Cancer PROGRAMS

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AJCC

American Joint Committee on Cancer

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Lesson 13

Additional Material:
Staging for Residents, Nurses, and other Allied Health Personnel

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Inspiring Quality:
Highest Standards, Better Outcomes

100+years

Learning Objectives

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- 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

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Introduction

What is Staging

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- 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

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History of Staging

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- 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

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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

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- 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

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TNM Stage Process

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Determine timeframe for stage assignment

- At time of diagnostic workup - clinical
- After surgical resection - pathological

Assign categories: T, N, M, others

- Primary tumor
- Regional nodes
- Distant metastasis

Assign stage group that contains those categories

- 0
- I - IV

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TNM Stage Structure

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- 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

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- 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 System has chapters/protocols for
  - Each major organ or site of cancer
  - Histology specific such as separate chapters/protocols for Merkel Cell Carcinoma of the skin and Melanoma of the skin

Staging Systems Currently in Use

Staging Systems

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- 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

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- 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
  - Pathological
  - Posttherapy
  - Retreatment
  - Autopsy

AJCC Stage

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- 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

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- AJCC Cancer Staging Manual/System editions/versions
  - 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	2010-2017
8*	2016	2018-
Version 9*	2020+	2021-

*Annual rolling updates to gradually replace manual edition

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Summary Stage

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- Features
  - Broad categories that rarely change over time
  - Provides a simple grouping with longitudinal stability
  - Mainly used by population registries
- Consists of
  - In situ
  - Localized
  - Regional
    - Regional extension
    - Regional nodes
    - Regional both extension and nodes
  - Distant
- Less complex than other systems
  - Developed for epidemiologists who want some information
  - Do not need more detailed information

Summary Stage

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- 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 pathological exam of resected specimens

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Purpose of Staging

Purpose of Staging – Patient Care

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- 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

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- 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

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- 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

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- 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

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- 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 (Points in Time for Patient Care)

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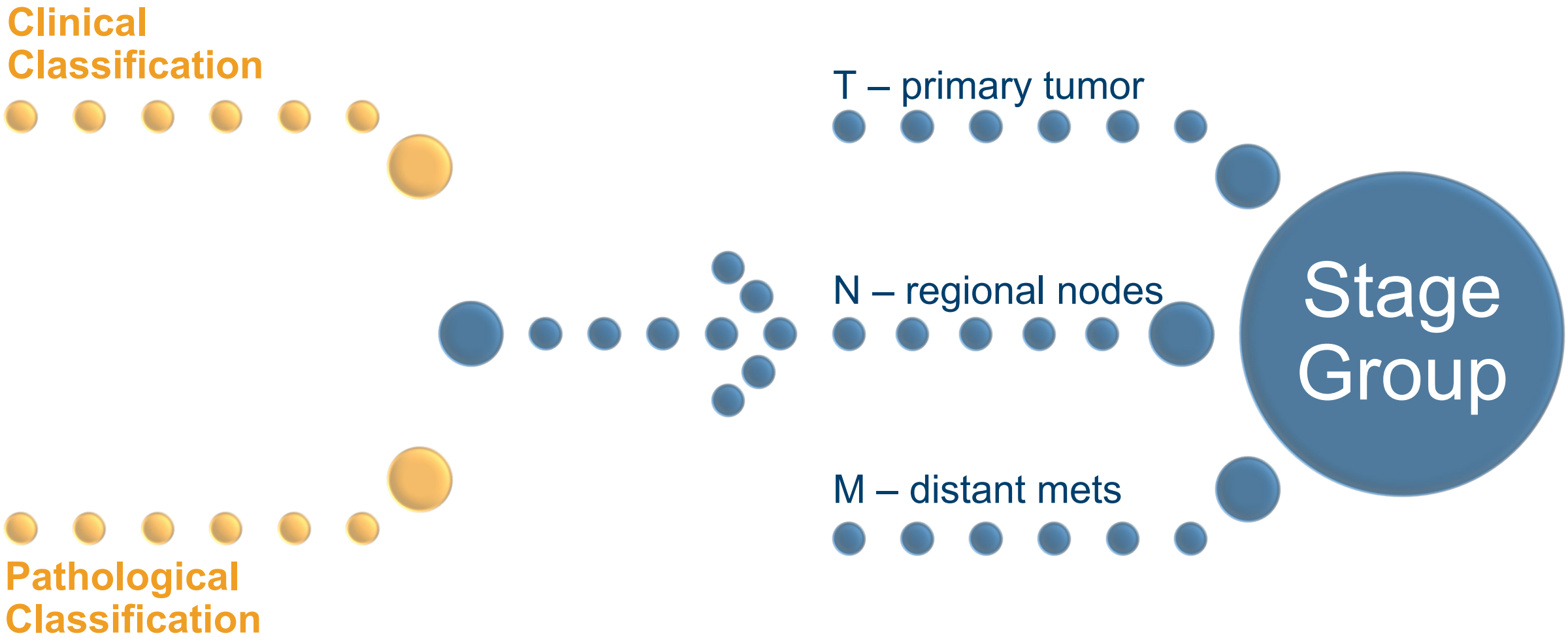

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Stage Classifications

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- Stage defined at a number of points in patient care
  - Clinical – before any treatment - c
  - Pathological – based on findings and pathology at time of surgery - p
  - Posttherapy – 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 pathological are the most commonly used

Clinical Stage Classification

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- 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
  - Surgical exploration
  - Other relevant examinations
- cT1 cN0 cM0 or T1N0M0, Clinical Stage I

Clinical Stage Classification

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- 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

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Clinical Stage Classification

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- 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

Pathological Stage Classification

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- Pathological classification based on
  - Information acquired before treatment (clinical stage) supplemented and modified by
  - Evidence acquired during and from surgery (surgical observations)
  - Particularly from pathological examination of resected tissues
  - Need sufficient tissue resected, criteria varies by chapter
- pT1 pN0 cM1 Pathological Stage IV

Pathological Stage Classification

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- Timing rule for pathological 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

Pathological Stage Classification

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- Need for pathological 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

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- Stage classification only includes information from that point in time, clinical or pathological
  - 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 pathological stage II

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Post Therapy/ Postneoadjuvant Therapy Classification

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- yc
  - Posttherapy clinical stage assigned after systemic and/or radiation therapy
- yp
  - Posttherapy pathological 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

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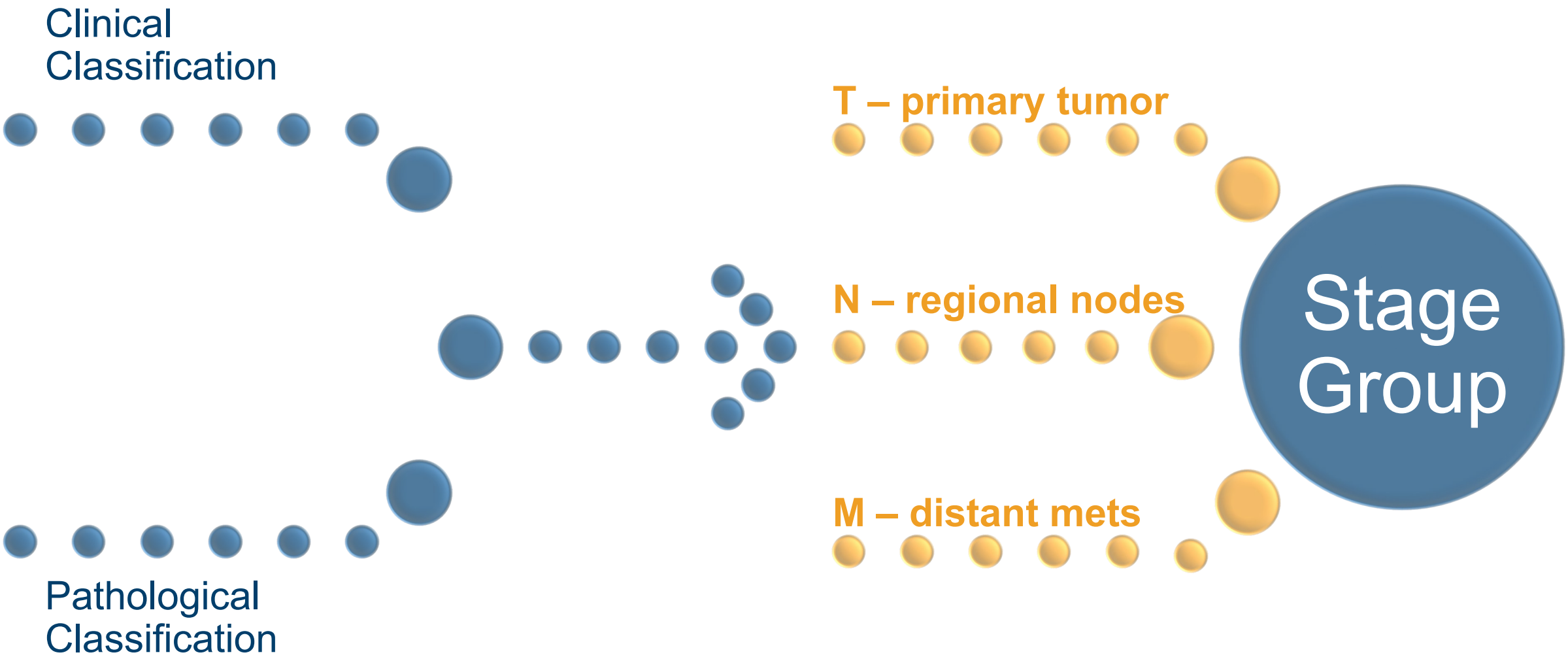
- Retreatment classification based on
  - Recurrence information after disease-free interval
- Retreatment stage
  - Used to select appropriate further treatment
- Biopsy confirmation
  - Important if clinically feasible
- rT2 rN1 rM1, Retreatment Stage IV

Autopsy Classification

- Autopsy classification based on
  - Postmortem examination
  - Cancer was not evident prior to death
  - Includes all clinical and pathological information obtained at time of death and autopsy
- aT3 aN1 aM0 Autopsy Stage III

Categories- T, N, M



- 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

- Breast
  - pT1a Tumor >1mm but <5mm in greatest dimension
- Lung
  - pT2a Tumor >3cm by < 4cm in greatest dimension
- Colon
  - pT3 Tumor invades through muscularis propria into pericolorectal tissues
- Prostate
  - cT2a Tumor involves one-half of one side or less

T Examples

- Breast
  - pT3 Tumor >50mm in greatest dimension
- Lung
  - cT2b Tumor >4cm but < 5 cm in greatest dimension
- Colon
  - pT4a Tumor invades through the visceral peritoneum
- Prostate
  - cT4 Tumor fixed or invades adjacent structures other than seminal vesicles

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

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- 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+)

N – Sentinel Lymph Node

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- 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

- 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

- Breast
  - pN3a Mets in 10 axillary nodes, at least one >2.0mm
- Lung
  - cN3 Mets in contralateral hilar and mediastinal nodes
- Colon
  - pN2b Seven or more regional lymph nodes positive
- 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
  - 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

- 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

- Breast
  - cM0 No distant metastasis
- Lung
  - cM0 No distant metastasis
- Colon
  - pM1a Metastasis confined to one organ or site (liver), without peritoneal metastasis
- Prostate
  - cM0 No distant metastasis

Combinations of T, N, M

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- 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

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Stage Group

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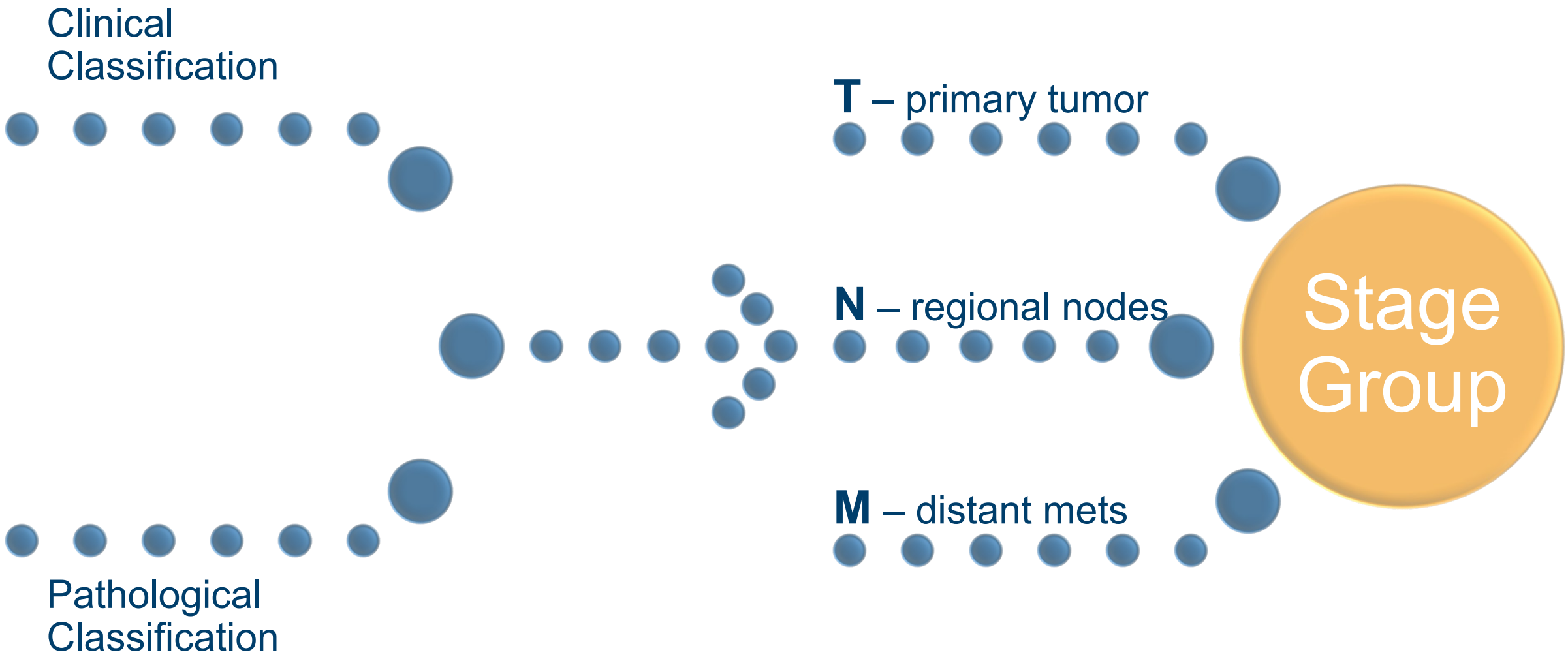

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Stage

- 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

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- Prognostic factors include anatomic and non-anatomic characteristics about a case

- Prognostic factors may
  - 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

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- Required for staging in various chapters
  - Grade
  - Tumor location
  - Mitotic rate
  - PSA (prostatic specific antigen)
  - Serum tumor markers for testis
  - HER2, ER, PR for Breast

- Relevant for clinical care
  - Many other factors are important to collect
  - Affect patient care or prognosis, but not used in staging

Prognostic Stage Group

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- Prognostic Stage Groups
  - New term for stage
  - Signifies inclusion of prognostic factors to assign group

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Stage Examples

- Breast
  - pT1a pN1a cM0(i+) G2 HER2- ER+ PR+ Pathological stage IA
- Lung
  - pT2a pN1 cM0 Pathological stage IIB
- Colon
  - pT3 pN0 cM0 Pathological stage IIA
- Prostate
  - pT2 pN0 cM0 PSA<20 Grade Group 2 Pathological stage IIB

Stage Examples

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- Breast
  - pT3 pN3a cM0 G2 HER2- ER+ PR+ Pathological stage IIIA
- Lung
  - cT2b cN3 cM0 Clinical stage IIIB
- Colon
  - pT4a pN2b pM1a Pathological stage IVA
- Prostate
  - cT4 cN0 cM0 PSA>20 Grade 4 Clinical stage IIIB

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Staging Guidelines

Staging Guidelines

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- 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

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- 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

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- 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

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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/versions of AJCC Cancer Staging Manual/System

Resources

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- AJCC Website
  - https://cancerstaging.org and
  - https://www.facs.org/quality-programs/cancer/ajcc
- Staging Moments – case-based scenarios, clarify finer points of staging
  - https://www.facs.org/quality-programs/cancer/ajcc/staging-education/moments
- YouTube AJCCancer Channel
  - http://www.youtube.com/user/AJCCancer

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