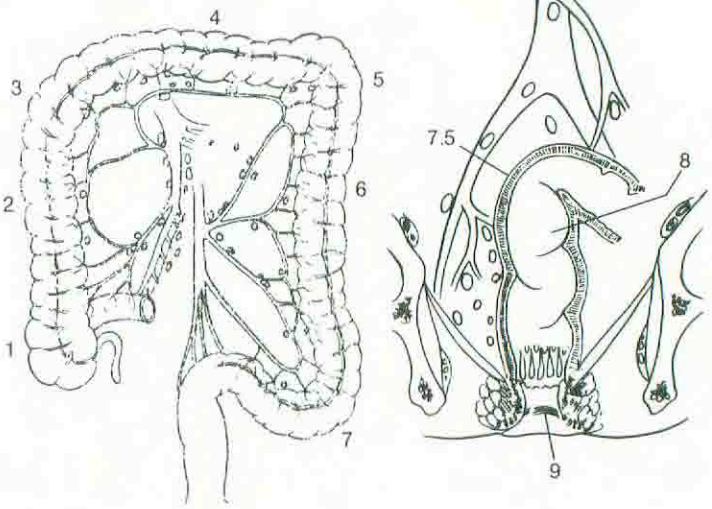
AJCC	Performance	ECOG Scale	Karnofsky Scale (%)
[ ] H0	Normal activity	0	90–100
[ ] H1	Symptomatic but ambulatory; cares for self	1	70–80
[ ] H2	Ambulatory more than 50% of time; occasionally needs assistance	2	50–60
[ ] H3	Ambulatory 50% or less of time; nursing care needed	3	30–40
[ ] H4	Bedridden; may need hospitalization	4	10–20

Anatomic Areas of Colon and Rectum

1. Cecum
2. Ascending colon
3. Hepatic flexure
4. Transverse colon
5. Splenic flexure
6. Descending colon
7. Sigmoid
7.5. Rectosigmoid
8. Rectum
9. Anal canal







For anatomic areas corresponding to numbers, see list above.

12

Liver and Biliary Tract

Staging of primary cancer of the liver, gallbladder, and biliary tract has just recently been proposed by a task force of the American Joint Committee. Suggestions for staging of these cancers are based on published data and the experience of members of the task force. Retrospective and prospective studies are needed to validate the proposed staging system in order to confirm the recommendations or suggest modifications. In the meantime, all pertinent information in individual cases which might contribute to staging should be recorded.

ANATOMY (ICD-O 155-156)

Primary Sites. The liver is the largest parenchymatous organ in the body and is situated in the right upper quadrant of the abdomen. It is divided into two major lobes. The intrahepatic ducts drain into large extrahepatic ducts, fusing into a single common bile duct, which drains into the duodenum through the ampulla of Vater. The gallbladder drains most often into the common hepatic bile duct, which is usually situated on the undersurface of the liver at the juncture of the right and left lobes. The lymphatics of the liver drain into regional hilar nodes and into those located along the common bile duct, and subsequently into the para-aortic lymph nodes.

TNM CLASSIFICATION

Primary Tumor (T)

TX Tumor is present but cannot be assessed.
T0 No evidence of tumor
T1 Small solitary tumor (<3.0 cm) confined to one lobe
T2 Large tumor (>3.0 cm) confined to one lobe
  T2a Single tumor nodule
  T2b Multiple tumor nodules (any size)
T3 Tumor involving both major lobes
  T3a Single tumor nodule (with direct extension)
  T4b Multiple tumor nodules
T4 Tumor invading adjacent organs

Nodal Involvement (N)

NX Nodes cannot be assessed.
N0 No histological evidence of metastasis to regional or distant lymph nodes
N1 Histologically confirmed spread to regional lymph nodes in porta hepatis
N2 Histologically confirmed spread to lymph nodes beyond porta hepatis

Distant Metastasis (M)

MX Not assessed
M0 No known metastasis
M1 Distant metastasis present
Specify site _____

Stage Grouping

Stage IA	T1, N0, M0, without cirrhosis
Stage IB	T1, N0, M0, with cirrhosis
Stage IIA	T2, N0, M0, without cirrhosis
Stage IIB	T2, N0, M0, with cirrhosis
Stage IIIA	T3, N0, N1; M0, without cirrhosis
Stage IIIB	T3, N0, N1; M0, with cirrhosis
Stage IVA	T4, N0-N2; M0, M1; without cirrhosis
Stage IVB	T4, N0-N2; M0, M1, with cirrhosis

Postsurgical Resection Residual Tumor (R)

R0 No residual tumor
R1 Microscopic residual tumor
R2 Macroscopic residual tumor

Other Site-Specific Information

Symptom [ ] Pain
[ ] Weight loss
Sign [ ] Jaundice
[ ] Ascites
[ ] Mass
Paraneoplastic syndrome; specify _____
Congenital or metabolic liver disease; specify _____

Laboratory Tests

Bilirubin _____ mg/dl
Alkaline phosphatase _____ U/ml (specify type of unit)
Albumin _____ mg/dl
ALT _____ U/ml
AFP _____ ng/ml
HBSAg Positive [ ] Negative [ ]
Other markers of HB infection; specify _____
Portal vein obstruction by angiography present [ ]

PERFORMANCE STATUS OF HOST (H)

Performance status of the host should be recorded because this information at times is pertinent to the treatment of the patient.

AJCC	PERFORMANCE	ECOG SCALE	KARNOFSKY SCALE (%)
H0	Normal activity	0	90-100
H1	Symptomatic but ambulatory; cares for self	1	70-80
H2	Ambulatory more than 50% of time; occasionally needs assistance	2	50-60
H3	Ambulatory 50% or less of time; nursing care needed	3	30-40
H4	Bedridden; may need hospitalization	4	10-20

HISTOPATHOLOGY

A. Epithelial Tumors
  A. Benign
    1. Liver cell adenoma (hepatocellular adenoma)
    2. Intrahepatic bile duct adenoma
    3. Intrahepatic bile duct cystadenoma
  B. Malignant
    4. Hepatocellular carcinoma (liver cell carcinoma)
    5. Hepatocellular carcinoma (fibrolamellar type)
    6. Cholangiocarcinoma (intrahepatic bile duct carcinoma)
    7. Mixed hepatocellular cholangiocarcinoma
    8. Bile duct cystadenocarcinoma
    9. Hepatoblastoma
      a. Predominantly fetal type
      b. Predominantly embryonal type
      c. Small cell undifferentiated type
    10. Undifferentiated carcinoma
B. Nonepithelial tumors
    11. Hemangioma
    12. Infantile hemangioendothelioma
    13. Embryonal sarcoma
    14. Other
      Specify _____
C. Miscellaneous tumors
    15. Teratoma
    16. Carcinosarcoma
    17. Other
      Specify _____
D. Unclassified tumors
E. Hemopoietic and lymphoid neoplasms

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Data Form for Cancer Staging

Patient identification
Name _____
Address _____
Hospital or clinic number _____
Age _____ Sex _____ Race _____

Institutional identification
Hospital or clinic _____
Address _____

Oncology Record

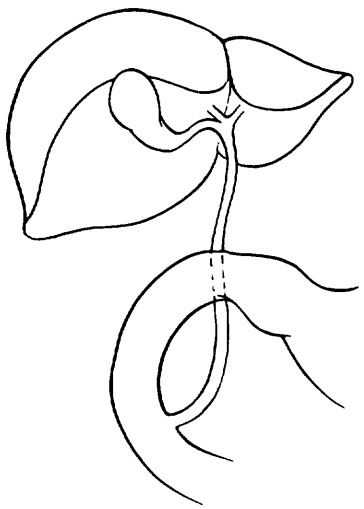
Anatomic site of cancer _____
Chronology of classification* [ ] Clinical-diagnostic (cTNM)
[ ] Surgical-evaluative (sTNM)
Date of classification _____

Histologic type _____ Grade (G) _____
[ ] Postsurgical resection–pathologic (pTNM)
[ ] Retreatment (rTNM) [ ] Autopsy (aTNM)

Definitions: TNM Classification

Primary Tumor (T)

[ ] TX Tumor is present but cannot be assessed.
[ ] T0 No evidence of tumor
[ ] T1 Small solitary tumor (<2.0 cm) confined to one lobe
[ ] T2 Large tumor (>2.0 cm) confined to one lobe
  [ ] T2a Single tumor nodule
  [ ] T2b Multiple tumor nodules (any size)
[ ] T3 Tumor involving both major lobes
  [ ] T3a Single tumor nodule (with direct extension)
  [ ] T3b Multiple tumor nodules
[ ] T4 Tumor invading adjacent organs



Indicate on diagram primary tumor and regional nodes involved.

Nodal Involvement (N)

[ ] NX Nodes cannot be assessed.
[ ] N0 No histological evidence of metastasis to regional or distant lymph nodes
[ ] N1 Histologically confirmed spread to regional lymph nodes in porta hepatis
[ ] N2 Histologically confirmed spread to lymph nodes beyond porta hepatis

* Use a separate form each time a case is staged.

Distant Metastasis (M)

[ ] MX Not assessed
[ ] M0 No known metastasis
[ ] M1 Distant metastasis present
Specify _____

Stage Grouping

[ ] Stage IA T1, N0, M0, without cirrhosis
[ ] Stage IB T1, N0, M0, with cirrhosis
[ ] Stage IIA T2, N0, M0, without cirrhosis
[ ] Stage IIB T2, N0, M0, with cirrhosis
[ ] Stage IIIA T3, N0, N1; M0, without cirrhosis
[ ] Stage IIIB T3, N0, N1; M0, with cirrhosis
[ ] Stage IVA T4, N0–N2; M0, M1; without cirrhosis
[ ] Stage IVB T4, N0–N2; M0, M1; with cirrhosis

Site-Specific Information

Symptom [ ] Pain
[ ] Weight loss
Sign [ ] Jaundice
[ ] Ascites
[ ] Mass
Paraneoplastic syndrome
Specify _____
Congenital or metabolic liver disease; specify _____

Laboratory Tests

Bilirubin _____ mg/dl
Alkaline phosphatase _____ U/ml (specify type of unit)
Albumin _____ mg/dl
ALT _____ U/ml
HBSAg Positive [ ] Negative [ ]
Other markers of HB infection
Specify _____
Portal vein obstruction by angiography present [ ]

Histologic Type of Cancer

A. Epithelial Tumors
  [ ] Benign
    [ ] Liver cell adenoma (hepatocellular adenoma)
    [ ] Intrahepatic bile duct adenoma
    [ ] Intrahepatic bile duct cystadenoma

Examination by _____ M.D.
Date _____

[ ] Malignant
  [ ] Hepatocellular carcinoma (liver cell carcinoma)
  [ ] Hepatocellular carcinoma (fibrolamellar type)
  [ ] Cholangiocarcinoma (intrahepatic bile duct carcinoma)
  [ ] Bile duct cystadenocarcinoma
  [ ] Hepatoblastoma
  [ ] Undifferentiated carcinoma

B. Nonepithelial Tumors
  [ ] Hemangioma
  [ ] Infantile hemangioendothelioma
  [ ] Embryonal sarcoma
  [ ] Other
    Specify _____

C. Miscellaneous Tumors
  [ ] Teratoma
  [ ] Carcinosarcoma
  [ ] Other
    Specify _____

D. Unclassified tumors

E. Hemopoietic and lymphoid neoplasms

Postsurgical Resection Residual Tumor (R)

[ ] R0 No residual tumor
[ ] R1 Microscopic residual tumor
[ ] R2 Macroscopic residual tumor
  Specify _____

Tumor Grade (G)

[ ] G1 Well differentiated
[ ] G2 Moderately well differentiated
[ ] G3–G4 Poorly differentiated

Performance Status of Host (H)

Several systems for recording a patient's activity and symptoms are in use and are more or less equivalent as follows:

AJCC	*Performance*	*ECOG Scale*	*Karnofsky Scale (%)*
[ ] H0	Normal activity	0	90–100
[ ] H1	Symptomatic but ambulatory; cares for self	1	70–80
[ ] H2	Ambulatory more than 50% of time; occasionally needs assistance	2	50–60
[ ] H3	Ambulatory 50% or less of time; nursing care needed	3	30–40
[ ] H4	Bedridden; may need hospitalization	4	10–20

13

Gallbladder

TNM CLASSIFICATION (ICD-O 156)

Primary Tumor (T)

TX Presence of tumor cannot be assessed.
T0 No evidence of tumor
Tis Carcinoma *in situ*
T1 Invasion limited to the submucosa or to the muscle layer
T2 Invasion limited to perimuscular connective tissue; no extension beyond serosa or into liver
T3 Involvement of all layers and direct extension beyond serosa or into one adjacent organ, or both (must be less than 2 cm into the liver)
T4 Involvement of all layers and direct extension 2 cm or more into liver or into two or more adjacent organs (includes stomach, duodenum, colon, pancreas, omentum, extrahepatic bile ducts, and any involvement of liver)

Nodal Involvement (N)

NX Minimum requirements to assess the regional nodes cannot be met.
N0 No histologic evidence of metastasis to regional lymph nodes
N1 Histologically proven metastasis to first station regional lymph nodes
N2 Histologically proven metastasis to second station regional lymph nodes

Distant Metastasis (M)

MX Not assessed
M0 No (known) distant metastasis
M1 Distant metastasis present

Stage Grouping

Stage 0	Tis, N0, M0
Stage I	T1, T2; N0, M0
Stage II	T3, T4; N0, M0
Stage III	T3, T4; N1, N2; M0
Stage IV	T3, T4; N0-N2; M1

Postsurgical Resection Residual Tumor (R)

R0 No residual tumor
R1 Microscopic residual tumor
R2 Macroscopic residual tumor
Specify _____

Other Site-Specific Information

Pain [ ] Yes
[ ] No
Duration _____
Jaundice [ ] Yes
[ ] No
Duration _____
Weight loss [ ] Yes
[ ] No
Pounds _____

Laboratory Tests

Alkaline phosphatase ___ U/ml (specify type of unit)
Total bilirubin _____ mg/dl
Alpha-fetoprotein (AFP) _____ ng/ml
Carcinoembryonic antigen (CEA) _____ ng/ml

HISTOPATHOLOGY

A. Malignant epithelial tumors
   1. Adenocarcinoma
      a. Well differentiated
      b. Papillary
      c. Intestinal type
      d. Pleomorphic giant cell
      e. Poorly differentiated, small cell
      f. Signet ring cell
      g. Clear cell
      h. Colloid
      i. With choriocarcinoma-like areas
   2. Squamous cell carcinoma
   3. Adenosquamous carcinoma
   4. Oat cell carcinoma
   5. Others
B. Malignant mesenchymal tumors
   1. Embryonal rhabdomyosarcoma (sarcoma botryoides)
   2. Leiomyosarcoma
   3. Malignant fibrous histiocytoma
   4. Others
C. Miscellaneous
   1. Carcinosarcoma
   2. Carcinoid tumor
   3. Malignant lymphoma
   4. Malignant melanoma
   5. Others

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Data Form for Cancer Staging

Patient identification
Name _____
Address _____
Hospital or clinic number _____
Age _____ Sex _____ Race _____

Institutional identification
Hospital or clinic _____
Address _____

Oncology Record

Anatomic site of cancer _____
Chronology of classification* [ ] Clinical-diagnostic (cTNM)
[ ] Surgical-evaluative (sTNM)
Date of classification _____

Histologic type _____ Grade (G)† _____
[ ] Postsurgical resection–pathologic (pTNM)
[ ] Retreatment (rTNM) [ ] Autopsy (aTNM)

Definitions: TNM Classification

Primary Tumor (T)

[ ] TX Presence of tumor cannot be assessed.
[ ] T0 No evidence of tumor
[ ] Tis Carcinoma *in situ*
[ ] T1 Invasion limited to the lamina propria or to the muscle layer
[ ] T2 Invasion limited to perimuscular connective tissue; no extension beyond serosa or into liver
[ ] T3 Involvement of all layers and direct extension beyond serosa or into one adjacent organ, or both (must be less than 2 cm into the liver)
[ ] T4 Involvement of all layers and direct extension 2 cm or more into liver or into 2 or more adjacent organs (includes stomach, duodenum, colon, pancreas, omentum, extrahepatic bile ducts, and any involvement of liver)

Nodal Involvement (N)

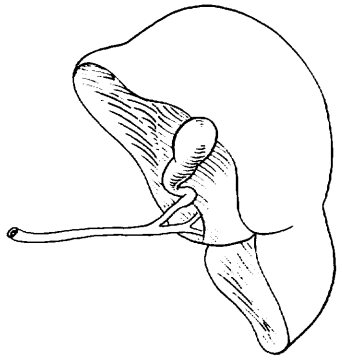
[ ] NX Minimum requirements to assess the regional nodes cannot be met.
[ ] N0 No histologic evidence of metastasis to regional lymph nodes
[ ] N1 Histologically proven metastasis to first station regional lymph nodes
[ ] N2 Histologically proven metastasis to second station regional lymph nodes

Distant Metastasis (M)

[ ] MX Not assessed
[ ] M0 No (known) distant metastasis
[ ] M1 Distant metastasis present

Stage Grouping

[ ] Stage 0 Tis, N0, M0
[ ] Stage I T1, T2; N0, M0
[ ] Stage II T3, T4; N0, M0
[ ] Stage III T3, T4; N1, N2; M0
[ ] Stage IV T3, T4; N0–N2; M1



Indicate on diagram primary tumor and regional nodes involved.

Site-Specific Information

Pain [ ] Yes
[ ] No
Duration _____
Jaundice [ ] Yes
[ ] No
Duration _____
Weight loss [ ] Yes
[ ] No
Pounds _____

Laboratory tests

Alkaline phosphatase _____ U/ml (specify type of unit)
Total bilirubin _____ mg/dl
Alpha-fetoprotein (AFP) _____ ng/ml
Carcinoembryonic antigen (CEA) _____ ng/ml

Histologic Type of Cancer

A. Malignant epithelial tumors
[ ] Adenocarcinoma
[ ] Well differentiated
[ ] Papillary
[ ] Intestinal type
[ ] Pleomorphic giant cell
[ ] Poorly differentiated, small cell

Examination by _____ M.D.
Date _____

*Use a separate form each time a case is staged.
†See reverse side for additional information.

[ ] Signet ring cell
[ ] Clear cell
[ ] Colloid
[ ] With choriocarcinoma-like areas
[ ] Squamous cell carcinoma
[ ] Adenosquamous carcinoma
[ ] Oat cell carcinoma
[ ] Others

B. Malignant mesenchymal tumors
[ ] Embryonal rhabdomyosarcoma (sarcoma botryoides)
[ ] Leiomyosarcoma
[ ] Malignant fibrous histiocytoma
[ ] Others

C. Miscellaneous
[ ] Carcinosarcoma
[ ] Carcinoid tumor
[ ] Malignant lymphoma
[ ] Malignant melanoma
[ ] Others

Postsurgical Resection Residual Tumor (R)

[ ] R0 No residual tumor
[ ] R1 Microscopic residual tumor
[ ] R2 Macroscopic residual tumor
Specify _____

Tumor Grade (G)

[ ] G1 Well differentiated
[ ] G2 Moderately well differentiated
[ ] G3–G4 Poorly differentiated

Performance Status of Host (H)

Several systems for recording a patient's activity and symptoms are in use and are more or less equivalent as follows:

AJCC	*Performance*	*ECOG Scale*	*Karnofsky Scale (%)*
[ ] H0	Normal activity	0	90–100
[ ] H1	Symptomatic but ambulatory; cares for self	1	70–80
[ ] H2	Ambulatory more than 50% of time; occasionally needs assistance	2	50–60
[ ] H3	Ambulatory 50% or less of time; nursing care needed	3	30–40
[ ] H4	Bedridden; may need hospitalization	4	10–20

14

Extrahepatic Bile Ducts (Exclusive of Ampulla and Intrapancreatic Bile Duct)

TNM CLASSIFICATION (ICD-O 156.1)

Primary Tumor (T)

TX Presence of tumor cannot be assessed.
T0 No evidence of tumor
Tis Carcinoma *in situ*
T1 Invasion limited to wall
T2 Invasion limited to periductal connective tissues
T3 Involvement of all layers and direct extension into one adjacent major vessel or organ
T4 Involvement of all layers and direct extension beyond secondary ductal bifurcation or into two or more adjacent organs including the following:
Liver
Pancreas
Duodenum
Stomach
Colon
Omentum
Gallbladder

Nodal Involvement (N)

NX Minimum requirements to assess regional nodes cannot be met.
N0 No histologic evidence of metastasis to regional lymph nodes
N1 Histologically proven metastasis to first station regional lymph nodes
N2 Histologically proven metastasis to second station regional lymph nodes

Distant Metastasis (M)

MX Not assessed
M0 No (known) distant metastasis
M1 Distant metastasis

Stage Grouping

Stage 0	Tis, N0, M0
Stage I	T1, T2; N0, M0
Stage II	T3, T4; N0, M0
Stage III	T3, T4; N1, N2; M0
Stage IV	T3, T4; N0-N2; M1

Postsurgical Resection Residual Tumor (R)

R0 No residual tumor
R1 Microscopic residual tumor
R2 Macroscopic residual tumor
Specify _____

Other Site-Specific Information

Location of tumor [ ] Upper third
[ ] Middle third
[ ] Lower third
[ ] Diffuse

Duct obstruction [ ] Complete
[ ] Incomplete

Jaundice [ ] Yes
[ ] No
Duration _____

Cholangiographic appearance [ ] Papillary or polypoid
[ ] Nodular or protuberant
[ ] Diffusely infiltrating or sclerosing
[ ] Annular stricture or constriction
[ ] Not classifiable

Laboratory Tests

Bilirubin _____ mg/dl
Alkaline phosphatase _____ U/ml (specify type of unit)
Carcinoembryonic antigen (CEA) _____ ng/ml
Alpha-fetoprotein (AFP) _____ ng/ml

HISTOPATHOLOGY

A. Malignant epithelial tumors
   1. Adenocarcinoma
      a. Well differentiated
      b. Papillary
      c. Intestinal type
      d. Pleomorphic giant cell
      e. Poorly differentiated, small cell
      f. Signet ring cell
      g. Clear cell
      h. Colloid
      i. With choriocarcinoma-like areas
   2. Squamous cell carcinoma
   3. Adenosquamous carcinoma
   4. Oat cell carcinoma
   5. Others
B. Malignant mesenchymal tumors
   1. Embryonal rhabdomyosarcoma (sarcoma botryoides)
   2. Leiomyosarcoma
   3. Malignant fibrous histiocytoma
   4. Others
C. Miscellaneous
   1. Carcinosarcoma
   2. Carcinoid tumor
   3. Malignant lymphoma
   4. Malignant melanoma
   5. Others

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EXTRAHEPATIC BILE DUCTS (ICD-O 156.1)

Data Form for Cancer Staging

Patient identification
Name _____
Address _____
Hospital or clinic number _____
Age _____ Sex _____ Race _____

Institutional identification
Hospital or clinic _____
Address _____

Oncology Record

Anatomic site of cancer _____
Chronology of classification* [ ] Clinical-diagnostic (cTNM)
[ ] Surgical-evaluative (sTNM)
Date of classification _____

Histologic type† _____ Grade (G) _____
[ ] Postsurgical resection–pathologic (pTNM)
[ ] Retreatment (rTNM) [ ] Autopsy (aTNM)

Definitions: TNM Classification

Primary Tumor (T)

[ ] TX Presence of tumor cannot be assessed.
[ ] T0 No evidence of tumor
[ ] Tis Carcinoma *in situ*
[ ] T1 Invasion limited to wall
[ ] T2 Invasion limited to periductal connective tissues
[ ] T3 Involvement of all layers and direct extension into one adjacent major vessel or organ
[ ] T4 Involvement of all layers and direct extension beyond secondary ductal bifurcation or into two or more adjacent organs including: liver, pancreas, duodenum, stomach, colon, omentum, gallbladder

Nodal Involvement (N)

[ ] NX Minimum requirements to assess regional nodes cannot be met.
[ ] N0 No histologic evidence of metastasis to regional lymph nodes
[ ] N1 Histologically proven metastasis to first station regional nodes
[ ] N2 Histologically proven metastasis to second station regional lymph nodes

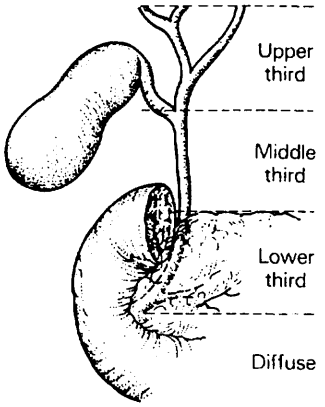
Distant Metastasis (M)

[ ] MX Not assessed
[ ] M0 No (known) distant metastasis
[ ] M1 Distant metastasis

Stage Grouping

[ ] Stage 0 Tis, N0, M0
[ ] Stage I T1, T2; N0, M0
[ ] Stage II T3, T4; N0, M0
[ ] Stage III T3, T4; N1, N2; M0
[ ] Stage IV T3, T4; N0–N2; M1

*Use a separate form each time a case is staged.
†See reverse side for additional information.



Indicate on diagram primary tumor and regional nodes involved.

Site-Specific Information

Location of tumor [ ] Upper
[ ] Middle
[ ] Lower
[ ] Diffuse
Duct obstruction [ ] Complete
[ ] Incomplete
Jaundice [ ] Yes
[ ] No
Duration _____
Cholangiographic appearance [ ] Papillary or polypoid
[ ] Nodular or protuberant
[ ] Diffusely infiltrating or sclerosing
[ ] Annular stricture or constriction
[ ] Not classifiable

Laboratory Tests

Bilirubin _____ mg/dl
Alkaline phosphatase _____ U/ml (specify type of unit)
Carcinoembryonic antigen (CEA) _____ ng/ml
Alpha-fetoprotein (AFP) _____ ng/ml

Examination by _____ M.D.
Date _____

Histologic Type of Cancer

A. Malignant epithelial tumor
- [ ] Adenocarcinoma
  - [ ] Well differentiated
  - [ ] Papillary
  - [ ] Intestinal type
  - [ ] Pleomorphic giant cell
  - [ ] Poorly differentiated, small cell
  - [ ] Signet ring cell
  - [ ] Clear cell
  - [ ] Colloid
  - [ ] With choriocarcinoma-like areas
- [ ] Squamous cell carcinoma
- [ ] Adenosquamous carcinoma
- [ ] Oat cell carcinoma
- [ ] Others

B. Malignant mesenchymal tumors
- [ ] Embryonal rhabdomyosarcoma (sarcoma botryoides)
- [ ] Leiomyosarcoma
- [ ] Malignant fibrous histiocytoma
- [ ] Others

C. Miscellaneous
- [ ] Carcinosarcoma
- [ ] Carcinoid tumor
- [ ] Malignant lymphoma
- [ ] Malignant melanoma
- [ ] Others

Postsurgical Resection Residual Tumor (R)

[ ] R0 No residual tumor
[ ] R1 Microscopic residual tumor
[ ] R2 Macroscopic residual tumor
Specify _____

Tumor Grade (G)

[ ] G1 Well differentiated
[ ] G2 Moderately differentiated
[ ] G3–G4 Poorly differentiated

Performance Status of Host (H)

Several systems for recording a patient's activity and symptoms are in use and are more or less equivalent as follows:

AJCC	*Performance*	*ECOG Scale*	*Karnofsky Scale (%)*
[ ] H0	Normal activity	0	90–100
[ ] H1	Symptomatic but ambulatory; cares for self	1	70–80
[ ] H2	Ambulatory more than 50% of time; occasionally needs assistance	2	50–60
[ ] H3	Ambulatory 50% or less of time; nursing care needed	3	30–40
[ ] H4	Bedridden; may need hospitalization	4	10–20

15

Pancreas

Collection of objective data to classify and stage cancer of the exocrine pancreas is still in progress. A protocol exists and can be obtained from the AJCC.* The following classification is recommended to be field-tested prospectively and evaluated for future refinement.

ANATOMY (ICD-O 157)

Primary Site. The *pancreas* is a long, lobulated structure that lies transversely in the posterior abdomen, located retroperitoneally in the concavity of the duodenum on its right end and touching the spleen on its left end. The shape of the pancreas may be compared to the letter "J" placed sideways. It is divisible into a head with an uncinate process, a neck, a body, and a tail.

Nodal Stations. There is a rich lymphatic network surrounding the pancreas, with left splenic and superior and inferior right side truncal drainage. The first station nodes include celiac, splenic, suprapancreatic, left gastropancreatic, hepatic artery, inferior pancreatic, juxta-aortic, anterior pancreatic duodenal, and posterior pancreatic duodenal. Juxtaregional nodes include the inferior portion of the para-aortic nodal drainage and mediastinal and mesenteric nodes.

Metastatic Sites. Distant spread occurs mainly to liver and lungs, with a lesser degree of involvement of bones and brain and other anatomic sites.

RULES FOR CLASSIFICATION

Clinical-Diagnostic Staging. The pancreas is inaccessible to physical examination. Laboratory and radiographic procedures are available but are largely diagnostic and investigative. These studies include upper gastrointestinal x-ray films, hypotonic duodenography, computed tomography (CT), pharmacodynamic angiography, ultrasonic scanning, aspiration biopsy or cytology of the pancreas, radioisotopic scanning of the pancreas,

*The American Joint Committee Office, 55 East Erie Street, Chicago, IL 60611

endoscopic retrograde cholangiopancreatography, and laparoscopy. Routine procedures to identify metastases include roentgenogram of the chest, SMA-12, and liver scan (radionuclide or CT).

Surgical-Evaluative Staging. Laparotomy and surgical exploration of the pancreas is a more accurate means of assessing the true anatomic extent of the tumor. Fine needle aspiration biopsy or biopsy of the tumor and associated nodes may confirm the anatomic and pathologic extent of the cancer.

Postsurgical Resection-Pathologic Staging. Complete or subtotal resection of the pancreas and its tumor and associated nodes with pathologic analysis is assigned to the pathologic classification.

Retreatment Staging. Biopsy is essential to establish recurrence of the disease, and complete workup of metastatic disease in other compartments is recommended.

TNM CLASSIFICATION

Primary Tumor (T)

TX Minimum requirements to assess the primary tumor cannot be met.
T0 No evidence of primary tumor
T1 No direct extension of the primary tumor beyond the pancreas
T2 Limited direct extension to duodenum, bile ducts, or stomach, still possibly permitting tumor resection
T3 Further direct extension (incompatible with surgical resection)

Regional Lymph Node Involvement (N)

NX Minimum requirements to assess the regional nodes cannot be met.
N0 Regional nodes not involved
N1 Regional nodes involved

Distant Metastasis (M)

MX Minimum requirements to assess the presence of distant metastasis cannot be met.
M0 No (known) distant metastasis
M1 Distant metastasis present
Specify _____

Specify sites according to the following notations:

Pulmonary	PUL	Bone marrow	MAR
Osseous	OSS	Pleura	PLE
Hepatic	HEP	Skin	SKI
Brain	BRA	Eye	EYE
Lymph nodes	LYM	Other	OTH

Add + to the abbreviated notation to indicate that the pathology (p) is proved.

POSTSURGICAL TREATMENT RESIDUAL TUMOR (R)

R0 No residual tumor
R1 Microscopic residual tumor
R2 Macroscopic residual tumor
Specify _____

STAGE GROUPING

Stage I T1, T2, N0, M0; no (or unknown) direct extension, or limited direct extension of tumor to adjacent viscera, with no (or unknown) regional node extension and absence of distant metastases. *Limited direct extension* is defined as involvement of organs adjacent to the pancreas (duodenum, common bile duct, or stomach) that could be removed *en bloc* with the pancreas if a curative resection were attempted.
Stage II T1-T3, N1, M0; regional node metastases tumor into adjacent viscera with no (or unknown) lymph node involvement and no distant metastases, which preclude surgical resection.
Stage III T1-T3, N1, M0; regional node metastases without clinical evidence of distant metastases
Stage IV T1-T3, N0-N1, M1; distant metastatic disease in liver or other sites

HISTOPATHOLOGY

Duct cell adenocarcinoma
Giant cell carcinoma (pleomorphic carcinoma)
Giant cell carcinoma (epulis type) with osteoid
Adenosquamous carcinoma
Microadenocarcinoma
Mucinous (colloid) carcinoma
Cystoadenocarcinoma
Acinar cell adenocarcinoma
Pancreatoblastoma
Papillary cystic tumor
Mixed type
Unclassified
Specify _____

TUMOR GRADE (G)

G1 Well differentiated
G2 Moderately well differentiated
G3-G4 Poorly to very poorly differentiated

Use whichever indicator is most appropriate (term or G + number).

BIBLIOGRAPHY

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Data Form for Cancer Staging

Patient identification
Name _____
Address _____
Hospital or clinic number _____
Age _____ Sex _____ Race _____

Institutional identification
Hospital or clinic _____
Address _____

Oncology Record

Anatomic site of cancer _____
Chronology of classification* [ ] Clinical-diagnostic (cTNM)
[ ] Surgical-evaluative (sTNM)
Date of classification _____

Histologic type _____ Grade (G)† _____
[ ] Postsurgical resection–pathologic (pTNM)
[ ] Retreatment (rTNM) [ ] Autopsy (aTNM)

Definitions: TNM Classification

Primary Tumor (T)

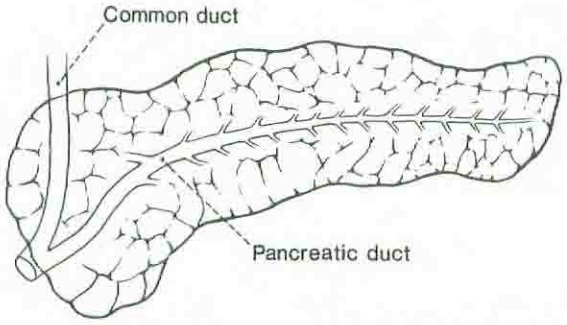
[ ] TX Minimum requirements to assess the primary tumor cannot be met.
[ ] T1 No direct extension of the primary tumor beyond the pancreas
[ ] T2 Limited direct extension to duodenum, bile ducts, or stomach, still possibly permitting tumor resection
[ ] T3 Further direct extension (incompatible with surgical resection)

Nodal Involvement (N)

[ ] NX Minimum requirements to assess the regional nodes cannot be met.
[ ] N0 Regional nodes not involved
[ ] N1 Regional nodes involved

Distant Metastasis (M)

[ ] MX Minimum requirements to assess the presence of distant metastasis cannot be met.
[ ] M0 No (known) distant metastasis
[ ] M1 Distant metastasis present
Specify _____



Indicate on diagram primary tumor and regional nodes involved.

Location in Pancreas

[ ] Head
[ ] Body
[ ] Tail
[ ] Diffuse
Size (largest diameter) _____ cm

*Use a separate form each time a case is staged.
†See reverse side for additional information.

Nodes

Number positive _____
Location _____

Stage Grouping

[ ] Stage I T1, T2; N0, M0
[ ] Stage II T3, N0, M0
[ ] Stage III T1–T3, N1, M0
[ ] Stage IV T1–T3, N0–N1, M1

Other Site-Specific Information

Diagnostic Confirmation

History
[ ] Pain Duration _____
[ ] Jaundice Duration _____
[ ] Weight loss Duration _____
[ ] Diabetes mellitus Duration _____

Physical findings
[ ] Abdominal mass
[ ] Ascitic fluid

Roentgenogram
[ ] Arteriography
[ ] CT scan
[ ] Endoscopic retrograde cholangiopancreatography (ERCP)
Ultrasound results _____

Cytology
[ ] Duodenal fluid
[ ] ERCP
[ ] Needle
[ ] Ascitic fluid

Pathology
[ ] From pancreas
[ ] Extrapancreatic
Type _____

Histopathology

[ ] Duct cell adenocarcinoma
[ ] Giant cell carcinoma (pleomorphic carcinoma)
[ ] Giant cell carcinoma (epulis type) with osteoid
[ ] Adenosquamous carcinoma
[ ] Microadenocarcinoma
[ ] Mucinous (colloid) carcinoma
[ ] Cystoadenocarcinoma
[ ] Acinar cell adenocarcinoma
[ ] Pancreatoblastoma
[ ] Papillary cystic tumor
[ ] Mixed type
[ ] Unclassified
Specify _____

Examination by _____ M.D.
Date _____

Postsurgical Resection Residual Tumor (R)

[ ] R0 No residual tumor
[ ] R1 Microscopic residual tumor
[ ] R2 Macroscopic residual tumor
Specify _____

Tumor Grade (G)

[ ] G1 Well differentiated
[ ] G2 Moderately well differentiated
[ ] G3–G4 Poorly to very poorly differentiated

Performance Status of Host (H)

Several systems for recording a patient's activity and symptoms are in use and are more or less equivalent as follows:

AJCC	*Performance*	*ECOG Scale*	*Karnofsky Scale (%)*
[ ] H0	Normal activity	0	90–100
[ ] H1	Symptomatic but ambulatory; cares for self	1	70–80
[ ] H2	Ambulatory more than 50% of time; occasionally needs assistance	2	50–60
[ ] H3	Ambulatory 50% or less of time; nursing care needed	3	30–40
[ ] H4	Bedridden; may need hospitalization	4	10–20

LUNG

16

ANATOMY (ICD-O 162)

Primary Site. The mucosa lining the bronchus is the usual site of origin of cancer of the lung. The trachea, which lies in the anterior mediastinum, divides into right and left main bronchi that extend into the right and left lungs, respectively, and then divide into lobar bronchi for the upper, middle, and lower lobes on the right and the upper and lower lobes on the left. The lungs are encased in membranes called visceral pleura and the chest cavity is lined by a similar membrane called parietal pleura. The potential space between these two membranes is the pleural space.

Nodal Stations. The first station lymph nodes are the intrapulmonary, peribronchial, and hilar lymph nodes, which are contained within the visceral pleural reflections. Second station lymph nodes are those in the mediastinum and may be paraesophageal, subcarinal, paratracheal, aortic, and pretracheal or retrotracheal. Involvement of scalene and more distant nodes is considered distant metastasis.

Metastatic Sites. Lung cancer may metastasize to any distant site, the more common being scalene, supraclavicular, and other cervical lymph nodes, liver, brain, bones, adrenals, kidney, and contralateral lung, including contralateral hilar lymph nodes.

RULES FOR CLASSIFICATION

Clinical-Diagnostic Staging. This should be based on the anatomic extent of the disease that can be detected by examination before thoracotomy or the implementation of any treatment. Such an examination may include a medical history, physical examination, routine and special roentgenograms, endoscopic examinations including bronchoscopy, esophagoscopy, mediastinoscopy, mediastinotomy, thoracentesis, or thoracoscopy, and any other examinations, including those used to demonstrate the presence of extrathoracic metastasis.

Postsurgical Resection-Pathologic Staging. The surgical pathology report and all other available data should be used to assign

a postsurgical treatment classification to those patients who have a resection.

Surgical-Evaluative Staging. This should be based on all of the data obtained for the clinical-diagnostic classification and on information obtained at the time of exploratory thoracotomy, including biopsy but not including that information obtained by complete examination of a therapeutically resected specimen.

Retreatment Staging. In the course of follow-up examinations, a patient may manifest evidence of progressive disease indicating treatment failure. Before initiating further treatment, the extent of tumor should be reassessed carefully, using all available information, and the patient should again be staged under the retreatment classification.

Autopsy Staging. In case of death of a lung cancer patient, the extent of the cancer, if any, found at autopsy may be recorded by the TNM system and an autopsy stage may be reported.

TNM CLASSIFICATION

Primary Tumor (T)

TX Tumor either proven by the presence of malignant cells in bronchopulmonary secretions but not visualized roentgenographically or bronchoscopically *or* cannot be assessed

T0 No evidence of primary tumor

Tis Carcinoma *in situ*

T1 A tumor that is 3.0 cm or less in greatest diameter, surrounded by lung or visceral pleura, and without evidence of invasion proximal to a lobar bronchus at bronchoscopy

T2 A tumor more than 3.0 cm in greatest diameter or a tumor of any size that either invades the visceral pleura or has associated atelectasis or obstructive pneumonitis extending to the hilar region. At bronchoscopy, the proximal extent of demonstrable tumor must be within a lobar bronchus or at least 2.0 cm distal to the carina. Any associated atelectasis or obstructive pneumonitis must involve less than an entire lung, and there must be no pleural effusion.

T3 A tumor of any size with direct extension into an adjacent structure such as the parietal pleura or chest wall, the diaphragm, or the mediastinum and its contents; a tumor bronchoscopically demonstrable to involve a main bronchus less than 2.0 cm distal to the carina; any tumor associated with atelectasis or obstructive pneumonitis of an entire lung or pleural effusion

Nodal Involvement (N)

NX Minimum requirements to assess the regional nodes cannot be met.

N0 No evidence of involvement of regional lymph nodes

N1 Metastasis to lymph nodes in the peribronchial or the ipsilateral hilar region, or both, including direct extension

N2 Metastasis to lymph nodes in the mediastinum

Distant Metastasis (M)

MX Minimum requirements to assess the presence of distant metastasis cannot be met.

M0 No evidence of distant metastasis

M1 Distant metastasis present
Specify _____

Specify sites according to the following notations:

Pulmonary	PUL	Bone marrow	MAR
Osseous	OSS	Pleura	PLE
Hepatic	HEP	Skin	SKI
Brain	BRA	Eye	EYE
Lymph nodes	LYM	Other	OTH

POSTSURGICAL TREATMENT RESIDUAL TUMOR (R)

R0 No residual tumor

R1 Microscopic residual tumor

R2 Macroscopic residual tumor
Specify _____

STAGE GROUPING

Occult Stage: TX, N0, M0

An occult carcinoma with bronchopulmonary secretions containing malignant cells but without other evidence of the primary tumor or evidence of metastasis to the regional lymph nodes or distant metastasis

Stage I: Tis, N0, M0

Carcinoma *in situ*

T1, N0, M0
T1, N1, M0
T2, N0, M0

A tumor that can be classified T1 without any metastasis or with metastasis to the lymph nodes in the peribronchial or ipsilateral hilar region only, or a tumor that can be classified T2 without any metastasis to nodes or distant metastasis

Note: TX, N1, M0 and T0, N1, M0 are also theoretically possible, but such a clinical diagnosis would be difficult if not impossible to make. If such a diagnosis is made, it would be included in stage I.

Stage II: T2, N1, M0

A tumor classified as T2 with metastasis to the lymph nodes in the peribronchial or ipsilateral hilar region only

Stage III

T3 with any N or M
N2 with any T or M
M1 with any T or N

Any tumor more extensive than T2, any tumor with metastasis to the lymph nodes in the mediastinum, or any tumor with distant metastasis

Note: Staging grouping is significant for all cell types listed under Histopathology except undifferentiated small cell (oat cell) carcinoma in which there is no significant relation between stage and survival rates. Nevertheless, the anatomic extent of small cell cancers may be recorded by the TNM system for future reference. This system has not been applied to the rarer lung tumors such as carcinoids, cylindromas, mucoepidermoids, and so forth.

HISTOPATHOLOGY

There are four major cells types of lung cancer:

1. Squamous cell (epidermoid) carcinoma
2. Adenocarcinoma including alveolar cell or terminal bronchiolar carcinoma
3. Undifferentiated large cell carcinoma
4. Undifferentiated small cell carcinoma including oat cell carcinoma

Tumor Grade (G)

G1	Well differentiated
G2	Moderately well differentiated
G3-G4	Poorly to very poorly differentiated

Use whichever indicator is most appropriate (term or G + number).

PERFORMANCE STATUS OF HOST (H)

Several systems for recording a patient's activity and symptoms are in use and are more or less equivalent as follows:

AJCC	PERFORMANCE	ECOG SCALE	KARNOFSKY SCALE (%)
H0	Normal activity	0	90-100
H1	Symptomatic but ambulatory; cares for self	1	70-80
H2	Ambulatory more than 50% of time; occasionally needs assistance	2	50-60
H3	Ambulatory 50% or less of time; nursing care needed	3	30-40
H4	Bedridden; may need hospitalization	4	10-20

SOME SUGGESTIONS FOR THE APPLICATION OF THE LUNG CANCER STAGING SYSTEM

The TNM system can be applied to most patients with lung cancer with certainty and the proper stage can be designated with consistency. One group of 15 patients was staged independently by 26 physicians and research assistants with more than 90% consistency in the TNM designation and the assignment of a stage for each patient.

However, it has become apparent that there are some areas of uncertainty and disagreement about the application of the system to certain confusing combinations of circumstances, and the following suggestions are made in the hope that they will increase the consistency of staging patients with lung cancer.

T0 is to be used when there is no demonstrable evidence of the primary tumor in the lung but there is evidence of metastatic cancer in a lymph node or elsewhere justifying an N1, N2, or M1 designation and it is concluded clinically that the primary is in the lung. T0 may also be used in the retreatment staging of a patient who had resection of his cancer and has proof of recurrence in the regional lymph nodes or a distant metastasis without evidence of recurrence in the lung.

TX is used when a patient has a positive sputum for malignant cells but a negative roentgenogram of the chest and a negative bronchoscopic examination. Such a designation is usually temporary because in most cases the source of the positive sputum can be localized and a proper T designation can be assigned. TX may also be used in the retreatment staging when it is impossible to evaluate the extent of residual primary tumor after radiotherapy and the development of radiation pneumonitis and fibrosis in the field of the radiotherapy.

Multiple synchronous tumors of different histologic cell types should be considered separate primary lung cancers and each one should be staged separately. If they are of the same cell type, they may be separate primaries or one may be the primary and the other one a metastasis. If there is evidence that both are primary lesions (*e.g.*, typical transition from normal bronchial epithelium to carcinoma *in situ* to invasive carcinoma), they should be staged separately even though they are of the same cell type. If there is inadequate evidence to support a diagnosis of separate primary cancers and the "metastatic lesion" is in the contralateral lung, the designation M1 should be used. If both lesions are in the same lung, it is recommended that the designation T2 be used unless there is evidence of T3 disease. This recommendation is based on preliminary unpublished data suggesting

that such cases have a relatively favorable prognosis following surgical treatment. However, more data are needed, so these cases should be analyzed in a separate group to determine the significance of such multiple ipsilateral lesions of the same cell type.

T2 is used when there is direct extension into the visceral pleura, but T3 is used if the lesion invades directly the parietal pleura covering the mediastinum and pericardium as well as that lining the chest wall and covering the diaphragm. Any ipsilateral discontinuous lesion or lesions in or on the visceral or parietal pleura should be designated T3. However, a discontinuous lesion outside the parietal pleura in the chest wall or diaphragm should be designated M1. In contrast, a similar lesion in the mediastinum is most likely a lymph node that has been replaced completely by cancer cells and should be designated N2.

Accurate clinical-diagnostic classification of hilar masses may be difficult. If the hilar mass can be separated from the mediastinum, hilar tomograms may indicate whether the mass is the primary tumor or metastatic disease in the hilar lymph nodes and the appropriate T and N designation may be assigned to the patient. If the hilar mass cannot be separated from the mediastinum, especially if there is a broad base of the lesion against the mediastinum, direct extension into the mediastinum is probable and the lesion should be designated T3. Vocal cord paralysis, superior vena caval obstruction, and compression of the trachea or the esophagus are usually related to metastases to the mediastinal lymph nodes and should be classified N2.

N1 is to be used whenever there is lymph node involvement within the lung or the hilar area within the reflections of the visceral pleura or its sagittal plane. Any nodal involvement medial to this should be considered mediastinal nodal metastasis and designated N2.

The M1 designation should be used *only* when there is reasonable proof of metastatic cancer, not just when it is possible. For example, elevated serum alkaline phosphatase without other evidence of metastatic cancer in liver or bone would not justify the designation M1.

In all cases, the designation of the greatest extent of disease that is applicable for a given patient should be used but only when there is reasonable evidence of that extent of the disease.

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Data Form for Cancer Staging

Patient identification
Name _____
Address _____
Hospital or clinic number _____
Age _____ Sex _____ Race _____

Institutional identification
Hospital or clinic _____
Address _____

Oncology Record

Anatomic site of cancer _____
Chronology of classification* [ ] Clinical-diagnostic (cTNM)
[ ] Surgical-evaluative (sTNM)
Date of classification _____

Histologic type† _____ Grade (G) _____
[ ] Postsurgical resection–pathologic (pTNM)
[ ] Retreatment (rTNM) [ ] Autopsy (aTNM)

Definitions: TNM Classification

Primary Tumor (T)

[ ] TX Tumor proven by the presence of malignant cells in bronchopulmonary secretions but not visualized roentgenographically or bronchoscopically; any tumor that cannot be assessed
[ ] T0 No evidence of primary tumor
[ ] Tis Carcinoma *in situ*
[ ] T1 Tumor 3.0 cm or less in greatest diameter, surrounded by lung or visceral pleura, and without evidence of invasion proximal to a lobar bronchus at bronchoscopy
[ ] T2 Tumor more than 3.0 cm in greatest diameter, or a tumor of any size that either invades the visceral pleura or has associated atelectasis or obstructive pneumonitis extending to the hilar region. At bronchoscopy, the proximal extent of demonstrable tumor must be within a lobar bronchus or at least 2.0 cm distal to the carina. Any associated atelectasis or obstructive pneumonitis must involve less than an entire lung and there must be no pleural effusion.
[ ] T3 Tumor of any size with direct extension into an adjacent structure such as the parietal pleura or the chest wall, the diaphragm, or the mediastinum and its contents; a tumor bronchoscopically demonstrable to involve a main bronchus less than 2.0 cm distal to the carina; any tumor associated with atelectasis or obstructive pneumonitis of an entire lung or pleural effusion

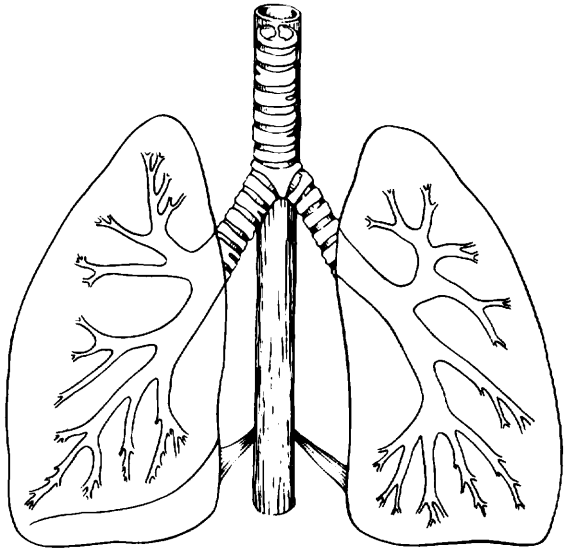
Nodal Involvement (N)

[ ] NX Minimum requirements to assess the regional nodes cannot be met.
[ ] N0 No evidence of involvement of regional lymph nodes
[ ] N1 Metastasis to lymph nodes in the peribronchial or the ipsilateral hilar region, or both, including direct extension
[ ] N2 Metastasis to lymph nodes in the mediastinum

Distant Metastasis (M)

[ ] MX Minimum requirements to assess the presence of distant metastasis cannot be met.
[ ] M0 No evidence of distant metastasis
[ ] M1 Distant metastasis present
Specify _____

Further definition of T, N, M can be found on reverse side.



Show primary tumor, indicating size in cm (greatest diameter) and measurability:

EV = evaluable
ME = measurable
NE = nonevaluable

Show lymph node metastasis.

Stage Grouping

[ ] Occult stage TX, N0, M0
Occult carcinoma with bronchopulmonary secretions containing malignant cells but without other evidence of the primary tumor or evidence of metastasis to the regional lymph nodes or distant metastasis
[ ] Stage I Tis, N0, M0
Carcinoma *in situ*
T1, N0, M0
T1, N1, M0
T2, N0, M0
Tumor that can be classified T1 without any metastasis or with metastasis to the lymph nodes in the peribronchial or ipsilateral hilar region only *or* a tumor that can be classified T2 without any metastasis to nodes or distant metastasis
Note: TX, N1, M0 and T0, N1, M0 are also theoretically possible, but such a clinical diagnosis would be difficult if not impossible to make. If such a diagnosis is made, it should be included under stage I.

Examination by _____ M.D.
Date _____

*Use a separate form each time a case is staged.
†See reverse side for additional information.

[ ] Stage II T2, N1, M0
Tumor classified as T2 with metastasis to the lymph nodes in the peribronchial or ipsilateral hilar region only

[ ] Stage III T3 with any N or M
N1 with any T or M
N2 with any T or M

Any tumor more extensive than T2, any tumor with metastasis to the lymph nodes in the mediastinum, or any tumor with distant metastasis

Histopathology

Squamous cell carcinoma, adenocarcinoma, undifferentiated small cell (oat cell) cancer

Cell type (check one):
- [ ] Squamous
- [ ] Small
- [ ] Large
- [ ] Adenocarcinoma
- [ ] Alveolar
- [ ] Other _____

Histologic Grade

- [ ] G1 Well differentiated
- [ ] G2 Moderately well differentiated
- [ ] G3–G4 Poorly to very poorly differentiated

Postsurgical Resection–Pathologic Residual Tumor (R)

- [ ] R0 No residual tumor
- [ ] R1 Microscopic residual tumor
- [ ] R2 Macroscopic residual tumor
  Specify _____

Performance Status of Host (H)

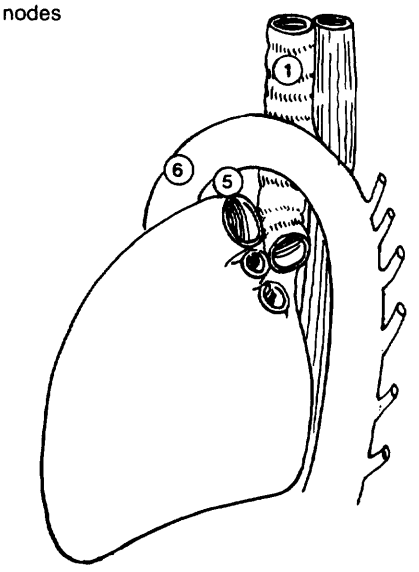
Performance status of the host should be recorded because this information at times is pertinent to the treatment of the patient.

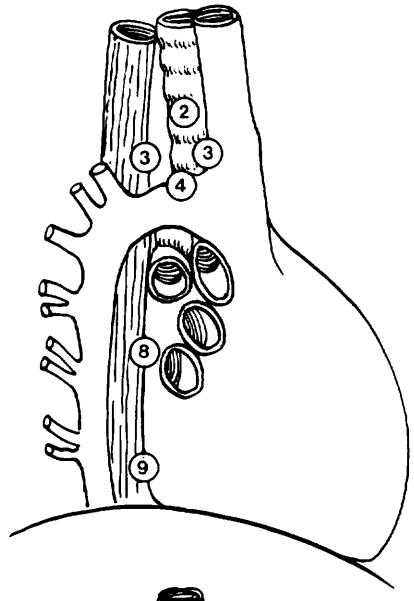
AJCC	*Performance*	*ECOG Scale*	*Karnofsky Scale (%)*
[ ] H0	Normal activity	0	90–100
[ ] H1	Symptomatic but ambulatory; cares for self	1	70–80
[ ] H2	Ambulatory more than 50% of time; occasionally needs assistance	2	50–60
[ ] H3	Ambulatory 50% or less of time; nursing care needed	3	30–40
[ ] H4	Bedridden; may need hospitalization	4	10–20

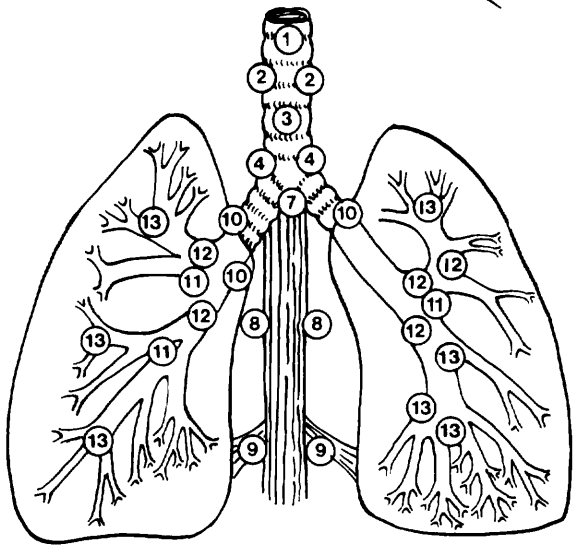
TNM Classification

Primary Tumor					
Size	*Intrabronchial Location*	*Extrapulmonary Extension*	*Atelectasis or Pneumonitis*	*Pleural Effusion*	*TNM Classification*
Positive bronchopulmonary secretions without demonstrable tumor or cannot be assessed				☐	TX
No evidence of primary tumor				☐	T0
Carcinoma *in situ*				☐	Tis
3 cm or less ☐	Not proximal to lobar bronchus ☐	None ☐	None or peripheral only ☐	None ☐	T1
More than 3 cm ☐	⩾2 cm distal to carina ☐	None ☐	Extends to hilar region but < entire lung ☐	None ☐	T2
Any size ☐	<2 cm distal to carina ☐	Chest wall, diaphragm, or mediastinum ☐	Involves entire lung ☐	Present ☐	T3
Regional Nodes					
No demonstrable metastasis to regional lymph nodes				☐	N0
Metastasis to peribronchial or ipsilateral hilar nodes				☐	N1
Metastasis to mediastinal lymph nodes				☐	N2
Distant Metastasis					
No (known) distant metastasis				☐	M0
Distant metastasis present (specify)				☐	M1

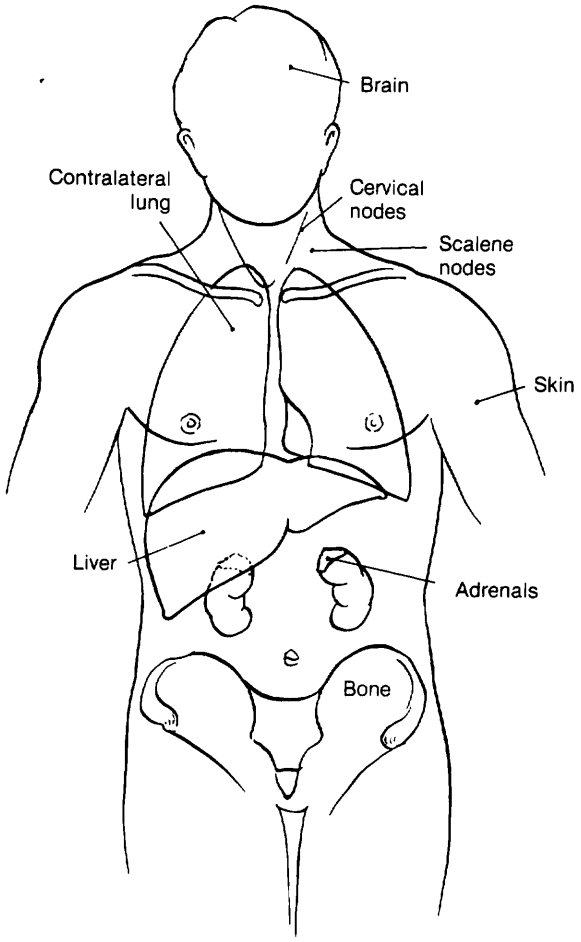
N-Regional nodes







Indicate on diagrams primary tumor and regional nodes involved.



Distant metastases beyond hemithorax

Indicate all known metastases.

N2 Nodes

Superior mediastinal nodes

1. Highest mediastinal
2. Upper paratracheal
3. Pre- and retrotracheal
4. Lower paratracheal (including azygos nodes)

Aortic nodes

5. Subaortic (aortic window)
6. Para-aortic (ascending aorta or phrenic)

Inferior mediastinal nodes

7. Subcarinal
8. Paraesophageal (below carina)
9. Pulmonary ligament

N1 Nodes

10. Hilar
11. Interlobar
12. Lobar
13. Segmental

MUSCULOSKELETAL SITES

17

Bone

Classification and staging of bone tumors is still being considered by the Task Force on Bone Tumors, and further recommendations may be made in the future. In the meantime, it is suggested that the following definitions and stage grouping be used.

TNM CLASSIFICATION (ICD-O 170)

Primary Tumor (T)

TX Minimum requirements to assess primary tumor cannot be met.
T0 No evidence of primary tumor
T1 Tumor confined within the cortex of the bone
T2 Tumor extending beyond the cortex of the bone

Note: Juxtacortical (parosteal) sarcomas should be considered separately.

Regional Lymph Nodes (N)

NX Minimum requirements to assess the regional nodes cannot be met.
N0 Regional lymph nodes do not contain metastatic deposits.
N1 Regional lymph nodes contain metastatic deposits.

Distant Metastasis (M)

MX Minimum requirements to assess the presence of distant metastasis cannot be met.
M0 No (known) metastasis
M1 Distant metastasis
Specify _____

Histologic Grade

G1 Well differentiated
G2 Moderately well differentiated
G3-G4 Poorly differentiated, anaplastic

Note: Ewing's sarcoma and malignant lymphoma are G3-G4.

STAGE GROUPING

Stage IA	G1, G2; T1, N0, M0
Stage IB	G1, G2; T2, N0, M0
Stage IIA	G3-G4; T1, N0, M0
Stage IIB	G3-G4; T2, N0, M0
Stage III	None yet defined
Stage IVA	Any G, any T, N1, M0
Stage IVB	Any G, any T, any N, M1

HISTOPATHOLOGY

See bibliography for reference material.

A. Bone-forming
   1. Osteosarcoma (osteogenic sarcoma)
   2. Juxtacortical osteosarcoma (parosteal osteosarcoma)
B. Cartilage-forming
   1. Chondrosarcoma
   2. Juxtacortical chondrosarcoma
   3. Mesenchymal chondrosarcoma
C. Giant cell tumor, malignant
D. Marrow tumors
   1. Ewing's sarcoma
   2. Malignant lymphoma of bone
   3. Myeloma
E. Vascular tumors
   1. Hemangioendothelioma
   2. Hemangiopericytoma
   3. Angiosarcoma
F. Connective tissue tumors
   1. Fibrosarcoma
   2. Liposarcoma
   3. Malignant mesenchymoma
   4. Undifferentiated sarcoma
G. Other tumors
   1. Chordoma
   2. "Adamantinoma" of long bones

RESIDUAL TUMOR (R)

R0 No residual tumor
R1 Microscopic residual tumor
R2 Macroscopic residual tumor
Specify _____

PERFORMANCE STATUS OF HOST

Performance status of the host should be recorded because this information at times is pertinent to the treatment of the patient.

AJCC	PERFORMANCE	ECOG SCALE	KARNOFSKY SCALE (%)
H0	Normal activity	0	90-100
H1	Symptomatic but ambulatory; cares for self	1	70-80
H2	Ambulatory more than 50% of time; occasionally needs assistance	2	50-60
H3	Ambulatory 50% or less of time; nursing care needed	3	30-40
H4	Bedridden; may need hospitalization	4	10-20

PROCEDURES RECOMMENDED FOR STAGING BY AJCC SYSTEM

A. Essential procedures
   1. History
   2. Physical examination
   3. Usual admission clinical pathology tests (such as blood chemistry, *etc.*)
   4. Plain radiography of involved site
   5. Cytohistologic examination of the lesion
      (Plan biopsy site anticipating field of later therapy.)
B. Selected procedures
   1. Computed tomography for lesions of trunk, pelvic girdle, shoulder girdle to determine anatomic extent and site for biopsy
   2. The following are indicated if plain radiograph indicates malignant tumor:
      a. Radiographs of chest
      b. Radionuclide bone scan
         Comparison radiograph of positive areas
   3. If biopsy diagnosis is primary sarcoma of bone and not a metastasis, perform pulmonary tomography or computed tomography.

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Data Form for Cancer Staging

Patient identification
Name _____
Address _____
Hospital or clinic number _____
Age _____ Sex _____ Race _____

Institutional identification
Hospital or clinic _____
Address _____

Oncology Record

Anatomic site of cancer _____
Chronology of classification* [ ] Clinical-diagnostic (cTNM)
[ ] Surgical-evaluative (sTNM)
Date of classification _____

Histologic type _____ Grade (G)† _____
[ ] Postsurgical resection–pathologic (pTNM)
[ ] Retreatment (rTNM) [ ] Autopsy (aTNM)

Definitions: TNM Classification

Primary Tumor (T)

[ ] TX Minimum requirements to assess the primary tumor cannot be met.
[ ] T0 No evidence of primary tumor
[ ] T1 Tumor confined within the cortex of the bone.
[ ] T2 Tumor extends beyond the cortex of the bone.

Note: Juxtacortical (parosteal) sarcomas should be considered separately.

Regional Lymph Nodes (N)

[ ] NX Minimum requirements to assess the regional nodes cannot be met.
[ ] N0 Regional lymph nodes do not contain metastatic deposits.
[ ] N1 Regional lymph nodes contain metastatic deposits.

Distant Metastasis (M)

[ ] MX Minimum requirements to assess the presence of distant metastasis cannot be met.
[ ] M0 No (known) metastasis
[ ] M1 Distant metastasis
Specify _____

Describe location, size, and characteristics of tumor.

_____
_____
_____
_____
_____
_____
_____
_____

Stage Grouping

[ ] STAGE I
  [ ] IA: G1, G2; T1, N0, M0
  [ ] IB: G1, G2; T2, N0, M0
[ ] STAGE II
  [ ] IIA: G3–G4, T1, N0, M0
  [ ] IIB: G3–G4, T2, N0, M0
[ ] STAGE III
  None yet defined
[ ] STAGE IV
  [ ] IVA: Any G, any T, N1, M0
  [ ] IVB: Any G, any T, any N, M1

* Use a separate form each time a case is staged.
† See reverse side for additional information.

Procedures Recommended for Staging by AJCC System

Essential for staging

1. History
2. Physical examination
3. Usual admission clinical pathology tests (blood chemistry, etc.)
4. Plain radiography of involved site
5. Cytohistologic examination of the lesion
   Plan biopsy site, anticipating field of later therapy.

Selected procedures

1. Computed tomography for lesions of the trunk, pelvic girdle, and shoulder girdle to determine the anatomic extent of the tumor and the site for biopsy
2. The following are indicated if the plain radiograph indicates the presence of a malignant tumor:
   a. Radiographs of the chest
   b. Radionuclide bone scan
      Comparison radiograph of positive areas
3. If the biopsy diagnosis is a primary sarcoma of the bone and not a metastasis:
   Pulmonary tomography or computed tomography

Histopathology‡

A. Bone-forming tumors
  [ ] Osteosarcoma (osteogenic sarcoma)
  [ ] Juxtacortical osteosarcoma (parosteal osteosarcoma)
B. Cartilage-forming tumors
  [ ] Chondrosarcoma
  [ ] Juxtacortical chondrosarcoma
  [ ] Mesenchymal chondrosarcoma
C. Giant cell tumor, malignant
D. Marrow tumors
  [ ] Ewing's sarcoma
  [ ] Malignant lymphoma
  [ ] Myeloma
E. Vascular tumors
  [ ] Hemangioendothelioma
  [ ] Hemangiopericytoma
  [ ] Angiosarcoma
F. Connective-tissue tumors
  [ ] Fibrosarcoma
  [ ] Liposarcoma
  [ ] Malignant mesenchymoma
  [ ] Undifferentiated sarcoma

‡World Health Organization: Histological Typing of Bone Tumours: International Classification of Tumours, No. 6. Geneva, World Health Organization, 1972

Examination by _____ M.D.
Date _____

G. Other tumors
[ ] Chordoma
[ ] Adamantinoma of long bones

Histologic Grade

[ ] G1 Well differentiated
[ ] G2 Moderately well differentiated
[ ] G3–G4 Poorly to very poorly differentiated

Postsurgical Resection–Pathologic Residual Tumor (R)

Does not enter into staging but may be a factor in deciding further treatment.

[ ] R0 No residual tumor
[ ] R1 Microscopic residual tumor
[ ] R2 Macroscopic residual tumor
Specify _____

Performance Status of Host (H)

Several systems for recording a patient's activity and symptoms are in use and are more or less equivalent as follows:

AJCC	*Performance*	*ECOG Scale*	*Karnofsky Scale (%)*
[ ] H0	Normal activity	0	90–100
[ ] H1	Symptomatic but ambulatory; cares for self	1	70–80
[ ] H2	Ambulatory more than 50% of time; occasionally needs assistance	2	50–60
[ ] H3	Ambulatory 50% or less of time; nursing care needed	3	30–40
[ ] H4	Bedridden; may need hospitalization	4	10–20

18

Soft Tissues

The staging system applies to all soft-tissue sarcomas except Kaposi's sarcoma, dermatofibrosarcoma, and fibrosarcoma grade 1 (desmoid type). Excluded from the soft-tissue category are those sarcomas arising within the confines of the dura mater, including the brain, and sarcomas arising in parenchymatous organs and from hollow viscera. The system is based on an analysis of 1215 cases obtained from 13 institutions. Cases were collected on the basis of the histology, diagnosis, and type of soft tissue and included cases from all age groups.*

In the analysis of the collected material, it was determined early in the study that, in addition to clinical information, the histologic type and grade of the tumor, as well as its size, were essential information for a meaningful staging system. The histologic diagnosis identifying the type of tumor and the pathologist's assessment of the inherent degree of malignancy of that type are fundamentals on which staging must be based.

Determination of the histologic grade and type of tumor is required for staging soft-tissue sarcomas and must be established by a qualified pathologist working with adequate sampling of the tumor.

HISTOPATHOLOGY

Tumor Type

Tumors included in the analysis and evaluations are listed below:

Alveolar soft-part sarcoma
Angiosarcoma
Epithelioid sarcoma
Extraskeletal chondrosarcoma
Extraskeletal osteosarcoma
Fibrosarcoma
Leiomyosarcoma
Liposarcoma

*For the most part, and with only a few variations, recommendations regarding staging of soft-tissue sarcoma in children are similar to those of the task force on this cancer. Grading of soft-tissue sarcoma has not been utilized, however, in the stage grouping of pediatric tumors.

Malignant fibrous histiocytoma
Malignant hemangiopericytoma
Malignant mesenchymoma
Malignant schwannoma
Rhabdomyosarcoma
Synovial sarcoma
Sarcoma, unclassified
Sarcoma, other

Tumor Grade (G)

G1 Well differentiated
G2 Moderately well differentiated
G3 Poorly differentiated

Once the histologic type has been determined, the tumor should be graded according to the accepted criteria of malignancy, including cellularity, cellular pleomorphism, and mitotic activity. In addition, the amount of intercellular substance such as collagen or mucoid material should be considered as a favorable factor in assessing the grade.

Also, there are tumors that are highly malignant regardless of their cellular differentiation, and they should be classified as grade 3 neoplasms. The most common of these are rhabdomyosarcoma and certain types of angiosarcoma and synovial sarcoma. The age of the patient may also be an important factor in determining the aggressiveness of a given tumor. For example, the prognosis of childhood fibrosarcoma is better than that of the adult forms of this neoplasm. Moreover, superficially located tumors have a more favorable prognosis than those deeply located. For the sake of simplicity, these features have been incorporated into the "G" designation, which has, in turn, been added to the TNM scheme for tumor evaluation.

ANATOMY (ICD-O 171)

Primary Site. A large variety of soft tissues can give rise to these sarcomas. The tissues include fibrous connective tissue, fat, smooth and striated muscle, vascular tissue, and peripheral neural tissue, as well as undifferentiated mesenchyme. Depending upon the location, different structures are at risk and they are included in the "T" classification.

Nodal Stations. Nodal stations or regions are related to site of origin of the sarcoma (see bibliography).

Metastatic Sites. The lung is the most common site that may be involved, but any viscous (liver, brain, *etc.*) or other site may be implicated.

RULES FOR CLASSIFICATION

The time of staging a tumor must be identified by a subset so it will be clearly understood when, in the course of diagnosis and treatment, the stage of disease was established.

cGTNM Clinical-diagnostic stage
pGTNM Postsurgical pathologic stage if the lesion is considered definitively treated by operation
rGTNM Retreatment stage

Initial steps for diagnosis and treatment planning include physical examination and roentgenographic evaluation of primary and metastatic sites, including chest films and skeletal survey, blood chemistries, blood counts, and other laboratory tests. Lymphangiography is an optional procedure. Radioisotopic, CT, ultrasonographic, and radionucleotide scans should be obtained as indicated. These procedures are of benefit in evaluating the patient's condition and in determining the optimal treatment; they are not necessarily required for staging. Biopsy of the tumor *is* required for diagnosis and grading.

Postsurgical pathologic (pGTNM) staging consists of the removal and pathologic evaluation of the primary tumor and, if indicated, of extensions of the tumor, nodes, or suspected metastases.

In retreatment (rGTNM) staging, questionable metastases or recurrences must be examined by biopsy and, if confirmed, complete restaging must be carried out.

TNM CLASSIFICATION

Primary Tumor (T)

TX Minimum requirements to assess the primary tumor cannot be met.
T0 No demonstrable tumor
T1 Tumor 5 cm or less in diameter
T2 Tumor more than 5 cm in diameter
T3 Clear radiographic evidence of destruction of cortical bone, with invasion; histopathologic confirmation of invasion of major artery or nerve

Nodal Involvement (N)

NX Minimum requirements to assess the regional nodes cannot be met.
N0 No histologically verified metastases to lymph nodes
N1 Histologically verified regional lymph node metastasis

Distant Metastasis (M)

MX Minimum requirements to assess the presence of distant metastasis cannot be met.
M0 No (known) distant metastasis
M1 Distant metastasis present
Specify _____

[ ] Pulmonary
[ ] Osseous
[ ] Hepatic
[ ] Brain
[ ] Lymph Nodes
[ ] Bone Marrow
[ ] Pleura
[ ] Skin
[ ] Eye
[ ] Soft Tissue
[ ] Other

POSTSURGICAL RESECTION RESIDUAL TUMOR (R)

R0 No residual tumor
R1 Microscopic residual tumor
R2 Macroscopic residual tumor
Specify _____

PERFORMANCE STATUS OF HOST (H)

Performance status of the host should be recorded because this information at times is pertinent to the treatment of the patient.

AJCC	PERFORMANCE	ECOG SCALE	KARNOFSKY SCALE (%)
H0	Normal activity	0	90-100
H1	Symptomatic but ambulatory; cares for self	1	70-80
H2	Ambulatory more than 50% of time; occasionally needs assistance	2	50-60
H3	Ambulatory 50% or less of time; nursing care needed	3	30-40
H4	Bedridden; may need hospitalization	4	10-20

STAGE GROUPING

Stage IA G1, T1, N0, M0, well-differentiated tumor 5 cm or less in diameter; no regional lymph nodal or distant metastases
Stage IB G1, T2, N0, M0, well-differentiated tumor more than 5 cm in diameter; no regional lymph nodal or distant metastases
Stage IIA G2, T1, N0, M0, moderately differentiated tumor 5 cm or less in diameter; no regional lymph nodal or distant metastases
Stage IIB G2, T2, N0, M0, moderately differentiated tumor more than 5 cm in diameter; no regional lymph nodal or distant metastases
Stage IIIA G3, T1, N0, M0, poorly differentiated tumor 5 cm or less in diameter; no regional lymph nodal or distant metastases
Stage IIIB G3, T2, N0, M0, poorly differentiated tumor more than 5 cm in diameter; no regional lymph nodal or distant metastases
Stage IIIC Any G, T1, T2; N1, M0, tumor of any differentiation, any size; regional lymph nodal metastases but no distant metastases
Stage IVA Any G, T3, any N, M0, tumor of any differentiation of malignancy demonstrating clear radiographic evidence of destruction of cortical bone (with invasion) and histopathologic confirmation of invasion of major artery or nerve, with or without regional lymph nodal metastases but without distant metastases
Stage IVB Any G, any T, any N, M1, tumor with distant metastases

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Data Form for Cancer Staging

Patient identification
Name _____
Address _____
Hospital or clinic number _____
Age _____ Sex _____ Race _____

Institutional identification
Hospital or clinic _____
Address _____

Oncology Record

Anatomic site of cancer _____
Chronology of classification* [ ] Clinical-diagnostic (cTNM)
[ ] Surgical-evaluative (sTNM)
Date of classification _____

Histologic type† _____ Grade (G) _____
[ ] Postsurgical resection–pathologic (pTNM)
[ ] Retreatment (rTNM) [ ] Autopsy (aTNM)

Histopathology (Tumor Type)

[ ] Alveolar soft-part sarcoma
[ ] Angiosarcoma
[ ] Epithelioid sarcoma
[ ] Extraskeletal chondrosarcoma
[ ] Extraskeletal osteosarcoma
[ ] Fibrosarcoma
[ ] Leiomyosarcoma
[ ] Liposarcoma
[ ] Malignant fibrous histiocytoma
[ ] Malignant hemangiopericytoma
[ ] Malignant mesenchymoma
[ ] Malignant schwannoma
[ ] Rhabdomyosarcoma
[ ] Synovial sarcoma
[ ] Sarcoma, unclassified
[ ] Sarcoma, other

Definitions: TNM Classification

Primary Tumor (T)

[ ] TX Minimum requirements to assess the primary tumor cannot be met.
[ ] T0 No demonstrable tumor
[ ] T1 Tumor less than 5 cm in diameter
[ ] T2 Tumor 5 cm or more in diameter
[ ] T3 Clear radiographic evidence of destruction of cortical bone, with invasion; histopathologic confirmation of invasion of major artery or nerve

Nodal Involvement (N)

[ ] NX Minimum requirements to assess the regional nodes cannot be met.
[ ] N0 No histologically verified metastases to lymph nodes
[ ] N1 Histologically verified regional lymph node metastasis

Distant Metastasis (M)

[ ] MX Minimum requirements to assess the presence of distant metastasis cannot be met.
[ ] M0 No (known) distant metastasis
[ ] M1 Distant metastasis present; specify: _____
[ ] Pulmonary
[ ] Osseous
[ ] Hepatic
[ ] Brain
[ ] Lymph nodes
[ ] Bone marrow
[ ] Pleura
[ ] Skin
[ ] Eye
[ ] Soft tissue
[ ] Other

Tumor Grade

[ ] G1 Well differentiated
[ ] G2 Moderately well differentiated
[ ] G3 Poorly differentiated

Stage Grouping

[ ] Stage I
Well-differentiated tumor 5 cm or less in diameter, no regional lymph nodal or distant metastases
[ ] IA: G1, T1, N0, M0
Well-differentiated tumor more than 5 cm in diameter, with no regional lymph nodal or distant metastases
[ ] IB: G1, T2, N0, M0

[ ] Stage II
Moderately differentiated tumor 5 cm or less in diameter, with no regional lymph nodal or distant metastases
[ ] IIA: G2, T1, N0, M0
Moderately differentiated tumor, more than 5 cm in diameter, with no regional lymph nodal or distant metastases
[ ] IIB: G2, T2, N0, M0

[ ] Stage III
Poorly differentiated tumor 5 cm or less in diameter, with no regional lymph nodal or distant metastases
[ ] IIIA: G3, T1, N0, M0
Poorly differentiated tumor, more than 5 cm in diameter with no regional lymph nodal or distant metastases
[ ] IIIB: G3, T2, N0, M0
Tumor of any differentiation, any size, with regional lymph nodal metastases but without distant metastases
[ ] IIIC: Any G, T1, T2; N1, M0

[ ] Stage IV
Tumor of any differentiation of malignancy, demonstrating clear radiographic evidence of destruction of cortical bone (with invasion) and histopathologic confirmation of invasion of major artery or nerve, with or without regional lymph nodal metastases but without distant metastases
[ ] IVA: Any G, T3, any N, M0
Tumor with distant metastases
[ ] IVB: Any G, any T, any N, M1

Examination by _____ M.D.
Date _____

*Use a separate form each time a case is staged.
†See reverse side for additional information.

Site-Specific Information

Clinical Information

Anatomic site (S)
[ ] Head and neck
[ ] Trunk
[ ] Extremities
  [ ] Shoulder or arm
  [ ] Elbow or below
  [ ] Buttocks or thigh
  [ ] Knee or below
[ ] Retroperitoneum or mediastinum
[ ] Other
  Specify _____

Major localization
[ ] Subcuti
[ ] Muscle

Secondary invasion
[ ] Bones
[ ] Blood vessels
[ ] Other

Tumor size (largest dimension in cm)
[ ] Less than 5 cm
[ ] 5 cm or larger

Regional lymph node involvement
[ ] Not assessed
[ ] Negative
[ ] Positive

Metastasis
[ ] None
[ ] Bone
[ ] Lymph Node
[ ] Lung
[ ] Liver
[ ] Soft Tissue
[ ] Other
  Specify _____

Oncogenic exposure
[ ] Irradiation
[ ] Chemical
[ ] Other
  Specify _____

Pathologic Information

Site or origin
[ ] Subcutis
[ ] Muscle
[ ] Tendon
[ ] Major nerve
[ ] Other
  Specify _____

Histologic type
[ ] Alveolar soft-part sarcoma
[ ] Angiosarcoma
[ ] Epithelioid sarcoma
[ ] Extraskeletal chondrosarcoma
[ ] Extraskeletal osteosarcoma
[ ] Fibrosarcoma
[ ] Leiomyosarcoma
[ ] Liposarcoma
[ ] Malignant fibrous histiocytoma
[ ] Malignant hemangiopericytoma
[ ] Malignant mesenchymoma
[ ] Malignant schwannoma
[ ] Rhabdomyosarcoma
[ ] Synovial sarcoma
[ ] Sarcoma, unclassified
[ ] Sarcoma, other

Tumor invasion
[ ] Skin
[ ] Subcutis
[ ] Muscle
[ ] Blood vessel
[ ] Nerve
[ ] Bone
[ ] Viscus
[ ] Other
  Specify _____

Margin evaluation
[ ] Negative
[ ] Positive

Grade of malignancy
[ ] G1 Well differentiated
[ ] G2 Moderately well differentiated
[ ] G3 Poorly differentiated

Tumor size
[ ] Less than 5 cm
[ ] 5 cm or larger

Postsurgical residual tumor
[ ] Negative
[ ] Positive
[ ] Gross residual tumor

Lymph node involvement
[ ] Not assessed
[ ] Negative
[ ] Positive

Distant metastasis
[ ] None
[ ] Lung
[ ] Bone
[ ] Liver
[ ] Lymph node
[ ] Other
  Specify _____

Postsurgical Resection–Pathologic Residual Tumor (R)

[ ] R0 No residual tumor
[ ] R1 Microscopic residual tumor
[ ] R2 Macroscopic residual tumor
  Specify _____

Performance Status of Host (H)

Performance status of the host should be recorded because this information at times is pertinent to the treatment of the patient.

AJCC	*Performance*	*ECOG Scale*	*Karnofsky Scale (%)*
[ ] H0	Normal activity	0	90–100
[ ] H1	Symptomatic but ambulatory; cares for self	1	70–80
[ ] H2	Ambulatory more than 50% of time; occasionally needs assistance	2	50–60
[ ] H3	Ambulatory 50% or less of time; nursing care needed	3	30–40
[ ] H4	Bedridden; may need hospitalization	4	10–20