

Staging for Residents, Nurses, and Multidisciplinary Health Care Team

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AJCC

American Joint Committee on Cancer

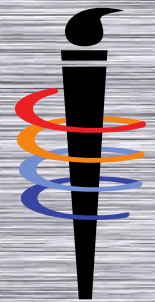
Validating science. Improving patient care.

Learning Objectives

- Introduce the concept and history of stage
- Recognize the reason for assigning stage
- Understand the various uses of staging: patient care, research, surveillance
- Understand stage classification based on different points in time of a patient's care
- Learn the components of stage
- Appreciate the general guidelines



Introduction



What is Staging

- Staging is a common language
 - Developed by medical professionals
 - Used to communicate information about a disease to others
- Staging is designed to
 - Aid in the planning of treatment
 - Give some indication of prognosis
 - Assist in evaluation of the results of treatment
 - Facilitate the exchange of information
 - Contribute to the continuing investigation of cancer
 - Support cancer control activities



History of Staging

- Concept of describing disease by stage or extent of the disease
 - Introduced in 1929 by League of Nations' World Health Organization
 - TNM introduced by Pierre Denoix in France in 1940's
- Globally accepted method of describing extent of cancer is TNM



Disease Process of Cancer

Theory of cancer growth or natural history

- Cancer originates in a single cell
- Cell continues to divide and grow
 - In organ of origin
 - Spreads to adjacent tissue or regional node drainage areas
 - Spreads to distant organs or structures
- Cancer spreads
 - From organ of origin through bloodstream or lymphatics into distant organs
 - Without involving adjacent organs and regional nodes



Disease Process of Cancer

- Many cancers go through a matured course
 - Advancing in tumor size or involvement
 - To regional nodal involvement
 - Eventually to distant metastasis

- Small tumors can metastasize
 - First sign of cancer is metastatic disease



TNM Stage Process

Determine
timeframe for
stage
assignment

- At time of diagnostic workup
- After surgical resection

Assign
categories:
T, N, M,
others

- Primary tumor
- Regional nodes
- Distant metastasis

Assign stage
group that
contains those
categories

- 0
- I - IV



TNM Stage Structure

- Stage groups are 0, I, II, III, and IV
- Groups consist of detailed anatomic categories
 - Local tumor extent, spread from organ/site of origin (primary site) - T category
 - Involvement of regional lymph nodes – N category
 - Distant metastatic spread – M category
- Groups increasingly use non-anatomic factors
 - Additional prognostic information
 - Potentially predict value of specific therapies

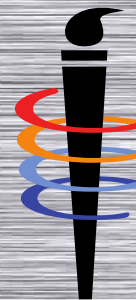


TNM Stage by Type of Cancer

- Definition of each category depends on
 - Site of cancer
 - Histology of cancer
- Definitions for breast T, N, M are not the same as those for colon, prostate, and other sites
- AJCC Cancer Staging Manual has chapters for
 - Each major organ or site of cancer
 - Histology specific such as separate chapters for Merkel Cell Carcinoma of the skin and Melanoma of the skin



Staging Systems Currently in Use



Staging Systems

- Two main staging systems in use
 - AJCC TNM
 - Shared with Union for International Cancer Control (UICC)
 - Used throughout the world to describe cancer and help make treatment decisions
 - Summary Stage
 - Used for tracking cancer data for epidemiologic purposes
- Each serves a different purpose



AJCC Stage

- Features
 - Provides more detailed information
 - Adds in assigning stage at different points in patient's care
 - Allows analysis of cases at the same point in their care
 - Ensures comparison of cases at similar times
- Different points in time of the patient's care are:
 - Clinical
 - Pathologic
 - Neoadjuvant Therapy
 - Retreatment
 - Autopsy



AJCC Stage

- Meets decision making needs of clinicians
 - Incorporated in most diagnostic and treatment guidelines
 - Choose appropriate treatment methods
 - Evaluation of treatment results
- Revised as medical science progresses
- Changes when data analysis proves it is necessary
 - Provides forward flexibility and clinical utility
 - Choosing treatment and estimating prognosis for individual cancer cases



AJCC Stage

- AJCC Cancer Staging Manual editions
 - New editions developed when significant changes warrant it
 - Each edition is used for specific years, Jan 1 – Dec 31

Edition	Publication Date	Effective for Cancers Diagnosed
1	1977	1978 – 1983
2	1983	1984 – 1988
3	1988	1989 – 1992
4	1992	1993 – 1997
5	1997	1998 – 2002
6	2002	2003 – 2009
7	2009	2010 –



Summary Stage

- Features
 - Broad categories that rarely change over time
 - Provides a simple grouping with longitudinal stability
 - Mainly used by population registries
- Less complex than other systems
 - Developed for epidemiologists who want some information
 - Do not need more detailed information

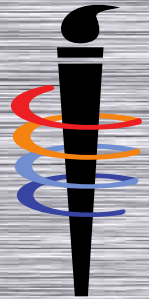


Summary Stage

- Useful when a series of cases is small
 - Only general categories produce enough data for meaningful analysis
- Only captures data once
 - Put together best information from diagnostic workup and pathologic exam of resected specimens



Purpose of Staging



Purpose of Staging – Patient Care

- Adequately assess extent of cancer in order to treat in most appropriate manner
- Understanding extent of disease assists the physician in determining treatment to
 - Cure the disease
 - Decrease the tumor burden
 - Relieve symptoms
- Allows clear communication with the patient and other physicians



Purpose of Staging – Patient Care

- Staging used to indicate prognosis
 - Data from historical sources provide estimate of expected survival rate for the patient
 - Determines prognosis and quality of survival along with
 - Histology
 - Tumor grade
 - Age
 - Sex
 - Race
 - Efficacy of therapy



Purpose of Staging – Quality Improvement

- Staging provides a means of comparing local institutional experience with national data
 - Used to compare treatment results based on common criteria
 - Staging expedites exchange of data and assists in continuing research
 - Health information record is primary source of documentation for staging



Purpose of Staging - Research

- Research types
 - Clinical
 - Epidemiologic
 - Health services

- Purpose of research
 - Evaluate cause and effect
 - Evaluate new diagnostic tests and procedures
 - Monitor efficacy of treatment modalities



Purpose of Staging - Research

- Comparative effectiveness research for cancer
 - Identify new and emerging clinical interventions
 - Review and synthesize current medical research
 - Identify gaps between existing medical research and the needs of clinical practice
 - Promote and generate new scientific evidence and analytic tools
 - Train and develop clinical researchers
 - Translate and disseminate research findings to diverse stakeholders
 - Reach out to stakeholders via a citizens forum



Purpose of Staging - Surveillance

- Population surveillance
 - Cancer incidence trends over time
 - Cancer diagnosed at early or late stages
 - Show cancer patterns in various populations
 - Guide planning and evaluation of cancer control programs
 - Mortality information

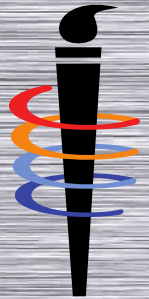


Purpose of Staging - Surveillance

- Public health information available to
 - Identify underserved communities
 - Determine need for screening
 - Determine need for awareness campaigns
 - Identify access to care issues
 - Maximize effectiveness of limited funds
 - Help set priorities for allocating health resources

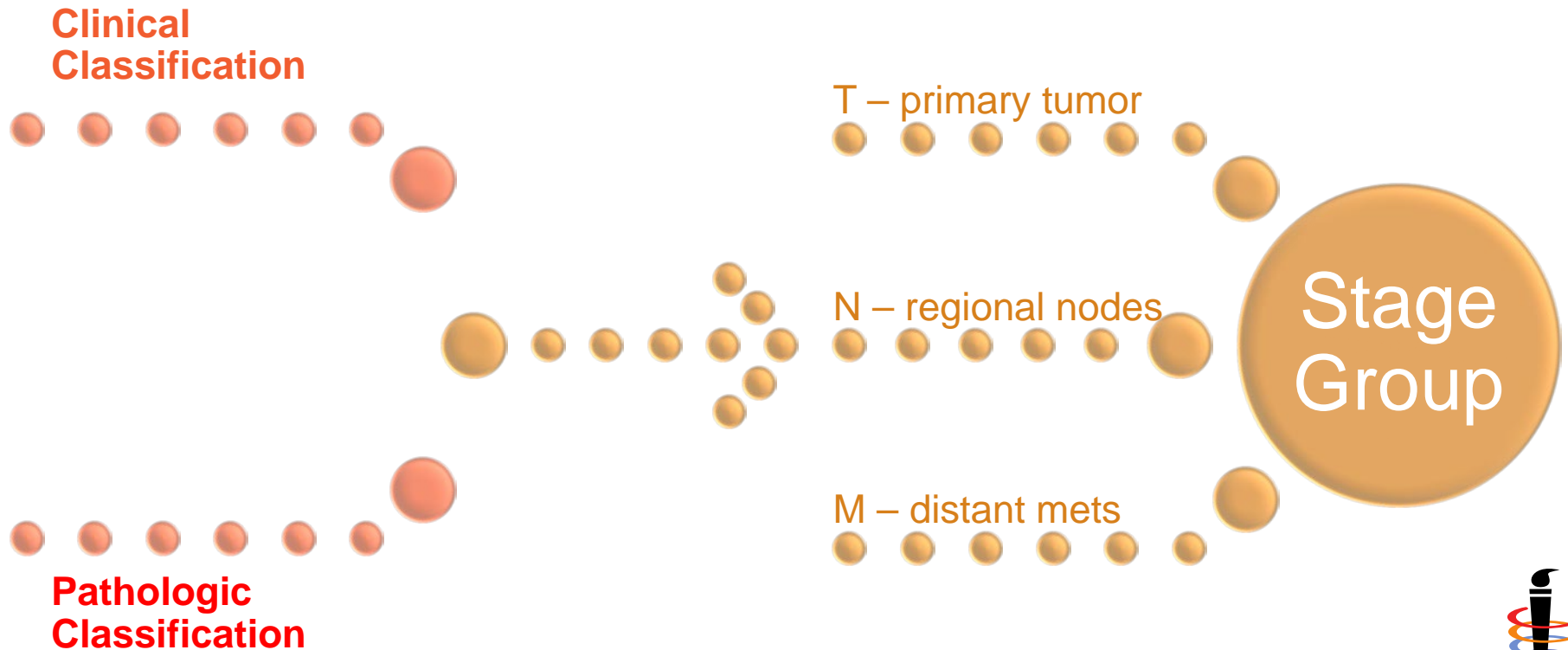


Stage Classifications



Stage Classifications

Points in Time for Patient Care



Stage Classifications

- Stage defined at a number of points in patient care
 - Clinical – before any treatment - **c**
 - Pathologic – based on pathology at time of surgery - **p**
 - Posttreatment – after neoadjuvant therapy - **y**, used as **yc** or **yp**
 - Retreatment – recurrence after disease free interval - **r**
 - Autopsy – unsuspected prior to death, incidental finding - **a**
- Clinical and pathologic are the most commonly used



Clinical Stage Classification

- Clinical classification uses diagnostic workup
 - History
 - Physical examination
 - Imaging
 - Endoscopy
 - Biopsy of primary site
 - Biopsy of single node or sentinel nodes as part of diagnostic workup
 - Biopsy of metastatic sites as part of diagnostic workup
 - Surgical exploration
 - Other relevant examinations
- cT1N0M0 or T1N0M0, Clinical Stage I



Clinical Stage Classification

- Timing rule for clinical staging includes
 - Any information about extent of cancer before initiation of definitive treatment
 - Surgery
 - Systemic therapy
 - Radiation therapy
 - Active surveillance
 - Palliative care
 - Or within four months after date of diagnosis
 - Whichever is **shorter**
 - Has NOT clearly progressed during that time



Clinical Stage Classification

- Need for clinical stage clearly identified
 - Monitoring of appropriateness of treatment
 - Treatment based on clinical stage
 - Treatment guidelines assess appropriateness
 - Only point in time where all cases can be compared
 - Clinical stage takes place prior to treatment
 - All cases can be compared regardless of treatment
 - Not all patients have surgery and Pathological Stage
 - By staging at diagnosis, the validity of epidemiological analysis, screening, analysis of treatment outcomes and proper healthcare planning is ensured



Pathologic Stage Classification

- Pathologic classification based on
 - Information acquired before treatment supplemented and modified by
 - Evidence acquired during and from surgery (surgical observations)
 - Particularly from pathologic examination of resected tissues
 - Need sufficient tissue resected, criteria varies by chapter
- pT1N0M1 Pathologic Stage IV



Pathologic Stage Classification

- Timing rule for pathologic staging includes
 - Any information obtained about extent of cancer through completion of definitive surgery in first course treatment
 - Or within four months after date of diagnosis
 - Whichever is ***longer***
 - No systemic or radiation therapy initiated
 - Has not clearly progressed during that time



Pathologic Stage Classification

- Need for pathologic stage clearly identified
 - Used to determine further postoperative therapy
 - Estimate prognosis and survival for individual patient
 - Monitoring of outcomes and survival
 - By stage group
 - By treatment choices – compare efficacy of treatment



Stage Classification Rules

- Stage classification only includes information from that point in time, clinical or pathologic
 - cT and cN or pT and pN
 - Cannot mix and match c and p
- Exception
 - M designation can be either c or p
 - Based on how the metastases are determined: physical exam and imaging, or biopsy/surgery
- Examples
 - cT1 cN2 pM1 clinical stage IV
 - pT3 pN1 cM0 pathologic stage II



Post Therapy / Postneoadjuvant Therapy Classification

- yc prefix
 - Clinical stage assigned after systemic and/or radiation therapy
- yp prefix
 - Pathologic stage assigned after surgical resection following the neoadjuvant (systemic and/or radiation) therapy
- yp stage
 - Utilized in conjunction with clinical stage
 - Assess response to neoadjuvant therapy



Retreatment Classification

- Retreatment classification based on
 - Recurrence information after disease-free interval
 - Progression of disease needing subsequent treatment
- Retreatment stage
 - Used to select appropriate further treatment
- Biopsy confirmation
 - Important if clinically feasible
- rT2N1M1, Retreatment Stage IV



Autopsy Classification

- Autopsy classification based on
 - Postmortem examination
 - Cancer was ***not*** evident prior to death
 - Includes all clinical and pathologic information obtained at time of death and autopsy
- aT3N1M0 Autopsy Stage III

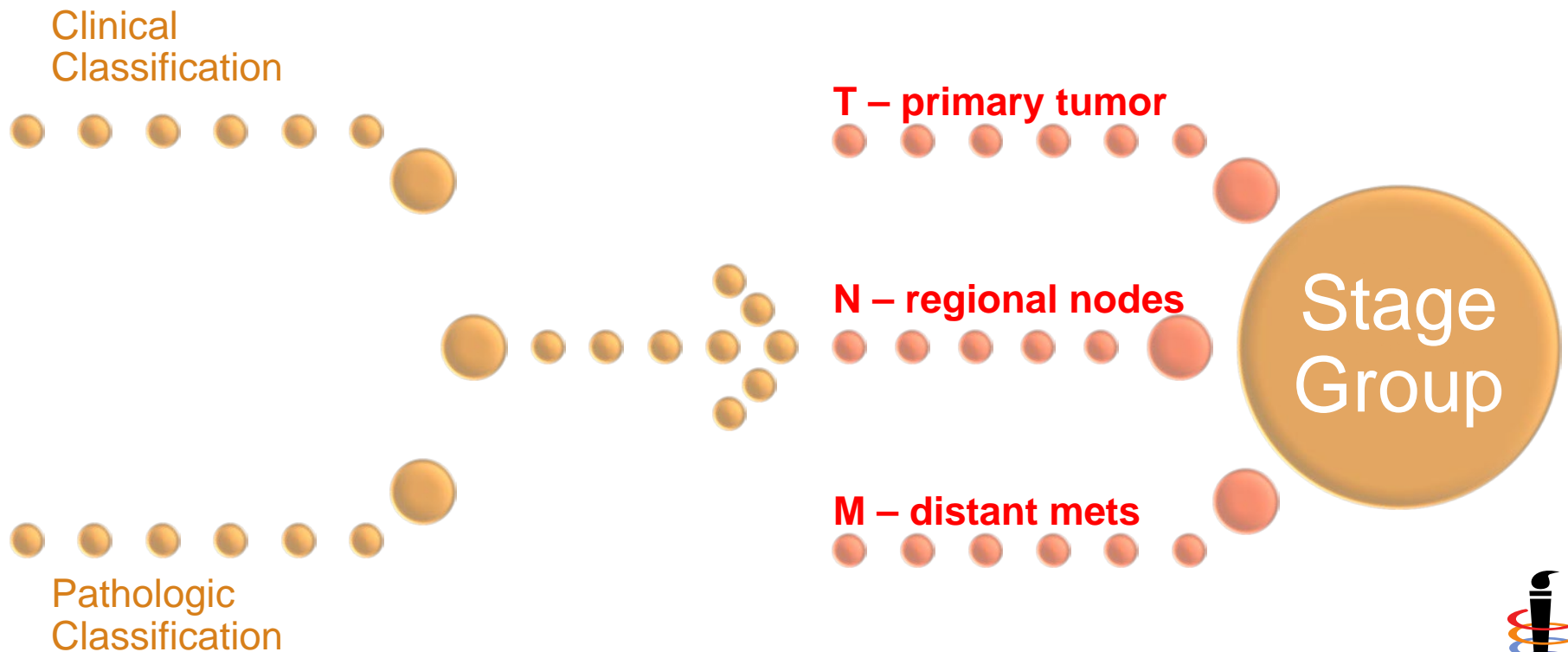


Categories – T, N, M



Categories – T, N, M

Assigning the T, N, and M



T

- T category
 - Designates size and invasiveness of primary tumor
 - Numerical value increases with size and invasiveness
 - Categories range from 0 - 4
 - For example
 - Small lesion confined to the organ – T1
 - Larger size or deeper extension into adjacent structures – T2
 - Larger size or extension confined to the region – T3
 - Massive lesion or directly invades another organ – T4



T Examples

- Obvious differences, some use size, invasion of tissues, or location
- Breast
 - pT1a Tumor >1mm but \leq 5mm in greatest dimension
- Lung
 - pT2a Tumor >3cm, invades visceral pleura (PL1)
- Colon
 - pT3 Invades through muscularis propria into pericolic tissues
- Prostate
 - pT2a Unilateral, one-half of one side or less



T Examples

- Even with similar size the T category is not the same, and some use involvement of other structures
- Breast
 - pT3 Tumor >50mm in greatest dimension
- Lung
 - cT2b Tumor >5cm but \leq 7cm, invades visceral pleura (PL1)
- Colon
 - pT4a Tumor penetrates to surface of visceral peritoneum
- Prostate
 - cT4 Tumor fixed to rectum and bladder



N

- N category
 - Designates presence or absence of regional node involvement
 - Numerical value based on number or location or nodes
 - Increasing numerical value based on size, fixation, capsular invasion, or multiple node involvement
 - Categories range from 0 - 3



N - Isolated Tumor Cells

- Isolated tumor cells (ITC) are single tumor cells or small clusters of cells not more than 0.2 mm in greatest extent that can be detected by routine H and E stains or immunohistochemistry
- ITCs do not typically show evidence of metastatic activity (e.g., proliferation or stromal reaction)
- Considered N0 – negative lymph nodes for most sites
- N0(i+) or N0(i-)



N - Sentinel Lymph Node

- Sentinel lymph node is first lymph node to receive lymphatic drainage from a primary tumor
- If it contains metastatic tumor this indicates that other lymph nodes may contain tumor
- If it does not contain metastatic tumor, other lymph nodes are not likely to contain tumor
- May be more than one sentinel lymph node



N Examples

- Obvious differences, some use size, number positive, or location (nodal chain)
- Breast
 - pN1a Mets in 1-3 axillary nodes, at least one >2.0mm
- Lung
 - pN1 Mets in ipsilateral hilar nodes
- Colon
 - pN0 No regional node metastasis
- Prostate
 - pN0 No regional node metastasis



N Examples

- Even with similar number the category is not the same, and some use which nodal chains are involved, and whether ipsilateral or contralateral
- Breast
 - pN3a Mets in 11 axillary nodes, at least one >2.0mm
- Lung
 - cN3 Mets in contralateral hilar and mediastinal nodes
- Colon
 - pN2b Metastasis in 8 regional nodes
- Prostate
 - cN0 No regional node metastasis



M

- M category
 - Identifies presence or absence of distant metastases
 - Including lymph nodes that are not regional
 - Categories range from 0 - 1
 - AJCC 7th Edition added concept of isolated tumor cells in metastatic sites
 - Circulating tumor cells are found in blood (CTCs)
 - Disseminated tumor cells are found in bone marrow or other structures (DTCs)
 - Considered M0 similar to the concept of isolated tumor cells in lymph nodes, M0(i+)



M Examples

- Note, isolated tumor cells are still considered M0
- Breast
 - cM0(i+) No distant metastasis but microscopically detected tumor cells in circulating blood
- Lung
 - cM0 No distant metastasis
- Colon
 - cM0 No distant metastasis
- Prostate
 - cM0 No distant metastasis



M Examples

- Note, some sites with subcategories for M1, such as colon with M1a and M1b
- Breast
 - cM0 No distant metastasis
- Lung
 - cM0 No distant metastasis
- Colon
 - pM1a Metastasis confined to one organ or site (liver)
- Prostate
 - cM0 No distant metastasis

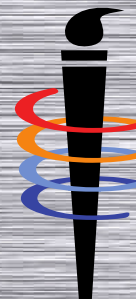


Combinations of T, N, M

- Physician chooses T, N, and M that best describes the patient's cancer
- Many possible combinations of T, N, M
 - For example:
 - T1 N0 M0
 - T2 N1 M0
 - T4 N2 M1

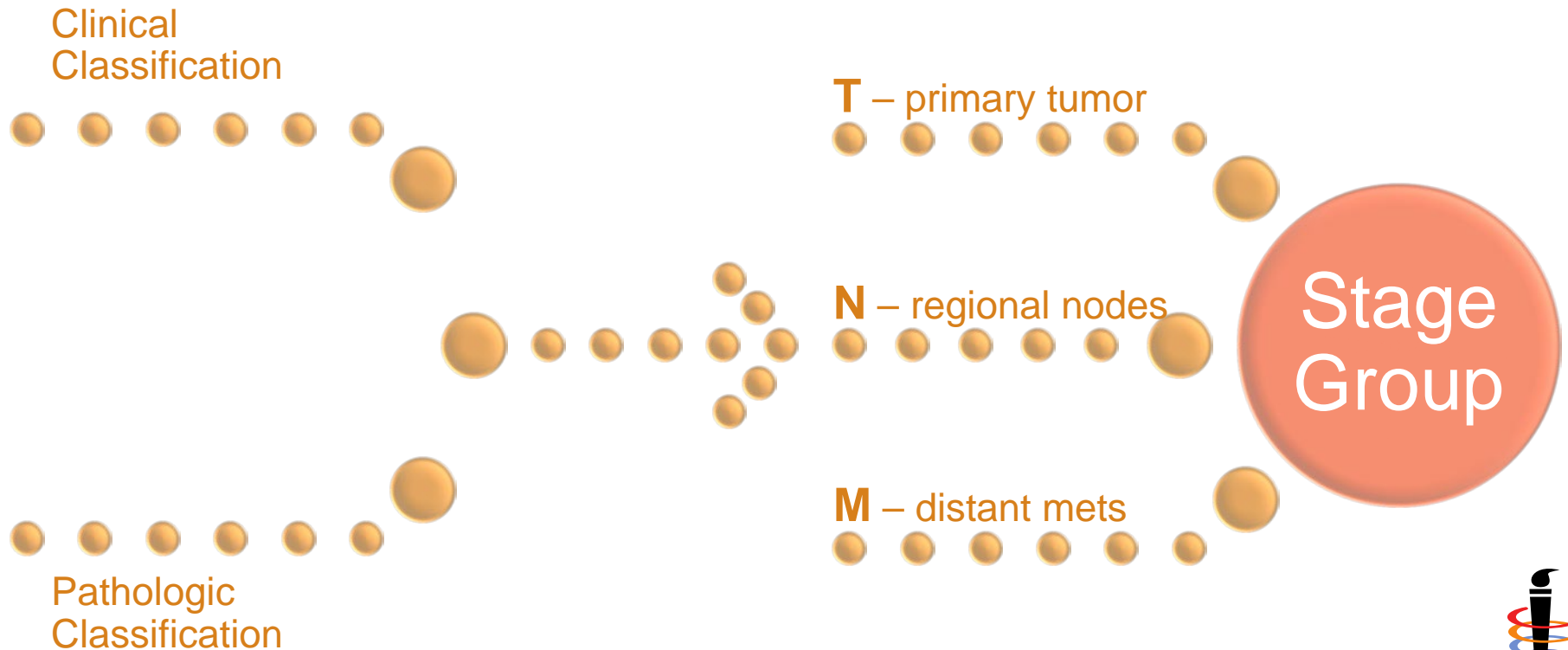


Stage Group



Stage Group

Assigning the Stage Group



Stage

- The combinations of T, N, and M are put into what is called a *stage group*, or simply, *stage*
- Stage
 - There are many possible combinations of the numbered categories for T, N, and M
 - Organizes combinations into four or five main stages
 - Allows for easier comparison of cases



Stage

- Stage is assigned a Roman numeral (0, I, II, III, IV)
 - Higher numbers indicate more extensive disease
 - Stage 0 is minimal involvement, usually carcinoma in-situ
 - Stage I is minimal disease
 - Stage IV is greatest tumor involvement or distant metastasis
 - Some stages have subdivisions
 - Listed as IIA, IIB
 - Based on survival rates



Prognostic Factors

- Prognostic factors include anatomic and non-anatomic characteristics about a case
- Prognostic factors can
 - Play a role in describing the disease and
 - May be a part in how a stage group is assigned
- Prognostic factors
 - Personalize the information for that patient
 - Provide information for individualized or personalized prognosis



Prognostic Factors

- Required for staging in various chapters
 - Grade
 - Tumor location
 - Mitotic rate
 - PSA (prostatic specific antigen)
 - Gleason score
 - Serum tumor markers for testis
- Clinically significant
 - Many other factors are important to collect
 - Affect patient care or prognosis, but not used in staging



Anatomic Stage/Prognostic Group

- In the 7th edition Stage Group was renamed
 - Commonly referred to as “stage”
- Anatomic Stage/Prognostic Groups
 - New term for stage
 - Signifies inclusion of prognostic factors to assign group



Stage Examples

- Criteria for assigning stage is specific to each chapter
 - All cases are stage IIA
 - Vary from T1 to T3, and from N0 to N1
- Breast
 - pT1a pN1a cM0(i+) Pathologic stage IIA
- Lung
 - pT2a pN1 cM0 Pathologic stage IIA
- Colon
 - pT3 pN0 cM0 Pathologic stage IIA
- Prostate
 - pT2a pN0 cM0 PSA<20 Gleason 7 Pathologic stage IIA

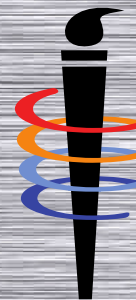


Stage Examples

- Different criteria by site
 - Differences in stage III and in stage IV
 - Note prostate is stage IV without distant mets (M1)
- Breast
 - pT3 pN3a cM0 Pathologic stage IIIC
- Lung
 - cT2b cN3 cM0 Clinical stage IIIB
- Colon
 - pT4a pN2b pM1a Pathologic stage IVA
- Prostate
 - cT4 cN0 cM0 PSA>20 Gleason 8 Clinical stage IV



Staging Guidelines



Staging Guidelines

- Rules for assigning stage ensure data consistency
- Stage applied to cancers that are similar
 - Specific criteria for different primary sites
 - Some specific criteria are based on histology
 - Some specific criteria are based on both site and histology
- Accurate and complete assessment necessary
 - Important to seek further information if staging documentation is unclear

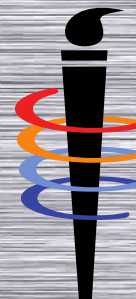


Staging Guidelines

- A few cases are unstageable
 - Unknown stage if unable to identify extent of disease
 - Site or histology do not meet criteria for staging
 - No system for rare sites with not enough cases to establish validated criteria
- Mandatory to stage uniformly using the same staging system
 - In order to compare data or results



Summary



Summary

- Stage allows for clear communication between multidisciplinary physicians involved in cancer care
- Many patients understand broad concept of stage
 - Stage used in physician discussions with the patient
- Patient's treatment based on stage
 - Many national treatment guidelines available
- Prognosis estimated by stage and other factors
 - Patients want to know their prognosis



Summary

- Uses of stage
 - Monitor patient care and outcomes
 - Clinical trials, research studies, data analysis
 - Monitor regional/national treatment patterns and outcomes
- Survival data by stage monitored over the years
 - Influences subsequent editions of *AJCC Cancer Staging Manual*



Resources

- Staging Moments – case-based scenarios, clarify finer points of staging, <https://cancerstaging.org/CSE/general/Pages/Staging-Moments.aspx>
- On-Demand AJCC Webinars – various topics, <https://cancerstaging.org/CSE/Physician/Pages/Webinars.aspx>
- Staging Posters – breast, cervix, colorectal, lung, melanoma, pancreas, and prostate, <https://cancerstaging.org/references-tools/quickreferences/Pages/default.aspx>
- You Tube AJCCancer Channel – <http://www.youtube.com/user/AJCCancer>
- More resources under Cancer Staging Education on AJCC website, <https://cancerstaging.org/Pages/default.aspx>



TNM Staging: *The Common Language of Cancer*

AJCC Web Site: <http://cancerstaging.org>

