

**University of Washington
Anatomic Pathology**

**2005-2006 Surgical Pathology Guidelines
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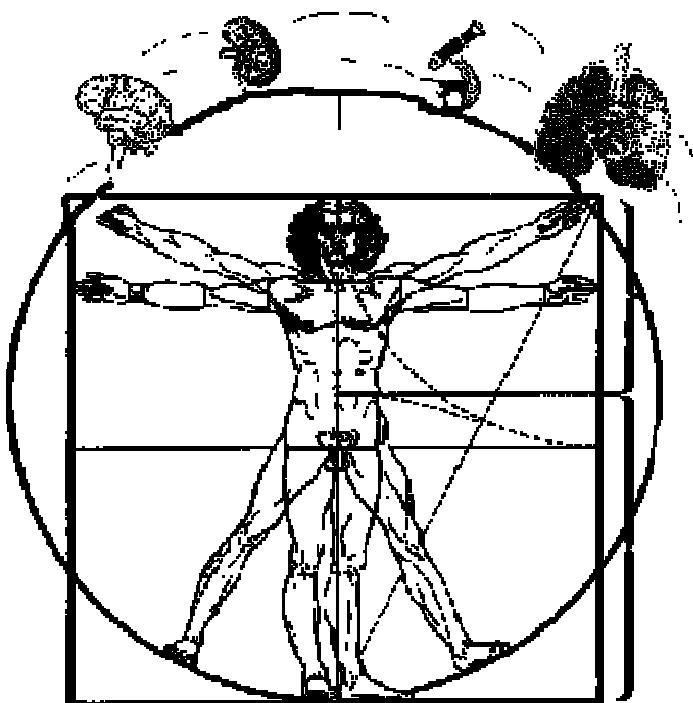
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Based on Ackerman's
Surgical Pathology, 8th
ed.

GO TO
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[INTRAWEB](#)

Handling Surgical Pathology Specimens



For all residents, read:

[Murphy WM](#): Ethical issues in anatomic pathology: are we going the way of the financial sector? *AJSP* 2003; 27:392-5.

This site contains the procedures and references for the handling of surgical pathology specimens within the Anatomic Pathology Department at the University of Washington Medical Center and the Department of Pathology. This document is published once a year in hard copy. All changes made during the year are updated on the web document.

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Gross Techniques

Section 1 - Gross Room Procedures

Author: Rochelle Garcia, MD

Section 2 - Gross Exam

Author: Medical Staff Administrative Committee

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Gross Room Procedures

Rochelle L. Garcia, MD

PATIENT CARE

GROSS PATHOLOGIC EXAM AND DESCRIPTION

"For me, the surgical pathology report is, and always will be, the distillation of the pathologist's experience, knowledge, and wisdom. It reflects the dignity of the profession and a pride in one's work. As a pathologist, I am a consultant to my fellow clinicians. Pathologists need to act and behave as true consultants and not as substitutes for computerized slide-readers. In our reports we should reflect on the diagnosis and its biologic and/or therapeutic significance to the patient. Complete reports not only enable pathologists to maintain standards of excellence but further our role as vital members of the health care team." (From *Human Pathology* 1984, 15(1))

DEFINITIONS

Gross: Total, without deductions, whole, utter, brutish, coarse, offensive

Gross Anatomy: the study of organs, parts and structure of the body that are visible to the naked eye

Pathology: Scientific study of disease and its causes, processes, developments and consequences

ASK QUESTIONS!

The gross pathologic description is one of the vital parts of the surgical pathology report - just as vital (and sometimes more so) as the Final Diagnosis. It should be a concise, clear and meaningful description of the specimen received, any abnormalities present and the relationship between those abnormalities to the normal tissue and margins, what was done to the specimen and what sections were taken. Although this exam focuses on visual inspection, tactile (especially for masses, nodes) and olfactory senses are also important tools in the gross exam.

SMALL BIOPSIES - DIAGNOSTIC SPECIMENS

Purpose of gross description - to document amount present (#, approximate volume). Three dimensions are not necessary, and in fact a waste of time. Color is also of little consequence though presence of blood and mucus is.

Skin shave biopsies – may ink (under surface only), but is not necessary and is not for margin determination, but to aid in orientation, bisect and/or trisect. Do describe any abnormalities present.

Skin punch biopsies – may ink, but not necessary, same as above

MEDIUM-SIZED SPECIMENS

Removed for treatment and sometimes diagnosis, e.g., gallbladder, appendixes, skin excisions (inking). These are typically NOT biopsies but excisions/resections. Sometimes they are partial excisions (e.g. tubal ligation). Lymph nodes resections/dissections (for staging) are for both diagnosis and treatment and also are NOT biopsy specimens. (Mediastinal lymph nodes are typically biopsies and SHOULD NOT be counted.)

LARGE AND COMPLEX SPECIMENS

THINK!!!

UNDERSTAND NORMAL ANATOMY

UNDERSTAND WHEN TO FIX

USE TEMPLATES - only as a guide

For any complex specimen, call the attending of the day or other faculty member to view.

DESCRIBE

What - was received (all components present)? If it is recognizable as a gallbladder, received is a (dimensions) gallbladder not a round, sack like structure.

What - type of procedure was performed for removal (e.g. radical versus simple hysterectomy, lumpectomy, lymph node dissection versus biopsy, type of mastectomy)? This is actually to be sure that the correct specimen is identified, not the procedure per se.

How - was the specimen received? e.g., fresh, in formalin, intact, etc.

Why - This information should be filled out by the clinician under clinical info or pre-op diagnosis. It is incumbent on us to determine this relevant clinical information if it is not provided on the form or if something does not fit. USE MINDSCAPE or THE PHONE!

WHAT IS A MARGIN AND WHEN IS IT IMPORTANT?

A margin is a cut surface, - one made by the surgeon. The skin surface, any mucosal surface or serosal surfaces (e.g. pleural, peritoneal, uterine serosa, liver surface) are not margins!!

Margins that closely approximate neoplasm are important to sample! Those far away (e.g. the proximal and distal ends of a colon resection for carcinoma) are not important.

In inflammatory conditions grossly unremarkable margins may be important to sample (e.g. IBD, dead bowel).

Margin sampling depends on specimen type and proximity of tumor. Shave margins in some cases, perpendicular in others.

REMEMBER - SEROSAL SURFACES ARE NOT MARGINS. It is not nearly as significant that a neoplasm approaches to less than 1 mm of a serosal surface as a cut margin.

TO INK OR NOT TO INK

Ink before you think - NO, NOT NECESSARILY

Ink for orientation and determination of margins.

DO NOT ink epithelial surfaces (mucosal, skin). Inking serosa is O.K.

FORMAT OF REPORT

Receive (fresh, fixed, in multiple parts, intact, etc.), labeled "name specimen", is a _____ gm ____x____x____ uterus/complex specimen including ____x____x____ pancreas and attached spleen, etc. The external surfaces are _____. Sections of _____ are removed for frozen section evaluation and the specimen is fixed overnight. Serially sectioning reveals a ____x____x____ mass located _____. Etc. The following sections are taken:

A1:

A2:

etc.

DISSECTION

Initially cuts should be made in one plane. Think about that first cut (it doesn't always have to be the same). Once initial dissection is done and sections taken, if results are not clear, GO BACK and take more. Although retention of orientation is nice, sometimes one must sacrifice the gross appearance in order to take appropriate sections. In general cuts should be made all the way through the specimen rather than trying to keep pieces together.

SECTIONS

Please THINK about what and how many sections to take. A "rule of thumb" may not apply in a specific case. In general if a sample is taken for staging purposes (e.g. lymph node dissection, omentectomy), multiple sections should be taken if the sample is grossly negative but relatively few and frequently only one if it is grossly positive.

Lymph nodes should be totally submitted unless grossly positive.

READ YOUR REPORT

Remember this should be a description that allows the reader to reconstruct the specimen, what was done to it and how the sections relate to the specimen. Don't be scared to edit the report (you should!), and if you discover an error, fix it!!

PLEASE use proper English grammar and spelling. Errors are unprofessional and distract one from proper interpretation of the report. Most gross descriptions are in present tense. Past tense is O.K., but whichever is used must be consistent.

TERMS TO AVOID (Some are my own biases)

Shows: No specimen shows you anything - it either has something or does not.

Ulceration: It should be ulcer.

Adhesed: The proper term is adherent. (Dr. Haggitt especially hated this.)

Tumor: Unless one uses the term to refer to a mass, although mass is a better descriptor. It is my personal bias that "tumor" should NOT be used in the diagnostic line.

OTHER TERMS FREQUENTLY MISUSED

Bivalve: This is a descriptor for something that is sectioned into 2 symmetric halves. Often used when bisect or sectioned is the appropriate term.

Macerated: This term implies/means that some degree of degeneration (before removal) has taken place, e.g., macerated fetus died before termination (alternative words are disrupted or fragmented).

Fragmented: Should be truly fragmented and not sectioned by us.

Serosal Margin: Again, it is not a margin.

Mucosal Margin: e.g., in a colon resection the proximal and distal margins contain more than mucosa (they contain bowel wall).

Colors and other descriptors are fine if not overdone, but much less important than sizes and relationships.

THINK about what is needed to properly assess the questions present.

AND REMEMBER

ASK QUESTIONS!

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Gross Exam

LIST OF TISSUES TO BE EXEMPTED FROM ACCESSIONING IN THE DIVISION OF ANATOMIC PATHOLOGY

Note: The removal of such tissues and their disposition must be documented in the patient's chart.

- Foreskin from infants
- Placentas in the absence of clinical indications for pathologic examination
- Medical devices such as orthopedic hardware, pacemakers, catheters, etc. **EXCEPTION: Any device removed for apparent failure must be retained by the Hospital (as required by the Safe Medical Devices Act). Send them to Pathology with completed Path slip, indicating, "HOLD FOR RISK MANAGEMENT".**
- Foreign body, unless the physician requests an identification
- Crystalline lens
- Teeth
- Research specimens previously authorized in writing by UWMC Medical Director for transmission to various research labs
- Tissues and organs for transplantation, including bone submitted to the bone bank
- Portions of bone and other tissues removed for access to an operative field, such as segments of rib removed for access to the lung and fibrous tissue and muscle removed for access to a joint
- With few exceptions, such as tumors of the central nervous system, tissues removed via suctioning are not considered surgical specimens.
- Tissues removed by burring, scraping, reaming, or in any manner that morcellizes them so that pathologic examination is rendered unfruitful
- Residual tissue from frozen sections on margins of Mohs micrographic surgical specimens
- Thrombi removed from vascular grafts
- Products of conception where a gross examination has been performed by the attending physician who performed the procedure, there is documentation that fetal tissue, a chorionic sac or chorionic villi have been identified, and in which there is absence of a hydropic appearance or other abnormality
- Nasal septum
- Bunions, bone spurs, condylectomies and tendonectomies unless significant pathologic process is suspected
- Skin from plastic and/or reconstructive procedures, other than those done for malignant neoplasms
- Renal calculi - send directly to chemistry
- Varicose veins
- Tissue accompanying a foreign body
- Cholesteatomas (when tissue is available)
- Knee cartilage other than those removed by morcellization
- Loose bodies from joints
- Skin, scar (no previous neoplasm)
- Tattoos
- Ureter from donor nephrectomy

TISSUES FOR GROSS EXAMINATION ONLY

- Middle ear ossicles
- Atherosclerotic plaques
- Traumatic amputation specimens of digits and portions of extremities

- Portions of bone (such as patella, radial head) removed for traumatic fracture or to revise the anatomy of the structure (such as radial head removed for shortening the radius)
- Hernial sacs (to be examined histologically if grossly abnormal)

TISSUES TO BE EXAMINED AND ASSIGNED A *TISSUE IDENTIFICATION CHARGE* ONLY (GENERATES AT LEAST ONE HISTOLOGICAL SLIDE)

- Anal tag
- Fallopian tubes
- Hydrocele
- Intervertebral discs
- Skin tags
- Sympathetic ganglia
- Tonsils
- Vaginal wall tissue, vaginal mucosa, alone
- Vagus nerves
- Vasa deferentia
- Foreskin (prepuce) from adults

Approved by the Medical Staff Administrative Committee (MSAC) May 11, 1998.

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Special Techniques

Section 1 - DNA Flow Cytometry
Author: Peter Rabinovitch, MD

Section 2 - Ordering IHC Online
Author: Tracie Evans & Farinaz Shokri

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DNA Flow Cytometry

Peter Rabinovitch, MD

CATEGORIES OF RELEVANCE TO PROGNOSIS OR DIAGNOSIS

VALUE FOR PATIENT CARE

- Breast
- Endometrial carcinoma
- Ovarian carcinoma
- Prostate carcinoma
- Urinary bladder carcinoma
- Barrett's esophagus
- Non-Hodgkin's lymphomas
- Hydatidiform mole
- Ulcerative Colitis

RESEARCH INTEREST AND POTENTIAL VALUE FOR PATIENT CARE

- Carcinomas of kidney, cervix (squamous), colon, lung (squamous)
- Adrenal cortical neoplasms
- Melanoma
- Multiple myeloma
- Glioma
- Soft tissue sarcomas, chondrosarcoma, osteogenic sarcoma

UNCERTAIN VALUE

- Thyroid neoplasms
- Carcinoid tumors
- Mesothelioma
- Meningioma

At UWMC, DNA flow cytometry is done when requested by the clinician, particularly for breast carcinomas, sarcomas for ploidy and S phase analysis and P.O.C. (moles) for exclusion of triploidy. If you have a specimen for which you think flow cytometric evaluation would be of interest, please contact the Flow Cytometry Lab (598-6415). If you are not certain whether the clinicians will request flow cytometric analysis, place a representative sample in Flow Media and submit, marked "HOLD."

Ordering IHC Online

Farinaz Shokri, MT, ASCP

PRINCIPLE

The purpose of this procedure is to expedite on line ordering of ICC by Pathologists and Residents.

Turnaround Time: If the order is placed before 4:30 pm during weekdays assuming that the procedure is followed step by step and that the slides were cut by Histology or GI lab, the case will be run the following day (except for EBV probe and FISH probes which are run twice a week and once a week respectively).

Comment: Residents must consult with an attending physician regarding antibody choice before they place their order on line. You are not allowed to delete any charges once the antibodies are run.

PROCEDURE

1. Log in to PowerPath 2000 and open your case .
2. Click on “ Specimen” Tab.
3. Click on “ Specimen” sub-tab.
4. If the received date on the specimen is more than 30 days past the ordering date, have the office staff reaccession the case for billing purposes. If it is not caught at the time of ordering, it will be an extra day delay to run the case.
5. If the case is within the 30 days time frame, proceed to the next step.
6. Click on “Material tree” sub- tab.
7. Click on the block of interest(not on the specimen, nor on the unstained slides) and right click.
8. Choose the “New Order” from the list
9. Choose one of the codes listed in the table below that best matches your need and type it in the box under code. Order twice the number of unstained slides as antibodies ordered in case you need additional studies later.

of unstained slides needed = # of antibodies to be ordered x 2

Example: if you need to order 5 antibodies, the number of unstained slides you need to order is 10 therefore the code to use is: ICC 110.

Code	Description
icc 15	1 recut + 5 unstained
icc 18	1 recut + 8 unstained
icc 110	1 recut + 10 unstained
icc 112	1 recut + 12 unstained
icc 115	1 recut + 15 unstained
icc 312	3 recuts + 12 unstained
icc recut	To order H&E only
icc us	To order unstained slides only
icc slides	To order unstained slides from GI lab

10. If you choose one of the last 3 codes from the above table ("icc recut", "icc us", "icc slides"), then tab over to "Quantity" box and choose the correct number of slides you need to order for each.
11. Tab over to the instruction section at the bottom half of the screen and type any special cutting instructions to Histology or GI lab as the above orders will only show up on their worklists. (example : "Don't waste tissue", " number the slides as you cut them")
12. Return to "Code" and down arrow to have a blank space and type the IP code from the IP code list provided to you . If you don't have that list handy, just type "IP"and tab. It will show you the complete IP list. Select the antibody you need from the list.
13. Tab over to "Source material" and choose any additional blocks that need the same IP code.
14. Tab over to the instruction section at the bottom half of screen and type in the differential diagnosis / clinical history only on the first antibody ordered. These instructions will appear on the ICC worklist.
15. **Repeats and/or Additional Studies:** When ordering additional markers on a case that already had some IHC run on it previously, make sure you type in "ADD'L" in the instruction field of the marker requested. In addition, please contact IHC lab staff to verify they have enough unstained slides in the file. Otherwise they will instruct you to order more unstained slides. Do not order another H&E . These steps need to be followed to prevent delays on the case. **Exceptions:** Any repeat studies need to be ordered by the IHC staff. Please fill out the "*ICC Request Form*", indicate that it is a repeat and the reason for wanting to repeat the study. This is to assure the patient does not get charged twice for the same test.

16. Repeat step 10 to 13 for any additional antibodies you need.
17. Order "IP neg" for a negative control on all new cases for IHC.
Additional IHC studies do not need a negative control.
18. After you have ordered all your antibodies, click "OK" at the bottom of the screen.
19. Check the bottom half of the screen. Everything you ordered must be there. Make sure the number of unstained slides is twice the number of antibodies ordered.
20. press F10 to save all the changes .

Revised 3/25/05

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Autopsy

Section 1 - Medical Examiner Reporting

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Section 3 - Fetal Autopsy Procedure

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Medical Examiner Reporting

Corinne Fligner, MD

TYPES OF DEATH TO BE REPORTED TO THE KING COUNTY MEDICAL EXAMINER'S OFFICE, SEATTLE, WASHINGTON

Jurisdiction is vested in the King County Medical Examiner over all bodies who come to their death as described in RCW 68.08.010. This section explains the types of deaths in that statute. All of them must be reported to the Medical Examiner's Office. Although we have tried to be as complete and specific as possible in compiling this list, we realize there will always be cases that may not fit the criteria exactly. Please call the Medical Examiner's Office, 206-731-3232, if you are uncertain whether a case falls within our jurisdiction.

1. Persons who die suddenly when in apparent good health and without medical attendance within thirty-six (36) hours preceding death. This category should be reserved for the following situations:
 - A. Sudden death occurring in a person without a known natural cause;
 - B. Death during an acute or unexplained rapidly fatal illness, for which a reasonable natural cause has not been established;
 - C. Deaths occurring in anyone not under the care of a licensed physician;
 - D. Deaths of persons in nursing homes or other institutions where medical treatment is not provided by licensed medical personnel.
2. Circumstances indicate death caused entirely OR IN PART by unnatural or unlawful means. This category includes but is not limited to:
 - A. Drowning, suffocation, smothering, burns, electrocution, lightning, radiation, chemical or thermal injury, starvation, environmental exposure, neglect;
 - B. Unexpected deaths during, associated with, or as a result of, diagnostic or therapeutic procedures;
 - C. All deaths in the operating room whether due to surgical or anesthetic procedures;
 - D. Narcotics or other addictions, other drugs including alcohol or toxic agents, or toxic exposure;
 - E. Death thought to be associated with, or resulting from the decedent's occupation; this includes chronic occupational disease such as asbestosis and black lung;
 - F. Death of the mother caused by known or suspected abortion;
 - G. Deaths occurring from apparent natural causes during the course of a criminal act, i.e., victim collapses during a robbery.
 - H. Deaths that occur within one year following an accident even if the accident is not thought to have contributed to the cause of death;
 - I. Death following all injury producing accidents, if recovery was considered incomplete or if the accident is thought to have or may have contributed to the cause of death (regardless of the interval between accident and death).
3. Suspicious circumstances. This category includes but is not limited to deaths under the following circumstances.
 - A. Deaths resulting from apparent homicide or stabbing;
 - B. Hanging, gunshot wounds, stabs, cuts, strangulation, etc.;
 - C. Alleged rape, carnal knowledge, or sodomy;

- D. Deaths during the course of, or precipitated by, a criminal act;
 - E. Deaths that occur while in a jail, prison, in custody of law enforcement, or other non-medical public institutions.
-
- 4. Unknown or obscure causes. This category includes:
 - A. Bodies that are found dead (see criteria #1);
 - B. Deaths during or following an unexplained coma.

 - 5. Deaths caused by any violence whatsoever, whether the primary cause or any contributory factor in the death. This category includes but is not limited to:
 - A. Injury of any type including falls;
 - B. Any deaths due to, or contributed to, by any type of physical trauma.

 - 6. Contagious disease. This category includes only those deaths wherein the diagnosis is undetermined, and a contagious disease which may be a public health hazard is a suspected cause of death.

 - 7. Bodies that are not claimed. This category is limited to cases where no next-of-kin or other legally responsible representatives can be identified for disposition of the body.

 - 8. Premature and stillborn infants. This category includes only those stillborn or premature infants whose birth was precipitated by maternal injury, criminal or medical negligence, or abortion under unlawful circumstances.

**UWMC Autopsy Service
Technical Competence**

Resident Name:	R1 R2 Other
Rotation Dates:	

Task	Case/Date	Competence (Date/Evaluator)
1) Adult evisceration (Total including bowel and tie-off of vessels) (5)	Performed: UF ____ / ____	
	Performed: UF ____ / ____	
	Performed: UF ____ / ____	
	Performed: UF ____ / ____	
	Performed: UF ____ / ____	
2) Adult Pelvic Organs (5) Observed: UF _____	Performed: UF ____ / ____	
	Performed: UF ____ / ____	
	Performed: UF ____ / ____	
	Performed: UF ____ / ____	
	Performed: UF ____ / ____	
3) Adult brain removal (10) Observed: UF _____	Performed: UF ____ / ____	
	Performed: UF ____ / ____	
	Performed: UF ____ / ____	
	Performed: UF ____ / ____	
	Performed: UF ____ / ____	
	Performed: UF ____ / ____	
	Performed: UF ____ / ____	
	Performed: UF ____ / ____	
	Performed: UF ____ / ____	
	Performed: UF ____ / ____	
4) Adult Spinal Cord Removal (5) Observed: UF _____	Performed: UF ____ / ____	
	Performed: UF ____ / ____	
	Performed: UF ____ / ____	
	Performed: UF ____ / ____	
	Performed: UF ____ / ____	
5) Adult heart dissection (5) Observed: UF _____	Performed: UF ____ / ____	
	Performed: UF ____ / ____	
	Performed: UF ____ / ____	
	Performed: UF ____ / ____	
	Performed: UF ____ / ____	

Task	Case/Date	Competence (Date/Evaluator)
6) "Run" adult bowel (3) Observed: UF _____	Performed: UF ____ / ____	
	Performed: UF ____ / ____	
	Performed: UF ____ / ____	
7) Adult neck organ removal (3) Observed: UF _____	Performed: UF ____ / ____	
	Performed: UF ____ / ____	
	Performed: UF ____ / ____	
8) Sew adult body (2) P Observed: UF _____	Performed: UF ____ / ____	
	Performed: UF ____ / ____	
9) Adult testicle removal (3) Observed: UF _____	Performed: UF ____ / ____	
	Performed: UF ____ / ____	
	Performed: UF ____ / ____	
10) Inflate lungs (2) Observed: UF _____	Performed: UF ____ / ____	
	Performed: UF ____ / ____	
11) Fetal dissection (3) Observed: UF _____	Performed: UF ____ / ____	
	Performed: UF ____ / ____	
	Performed: UF ____ / ____	
12) Fetal/Infant Brain removal (3) Observed: UF _____	Performed: UF ____ / ____	
	Performed: UF ____ / ____	
	Performed: UF ____ / ____	
13) Fetal/Infant Spinal Cord removal (3) Observed: UF _____	Performed: UF ____ / ____	
	Performed: UF ____ / ____	
	Performed: UF ____ / ____	
14) Sew baby body (1) Observed: UF _____	Performed: UF ____ / ____	
15) Cisternal CSF removal Adult (2) Infant (2) Observed: UF _____	Performed: UF ____ / ____	
	Performed: UF ____ / ____	
	Performed: UF ____ / ____	
	Performed: UF ____ / ____	
16) Vitreous sampling (2) Observed: UF _____	Performed: UF ____ / ____	
	Performed: UF ____ / ____	
17) Central & peripheral blood sampling (adult) (3) Observed: UF _____	Performed: UF ____ / ____	
	Performed: UF ____ / ____	
	Performed: UF ____ / ____	
18) Take gross photos (4) Observed: UF _____	Performed: UF ____ / ____	
	Performed: UF ____ / ____	
	Performed: UF ____ / ____	
	Performed: UF ____ / ____	
19) Take X-Ray (3) – infant and specimen Observed: UF _____	Performed: UF ____ / ____	
	Performed: UF ____ / ____	
	Performed: UF ____ / ____	
20) Sharpen knife (3) P Observed: UF _____	Performed: UF ____ / ____	
	Performed: UF ____ / ____	
	Performed: UF ____ / ____	
21) Put body into & remove from crypt (2 each) Observed: UF _____	Performed: UF ____ / ____	
	Performed: UF ____ / ____	
22) Release body (2) Observed: UF _____	Performed: UF ____ / ____	
	Performed: UF ____ / ____	
23) Muscle biopsy (2) Observed: UF _____	Performed: UF ____ / ____	
	Performed: UF ____ / ____	
24) Cut adult brain (5) Observed: UF _____	Performed: UF ____ / ____	
	Performed: UF ____ / ____	
	Performed: UF ____ / ____	
	Performed: UF ____ / ____	
	Performed: UF ____ / ____	

UWMC Autopsy Service Technical Competence

One of the educational goals for the UWMC Autopsy Service is achieving competence in the technical aspects of the autopsy, for both adult and perinatal/fetal autopsies.

It is expected that the resident shall have demonstrated technical competence in the following aspects of autopsy practice. In addition, competence in standard adult and fetal/infant dissection techniques is expected, but is not separately evaluated by the attached form (that evaluation will be done in the general rotation evaluation). Each resident is expected to complete the technical competency activities, and submit the completed documentation form to the Residency Director at the end of the first year UWMC Autopsy Service rotation. If the required competencies have not been achieved, they can be completed during the second year rotation. Forms will be included in the resident's permanent file.

Document case numbers and dates for the observation and performance of the required activities. All activities must be completed and competency must be observed and documented for each activity by either an attending pathologist, the Autopsy Service Director, or the Autopsy Coordinator (or by another person, as approved by the Autopsy Service Director).

Activities are as follows:

- Adult evisceration
- Adult pelvic organs
- Adult brain removal
- Adult spinal cord removal
- Adult heart dissection
- Run adult bowel
- Adult neck organ removal
- Sew adult body
- Adult testicle removal
- Inflate adult
- Fetal evisceration and dissection
- Fetal/infant brain removal
- Fetal/infant spinal cord removal
- Sew baby body
- Cisternal CSF removal—Adult and infant
- Vitreous sampling-adult
- Central and peripheral blood sampling—adult
- Take gross photos on photo stand
- Take xray—infant and specimen
- Sharpen knife
- Put body into and remove from crypt
- Release body
- Muscle biopsy
- Cut adult brain

Fetal Autopsy Procedure

Corinne L. Fligner, MD

To: **UWMC Prenatal Diagnosis /OB Attendings and Fellows**
(Drs. Easterling, Shields, Cheng, O'Reilly, Hitti, Carr, Benedetti, Ridgeway, Gopalani, Amory, Tran, and others)
UWMC Prenatal Diagnosis Genetics Counselors (Stefanie Uhrich, Leslie Carpenter, Linda Knight)
UWMC Anatomic Pathology (Drs. Parks, Swanson, Upton; Janet Miller, Jessica Norberg, Tom Small, Dan Luff)

From: Dr. Corinne Fligner, Director
UWMC Decedent Affairs/Autopsy Service

Date: September 21, 2004

This memo is written to clarify how pathology examinations are performed at UWMC on intact and fragmented fetuses ("POC specimens"), in order that patients receive accurate information, and the appropriate consent forms are completed only when necessary.

Fragmented fetuses, which are specimens commonly termed "POC" or "products of conception," consist of fragmented fetal and placental tissue, and are considered to be surgical pathology specimens, which are routinely examined per hospital protocol, no matter what the gestational age. Thus, any uterine evacuation or termination of pregnancy ("D and E"), which results in fragmented fetal and placental tissue, is examined as a surgical specimen, and **no special consent to examine is needed**. These examinations are performed per routine procedure, under hospital guidelines that require that this type of specimen be sent to Anatomic Pathology for examination, and by virtue of the general consent to care signed by patients who are admitted to the hospital. **This examination is not an autopsy examination**. In the usual circumstance, these specimens are examined by pathology residents under the direction of general surgical pathology attendings, who have no special expertise in perinatal/fetal pathology. If it is desired by the attending OB physician that the examination be performed by a pathologist with expertise in fetal/perinatal pathology, that should be indicated on the Pathology request form ("Attention: Dr. Fligner or Dr. Parks"), and the examination will be performed by one of those pathologists.

Intact fetuses are evaluated under different guidelines, and the requirement for examination is different depending on gestational age. These guidelines take into consideration legal views of fetuses with respect to requirement for death certificates (not required for age less than 20 weeks or weight less than 500 grams). Examination of the intact body after death is termed an autopsy. For **intact fetuses less than 20 weeks** gestation, the fetus will routinely be examined **externally only**, along with the placenta, if placental examination is indicated, and no matter what the cause of the fetal demise. This external examination in the less than 20-week gestation fetus does not require an autopsy consent (note that an autopsy consent is required if internal examination/dissection is desired). **However, for fetuses older than 20 weeks, no examination (including no external examination) will be performed unless specific autopsy consent is granted.**

No dissection will be performed on any intact fetus, no matter what the gestational age, without a properly witnessed, completed autopsy consent. Any incisions on the body after death, even for a specimen for cytogenetics, require a properly completed autopsy consent. The Fetal/infant Expiration Packet contains all the paperwork necessary for handling the fetal deaths when the fetus is intact.

In summary:

Intact fetus: **Autopsy consent is required for internal examination for all intact fetuses, no matter what the gestational age.**

No exam for > 20 weeks, without autopsy consent

External exam only for < 20 weeks, even without autopsy consent.

Any incision on the body requires specific autopsy consent.

Fragmented fetus: **Routinely examined as surgical specimen.**

No special consent form needed.

If perinatal/fetal pathology involvement is desired, indicate on the surgical pathology request form, and ideally contact the pathologist to indicate the clinical concerns.

Please contact the Decedent Affairs/ Autopsy Office (598-4205) or me (598-6403 or fligner@u.washington.edu) if you have any questions or concerns about these guidelines.

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[Section 2](#)
[Section 3](#)

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Skin

Section 1 - Skin Cutting Guidelines

Author: Greg Wolgamot, MD PhD

Section 2 - Melanoma: Sentinel Lymph Node Sampling

Author: Larry True, MD & Tom Lawton, MD

Section 3 - CAP Cancer Protocols and Checklists

Including: Carcinoma of the Skin, Melanoma of the Skin

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Technical Editor: [Larry True, MD](#) Web Editor: [Michelle Rickard](#)

Skin Cutting Guidelines

Greg Wolgamot, MD PhD

TRIAGE

1. Punches, shaves, and unoriented excisions go to the pathology staff.
2. Oriented excisions go to the dermatologist.
3. Big specimens (i.e. cross section of an ellipse will not fit into a cassette, or 1/2 cross section of a round excision will not fit into cassette) from dermatologists go to the dermatologist.
4. Large re-excisions from non-dermatologists go to the resident on general surgicals.

Derm Faculty	
Argenyi, Zsolt	Hornung, Robin
Asgari, Maryann	Hurst, Stan
Barnes, Sanford	Kirby, Phil
Berg, Daniel	Kuechle, Melanie
Bub, Jennifer	Olerud, John
Chen, Andy	Piepkorn, Michael
Colven, Roy	Sidbury, Robert
Davis, Claudia ARNP	Wang, Hao
Fleckman, Philip	Welch, Marshall

5. Plastics specimens go to the resident on general surgicals.
6. Specimens with unusual issues go to the resident on dermatology. "Unusual issues" constitutes anything that makes the pathology staff uncertain how to proceed.
7. Before grossing, the pathology staff may page the dermatologist or gross room supervisor who will review the cases to identify unusual tissues (like bullous diseases, special stains, etc.)
8. The gross room supervisor can triage specimens to the pathology staff or general surgicals by mutual agreement with the party receiving the specimen.

SURGICAL GROSSING

General

1. All specimens should be described with 3-dimensional measurements and number of tissue pieces received. (This is important in identifying cross-labeled specimens.)
2. Ink all margins on specimens >0.3 cm, but not the epithelial surface; i.e., no "dunking" in ink (black and blue are preferred colors). Smaller biopsies should have the epidermis marked with orange to aid the imbedding technologist.
3. Tiny specimens should be submitted wrapped in tissue paper; a spot of eosin may be helpful so the embedding technologist can find the specimen.
4. If more than one specimen is received in the same container, ink in different colors.
5. Generally put no more than 3 pieces in the same block, except for curettings or nails.
6. Pieces > 1 cm² should be singly placed in a block.
7. Place the side to be cut facing down in the cassette.
8. Do not cut through bullae or vesicles (blisters); submit whole and communicate with embedding technologist on "Special embedding & Cutting Requests" sheet. Such specimens can be identified by an additional specimen received for immunofluorescence, by seeing "blister",

"bullae", or "vesicles" in the clinical history, or by consultation with the resident rotating on dermatopathology.

9. If a PAS is requested on the requisition sheet, order it up front by communicating with the embedding technologist. Other requested stains should be cleared with the derm resident; unstained slides should be ordered if the resident is not available. Indicate on the requisition sheet what has been ordered.
10. Order a PAS for funguses up front on all nail specimens with the "Special Embedding & Cutting Requests" sheet. Indicate on the requisition sheet that it has been ordered.
11. Put all skin biopsies on the long processor run.
12. Note special cases on the "Special Embedding & Cutting Requests" sheet, which the embedding histotechnologist will use to know which cases require special stains, have bullous lesions, etc.
13. When dictating, please be diligent about reading the patient's name and specimen designation on the bottle, and correlate with paperwork.
14. Direct questions to the pathology resident on dermpath rotation.
15. Ultimately, no set of rules can replace common sense and logic about the best way to handle a specimen, show margins, etc. (which is why these are referred to as "guidelines" rather than "rules"!)

Shaves

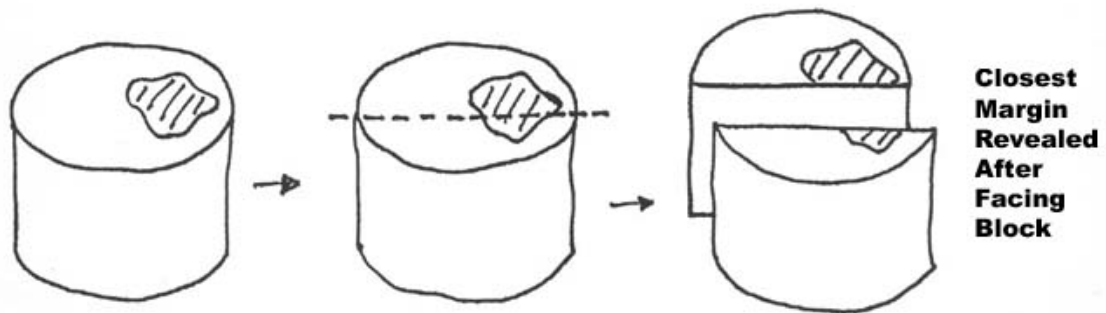
1. Ink margin.
2. Section in 1-3 mm intervals.
3. Wrap in tissue paper.

Sample dictation: *"Received in formalin labeled 'cheek lesion' is a shave biopsy (0.5 x 0.4 x 0.1 cm). In the center of the light tan skin is a verrucous lesion (0.2 cm) that comes to within 0.1 cm of the nearest edge. The surgical margin is inked blue, the specimen is sectioned, and entirely submitted for histological examination. A1: shave, 3 pieces."*

Punches

1. Ink margin, both lateral and deep.
2. Section based on diameter:
 1. 2-3 mm: Submit whole; do not cut.
 2. 4 mm: Bisect (see note).
 3. 6-8 mm: Trisect with a thin central slice.

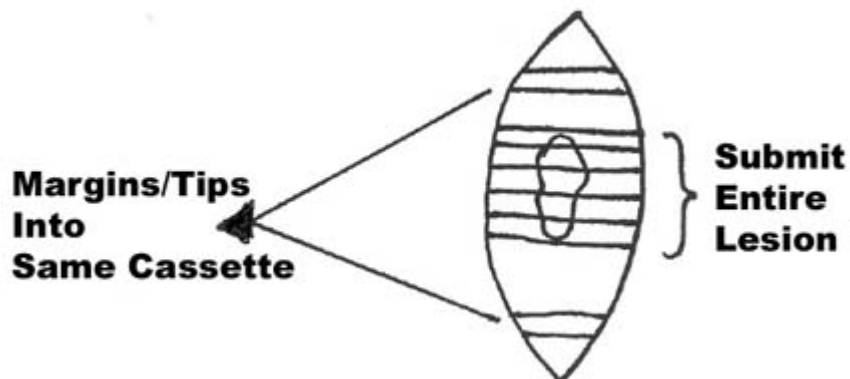
Note: Section so that the closest margin, as well as the central portion of the lesion, is demonstrated on the glass slide. This is best accomplished by cutting just to the side of the lesion, to account for tissue that is lost during facing of the block. Do not section blisters; these should be processed whole and then sectioned after embedding by the histotechnologist.



Sample dictation: "Received in formalin labeled 'cheek lesion' is a punch biopsy (6 mm x 6 mm deep). In the center of the brown skin is a hypopigmented papule (0.2 cm) that comes to within 0.1 cm of the nearest edge. The surgical margin is inked blue, the specimen is sectioned, and entirely submitted for histological examination. A1: punch, 3 pieces."

Unoriented Ellipses

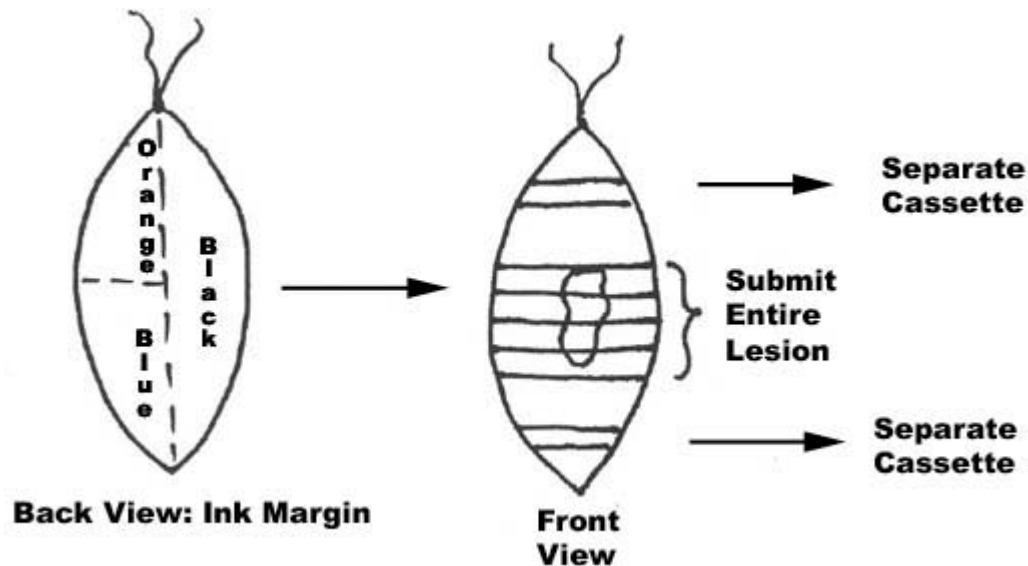
1. Ink margin one color.
2. Section in 2-3 mm intervals.
3. Submit with tips both in same cassette.
4. For large excisions with grossly visible lesions, the entire specimen need not be submitted. Submit the entire lesion or scar, and then submit grossly normal skin between the lesion and the tips in the same cassette. (The tips can later be submitted if the grossly normal skin is positive for neoplasm.)



Sample dictation: "Received in formalin labeled 'cheek lesion' is an unoriented excision (6 x 1.5 x 0.6 cm deep). In the center of the tan skin is a smooth, hypopigmented scar (1.4 cm) that comes to within 0.5 cm of one lateral margin. The surgical margin is inked blue, the specimen is sectioned. Representative sections, including the entire scar, are submitted for histological examination. A1: skin between scar and tips, 2 pieces; A2-A3: scar, 4 pieces."

Oriented Ellipses

1. Examine specimen and requisition sheet. Orient the suture according to the surgeon's request. If no designation is given, orient the suture at 12 o'clock and dictate that you, not the surgeon, have designated it at 12 o'clock.
2. Ink in 3 colors, as shown in the diagram. Dictate ink colors as if you were looking at the skin, not the deep aspect. (Two colors can be used, with the ink junction on the midline/"spine" of the specimen, but then the specimen needs to be organized into cassettes so that the two ends can be differentiated.)
3. Section in 2-3 mm intervals.
4. Submit with tips in different cassettes.
5. For large excisions with grossly visible lesions, the entire specimen need not be submitted. Submit the entire lesion or scar, and then submit grossly normal skin between the lesion and the tips in separate cassettes as if they were the tips. (The tips can later be submitted if the grossly normal skin is positive for neoplasm.)

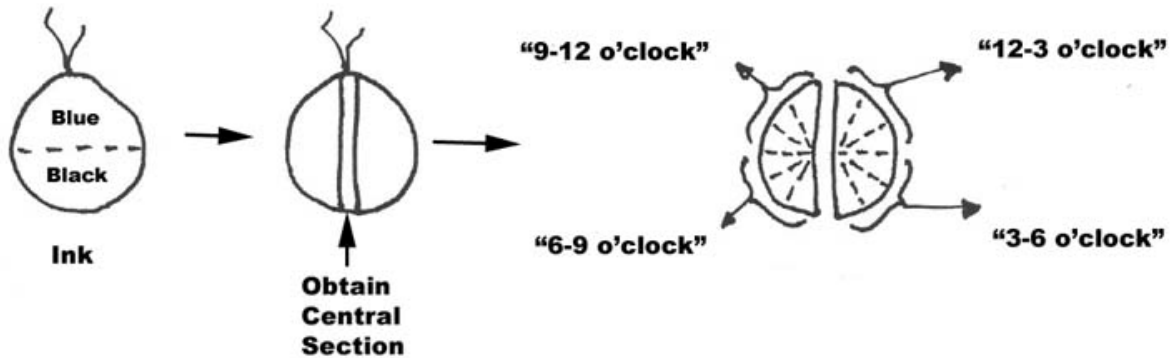


Sample dictation: "Received in formalin labeled 'cheek lesion' is an oriented excision (6 x 1.5 x 0.6 cm deep). A suture present at one tip is designated 12 o'clock by the surgeon. In the center of the tan skin is a smooth, hypopigmented scar (1.4 cm) that comes to within 0.5 cm of one lateral margin. The margin from 12 o'clock to 3 o'clock is inked orange, from 3 o'clock to 6 o'clock is inked blue, and from 6 o'clock to 12 o'clock is inked black. The specimen is sectioned, and representative sections, including the entire scar, are submitted for histological examination. A1: skin between scar and 12 o'clock tip, 1 piece; A2-A3: scar, 4 pieces; A4: skin between scar and 6 o'clock tip, 1 piece."

Round Excisions

1. Ink margins. If the specimen is oriented *and* of a workable size, ink the 12 o'clock half blue and the 6 o'clock half black.
2. If a complete cross-section will fit into one cassette, take a central vertical cross-section. Put the remaining pieces back together, and radially section.

3. If a complete cross-section will not fit into one cassette, use your judgment about whether a central section to show the complete lesion is feasible. Radially section the remainder for examination of margins.
4. If you suspect that the specimen will be difficult to embed, make notes on the "Special Embedding & Cutting Requests" sheet.



Sample dictation: "Received in formalin labeled 'cheek lesion' is an oriented, round excision (2 cm diameter x 0.8 cm deep). A suture present at one edge is designated 12 o'clock by the surgeon. In the center of the tan skin is a symmetric, verrucous papule with a central keratin plug (1.4 cm) that comes to within 0.2 cm of the 3 o'clock lateral margin. The margin of the 12 o'clock half is inked blue, and the 6 o'clock is inked black. After a central, complete cross-section is obtained, the remainder of the specimen is radially sectioned. The entire specimen is submitted for histological examination. A1: cross section from 12 o'clock to 6 o'clock, 1 piece; A2: 12 o'clock to 3 o'clock, 3 pieces; A3: 3 o'clock to 6 o'clock, 3 pieces; A4: 6 o'clock to 9 o'clock, 3 pieces; A5: 9 o'clock to 12 o'clock, 3 pieces.

Skin Tags

1. Ink the base if it can be identified.
2. If the specimen is >3 mm, bisect the specimen perpendicular to the base. If <3 mm, submit whole.

Sample dictation: "Received in formalin labeled 'right axilla' is a skin tag (1.2 x 1.0 x 1.0 cm). The cutaneous surface is light tan and wrinkled. The surgical margin is inked blue, the specimen is bisected, and entirely submitted for histological examination. A1: skin tag, 2 pieces."

Nails

1. If oriented, gross as one would any oriented excision, but it is not necessary to ink nails.
2. If not oriented (most cases), section into 2-3 mm pieces and entirely submit in one cassette. More than 3 pieces are permitted.
3. Order a PAS stain up front.

Sample dictation: "Received in formalin labeled 'left thumb' is a nail plate (0.9 x 0.5 x 0.1 cm). The cutaneous surface is cracked, with focal pitting. The specimen is sectioned and entirely submitted for histological examination. A1: nail, 3 pieces."

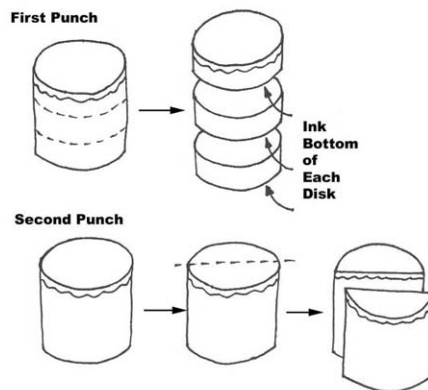
Curettings

1. Do not ink.
2. Submit entirely.
3. More than 3 pieces can be placed in a cassette, as seems reasonable.

Sample dictation: *"Received in formalin labeled 'festering hip lesion' are multiple fragments of tan soft tissue (1 x 1 x 0.5 cm in aggregate). The specimen is entirely submitted for histological examination. A1-A5: curettings, multiple pieces."*

Scalp Biopsies Designated "Alopecia protocol"

1. Two punch biopsies are usually submitted; one is for horizontal sectioning, and the second is for standard vertical sectioning.
2. Section one biopsy parallel to the skin surface, making disks, each 1-2 mm thick.
3. Put ink on the deep surface of each disk, for orientation (not margins).
4. Place into cassette, ink side down, and indicate on the "Special Embedding & Cutting Requests" sheet that the specimens be cut from the inked side.
5. Cut the second punch biopsy in the standard fashion, perpendicular to the cutaneous surface, and submit in a separate cassette.



Sample dictation: *Received in formalin labeled 'scalp, alopecia protocol' are two punch biopsies (each 4 mm diameter x 6 mm deep) with smooth light tan skin. No hair is present. One specimen is sectioned parallel to the cutaneous surface, and the other is sectioned perpendicular to the cutaneous surface. Both are entirely submitted for histological examination. A1: Punch, cut parallel to surface, 3 pieces; A2: Punch, cut perpendicular to surface, 2 pieces."*

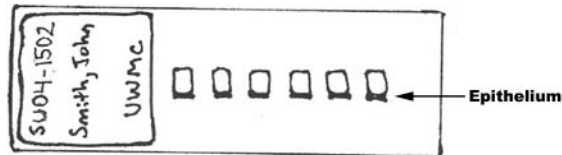
HISTOLOGIC EMBEDDING AND CUTTING

Proper embedding of dermatopathology specimens is crucial because accurate interpretation is critically dependent on orientation, perhaps more than any other type of biopsy. Accurate interpretation is especially important for melanocytic lesions. (Misdiagnosing a melanoma can have tremendous medicolegal implications!) Evaluation of margins is critical, especially in specimens taken from the face, genitalia, hands and feet, where additional surgery is especially disfiguring.

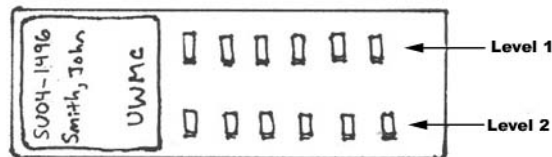
1. Embed so that the pathologist can view a cross-section of the skin, from superficial to deep (except disks for "alopecia protocol"; see #2 below). Shaves are embedded on edge.
2. Multiple round disks with one surface inked are to evaluate "alopecia" (hair loss). These have been cut parallel to the skin surface and should be embedded to view round disks. One side of

each should be inked for your orientation; embed inked side down so that the inked surface is leveled into first on the microtome.

3. Embed pieces close to one another in the block. (It is easy to overlook a piece when looking through a microscope, which has a limited field of view.)
4. Organize pieces in a row, not haphazardly.
5. Generally put a serial ribbon of 6-8 sections on a slide; see diagram. (6-8 sections may not fit if the sections are too big.)



6. For smaller pieces, two levels can be placed on a single slide, with each level in a row.



7. Ensure that the cut slides are representative of the tissue in the block. (This may be important when a specimen is not bisected, so that the specimen must be leveled into in order to obtain a representative section. The lesion is almost always at the center of the biopsy.)
8. Ensure that all of the epithelium is present on the slide. (The most common reason for ordering recuts is because epithelium is missing.)
9. In cases that special stains are ordered up front, please cut extra unstained slides to begin the stains as request on the "Special Embedding & Cutting Requests" sheet.

SPECIAL EMBEDDING & CUTTING REQUESTS

Case # SU04-1281 Block # A2

☐ Embed on end

☐ Embed on edge

☐ Rush case

☐ Unstained slides for IHC

☐ Unstained slides for Specials

☐ Tiny/scant tissue

☒ Do not embed/Hold for instructions

☒ Additional comments: ORIENTATION IS CRITICAL -
please page me when you are ready to
embed. Thanks Howard p:603-1234

Melanoma: Sentinel Lymph Node Sampling

Larry True, MD & Tom Lawton, MD

GROSS DESCRIPTION

- Size and shape of specimen.
- Describe and measure the pigmented lesion, commenting upon gross proximity to surgical margins, shape of lesion, i.e., symmetrical ?, regular margins?, etc., color, i.e., variegated, homogeneous, etc.

SECTIONS

- Ink the lateral and deep margins
- Section sequentially from one end of the specimen to the other through the short axis, i.e., in a "bread loaf" manner
- Optimally, sectioning is done at 1 mm intervals. Submit the entire specimen if small (less than 8 cassettes, the scar if large, or discuss with attending).

DIAGNOSTIC REPORT

Comment upon the following:

- Extent of invasion (vertical gross phase), represented both by Clark's levels and Breslow's measurement (in mm).
- Type of radial growth phase (if present); i.e., superficial spreading versus lentigo maligna type.
- Presence or absence of satellitosis and/or ulceration.
- Qualitative assessment of mitotic rate.
- Nature and extent of inflammatory cell reaction.
- Proximity of lesion to inked surgical margins.

Definition of TNM - Primary Tumor (T)	
AJCC, 2002	
TX	Primary tumor cannot be assessed.
T0	No evidence of primary tumor.
Tis	Melanoma <i>in situ</i> (atypical melanocytic hyperplasia/severe dysplasia; Clark's level I)
T1	Tumor 2 cm or less in greatest dimension (from top of granular layer or base of ulceration).
T2	Tumor more than 2 cm, but not more than 5 cm, in greatest dimension and/or invades to papillary-reticular interface (Clark's level III)
T3	Tumor more than 5 cm in greatest dimension and/or invades the reticular dermis (Clark's level IV)
T4	Tumor invades deep extradermal structures (i.e., cartilage, skeletal muscle, or bone) and/or invades subcutaneous tissue (Clark's level V) and/or there are satellite nodules of tumor within 2 cm of the primary tumor
Note: In case of multiple simultaneous tumors, the tumor with the highest T category will be classified and the number of separate tumors will be indicated in parentheses, e.g., T2 (5).	

Definition of TNM - Regional Lymph Nodes (N)	
AJCC, 2002	
NX	Regional lymph nodes cannot be assessed.
N0	No regional lymph node metastasis.
N1	Regional lymph node metastasis.

REFERENCES

-  American Joint Committee on Cancer. *AJCC Cancer Staging Handbook, 6th ed.* New York: Springer, 2002.

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 Technical Editor: [Larry True, MD](#) Web Editor: [Michelle Rickard](#)
 Last modified: Wednesday, July 13, 2005

CAP Cancer Protocols and Checklists

Skin

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Carcinoma of the Skin	Checklist	Full Protocol
Melanoma of the Skin	Checklist	Full Protocol

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Head & Neck

**Section 1 - Otolaryngology including larynx, neck, mandible
and glandular structures**

Author: Marc Coltrera, MD

Section 2 - Hypopharyngeal Cancer

Author: National Cancer Institute - cancer.gov

**Section 3 - CAP Cancer Protocols and Checklists
Including: Upper Aerodigestive Tract (Including
Salivary Glands)**

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Otolaryngology

Marc Coltrera, MD

The purpose of this handout is to acquaint the surgical pathologist with the general anatomy and questions that an Otolaryngology - Head and Neck surgeon is concerned with. Suggestions are made which may or may not be already obvious or which may not meet with your basic methods of handling specimens. The techniques presented here are distilled from experience as an Otolaryngology - Head and Neck surgery resident in the Pathology Department of the Massachusetts General Hospital. Please feel free to inform me of any improvements or additions that you may find helpful.

GENERAL HANDLING OF SPECIMENS

Fixation of tissues prior to sectioning will allow easier sectioning. This is especially true in laryngeal specimens. The one exception is neck dissections, which are much easier to process as unfixed (fresh) specimens.

Ossified cartilage and bone will need decalcification. Fixation is required prior to decalcification since the acid used (usually 10% HNO₃) will digest non-fixed tissue. Even then decalcifications will wash out detail; therefore, soft tissue resection margins should be sampled prior to decal.

Ink all resection margins. In glandular specimens and partial laryngectomy procedures where the attached cartilage tends to pull away in cutting/processing, the actual resection margin may be hard to discern on the pathology slide.

In the dictated description of the specimen include the important anatomic structures that give an indisputable clue as to the tissue actually removed. For example in the case of a radical neck dissection the specimen tends to shrink after removal. By measuring the length of internal jugular vein included it will be clear just how thorough the surgeon was in his dissection superiorly and inferiorly.

SPECIMEN HANDLING

Four basic types of specimens are discussed:

- Larynx.
- Radical neck dissection/functional neck dissection.
- Composite resection.
- Glandular structures (parotid, submandibular, thyroid).

LARYNX

- Anatomy: schematic of a larynx with the pertinent structures noted. (Figure 1)
- Before fixation of the specimen, describe the specimen and record the dimensions as you would normally do. Include the number of tracheal rings resected in the case of a total laryngectomy. Then split the specimen in the posterior midline and hold it open with a Q-tip shaft. After fixation, it will remain open allowing for easier sectioning. Ink all mucosal margins. If the tumor is very large, ink the soft tissue margins as well (i.e., the strap muscles anteriorly). When measuring the tumor's dimensions include any subglottic extension measured from the level of the true cords: note where the measurement is taken from (anterior, middle or posterior: the significance of subglottic extension varies with position.) (Figure 2)

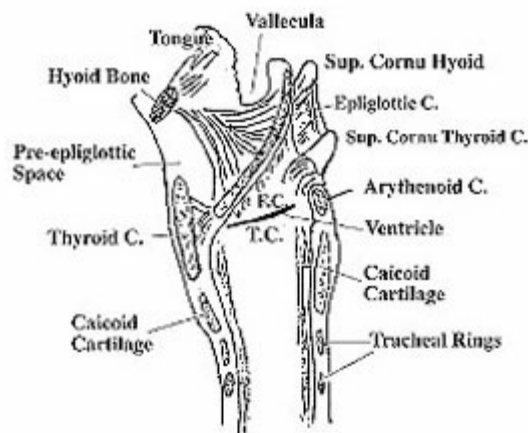


Figure 1.

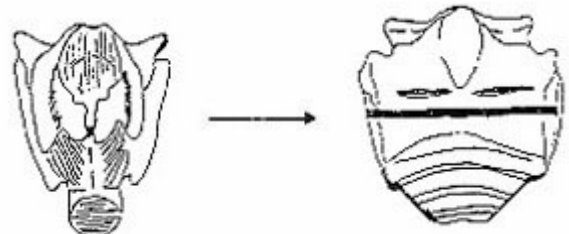


Figure 2.

- Standard sections: These should be done on all larynx specimens. Partial laryngectomies will not include all these areas:

Margins		
I	Valleculas	
II	Piriform sinuses	
III	Postcricoid area	
IV	Tracheal resection margin	
II and III may be combined.		Figure 3.

- To document tumor invasion:
 - o Vertical section through anterior commissure: epiglottis, thyroid, cartilage, pre-epiglottic space and anterior soft tissue.
 - o Vertical section through false vocal cord ventricle, true cord, subglottic area and should include thyroid, cricoid and/or tracheal cartilage if part of the specimen on the involved side.
 - o Vertical section through arytenoid with or without cricoid cartilage on the involved side.
 - o Extra sections through any area that you feel might show cartilage invasion or extra-laryngeal spread which would affect the tumor staging.

Modified laryngectomy specimens fall into three basic categories:

- Hemilaryngectomy.
- Subtotal.
- Supraglottic.

Needless to say the surgical resection margins must all be evaluated. In a supraglottic laryngectomy the inferior resection margin is a thin strip of mucosa in the ventricle (see cross-section). The tumor may be breaking through or close to the surface of the false cord but remember that the medial and inferior surfaces of the false cord abut air spaces and are not surgical margins. It is particularly important in this specimen to ink the proper margin.

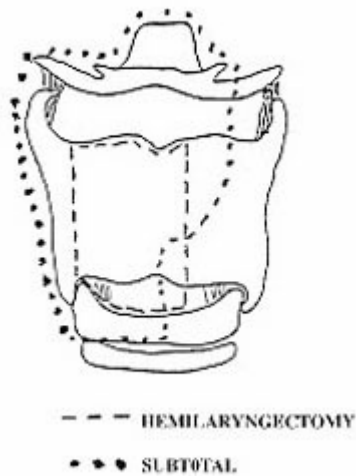


Figure 4.

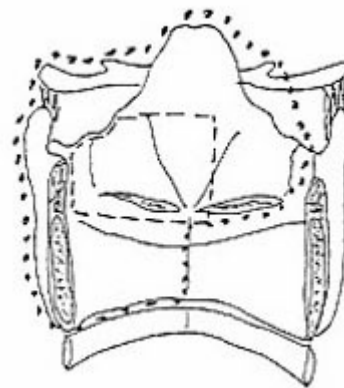


Figure 5.

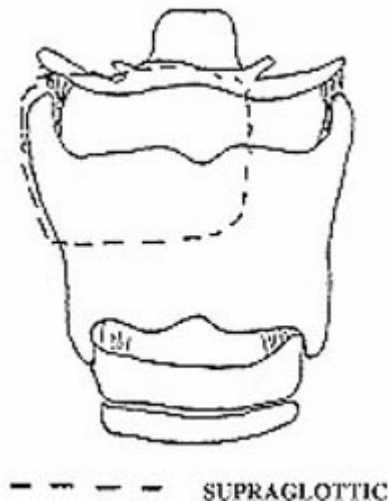


Figure 6.

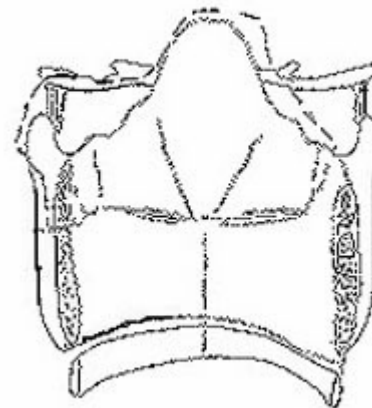


Figure 7.

RADICAL NECK SPECIMENS

Do not fix neck specimens. Refrigerate them if they need to wait overnight.

Orientation

In a radical neck resection the sternocleidomastoid (SCM) muscle will be included along with the internal jugular vein (IJ). The inferior portion of the muscle is usually larger (the two heads) and the IJ should be on the medial surface of the muscle with a silk tie on one or both ends. If included, the submaxillary gland lies at the superior end. The external jugular vein (EJ) occasionally can be very large and confused with the IJ. The clue in this case is the connective tissue, which is usually attached, in the surgical specimen only to the deep surface of the SCM.



Figure 8.

In a "functional neck resection" the SCM and IJ are not removed. The surgeons have done part of your work for you but it is up to them to properly tag one end of the specimen to orient high from low. Do not be confused by terms such as "modified radical neck". If they are using the term correctly, it means certain structure(s) have been spared. A "suprahyoid neck dissection" is a submandibular and submental clean out.

Description

Measure the IJ vein's length. Mention the submax glad if present and cut the gland from representative cross-sections. Gross involvement of any large vessel should be noted and the IJ opened to rule out intimal involvement.

Dissection

Divide the specimen into three portions: high, mid and low jugular. The posterior triangle dissection can be submitted separately or as part of the low jugular area. The muscle should be separated from the connective tissue that bears the nodes. One end of the tissue should be anchored while counter traction is applied with forceps. The tissue can then be thinned with a scapel blade. Nodes as small as 0.5 cm can be found in the thinned tissues. The average node count from a radical neck ranges from 25-45, less in irradiated necks. If there is involvement of extranodal structures (vein, muscle) include a cross-section of this area with the nodes/tumor attached.

COMPOSITE RESECTIONS

Orientation

The definition of a composite resection is a resection that includes bone (usually mandible) with attached soft tissue - tongue, pharyngeal wall, floor of mouth, neck dissection, etc. Orientation follows from the mandibular segment and the intraoral attachments.

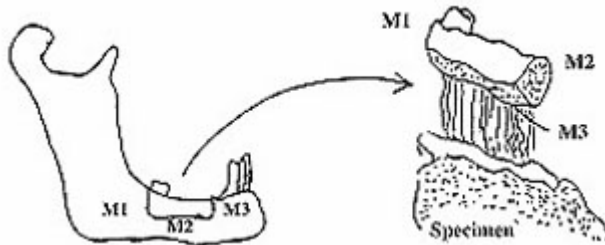


Figure 9.

Description

Relatively straightforward.

Handling of the margins is particularly important on the medial side (usually tongue). All margins should be inked and the mandible/soft tissue portion fixed. The soft tissue margins should be removed prior to decalcification of the mandible. The location of the margins submitted must be carefully documented (i.e., posteromedial deep tongue or floor of mouth).

Decalcification of the mandible can take 3-7 days. The teeth can be removed since they take longer. The bony margins should be inked and submitted since tumor spread takes place easily in the marrow cavity. If tumor appears to invade the mandible, a cross-section of this area should be submitted to the document depth of invasion.

GLANDULAR STRUCTURES

- Orientation is dependent on the surgeon making the specimen.
- Description is straightforward.
- Ink and fix the entire surface. Sectioning is usually perpendicular to the long axis. If tumor extends into an end, then sections oriented parallel to the axis will be required.

POINTS TO REMEMBER

The **T**(umor), **N**(ode), **M**(etastases) staging system as used by head and neck surgeons is a prospective staging system based on physical examination. The pre-op exam can be grossly inaccurate and the pathology findings are then crucial to the final choice of therapy. Therefore, it is imperative that certain standard sections be taken on each and every specimen you evaluate. The head and neck region is remarkable for marked differences in prognosis based on tumor spread between contiguous, easily identifiable structures. Lymphatic spread can be very compartmentalized depending on the tumor's location +/- a half a centimeter. With this in mind, I have summarized the surgical pathologist's findings, apart from clear margins and tumor histopathology that matter most. These are detailed in the text of this handout.

Larynx: Involvement of true cord only (T1)
Invasion of the cartilage, extension beyond the larynx
(see subglottic extension notes (T4))

Necks: Number of positive nodes (include total number found)
What levels did the positive nodes come from?

Composite: Depth of mandibular invasion
Marrow cavity at the margins

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Hypopharyngeal Cancer

National Cancer Institute

This information is located at the following website

http://www.cancer.gov/cancer_information/doc.aspx?version=1&viewid=20c10658-3cd7-47c0-a278-8970248b93bf

and is linked on the online version of this publication.

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Lungs & Pleura

Section 1 - Lung Resection for Carcinoma

Author: Rodney A. Schmidt, MD PhD

Section 2 - Open Lung Biopsy

Author: Rodney A. Schmidt, MD PhD

Section 3 - Lung Biopsies for Transplant Rejection

Author: Rodney A. Schmidt, MD PhD

Section 4 - Lung Biopsies for Pulmonary Hypertension

Author: Rodney A. Schmidt, MD PhD

Section 5 - CAP Cancer Protocols and Checklists

Including: Lung, Thoracic Mesothelium, Peritoneum

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Lung Resection for Carcinoma

Rodney A. Schmidt, MD PhD

Correct staging of lung cancers is dependent on cell type, tumor size, proximity of tumor to pleura and carina, and presence or absence of lymph node metastases (broken down by location).

PROCEDURE

- Ink the surface over the tumor.
- Submit sections of the primary tumor in formalin (at least one section per cm. of maximum tumor dimension), and (optionally) in flow medium, methacarn and EM fixative.
- Either obtain sections of the fresh tissue or inflate with formalin and fix. Sections should include:
 - o primary tumor.
 - o overlying pleura and/or chest wall (including the margin).
 - o bronchial margin.
 - o lymph nodes, including peribronchial nodes.
 - o lung parenchyma remote to the tumor.
 - o any other lesions.
- Histochemical stains:
 - o H and E's (routine).
 - o Movat elastic tissue stain of tumor/pleura relationship if tumor abuts pleura.
 - o (As needed), PAS, ICC and EM.

GROSS DESCRIPTION

It should explicitly comment on:

- Tumor size (one dimension minimum, 3 preferable)
- Relation of the tumor to the pleura.
 - o Does tumor abut the pleura?
 - o Is the overlying pleura puckered?
 - o Is there obvious extension through the pleura?
 - o Are chest wall tissues (incl. parietal pleura) present?
 - o Are there nodules or lesions suspicious of pleural tumor deposits or intralymphatic spread?
- Proximity of the tumor to the bronchial margin of resection and to the hilar margins (closest approach in cm).
- Is atelectasis or obstructive pneumonitis associated with the tumor?
 - o Does it extend to the hilum?
 - o Does it involve the entire lung?
- Lymph nodes. All lymph nodes must be dissected out of the specimen and submitted for histologic examination. The nodes fall into 3 groups for staging purposes:
 - o **N1 nodes** - Peribronchial and interlobar nodes (lobar and smaller bronchi, within the substance of the lung (groups 11, 12, 13, 14); basically any nodes within the visceral pleural envelope).
 - o **N2 nodes** - Nodes around the mainstem bronchus, subcarinal nodes, and ipsilateral mediastinal nodes (groups 10, 7, and ipsilateral 2 and 4). Although some of these nodes may be attached to a pneumonectomy specimen, they are usually submitted separately.
 - o **N3 nodes** - Contralateral mediastinal and supraclavicular nodes (submitted separately by the surgeon).
- Other pathology in the remote lung, such as emphysema, anthracotic pigment, fibrosis, etc.

MICROSCOPIC DETERMINATION

- Tumor cell type. Small cell vs. nonsmall cell; adenocarcinoma, squamous cell carcinoma or large cell undifferentiated. Do mucin stains (PASD - [PAS with diastase digestion] or mucicarmine) on tumors that appear to be large cell undifferentiated carcinomas.
- Involvement of the visceral pleura. The key criterion is whether the tumor extends through the visceral pleural elastica. An elastic tissue stain (Movat stain, preferably) should be done on cases where there is any question of pleural involvement.
- Extension into chest wall. The best landmark is chest wall fat or muscle.
- Extension of tumor to surgical margins of resection, including the hilar peribronchial margins.
- Other features which may be of prognostic value include:
 - o Lymphatic space invasion
 - o Arterial invasion
 - o Venous invasion
 - o Nuclear grade
 - o Location entirely within a bronchus (as defined by the cartilaginous plates).
- Presence or absence of metastatic carcinoma in each lymph node. Nodal involvement by direct extension is equivalent to a nodal metastasis for staging purposes.
- Any pathologic abnormalities in the remainder of the lung.

DIAGNOSIS

May take the following form but **must** include all staging information:

Type of surgical resection: Type and differentiation of tumor

- Staging information
 - o Size (T1 <3.0 cm greatest dimension).
 - o Extent
 - Confined within visceral pleural elastica.
 - Penetration of visceral pleural elastica (T2).
 - Extension into chest wall or mediastinum (T3).
 - Involvement of serosal surface/seeding of pleural cavity (T4).
 - o Involvement of mainstem bronchus or trachea (T3).
 - o Associated atelectasis or obstructive pneumonitis.
 - Extends to hilum? (T2)
 - Involves entire lung? (T3)
 - o Lymph nodes: number involved (even by direct extension) and uninvolved in each of the following broad groups:
 - N1: Peribronchial nodes (lobar and smaller bronchi) and intraparenchymal nodes
 - N2: Peribronchial nodes (around the mainstem bronchi and ipsilateral mediastinal nodes (including subcarinal nodes)
 - N3: Contralateral mediastinum, supraclavicular nodes (separately submitted by surgeon)
 - o Surgical margins - Include distance to bronchial margin, and hilar soft tissue margins, if applicable.
 - o Other features of the tumor
 - Arterial invasion
 - Venous or lymphatic invasion
 - (? Nuclear grade ?)
 - Association with large bronchus or bronchiole
 - o Any pathology in the rest of the lung tissue.

Open Lung Biopsy

Rodney A. Schmidt, MD PhD

SUMMARY

Open lung biopsies are most often done for diffuse lung disease and not for neoplasia. Thus, only in the infrequent situations where a lung tumor is wedged need consideration be given to handling the specimen as you should for a cancer operation, i.e. inking and paying attention to the status of margins.

- Verify that the surgeon has sent some tissue to Microbiology for appropriate stains and cultures.
- Touch preps (3 air-dried, 3 wet-fixed in 95% ETOH)- optional
- Frozen section - keep block frozen.
- Save a section in RPMI transport medium if there is any suspicion of a lymphoid lesion (also need 3 additional air-dried unstained touch preps).
- Fix a piece in Methacarn fixative.
- Inflate the remaining tissue with formalin using a syringe (preferably a tuberculin syringe) to gently instill fixative directly into the gas-exchange tissue.
- After fixation, submit all remaining tissue for histology except for a small representative piece, which should be transferred to 1/2 strength Karnovsky's fixative and set aside for possible EM.
- Arrange for timely processing.
- Arrange for special stains.

PROCEDURE - DETAILED COMMENTS

The pathologic work-up of the specimen is based on the clinical questions. The single most important question is whether the patient's disease is acute or chronic. You should obtain preliminary information to help in guiding your work-up by doing a frozen section to determine the category of disease in which the specimen falls.

FROZEN SECTION (may not be done in some cases)

Section perpendicular to the pleural surface. **Do not** thaw the tissue used for frozen section. After minimal thawing to remove the tissue from the metal block, put in a small zip-lock bag, label, seal and transfer to a -70° freezer. There is a box labeled "Open Lung Biopsies" in a freezer in the room opposite the EM lab. Remember that since the cryostat defrosts at night, the specimen has to be moved to the freezer by the end of the day.

The following tissue is then obtained before formalin fixation:

- **Microbiology (cultures and stains)**

Crushed tissue, i.e. from the staple line, is perfectly adequate for culture; keep the good tissue for histology. At UWMC it is the responsibility of the surgeon to submit tissue for micro studies from the operating room (where appropriate tubes and forms are kept). Generally, the lab needs a total of 1-2 cm³ of tissue. The microbiologic work-up is influenced by the clinical situation but the following is a general guideline:

Cultures

- o mycobacteria
- o fungi
- o aerobic and anaerobic bacteria
- o viruses (including shell-vial assay for CMV)

Stains

- o AFB
- o Gram Stain
- o Gram-Weigert (for pneumocystis)
- o Legionella - direct fluorescent antibody

- **Touch Preps (from freshly cut surface)**

3 air-dried (Wright-Giemsa stain for viral inclusions and foamy PCP exudates)
3 wet-fixed (95% ETOH) (cytology, viral inclusions)
Make extra air-dried slides in cases of possible lymphoma.

- **RPMI Transport Medium**

If there is any suspicious lymphoid infiltrate in the frozen section or any clinical question of a lymphoreticular malignancy, place a generous sample in transport medium for cell surface marker studies and transport it to the Hematopath lab (beeper of Hemepath resident/fellow is 540-8091) expeditiously. Have them "freeze and hold" the specimen pending histologic evaluation of the permanent sections.

- **Methacarn-fixed Tissue**

One representative section, including part of any gross lesion. Process routinely for H&E.

- **Inflation with Formalin**

Gently inflate the specimen with formalin by injecting fixative directly into the lung, preferably using a 25 g needle. After fixation, section perpendicular to the pleural surface.

- **Processing**

In most cases (and all cases of severe or rapidly progressive disease) the permanent sections need to be reviewed the next day. **ANY BIOPSY TAKEN BEFORE 7:00PM SHOULD BE PUT ON THE TISSUE PROCESSOR AS A "FIRST OUT" CASE.** Biopsies obtained after 7:00 PM should be hand-processed the next day unless it is clear that the biopsy results will not affect clinical decision-making that day. In some cases, the urgency of the clinical situation is such that a histology tech will need to be called in on a weekend to process the tissue.

- **Special Stains (Do if indicated)**

- o AFB - pneumonia or granulomatous disease
- o GAS - granulomatous disease, pneumonia, alveolar exudates
- o B&B - pneumonia
- o Giemsa - pneumonia
- o Steiner's - pneumonia (Legionella)
- o Movat's - interstitial lung disease

IHC may be needed for herpes-group viruses, characterizing tumors, or characterizing cellular infiltrates.

DIAGNOSTIC REPORT

The final diagnostic report should include:

- Histopathologic diagnosis
- Size and number of biopsies
- Results of ancillary studies, i.e. special stains.

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Lung Biopsies for Transplant Rejection

Rodney A. Schmidt, MD PhD

TISSUE ADEQUACY

The most recent (1995) consensus statement of the Lung Rejection Study Group (1) states that "at least five pieces of alveolated lung parenchyma each containing bronchioles and greater than 100 air sacs are necessary to confidently grade acute and chronic rejection". When the specimens don't meet this criteria "it is essential to note in the pathology report that the biopsy findings may not be fully representative of the changes in the pulmonary allograft".

HISTOLOGIC STAINS

H&E stains are performed at 3 levels. At UWMC, lung transplant biopsies are always stained with Movat pentachrome stain to aid in the detection of obliterative bronchiolitis, GAS for PCP and fungi, and Ziehl-Neelsen for acid-fast bacilli. Other special stains may be done if indicated.

REJECTION-RELATED PATHOLOGY

Acute (cellular) rejection

"The diagnosis of acute rejection is based exclusively on the presence of perivascular and interstitial mononuclear cell infiltrates" (1). The affected vessels are small ambiguous vessels within the lobule of alveolar lung tissue. Grading is based on how dense the infiltrate is and, more specifically, whether the infiltrate extends to involve neighboring alveolar septa. Acute rejection is a patchy process.

Airway inflammation (lymphocytic bronchiolitis/bronchitis)

Airway inflammation is defined as mononuclear cell infiltrates within the submucosa of the bronchioles. Higher grade inflammation is associated with damage to the overlying epithelium and lymphocyte presence in the epithelium. The significance of airway inflammation is controversial but it may be a harbinger of obliterative bronchiolitis. It is *optional to grade* airway inflammation.

Chronic airway rejection (obliterative bronchiolitis)

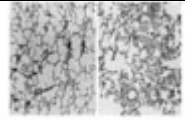
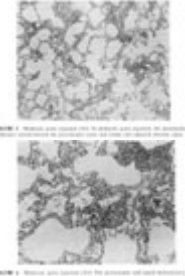
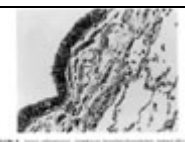
Obliterative (constrictive) bronchiolitis is a slowly progressive endoluminal scarring process that is patchy and involves membranous bronchioles. The mucosal elastica and airway smooth muscle are unaffected. Normally, the epithelial basement membrane is closely approximated to the elastica. The Movat stain is useful in demonstrating fibrous tissue or granulation tissue interposition between the two. It is a patchy process and may not be evident in transbronchial biopsies. OB rarely develops within the first 3 months after transplant and more typically occurs one year or more after surgery.

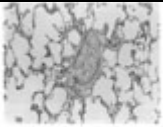
Chronic vascular rejection (accelerated vascular sclerosis)

Chronic vascular rejection is evident as progressive endoluminal scarring involving small arterioles and venules. It is similar to the accelerated atherosclerosis seen in some cardiac allografts.

Hyperacute rejection Hyperacute rejection is a controversial entity where rejection occurs immediately after engraftment due to the presence of circulating preformed antibodies or cells directed toward donor antigens. The diagnosis is made only in concert with clinical, serological, and immunofluorescence studies of allograft tissue.

GRADING OF REJECTION

Type	Grade	Criteria	Image(s)
Acute rejection	A0 – None	Mononuclear infiltrates absent in an adequate biopsy	
	A1 - Minimal	Scattered perivascular infiltrates not obvious at 4x; 2-3 cells thick and confined to adventitia	 FIGURE 1. Micrograph showing scattered perivascular infiltrates in the adventitia. The infiltrates are composed of mononuclear cells and are confined to the adventitia.
	A2 - Mild	Perivascular infiltrates are easily recognized at 4x; endotheliitis may be present but infiltrates don't extend to adjacent septa.	 FIGURE 2. Micrograph showing perivascular infiltrates and endotheliitis. The infiltrates are composed of mononuclear cells and are confined to the adventitia.
	A3 - Moderate	Dense perivascular mononuclear infiltrates with endotheliitis and extension into septa and airspaces. Eos and PMNs are common.	 FIGURE 3. Micrograph showing dense perivascular mononuclear infiltrates with endotheliitis and extension into septa and airspaces. Eos and PMNs are common.
	A4 - Severe	Diffuse perivascular, airspace, and interstitial infiltrates often associated with necrosis, hemorrhage, and hyaline membranes.	 FIGURE 4. Micrograph showing diffuse perivascular, airspace, and interstitial infiltrates often associated with necrosis, hemorrhage, and hyaline membranes.
Airway inflammation	B0 - None	No airway inflammation	
	B1 - Minimal	Rare scattered mononuclear cells in submucosa	 FIGURE 5. Micrograph showing rare scattered mononuclear cells in the submucosa.
	B2 - Mild	Circumferential band of mononuclear cells and some eos in submucosa	 FIGURE 6. Micrograph showing a circumferential band of mononuclear cells and some eos in the submucosa.
	B3 - Moderate	Dense circumferential submucosal infiltrate with epithelial apoptosis and intraepithelial lymphocytes	 FIGURE 7. Micrograph showing a dense circumferential submucosal infiltrate with epithelial apoptosis and intraepithelial lymphocytes.

	B4 - Severe	Dense infiltrate with detachment of epithelium, ulceration, apoptosis and fibrinopurulent exudates	
Obliterative bronchiolitis	a - active	Endobronchiolar scarring is accompanied by mononuclear cell infiltration and epithelial damage	
	b - inactive	Scarring with no associated inflammation or epithelial damage	
Chronic vascular rejection		(not graded)	

DIFFERENTIAL DIAGNOSIS

Reperfusion injury

Occurs within the first few days or weeks after engraftment and is similar to DAD or severe acute rejection but lacks the perivascular mononuclear cell infiltrates of the latter.

Pseudomembranous bronchitis

Occurs within the first few weeks of transplantation and is often exquisitely localized to the bronchial anastomotic site and distal mucosa. Probably reflects inadequate vascular supply to mucosa. Often superinfected with *Aspergillus* or *Candida*.

Infection

The most common infectious agents are *Aspergillus* and CMV, although *Candida* and bacterial infections are also frequent. *Pneumocystis*, *Legionella*, and mycobacteria need to be considered. Pneumonias and bronchitis may occur.

PTLD (post-transplant lymphoproliferative disorder)

PTLD is an EBV-driven B lymphocyte proliferation that occurs in immunosuppressed individuals. It comprises a spectrum from polymorphous infiltrates to atypical lymphoid infiltrates with all the morphologic and molecular features of a B cell lymphoma. In PTLDs, the atypical cells are always B lymphocytes and are always positive for EBV by in situ hybridization (and often by IHC). Rejection infiltrates are polymorphous and EBV-negative.

Recurrent disease

Sarcoidosis, lymphangioleiomyomatosis, and giant cell interstitial pneumonia are known to recur in the allograft.

SUGGESTED WORDING OF REPORTS

The following need to be included in the reports: specimen source; type of biopsy; interval since transplantation; specimen adequacy; acute rejection grade; presence of airway inflammation, OB, and vascular sclerosis; other types of pathology. A microscopic description is useful but is not required. The suggested style is:

FINAL DIAGNOSIS:

Right lower lobe of lung, transbronchial biopsy (6 months post-transplant):

1. Mild cellular rejection (grade A2)
2. Minimal airway inflammation (grade B1)
3. No evidence of obliterative bronchiolitis, vascular sclerosis, or infection by light microscopy and special stains (Movat, GAS, AFB)

COMMENT:

This set of biopsies includes 3 adequate-size samples of alveolar lung tissue and 2 samples of bronchial mucosa. Because 5 alveolar tissue samples are preferred to adequately grade rejection, there is a possibility that the biopsies do not accurately reflect the severity of the changes in the allograft.

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Lung Biopsies for Pulmonary Hypertension

Rodney A. Schmidt, MD PhD

GENERAL DESCRIPTION AND SUMMARY

Patients with pulmonary hypertension generally have one of 4 patterns of pulmonary vascular disease. Note that vascular changes may be subtle and **a Movat pentachrome stain should be performed on at least one block from every biopsy where pulmonary hypertension is part of the clinical history.**

The best general reference for pulmonary vascular disease is Chapter 29 in Thurlbeck and Churg's Pathology of the Lung, 2nd ed. by J. Michael Kay.

SUMMARY

Pattern	Most useful features	Associations/Etiologies
(Plexiform) Pulmonary arteriopathy	Symmetric medial hypertrophy, plexiform lesions, dilatation lesions, fibrinoid necrosis	Idiopathic pulmonary hypertension, left-to-right shunts, hepatic disease, schistosomiasis, anorexigenic drugs
Venous-dominant vasculopathy	Venous intimal sclerosis with sparing of arterioles; congestion and edema	Left-sided cardiac failure and other abnormalities causing pulmonary venous hypertension; veno-occlusive disease
Thrombotic pulmonary arteriopathy	Organizing thromboemboli	Chronic recurring pulmonary emboli
Hypoxic pulmonary arteriopathy	Medial hypertrophy of small arterioles with sparing of larger arterioles	Alveolar hypoxia

PATTERNS OF PULMONARY VASCULAR CHANGES

1. Pulmonary arteriopathy is characterized by symmetric or asymmetric medial hypertrophy of the arterioles, intimal cellular proliferation, intimal fibrosis, and, in the more severe states, plexiform lesions, dilatation lesions, and fibrinoid necrosis of the media. Both large and small arterioles are involved. Atherosclerotic lesions may be seen in the larger arteries. Pulmonary veins are generally spared. Pulmonary edema, hemosiderin-laden macrophages, and iron encrustation of the elastica are generally not seen. Plexiform lesions are angiomatoid proliferation that involve the intima and media of vessels but also usually extend to the adventitia and adjacent tissue. Dilatation lesions are dilated, thin-walled vascular channels that extend from abnormal small arterioles into surrounding tissue. Pulmonary arteriopathy is associated with high-flow congenital cardiac anomalies (left-to-right shunts), the hepatic disease, schistosomiasis, and anorexigenic drugs. Most cases of idiopathic (primary) pulmonary hypertension have the pulmonary arteriopathy pattern. Heath and Edwards have described a grading system for pulmonary arterial lesions in congenital heart disease. Grade 1-3 lesions are thought to be reversible while Grade 4-6 lesions are thought to be irreversible.

Grade 1: Medial hypertrophy of muscular pulmonary arteries.

Grade 2: Medial hypertrophy with cellular intimal proliferation.

Grade 3: Medial hypertrophy with intimal fibrosis.

Grade 4: Occlusive intimal fibrosis, generalized dilatation, Lexa formed lesions.

Grade 5: Vein-like branches; angiomatoid lesions.

Grade 6: Fibrinoid process; arteritis.

2. Venous-dominant vasculopathy is characterized primarily by intimal sclerosis of the veins and venules with a milder, secondary changes in the arterioles. The outer circumference of the veins remains normal but the intima is greatly expanded by hypocellular fibrous connective tissue. The intimal and luminal fibrosis often contains multiple residual lumina, so-called "colander" lesions. On H&E stains, the changes may be very subtle and an elastin or Movat pentachrome stain will highlight the features that enable you to make the diagnosis. Veins often become muscularized and develop a media so prominent that it is difficult to distinguish veins from arteries. Location of the abnormal vessel is key. Arterioles are found next to bronchioles whereas veins are found in secondary lobular septa. A major feature of venous-dominant vasculopathy is the presence of patchy pulmonary congestion with pulmonary edema and accumulation of hemosiderin-laden macrophages. Importantly, this feature is absent in pulmonary arteriopathy.

Venous-dominant vasculopathy is associated with venous hypertension due to left-sided cardiac failure (mitral valve disease, left atrial myxoma, cor triatriatum, stenosis or compression of major pulmonary veins, severe ischemic cardiac disease), and pulmonary veno-occlusive disease. Only about 10 percent of patients with idiopathic pulmonary hypertension have pulmonary veno-occlusive disease. There is no grading system for pulmonary veno-occlusive disease.

3. Thrombotic pulmonary arteriopathy is characterized by multiple organizing or organized pulmonary emboli. Intimal fibrosis may be present but is generally eccentric, in contrast to pulmonary arteriopathy. Localized pulmonary hemorrhage and edema may be present. Although multiple residual channels may be present in the recanalized thrombi, true plexiform lesions are not present.

Thrombotic arteriopathy is associated with any cause of chronic recurring pulmonary emboli. Blood clotting disorders should be considered, particularly in any young patient.

4. Hypoxic pulmonary arteriopathy is characterized primarily in body muscular station of small pulmonary arterioles (< 100 micron diameter). These develop a thick muscular media of circular smooth muscles sandwiched between distinct internal and a external elastica lamina. Medium-sized and larger pulmonary arterioles are spared.

Hypoxic pulmonary arteriopathy is associated with alveolar hypoxia. It may be seen with upper airway obstruction, chronic airflow obstruction, alveolar hypoventilation syndromes, thoracic skeletal disorders, and residence at high altitude.

SUGGESTED WORDING OF DIAGNOSIS

The diagnosis should indicate whether or not the features are consistent with pulmonary hypertension, the pattern of vascular abnormalities, and grade, if appropriate. For example:

Right upper lobe of lung, wedge biopsy: Vascular changes consistent with pulmonary hypertension, plexiform arteriopathy pattern, grade IV/VI (Heath-Edwards classification).

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Thymic System

Section 1 - Thymoma, Thymic Carcinoma, and Other Thymic Neoplasms

Author: Rodney A. Schmidt, MD PhD

Section 2 - CAP Cancer Protocols and Checklists Including: Thymoma and Thymic Carcinoma

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Thymoma, Thymic Carcinoma, and Other Thymic Neoplasms

Rodney A. Schmidt, MD PhD

REASONS FOR SURGERY

Thymomas are the most common neoplasms presenting in the thymus but thymic carcinoma, germ cell tumors, and lymphomas (Hodgkin's Disease and non-Hodgkin's lymphomas) also occur with considerable frequency. Certainly these neoplasms may spread locally if left untreated and most can metastasize. Thymomas, in particular are associated with paraneoplastic syndromes (myasthenia gravis, pure red cell aplasia, aplastic anemia) and the paraneoplastic symptoms may regress following resection of the thymoma. Similar paraneoplastic syndromes are also associated with thymic hyperplasia and thymic cysts, so surgery may also be performed for these indications. Biopsies of the thymus are rarely done because of the risk of contaminating the pleural space with neoplasm.

GROSS EXAMINATION

The goals of the gross exam are to identify any neoplasm that is present, to document gross features that determine tumor stage, and to take sections to evaluate tumor type, grade, and stage.

Procedure:

1. Document size of specimen (3 dimensions or weight) and presence/size of any mass (3 dimensions).
2. If a mass is present, ink the specimen. If given orientation by the surgeon, differentially ink the specimen so that tumor proximity to different margins may be unambiguously assessed.
3. Describe tissue overlying the mass – freely movable vs fixed; probable tumor vs normal tissue.
4. Breadloaf the specimen, leaving it hinged, if possible.
5. Assess/describe proximity of any tumor to margins.
6. Specifically note presence and relation to tumor of any included pleura or pericardium.
7. Carefully search for any evidence of tumor penetration of a fibrous capsule.
8. Submit sections of tumor (usually one piece per cm tumor diameter), any areas of possible capsular penetration, and relationship of tumor to margins.
9. If any lymph nodes are included in the specimen (uncommon) submit them for histologic examination.

MICROSCOPIC EXAMINATION

The most important issues for microscopic resolution are:

- Tumor type (thymoma, thymic carcinoma, thymic carcinoid, germ cell tumor, lymphoma, Hodgkin's disease)
- Tumor grade
- Tumor extent (confined within capsule, transcapsular invasion, invasion of other structures)

CLASSIFICATION AND GRADING OF THYMIC NEOPLASMS

Historically, several classifications systems for thymomas and thymic carcinomas have been promulgated but most suffer from poor reproducibility or lack of correlation with clinically important outcome measures, or both. At present, we use the WHO system (1,2) as listed below. In general, this system is based on the

degree of anaplasia and the predominance of lymphocytes. Tumors without anaplasia are called thymomas and those with anaplasia are called carcinomas. An intermediate category, called atypical, exists but is not well defined. Thymomas are subclassified according to the relative proportions of lymphocytes and epithelial cells while carcinomas are subclassified according to histologic appearance as carcinomas arising in other sites are. Be careful in the use of the term "thymic carcinoma" as the term has been used to mean different things in different historical classifications.

- Type A Thymoma (spindle cell, medullary)
- Type B Thymoma
 - o B1 thymoma (lymphocyte-rich, lymphocytic, predominantly cortical, organoid)
 - o B2 thymoma (cortical)
 - o B3 thymoma (epithelial, atypical, squamoid, well-differentiated thymic carcinoma)
- Type AB Thymoma (mixed)
- Type C Thymoma (thymic carcinoma)
 - o Epidermoid keratinizing (squamous cell) carcinoma
 - o Epidermoid nonkeratinizing carcinoma/lymphoepithelioma-like carcinoma
 - o Sarcomatoid carcinoma
 - o Carcinosarcoma
 - o Clear cell carcinoma
 - o Basaloid carcinoma
 - o Mucoepidermoid carcinoma
 - o Papillary carcinoma
- Undifferentiated carcinoma

STAGING OF THYMIC NEOPLASMS

Neither the AJCC or the UICC have an approved staging system for thymic neoplasms. Koga's modification of Masaoka's staging system (3-6) is widely used and should be utilized for UW reports. Note the importance of assessing capsular invasion in this system.

Stage I	Grossly and microscopically completely encapsulated (including microscopic invasion into the capsule)
Stage IIa	Microscopic transcapsular invasion
Stage IIb	Macroscopic capsular invasion into thymic or surrounding fat, or grossly adherent but not breaking through mediastinal pleura or pericardium
Stage III	Macroscopic invasion of neighboring organs (eg, pericardium, lung, great vessels, others)
Stage IVa	Pleural or pericardial dissemination
Stage IVb	Hematogenous or lymphatic dissemination

DIAGNOSIS

As for all neoplasms, the diagnoses for thymic tumors need to include descriptive features as well as grading and staging information. Because of the multiplicity of grading and staging systems in the literature, the diagnoses should explicitly reference the schemes being used. For example:

- A. Thymus, thymectomy: Thymoma with the following features.
1. Size: 3 x 2.5 x 2.0 cm
 2. Type: Lymphocyte-predominant (WHO type B1)
 3. Capsule: Thymoma microscopically extends through the fibrous capsule into adjacent fat in one focus.

4. Invasion of pleura or adjacent organs: Not present
5. Surgical margins: Thymoma is free of all margins examined; closest approach is to the anterior margin (0.2 cm).
6. Minimum pathologic stage: Stage IIa (Koga/Masaoka 1994).

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CAP Cancer Protocols and Checklists

Thymic System

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Endocrine System

Section 1 - Thyroid

Author: Mary Bronner, MD

Section 2 - Thyroid Staging & Grading of Thyroid Carcinoma

Author: Mary Bronner, MD

Section 3 - Parathyroid Glands

Author: Mary Bronner, MD

Section 4 - Adrenal & Extra-adrenal Paraganglia

Author: Mary Bronner, MD

The thyroid and parathyroid sections are excerpts from the "blue" AFIP fascicle series (3rd series); the thyroid material derives from the Rosai, et al. fascicle (number 5) and the parathyroid derives from the DeLellis fascicle (number 6).

Section 5 - Pituitary Gland (Included in Neuropathology)

Section 6 - CAP Cancer Protocols and Checklists Including: Thyroid, Adrenal Gland

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Thyroid

Mary Bronner, MD

FROZEN SECTIONS

In general, thyroid frozen section diagnosis has been largely replaced by preoperative fine needle aspiration (FNA). Only if no FNA diagnosis is available should a frozen section be performed. Among the more common requests from our surgical colleagues is to freeze a nodule called "cellular follicular lesion, possible follicular neoplasm, recommend excision". In this case, frozen section rarely, if ever, permits differentiation of adenoma or carcinoma, and therefore should not be performed. In such a case, a cytologic scrape prep of the lesion should be obtained as the best way to exclude papillary carcinoma, and if so, revert back to the "cellular follicular neoplasm, defer to permanents" diagnosis. Frozen sections are not recommended for papillary carcinoma, as freezing artifacts usually obscure the critical diagnostic nuclear features. Because of this, scrape preps are preferable. ([Bronner MP, Hamilton R, LiVolsi VA](#))

GROSS PROCESSING

- Weigh the specimen, and measure it in three dimensions.
- Orient the specimen, if feasible (help from the surgeon may be necessary).
- Search for parathyroid glands and lymph nodes in the surrounding fat.
- Paint the outer aspect of the specimen with India ink or similar dye.
- Make parallel serial cuts, 3 to 5 mm apart, either in the fresh state or after formalin fixation.

GROSS DESCRIPTION

- Indicate the type of specimen received; nodulectomy (an operation that has been abandoned in most institutions), lobectomy, lobectomy with isthmusectomy, subtotal thyroidectomy, or total thyroidectomy. For specimens other than the last one, indicate the side from which most or the entire specimen was obtained.
- State the weight, dimensions, shape, color, and consistency of the specimen.
- Examine the cut surface color and appearance. Note whether or not is homogeneous and whether it is smooth or nodular.
- When one or more nodules are present; note the number, size, shape, color; whether they are solid or cystic, calcified, hemorrhagic, or necrotic; and whether or not they are encapsulated.
- If a capsule is present, note whether it is thin or thick and regular or irregular. Note whether it is apparently intact or violated by the tumor growth and whether the main thyroid gland's capsule is intact or disrupted by tumor. Calculate the shortest distance from the edge of the nodule to the line of resection, and to the nearest main capsule of the thyroid gland itself.

EXAMPLE OF GROSS DESCRIPTION

"Received in the fresh state and labeled with the correct patient identification data, is a right thyroid lobectomy with isthmusectomy. A black suture is present at the isthmusectomy margin. The specimen weighs 30 g and measures 6.5 x 4.0 x 3.0 cm. The outer surface is smooth, and the consistency is homogeneously firm. An ill-defined bulging area is noted in the lower pole of the lobe. No parathyroid glands or lymph nodes are identified. Parallel serial sections of the specimen reveal a round nodule in the right lower lobe measuring 2.5 cm in diameter. It is entirely surrounded by a very thin fibrous capsule that shows no gross evidence of invasion. The cut surface of the nodule is solid, slightly bulging, and tan, with punctuate areas of fresh hemorrhage. The capsule of the nodule is 0.5 cm distant from the thyroid capsule and 1.2 cm distant from the surgical margin at the isthmus. The rest of the thyroid shows no

gross abnormalities. Sections are submitted as follows: A1, A2: nodule; B1, B2: remainder of right lobe; and C: surgical margin at the isthmus."

SECTIONS FOR HISTOLOGY

For all cases, submit all parathyroid glands and lymph nodes whenever found on gross inspection.

FOR SOLITARY NODULES OR MULTINODULAR GLANDS

- For solitary encapsulated nodules (identified after careful gross examination of serially sectioned tissue), measuring up to 6 cm in diameter, submit the entire central slice. Each block should have a portion of the capsule and tumor and adjacent thyroid tissue, if present. For a nodule measuring exactly 6 cm in diameter, six blocks will usually have to be made.
- For larger encapsulated nodules, submit one additional block for each centimeter over 6 cm (i.e., 7 blocks for a 7-cm nodule, or 10 blocks for a 10-cm nodule, etc.).
- For multinodular thyroid glands, submit a minimum of one section for each nodule (up to five nodules), including rim and adjacent gland. Submit additional sections for the nodules that are larger than and/or grossly different from the others.

FOR PAPILLARY OR MEDULLARY CARCINOMA

- For known papillary or medullary carcinoma, submit the entire gland and (separately) the line of resection, if the specimen is other than a total thyroidectomy.
- For grossly invasive carcinoma other than papillary or medullary, submit a minimum of three blocks from the tumor, three of non-neoplastic gland (if present), and one from the line of resection (if other than total thyroidectomy).

FOR DIFFUSE OR INFLAMMATORY DISEASE

- Take three sections from each lobe and one from the isthmus.

FEATURES TO BE SPECIFIED IN THE FINAL DIAGNOSIS

- Location of the resected specimen (right and/or left and/or isthmus) and type of thyroid surgery (nodulectomy, lobectomy, lobectomy with isthmusectomy, subtotal thyroidectomy, total thyroidectomy).
- Diagnosis: If cancer, indicate:
 - o the type (papillary, follicular, medullary, anaplastic, insular, lymphoma, etc.)
 - o the tumor size
 - o whether it is limited to the thyroid or invades through the main thyroid capsule into surrounding tissue
- Whether angiolymphatic and/or invasion of the tumor capsule is present.
- Indicate the status of all lymph node(s) and parathyroid(s) identified.

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Staging & Grading Thyroid Carcinoma

Mary Bronner, MD

CLINICAL STAGING

This is the clinical staging system recommended by the International Union Against Cancer (UICC) in the sixth edition of their manual. The [American Joint Committee on Cancer](#) has also adopted this system.

Definition of TNM - Primary Tumor (T)	
AJCC, 2002	
TX	Primary tumor cannot be assessed.
T0	No evidence of primary tumor.
T1	Tumor 2 cm or less greatest dimension limited to the thyroid.
T2	Tumor more than 2 cm but not more than 4 cm in greatest dimension limited to the thyroid.
T3	Tumor more than 4 cm in greatest dimension limited to the thyroid or any tumor with minimal extrathyroid extension (e.g., extension to sternothyroid muscle or perithyroid soft tissues).
T4a	Tumor of any size extending beyond the thyroid capsule to invade subcutaneous soft tissues, larynx, trachea, esophagus, or recurrent laryngeal nerve.
T4b	Tumor invades prevertebral fascia or encases carotid artery or mediastinal vessels.
<i>All anaplastic carcinomas are considered T4 tumors.</i>	
T4a	Intrathyroidal anaplastic carcinoma - surgically resectable.
T4b	Extrathyroidal anaplastic carcinoma - surgically unresectable.
Note: All categories may be subdivided: (a) solitary tumor, (b) multifocal tumor (the largest determines the classification).	

Definition of TNM - Regional Lymph Node (N)	
AJCC, 2002	
Regional lymph nodes are the central compartments, lateral cervical, and upper mediastinal lymph nodes.	
NX	Regional lymph nodes cannot be assessed.
N0	No regional lymph node metastasis.
N1	Regional lymph node metastasis.
N1a	Metastasis to Level VI (pretracheal, paratracheal, and prelaryngeal/Delphian lymph nodes).
N1b	Metastasis to unilateral, bilateral, or contralateral cervical or superior mediastinal lymph nodes.

Definition of TNM - Distant Metastasis (M)			
<u>AJCC, 2002</u>			
MX	Presence of distant metastasis cannot be assessed.		
M0	No distant metastasis.		
M1	Distant metastasis.		
Note: Category M1 may be further specified according to the following notation:			
PUL	Pulmonary	MAR	Bone Marrow
OSS	Osseous	PLE	Pleura
HEP	Hepatic	PER	Peritoneum
BRA	Brain	SKI	Skin
LYM	Lymph nodes	OTH	Other

PATHOLOGIC STAGING

The pathologic staging of thyroid carcinoma uses terminology and categories similar to the above-listed clinical staging. In this scheme, the pT, pN, and pM categories substitute for the T, N, and M categories, respectively.

STAGE GROUPING			
Separate stage groupings are recommended for papillary or follicular, medullary, and anaplastic (undifferentiated) carcinoma. <i>AJCC, 2002</i>			
Papillary or Follicular Carcinoma (patient < 45 years old)			
Stage I	any T	any N	M0
Stage II	any T	any N	M1
Papillary or Follicular Carcinoma (patient > 45 years old)			
<TDS Stage I	T1	N0	M0
Stage II	T2	N0	M0
Stage III	T3	N0	M0
	T1	N1a	M0
	T2	N1a	M0
	T3	N1a	M0
Stage IVA	T4a	N0	M0
	T4a	N1a	M0
	T1	N1b	M0
	T2	N1b	M0
	T3	N1b	M0
	T4a	N1b	M0

Stage IVB	T4b	Any N	M0
Stage IVC	Any T	Any N	M1
Medullary Carcinoma			
Stage I	T1	N0	M0
Stage II	T2	N0	M0
Stage III	T3	N0	M0
	T1	N1a	M0
	T2	N1a	M0
	T3	N1a	M0
Stage IVA	T4a	N0	M0
	T4a	N1a	M0
	T1	N1b	M0
	T2	N1b	M0
	T3	N1b	M0
	T4a	N1b	M0
Stage IVB	T4b	Any N	M0
Stage IVC	Any T	Any N	M1
Anaplastic Carcinoma All anaplastic carcinomas are considered Stage IV			
Stage IVA	T4a	Any N	M0
Stage IVB	T4b	Any N	M0
Stage IVC	Any T	Any N	M1

MICROSCOPIC GRADING

The UICC recommends that all carcinomas of head and neck sites (including thyroid) be graded microscopically as follows:

GX	Grade cannot be assessed
G1	Well differentiated
G2	Moderately well differentiated
G3	Poorly differentiated
G4	Undifferentiated

Most thyroid pathologists, based on the following information, in general, do NOT RECOMMEND this. It should be understood that this grading system was proposed mainly on the basis of the squamous cell carcinomas of the upper aerodigestive tract, for which it works quite well. In the thyroid, instead, most tumors arising from follicular cells belong to either the well differentiated or the undifferentiated types. The former includes nearly all the minimally invasive follicular carcinomas (including those of oncocytic type) and the papillary carcinomas of either conventional or follicular variant types, whereas the undifferentiated grade is synonymous with the undifferentiated (anaplastic) type of carcinoma. The term insular carcinoma has been proposed for poorly differentiated tumors of either follicular or papillary type that exhibit an insular pattern of growth associated with mitotic activity and necrosis. This category can be expanded to include other poorly differentiated tumors of follicular cell origin that do fit the insular pattern. No grading

system has been proposed for medullary carcinoma, even though the small cell variant of this tumor could be regarded as its poorly differentiated member.

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Parathyroid Glands

Mary Bronner, MD

MANDATORY READING FOR ALL AP RESIDENTS

[LiVolsi VA, Hamilton R:](#) Intraoperative assessment of parathyroid gland pathology. A complete review for the surgeon and the pathologist. *Am J Clin Pathol* 1994; 102:365-373.

INTRA-OPERATIVE AND FROZEN SECTION EXAMINATION

- Before leaving the Operating Room, obtain information from the surgeon regarding an estimate of what percentage of the suspected parathyroid gland was biopsied (100%, >5%, etc.)
- WEIGH in mg all material received for a parathyroid surgery for frozen section or routine processing. Indicate whether it is a fresh or fixed weight.
- If requested, freeze the entire sample if less than the size of a single frozen block; if larger, ask the attending for advice.
- If after reviewing the frozen section slides, the material is probable or definite parathyroid tissue, then **cut 2 unstained, unprocessed frozen section slides**, label them with the accession number, and leave them to air dry in a slide pallet, without any further processing. **Order oil red O (ORO) stains on these frozen section slides from histology.**

FAT STAINS

The use of fat stains for the evaluation of the parathyroid is based on the observation that the intracellular or parenchymal lipid content is decreased or absent in hyper-functioning chief cells as compared to the increased intracellular lipid in normal or suppressed chief cells. Studies have stressed that evaluation of intracellular fat content is considerably more important than the estimation of stromal fat content. A combination of fat staining and careful morphologic assessment of more than one gland provides an optimal approach.

GENERAL INFORMATION

The role of the pathologist during parathyroid exploration is first, to determine if the biopsied tissue is of parathyroid origin and second, to determine the nature of the underlying process (hyperplasia vs. adenoma vs. carcinoma).

Parathyroid may be difficult to distinguish grossly from a variety of other tissues in the neck including, fat, lymph node, thyroid, and ectopic thymus. The surgeon may request frozen sections on a number of such samples to confirm the presence or absence of parathyroid tissue.

Generally, the distinction between parathyroid and non-parathyroid tissue is readily accomplished by frozen section. Occasionally, however, it is difficult to differentiate a crushed lymph node from crushed parathyroid or a lobule of thyroid from parathyroid, particularly if the parathyroid biopsy shows follicular structures. Generally, the follicles in parathyroid tissue are smaller than those in normal thyroid and the cells have a clear or vacuolated cytoplasm. Deeper sections of such equivocal cases may reveal areas more typical of parathyroid tissue. The distinction between a fragment of microfollicular thyroid adenoma and parathyroid may be impossible on frozen section and may occasionally present considerable difficulties on permanent sections. IHC studies for thyroglobulin and parathyroid hormone may be needed to know with certainty.

Fragments of ectopic thymus may be composed almost exclusively of epithelial elements that are difficult to differentiate from parathyroid. The identification of Hassal's corpuscles clearly establishes a thymic origin in such instances.

The critical issue in distinguishing hyperplasia from adenoma at surgery is the determination of the number of enlarged parathyroid glands. Virtually all patients with parathyroid adenoma will have involvement of one gland, and the remaining glands will be of normal size and suppressed function with abundant intracellular lipid on fat staining.

In most instances, the surgeon will remove the largest gland first. The gland should be carefully weighed and a representative section, which includes the capsule, should be taken for frozen section examination. Since a rim of adjacent parathyroid is seen in 30 to 50 percent of cases at the time of frozen section, the pathologist cannot rely on this criterion alone to render a diagnosis of adenoma.

The presence of stromal fat cannot be used to exclude the diagnosis of adenoma, since adenomas may contain at least some stromal fat, and some adenomas contain an abundance of stromal fat. In many instances, the pathologist can only report that the resected gland is hypercellular and that it may represent adenoma or hyperplasia. The surgeon must then sample another gland. If this gland is of normal size and cellularity with abundant intracellular fat on ORO staining, both the surgeon and pathologist can be satisfied that the diagnosis is most likely adenoma. Sometimes the surgeon will proceed with a limited surgery on the basis of preoperational radionuclide scans indicating only a single gland is hyperfunctioning. The surgeon is willing to accept the low likelihood that the patient has 4-gland hyperplasia and only resect the single gland seen on scan. In this case, the pathologist with only a single gland cannot distinguish adenoma from hyperplasia.

The diagnosis of hyperplasia is likely when more than one gland is enlarged. It should be remembered, however, that hyperplasia may not involve all glands equally and that one dominant gland may be present. Biopsy of a second gland in this situation, particularly if the biopsy is from one of the poles, may reveal a relatively high proportion of stromal fat. In such instances, it is imperative to know the size of the gland; hence, the importance of finding out from the surgeon the percentage of the gland that was resected. If the second gland is enlarged, the likelihood of hyperplasia is high. Fat stains, as discussed below are helpful in making this distinction, **and must be obtained at frozen section.**

PROCEDURES FOR PERMANENT SECTIONS

- Features to include in gross description: weight in mg, size, the external appearance, color, consistency of each gland, multinodularity, possible fibrosis or scarring, capsule irregularity or gross evidence of invasion (discuss with surgeon); necrosis, and hemorrhage.
- Fix specimens in formalin [after taking frozen sections for ORO staining](#).
- Submit small specimens (those that can be accommodated in one or two blocks) completely. For larger specimens, an average of two blocks per cm³ is generally considered adequate. Be certain to sample any grossly unusual areas such as hemorrhagic areas, necrotic foci, and areas suspicious for scarring or capsular invasion.

FEATURES TO BE SPECIFIED IN THE FINAL DIAGNOSIS

- The location of the resected or biopsied tissue (upper vs. lower pole, right vs. left).
- The percentage of the gland from which the biopsy or resection was derived.
- Weight in mg.
- The diagnosis (normocellular parathyroid, parathyroid adenoma, parathyroid carcinoma, parathyroid hyperplasia (primary or secondary), etc.).
- If carcinoma, indicate the presence or absence of angiolymphatic invasion, mitotic rate, necrosis, and capsular invasion.

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Adrenal & Extra-Adrenal Paraganglia

Mary Bronner, MD

PROCEDURES FOR GROSS PROCESSING AND DESCRIPTION

- Indicate the location of the resected specimen.
- **WEIGH** the gross the specimen as well as measure it. The most important prognostic indicator for adrenal neoplasms is size and most studies refer to **weight**.
- Describe the relation to all other submitted structures (kidney, etc.) and the gross appearance of all other submitted structures.
- If normal adrenal gland is present describe its size and appearance, particularly if multinodular.
- Ink the surgical margins and serially section to aid fixation.
- Photograph adrenal tumors.

SECTIONS FOR HISTOLOGY

- Submit the entire lesion if this can be accomplished in less than ten blocks.
- For larger lesions than above, a good rule is to submit sections that demonstrate any areas of any suspected gross invasion, necrosis, or hemorrhage, the lesion's relation to other resected structures such as kidney, the remaining adrenal, etc. At least ten blocks of the lesion should be submitted to encompass all of these features.

FEATURES TO BE SPECIFIED IN THE FINAL DIAGNOSIS

- Location and weight of the resected specimen and the resection procedure.
- Classification of the tumor (adrenal cortical, pheochromocytoma, etc.) and/or non-tumor pathology. If tumor:
 - o Grade (well, moderately, poorly differentiated).
 - o Features of invasion (angiolymphatic, capsular, involvement of soft tissue or other organs, etc.).
 - o Report resection status (complete versus at or approaching resection margins and to within what distance).

EXAMPLE:

Adrenal, resection (152g): Adrenocortical carcinoma, invading into kidney & metastatic to 3 of 5 lymph nodes.

REFERENCES

-  [Medeiros LJ, Weiss LM](#): New developments in the pathologic diagnosis of adrenal cortical neoplasms. A review. *Am J Clin Pathol* 1992; 97:73-83.

Pituitary

See Neuropathology Section – page xxx

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Endocrine System

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Colorectal Carcinomas

Melissa Upton, MD

SURGICAL PATHOLOGY REPORT FORM

APPROACH TO THE GROSS EXAMINATION:

1. Palpate the specimen to identify any nodules or masses. If none is felt, open the specimen along the antimesenteric border, longitudinally. If a neoplasm or lesion is palpated, try to open the specimen along an uninvolved segment of the mucosa.
2. Clean the lumen with saline to remove residual blood.
3. Measure the neoplasm and its relationship to the margins prior to fixation.
4. Photograph the specimen prior to fixation.
5. Using blunt dissection, remove all fat from the serosal surface, but leaving the fat intact in the vicinity of the deep margin of the neoplasm, or in the region of diverticula. Dissect the fat in the fresh state to identify all lymph nodes or tumor nodules.
6. Apply ink to the radial/deep margin of the neoplasm.
7. Consult the attending pathologist prior to sectioning for advice and for the opportunity to discuss the approach to the gross and microscopic evaluation.

THE FOLLOWING FEATURES SHOULD BE INCLUDED IN THE GROSS DESCRIPTION:

- Location of resected segment (sigmoid, rectum, etc.).
- Length and circumference of segment.
- Thickness of bowel wall, and any variation in thickness because of tumor, hypertrophy, stricture or adhesions.
- Gross description of tumor(s) or lesion(s) (polypoid, annular, constricting, ulcerating, plaque, linitis plastica, etc.).
- Tumor measurements in 3 dimensions.
- Apparent depth of invasion (into muscularis propria, into pericolic fat, etc.).
- Evidence of invasion through visceral peritoneum with or without direct extension to other organs or structures.
- Distance to margins (mucosal & radial). Note the critical importance of inking the radial resection margin, especially in low rectal resections below the peritoneal reflection.
- Presence of other lesions (adenomas, colitis).
- Comment about size and number of retrieved lymph nodes. Submit all lymph nodes (only one representative section of grossly positive nodes is necessary). Also submit any soft tissue nodules in contiguity with the main tumor mass. Typically, at least 10 nodes can be found in any segmental resection.

THE FOLLOWING FEATURES SHOULD BE SPECIFIED IN THE FINAL DIAGNOSIS:

- Location of resected segment: cecum, ascending colon, hepatic flexure, transverse colon, splenic flexure, descending colon, sigmoid colon, rectosigmoid, or rectum.
- Classification of histopathologic type of carcinoma: adenocarcinoma, medullary carcinoma, mucinous carcinoma (>50% mucinous features), signet ring carcinoma (>50% signet ring cells), squamous cell carcinoma, adenosquamous carcinoma, small cell carcinoma, carcinoma, NOS.
- Grade (well, moderately, poorly differentiated).

- Depth of invasion (into muscularis propria, through muscularis propria, extension into contiguous organ, etc.).
- Presence of lymphatic invasion
- Presence of venous invasion
- Status of nodes (No. positive/No. present) Per AJCC Cancer Staging Manual, Sixth Edition (2002) to TNM system, a regional lymphadenectomy from a colorectal resection should contain at least 7-14 lymph nodes; however, in patients who have received preoperative radiation, only a few lymph nodes may be identified.
- Number and size of nodules in perirectal/pericolic fat. (Per 2002 AJCC Cancer Staging Manual: "A tumor nodule in the pericolic adipose tissue of a primary carcinoma without histological evidence of a residual lymph node in the nodule is classified in the Pn category as a regional nodal metastasis if the nodule has the form and smooth contour of a lymph node. If the nodule has an irregular contour, it should be classified in the T category and also coded as V1 (microscopic venous invasion) or as V2 (if it was grossly evident), because there is a strong likelihood that it represents venous invasion.")
- Status of mucosal and radial margins:

R0	Complete resection, margins histologically negative, no residual tumor left after resection
R1	Incomplete resection, margins histologically involved, microscopic tumor remains after resection of gross disease
R2	Incomplete resection, margins involved or gross disease remains after resection.
AJCC Cancer Staging Manual, Sixth Edition, 2002	

- Presence of other lesions (adenomas, colitis, perforation).
- Pathologic stage of primary tumor:

Tx	Primary tumor cannot be assessed.
Tis	Carcinoma in situ: intraepithelial or invasion of lamina propria.
T1	Tumor invades submucosa.
T2	Tumor invades muscularis propria.
T3	Tumor invades through muscularis propria into subserosa, or into non-peritonealized pericolic or perirectal tissues.
T4	Tumor directly invades other organs or structures, and/or perforates visceral peritoneum.
AJCC Cancer Staging Manual, Sixth Edition, 2002	

- Pathologic stage of regional lymph nodes:

NX	Regional nodes cannot be evaluated.
N0	No regional lymph node metastasis.
N1	Metastasis in 1 to 3 regional lymph nodes.
N2	Metastasis in 4 or more regional lymph nodes.
AJCC Cancer Staging Manual, Sixth Edition, 2002	

- Assessment of distant metastasis, if possible (such as presence of liver metastasis). According to the 2002 AJCC Cancer Staging Manual:

MX	Distant metastasis cannot be assessed.
M0	No distant metastasis.
M1	Distant metastasis.
AJCC Cancer Staging Manual, Sixth Edition, 2002	

- On a pathologic basis, we usually can say either M1 or MX, but we are unable to be definitive about no metastasis.

MICROSCOPIC SECTIONS:

- Tumor: ≤4 sections, showing relationship to adjacent mucosa, deepest extent, and relationship, if any, to adjacent organs.
- Other Lesions: Sample all other lesions, such as polyps, unless there are >10 present.
- Diverticula: Submit one representative section; if one is perforated, it should be sampled.
- Lymph Nodes: All are identified and submitted in cases of neoplasia.
- Surgical Margins: Submit the deepest/radial margin in all cases. If the neoplasm is <5 cm from the proximal and/or distal margin, sections should be taken to document, if possible, the closest approximation of the neoplasm to the margin, which should be inked.
- Normal: If not previously included, represent normal colonic and ileal mucosa, if present.
- Inflammatory Bowel Disease: If present, sequential sections are taken every 10 cm, especially sampling raised, ulcerated, polypoid or fissured areas, as well as grossly normal mucosa.
- Cassette Count: For typical colonic carcinoma with IBD: 6 cassettes maximum, not including lymph nodes. If more sections/cassettes are indicated, consult the attending pathologist.

ANCILLARY STUDIES (IF DONE):

- Flow cytometry.
- Immunostaining for MLH1 and MSH2 (markers of microsatellite instability).

EXAMPLE:

Right colon, right hemicolectomy: Colonic adenocarcinoma, moderately differentiated; invading through muscularis propria into subserosal fat; angiolymphatic invasion not identified; metastatic to 5 of 17 lymph nodes (T3,N2,MX)

REFERENCES

-  [Assn. of Directors of Anatomic and Surgical Pathology](#): Recommendations for Reporting of Resected Large Intestinal Carcinomas. *Hum Pathol* 1996; 27:5-8.

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Technical Editor: [Larry True, MD](#) Web Editor: [Michelle Rickard](#)
Last modified: Wednesday, July 13, 2005

Esophageal Cancers

Mary Bronner, MD

SURGICAL PATHOLOGY REPORT FORM

THE GROSS DESCRIPTION SHOULD COMMENT ON THE FOLLOWING:

- Length of esophageal and gastric (greater & lesser curvatures) segments, with precise anatomic location of all gross lesions
- Tumor measurements in 3 dimensions
- Apparent depth of invasion
- Distance to mucosal and radial margins; note importance of inking margins
- Presence of Barrett's esophagus (segment length)
- Comment on size and number of lymph nodes

THE FOLLOWING FEATURES SHOULD BE SPECIFIED IN THE FINAL DIAGNOSIS:

- Classification of tumor
- Grade (well, moderately, poorly differentiated)
- Depth of invasion
- Presence of angiolymphatic invasion
- Status of nodes (No. positive/No. present) * Per UICC Supplement (1993) to TNM system, a regional lymphadenectomy from an esophageal resection should contain 6 or more lymph nodes
- Status of mucosal and radial margins
- Presence of Barrett's esophagus and length of segment, defined by goblet cells in esophageal columnar mucosa (for adenocarcinomas)
- Presence of dysplasia

ANCILLARY STUDIES (IF DONE):

- Flow cytometry

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Technical Editor: [Larry True, MD](#) Web Editor: [Michelle Rickard](#)
Last modified: Wednesday, July 13, 2005

Barrett's Esophagus

Mary Bronner, MD

DEFINITION

The diagnosis of Barrett's esophagus requires both **endoscopic** and **histologic** evidence of metaplastic columnar epithelium. Endoscopically, there must be columnar epithelium within the esophagus. Histologically, the epithelium must be metaplastic, as defined by the presence of goblet cells. An Alcian blue stain at pH 2.5 stains the acidic mucin present in the goblet cells. The most common errors in the identification of goblet cells are: 1) "pseudogoblet" cells; and 2) Alcian blue positive cells that are not goblet cells.

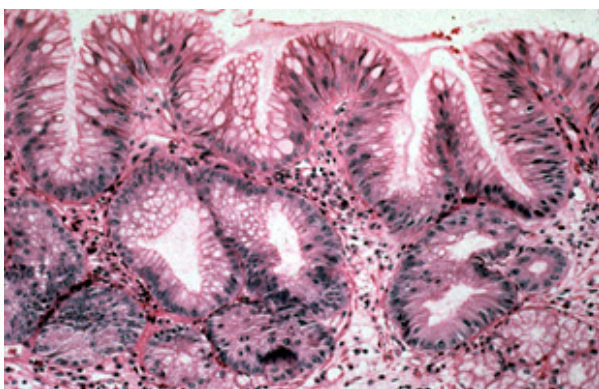
[Pseudogoblet cells](#) are barrel-shaped gastric surface or foveolar cells that do not stain with Alcian blue. These cells commonly have a blush of eosinophilia, due to neutral mucin, on H&E stained sections, in contrast to the blush of basophilia, imparted by the acidic mucin in goblet cells.

Alcian blue positivity in a columnar cell does not necessarily indicate a metaplastic goblet cell; it should have a barrel shape. Other types of cells that can be Alcian blue positive but which lack the barrel shape include: [reactive gastric foveolar cells](#), which may be present in the pits and on the mucosal surface, [mucous neck cells of the gastric glands](#), esophageal cardiac glands, and [submucosal glands](#) in the esophagus.

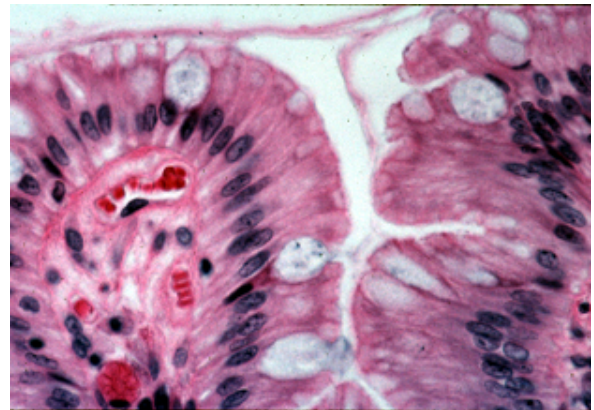
As stated above, the diagnosis of Barrett's esophagus requires both endoscopic and histologic evidence of metaplastic columnar epithelium. The significance of metaplastic columnar epithelium in a biopsy of the GE junction region when the endoscopist has not seen columnar epithelium within the esophagus has not been established.

Pseudogoblet Cells

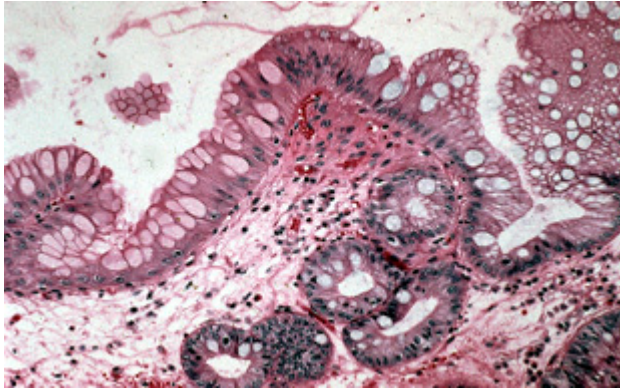
Columnar cells which have a barrel shape but which are Alcian blue negative should not be interpreted as goblet cells. Often these cells have a pink hue to them as compared to the bluish tinge to goblet cells.



Pseudogoblet cell with pink hue.



Goblet cell with barrel shape and bluish tinge.

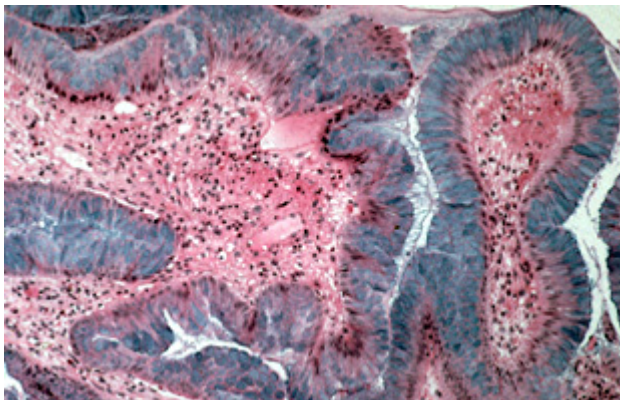


Pseudogoblet cells adjacent to true goblet cells.

Pitfalls in the Interpretation of Goblet Cells

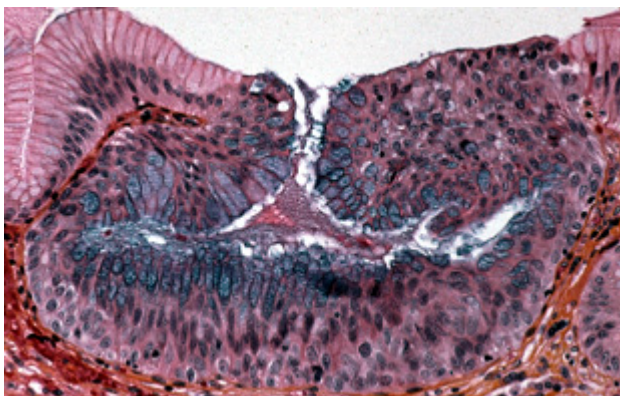
Alcian blue positive cells which are NOT goblet cells.

Alcian blue positivity alone does not define a cell as a goblet cell. We also like to see a barrel shape to the columnar epithelium.



Reactive gastric epithelium showing Alcian blue positivity.

Mucous neck cells of gastric glands are typically Alcian blue positive.



Submucosal esophageal glands can also show Alcian blue positivity.

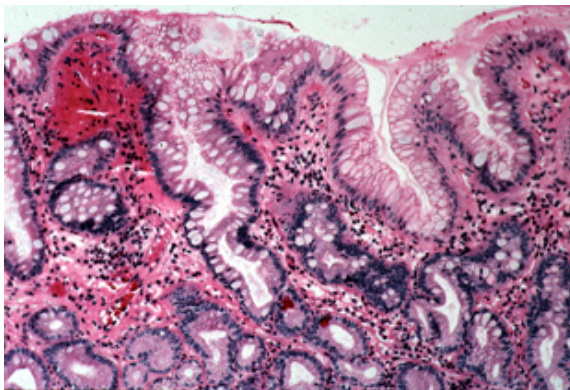
DEFINITION AND CHARACTERISTICS OF DYSPLASIA IN BARRETT'S ESOPHAGUS

Dysplasia is defined as neoplastic epithelium that remains confined within the basement membrane of the epithelial surface within which it arose. Questions regarding the diagnosis and grading of dysplasia arise commonly. We use a five-tiered system when evaluating Barrett's metaplastic epithelium for dysplasia or cancer: negative for dysplasia, indefinite for dysplasia, low-grade dysplasia, high-grade dysplasia, and intramucosal adenocarcinoma.

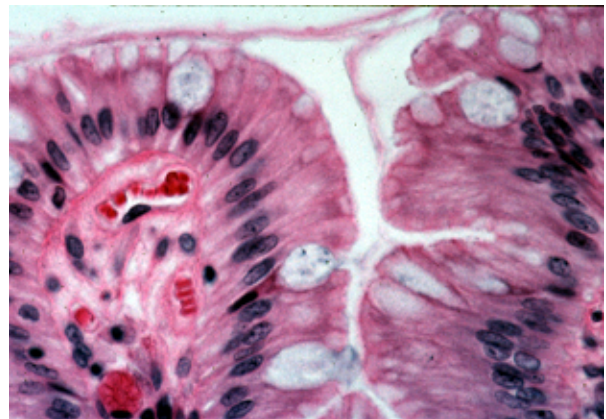
Negative for dysplasia: The metaplastic glands consistently show nuclear atypism when contrasted with normal columnar epithelium. This atypism comprises nuclear enlargement, crowding, hyperchromatism, prominence of nucleoli, and occasional mild stratification. These mild abnormalities may be misinterpreted as dysplasia, but can usually be separated from it because **they are confined to the lower portion of the glands, while the upper portion of the glands and surface epithelium shows less abnormality or is normal**; this feature is best recognized in well-oriented biopsy specimens.

Images of Barrett's Esophagus - Negative for Dysplasia

While cytologic abnormalities can be present in Barrett's esophagus, they are confined to the lower portion of glands. The mucosal surface shows less abnormality or is normal.

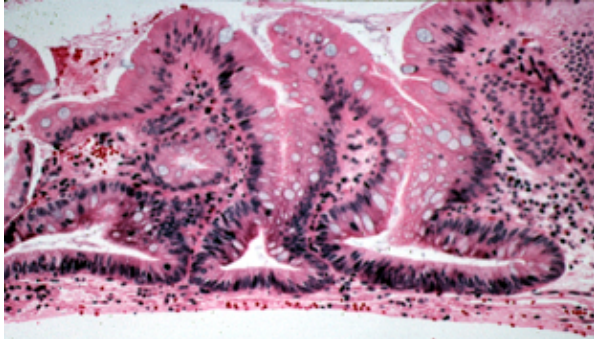


The deeper glands demonstrate mild nuclear atypia.

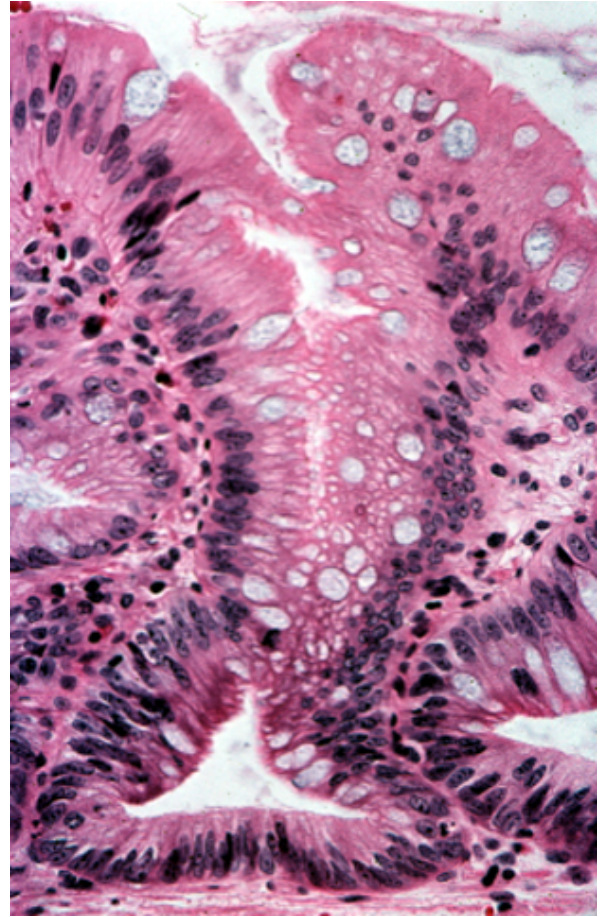


These changes, however, do not extend to the mucosal surface.

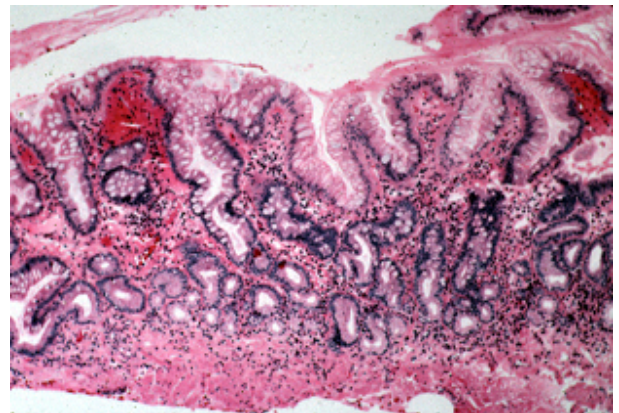
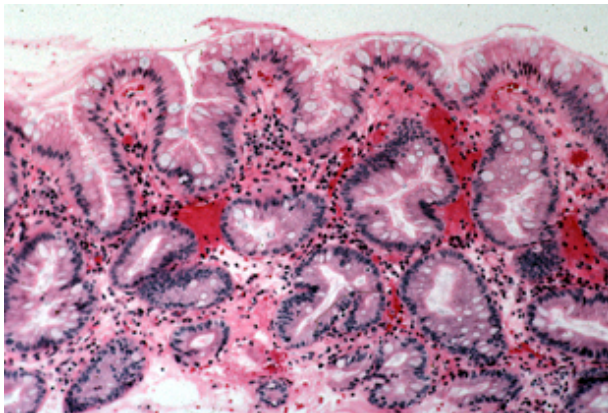
The mucosal surface demonstrates mucin caps with basally oriented nuclei lacking hyperchromatism, pleomorphism, or nuclear contour irregularity.

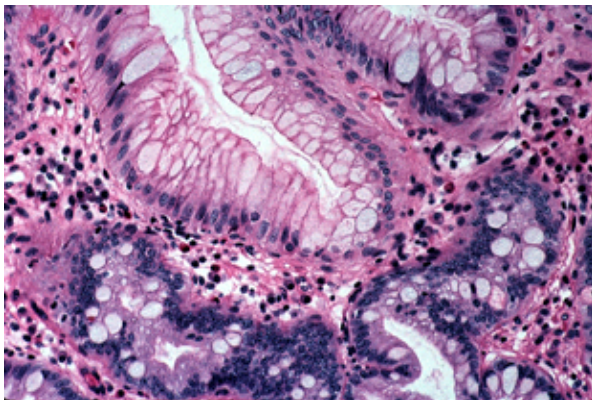
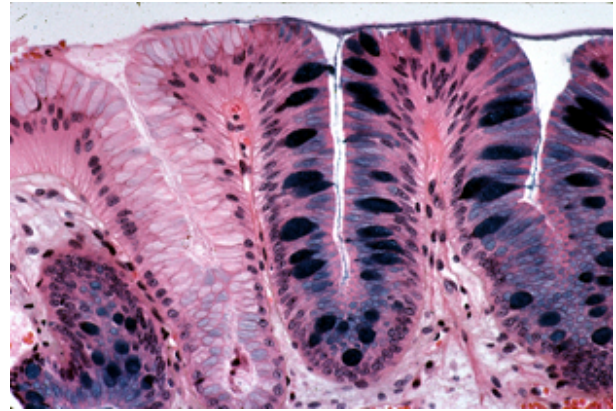
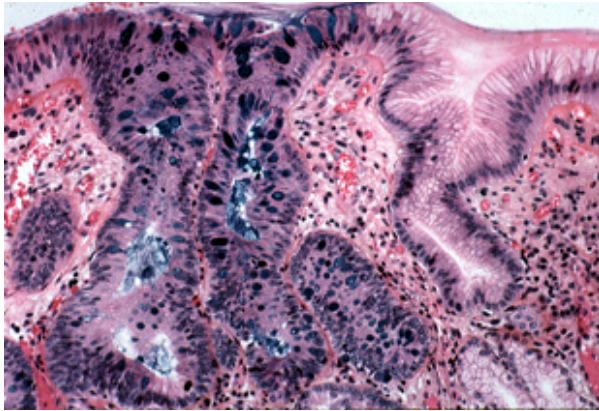


The deeper glands in Barrett's esophagus usually demonstrate some degree of nuclear atypia. However, there is maturation of the epithelium as it extends onto the mucosal surface.



Additional examples we would interpret as negative for dysplasia.





[Indefinite for dysplasia](#): This category is reserved for biopsies in which there is doubt as to the significance of the epithelial abnormalities. We use this term in several situations.

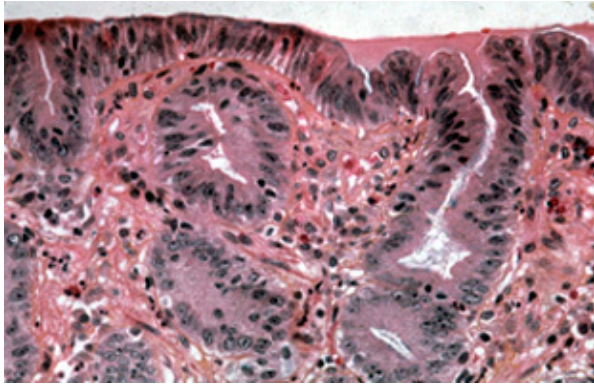
Often there is mild nuclear stratification of the surface epithelium, but the cytologic features fall short of those typical of dysplasia. The nuclei may be enlarged, but they are uniform in size and shape and have less hyperchromatism and irregularity of nuclear contour than seen in dysplasia.

When the nuclear features on the mucosal surface appear dysplastic, but there is prominent active inflammation, granulation tissue, or an adjacent ulcer, the diagnosis of dysplasia is difficult, and unless it is overt, we use the term "indefinite for dysplasia." Active inflammation can cause nuclear changes that mimic dysplasia; therefore we raise our threshold for dysplasia in its presence.

In poorly oriented biopsies, or in those with an eroded surface, the glands may appear dysplastic, but no surface epithelium is available for evaluation. We usually classify these biopsies as indefinite for dysplasia, or as dysplastic but without assigning a grade, depending on the degree of abnormality.

Images of Barrett's Esophagus - Indefinite for Dysplasia

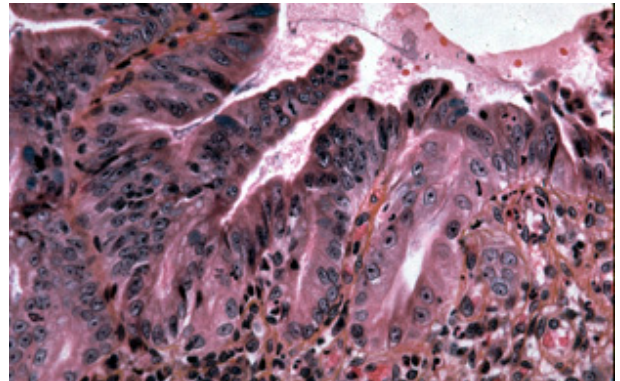
We use the term "indefinite for dysplasia" when we are in doubt of the significance of the epithelial abnormalities present in a biopsy. Examples of situations when we use this diagnosis are provided below.



Nuclear stratification without obvious dysplastic features.

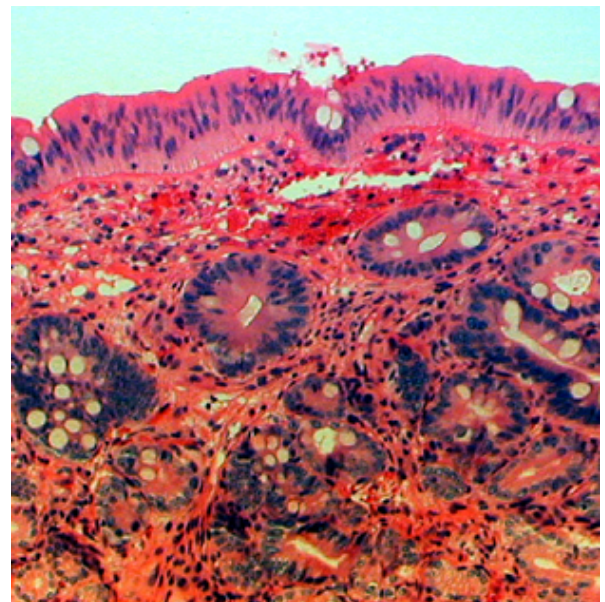
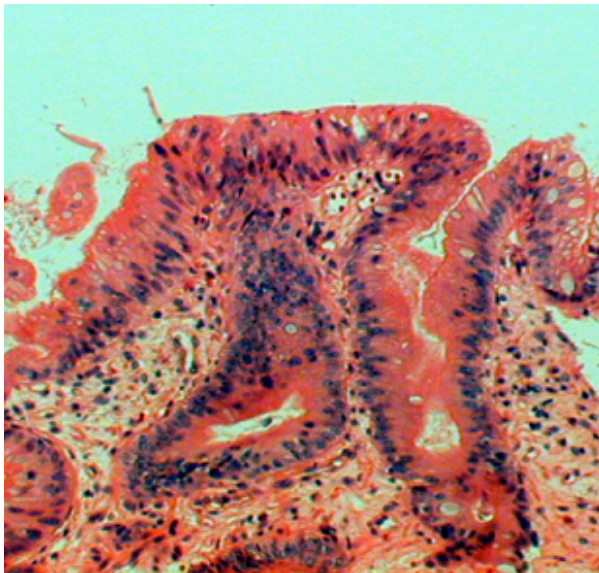
Active inflammation in area mimicking dysplasia.

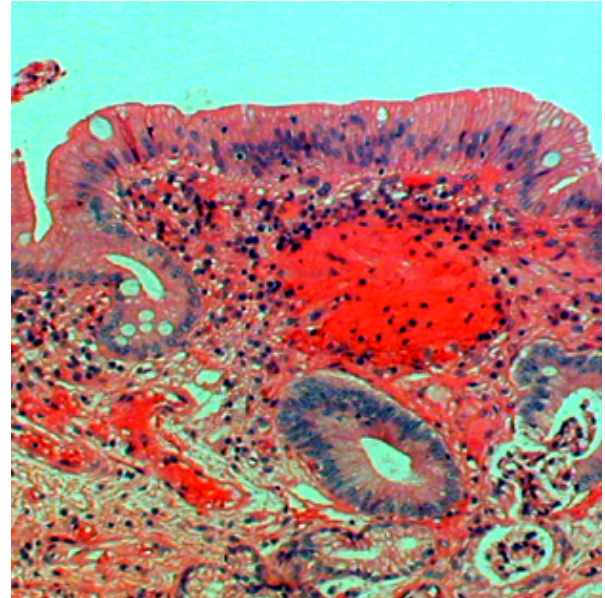
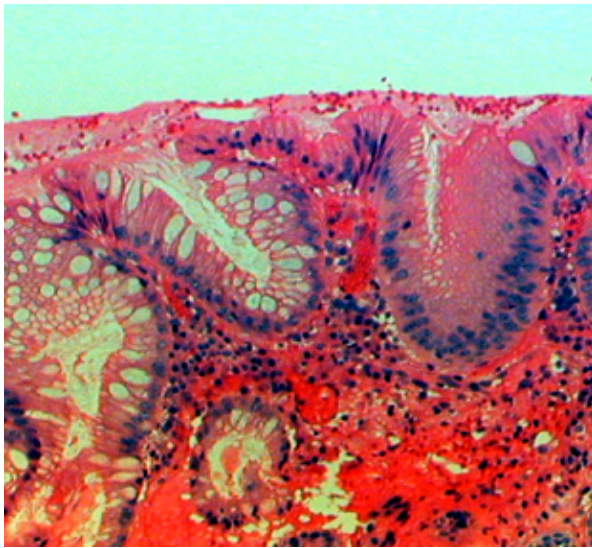
Highly atypical glands with no overlying epithelium for evaluation.



An area adjacent to an ulcer. The epithelium is highly atypical, but given the proximity to an ulcer, we would interpret these changes as indefinite for dysplasia.

Additional examples of cases we would interpret as indefinite for dysplasia.

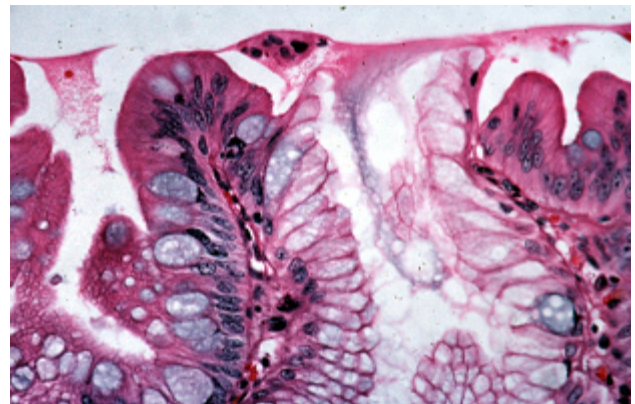
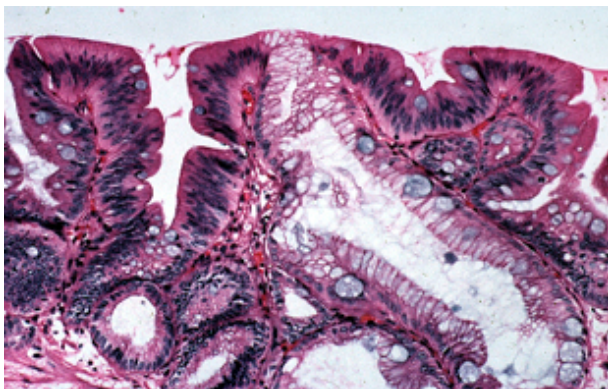




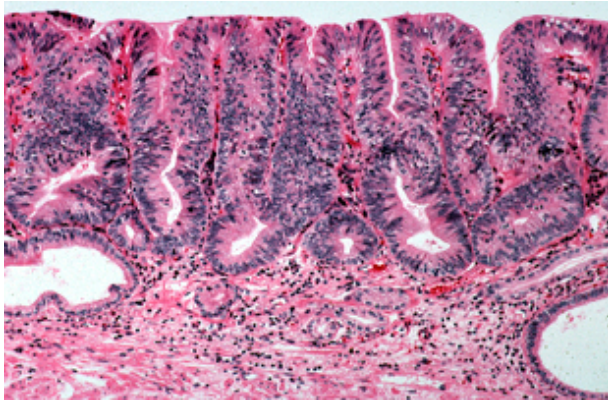
Low-grade dysplasia: The diagnosis of low-grade dysplasia can be difficult; however, it may be reassuring for the pathologist to know that the difference in patients with biopsies diagnosed as indefinite for dysplasia versus those with low-grade dysplasia may not be clinically relevant. The endoscopist may decrease the time interval between surveillance endoscopies and increase the number of biopsies, but therapeutic interventions are usually not initiated. There is significant interobserver and intraobserver variation in the diagnosis of dysplasia in Barrett's esophagus, particularly at the indefinite/low-grade interface. For this reason the categories of indefinite and low-grade dysplasia may be combined for clinical management purposes.

Images of Barrett's Esophagus - with Low-grade Dysplasia

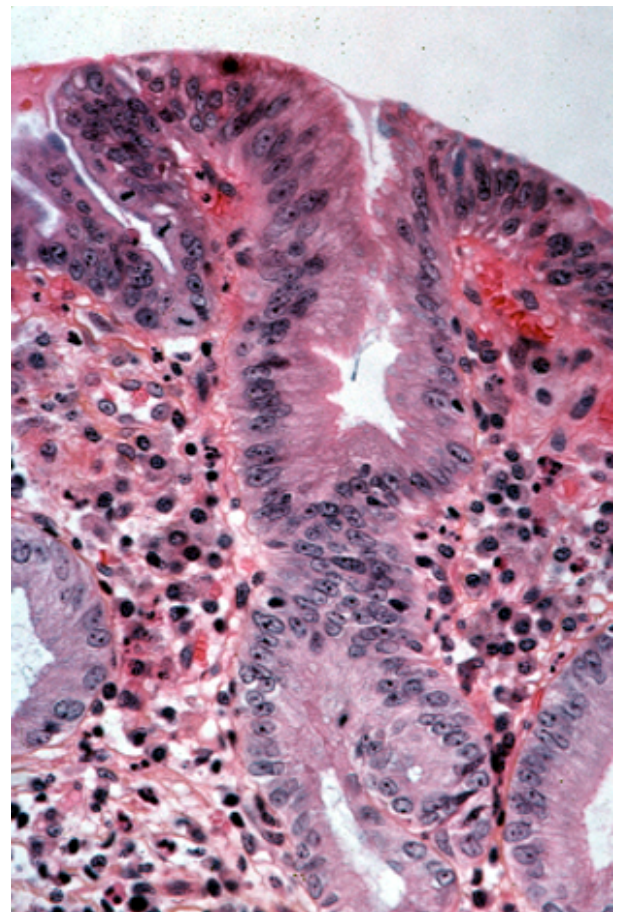
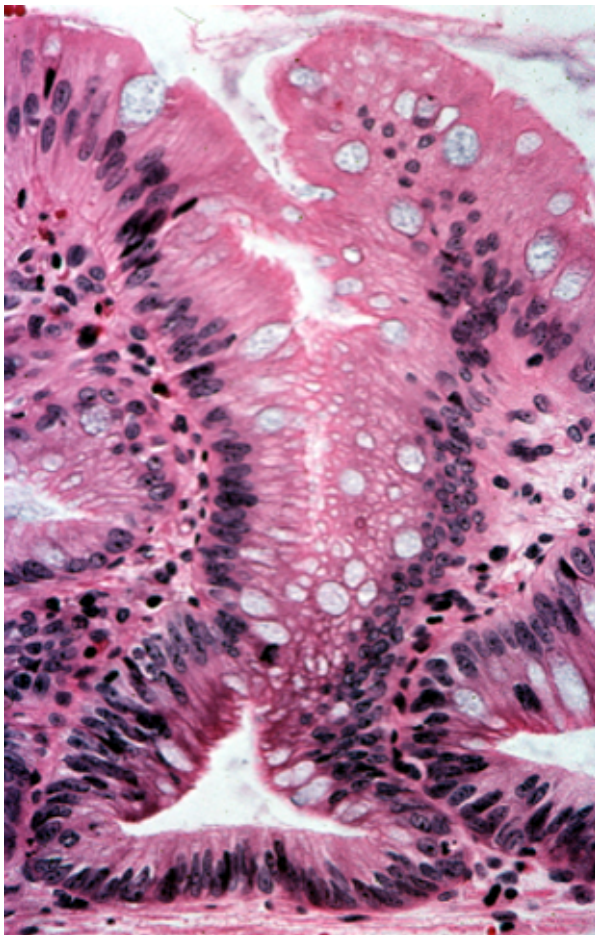
In low grade dysplasia, epithelial abnormalities extend onto the mucosal surface. The nuclei appear hyperchromatic, elongated, stratified, crowded, and may display loss of mucin production.



Low grade dysplasia is characterized by cells with enlarged, hyperchromatic, elongated, stratified nuclei that **extend onto the mucosal surface**. Typically there is decrease in the amount of mucin present a feature which can best be appreciated at low power.



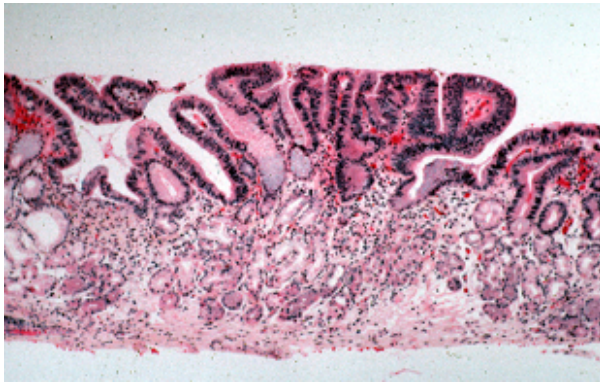
Loss of goblet cells can best be seen at low power in dysplastic areas.



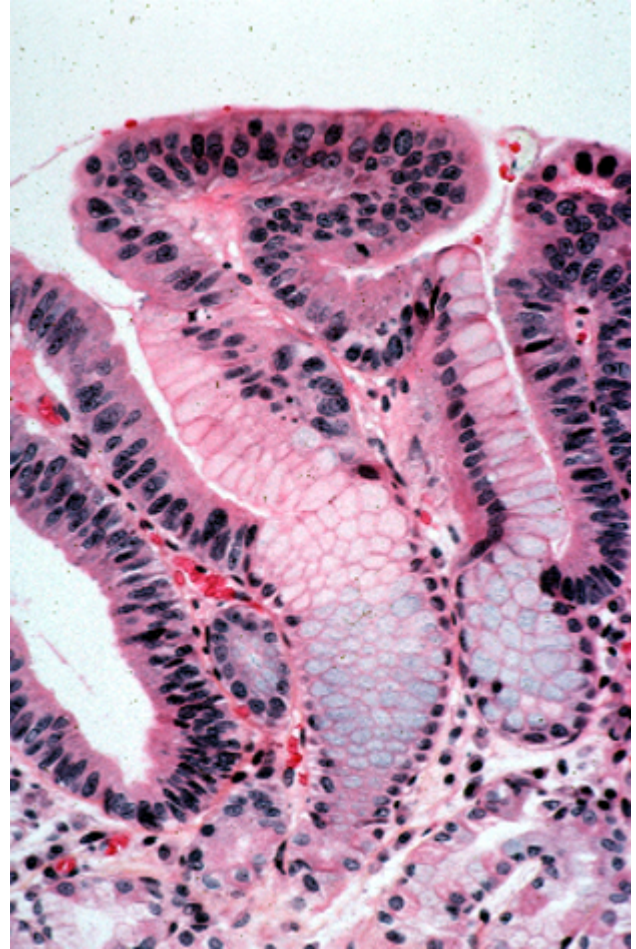
In dysplasia, the nuclear atypia extends onto the mucosal surface. Compare a biopsy with no evidence of dysplasia (on the right) with one that we felt represented low grade dysplasia (on the left).

Other phenotypes of dysplasia in Barrett's esophagus

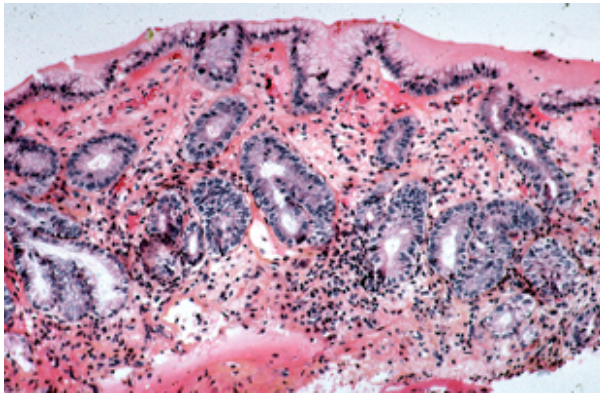
While it is more common to see mucosal surface involvement in combination with atypical deeper glands, situations may arise where only the mucosal surface demonstrates nuclear atypia while the deeper glands appear normal.



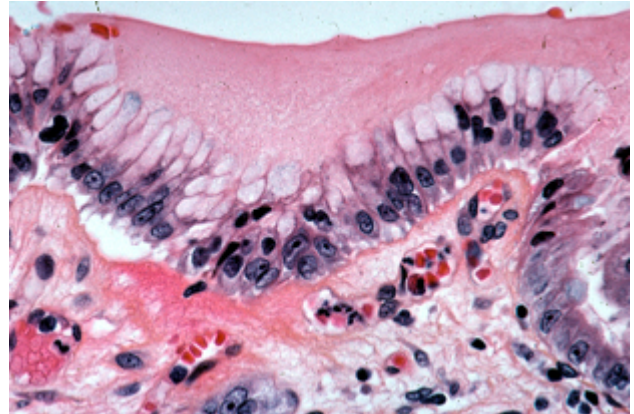
The dysplastic epithelium is present only on the mucosal surface with normal underlying glands.



A difficult phenotype of dysplasia to recognize occurs when there is retention of apical mucin and basally oriented nuclei. At low power, the biopsy may be called negative; however, at higher power, obvious atypical nuclei can be demonstrated.

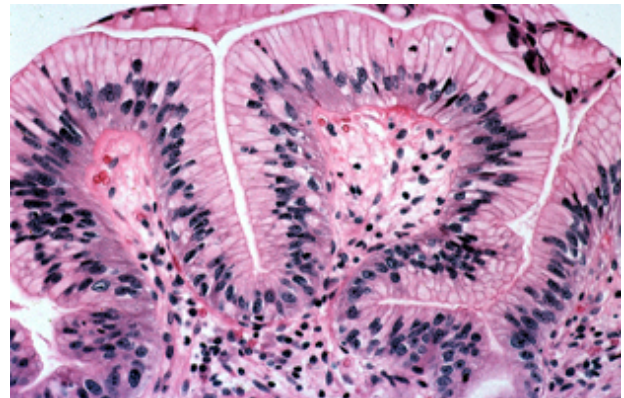
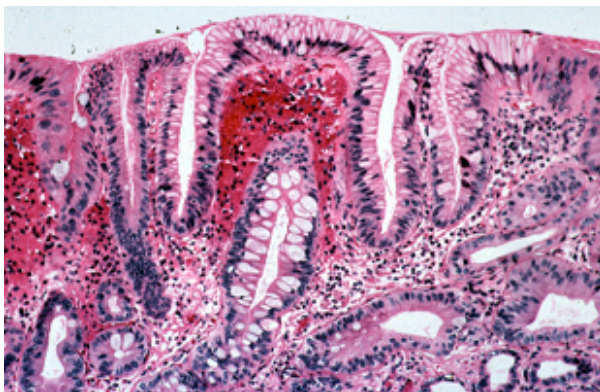
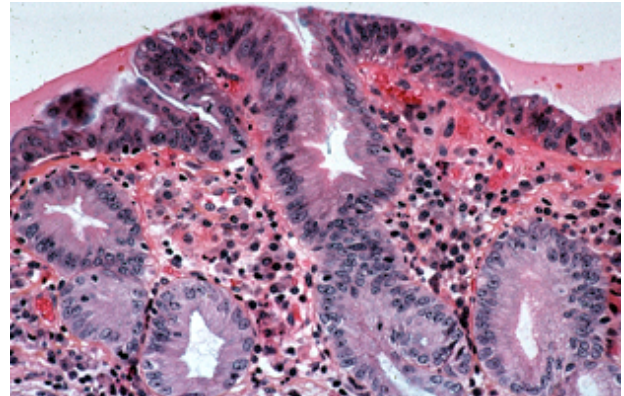
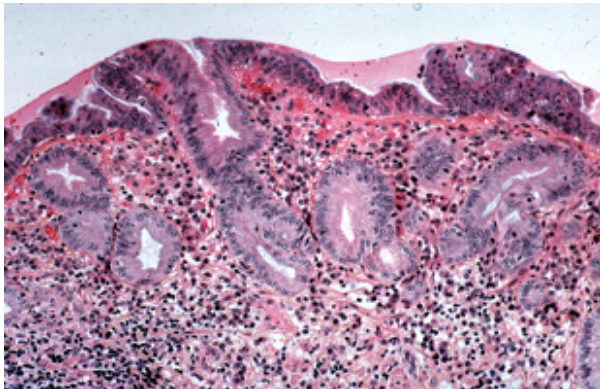


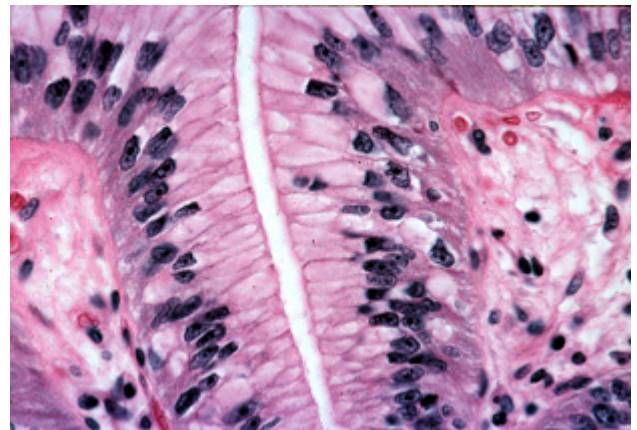
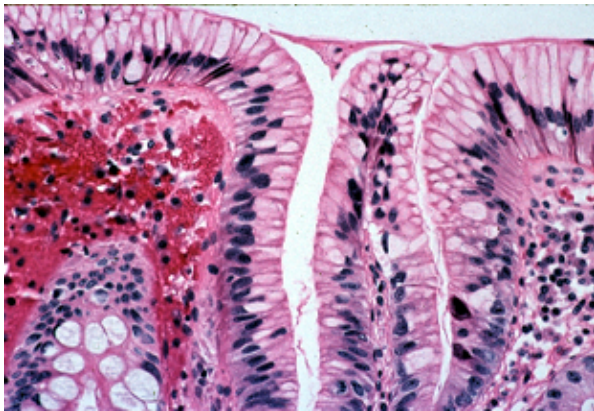
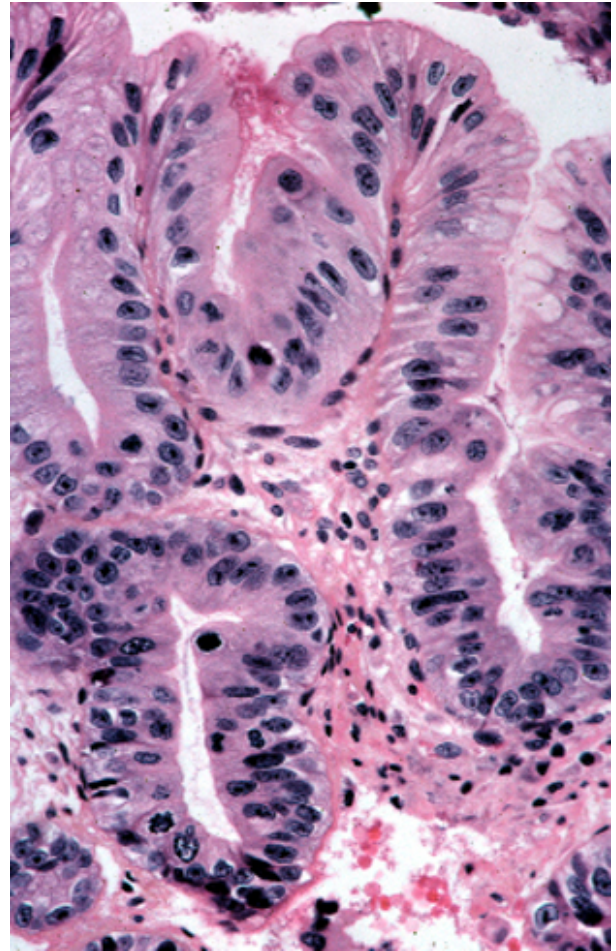
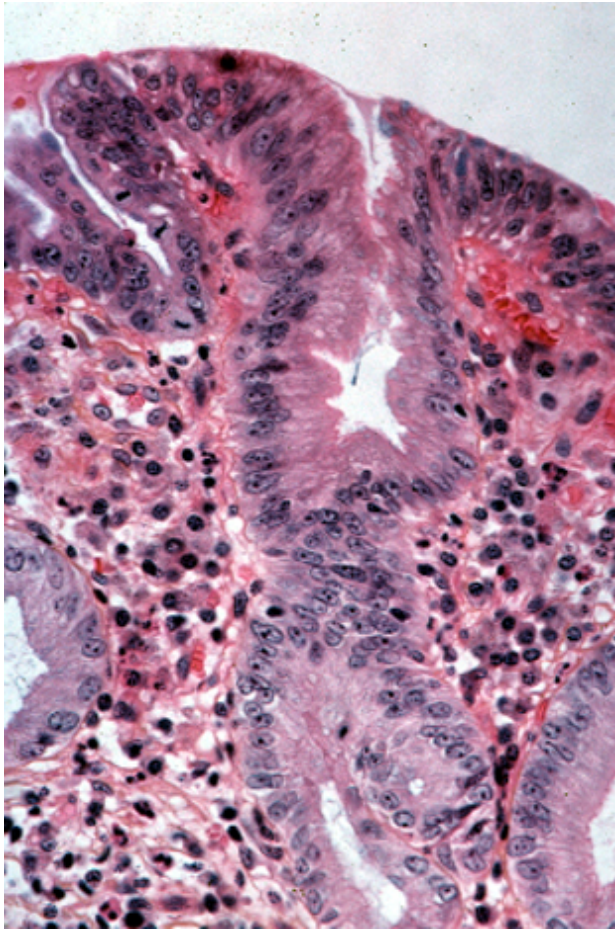
The abundant mucin seen at low power may elicit a diagnosis of negative for dysplasia

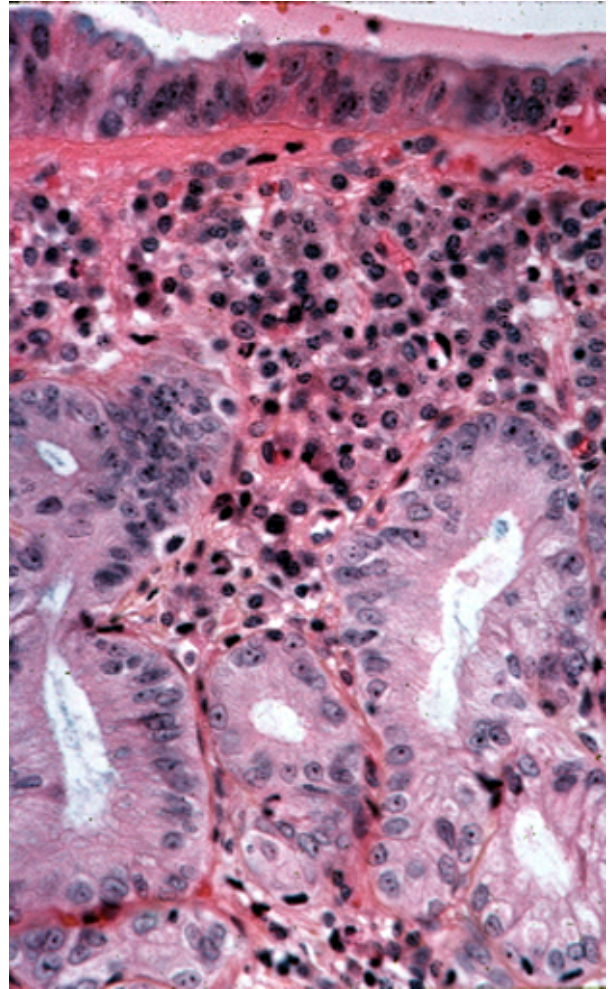


At higher power, however, obviously atypical nuclei can be seen at the mucosal surface, warranting a diagnosis of low grade dysplasia

Additional examples we would interpret as low-grade dysplasia.







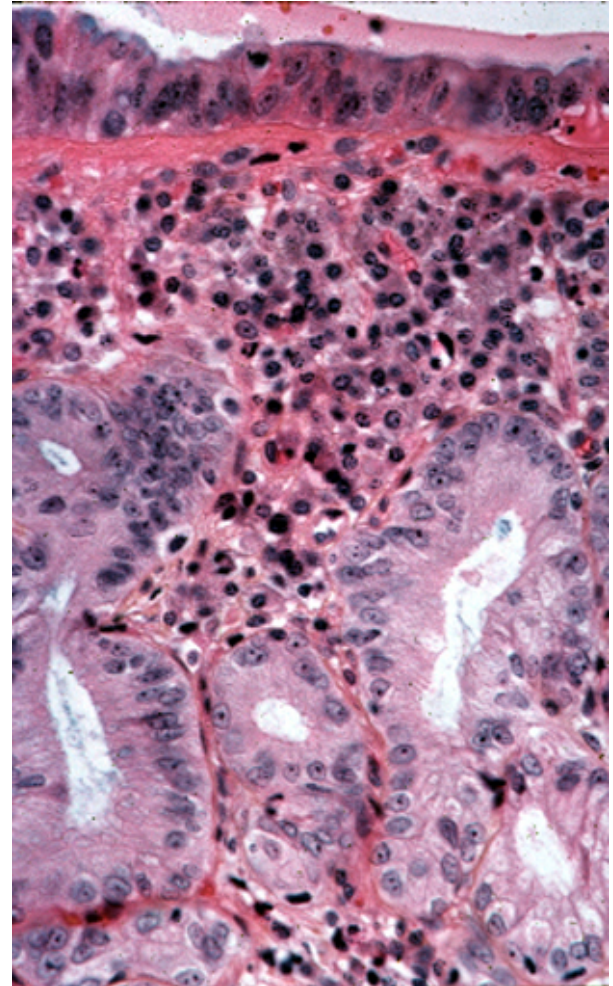
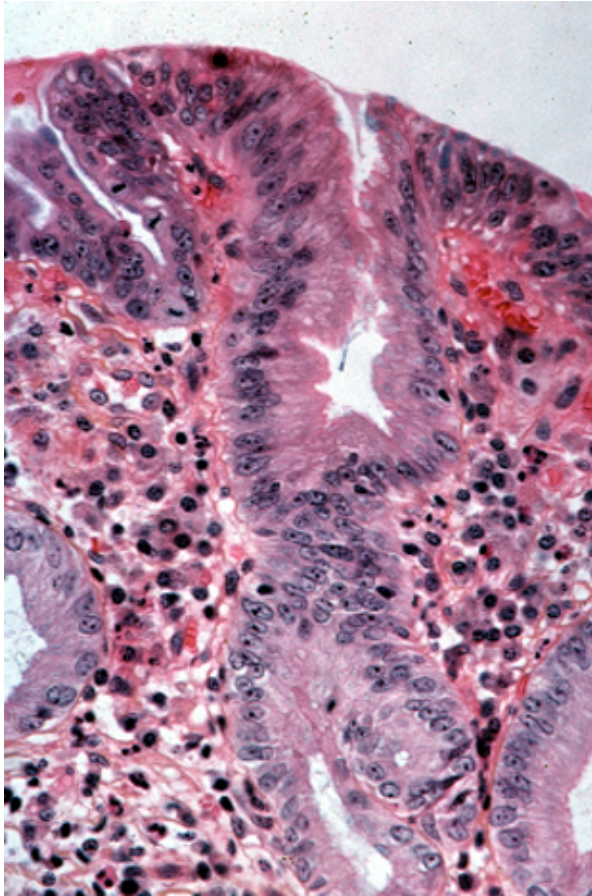
When the biopsy contains both abnormal and normal epithelium, or if a different biopsy from the same patient contains abnormal epithelium, the pathologist can obtain helpful clues about the diagnosis by comparing the nuclear features in the areas in question with those in the unaffected areas. The atypical nuclei of dysplastic epithelium extend onto the mucosal surface so both the surface and the glands contain nuclei that are much larger and hyperchromatic than the nuclei in unaffected epithelium.

We have observed two major phenotypes of abnormal epithelium in Barrett's esophagus. The first pattern is characterized by glands lined by cells with [crowded, stratified, hyperchromatic nuclei that extend onto the mucosal surface](#). Depending on the degree of cytologic atypism, this pattern may be interpreted as indefinite for dysplasia, or as low-grade dysplasia.

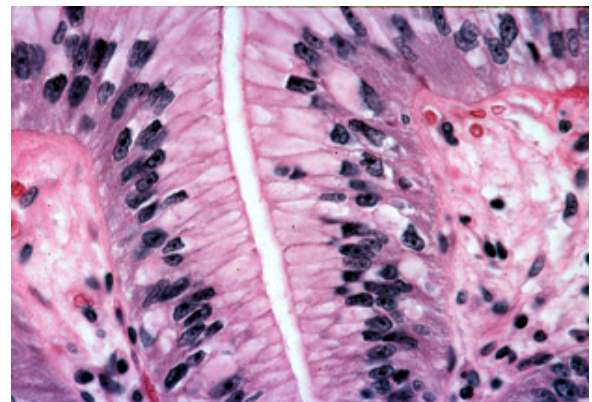
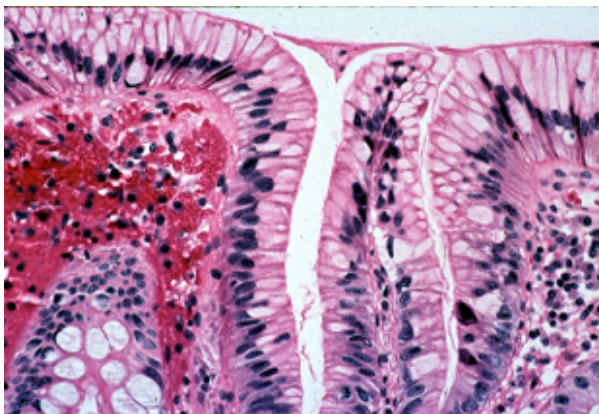
The second pattern consists of cells on the mucosal surface with [obviously dysplastic nuclei \(large, hyperchromatic, irregular contours\) that are basally located in the cell](#) with minimal or no stratification. This phenotype of dysplasia may be overlooked at low power as it often lacks goblet cells and may be confused with gastric cardiac epithelium.

Phenotypes of Dysplasia in Barrett's Esophagus

Stratified appearance of atypical nuclei



Basally located dysplastic nuclei



Clues to the Diagnosis of Dysplasia

At low power, certain clues that indicate dysplasia may be present, and they should prompt examination

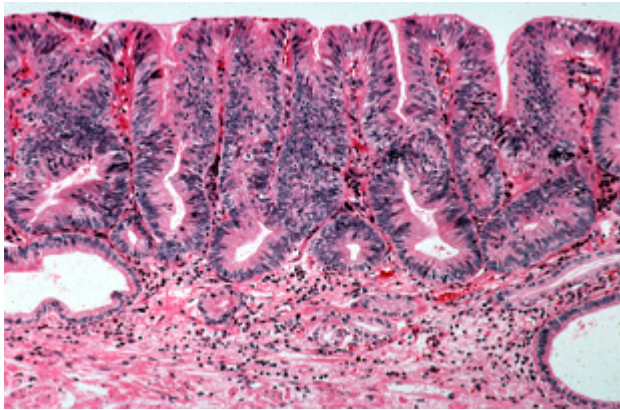
at a higher power to observe the nuclear features.

Frequently, [both an absence of goblet cells and mucin depletion in the non-goblet columnar cells](#) may be seen in dysplastic epithelium. At low power, these areas appear more hyperchromatic as compared to uninvolved areas. Entire biopsies composed of dysplastic epithelium may not contain goblet cells and may be confused with reactive gastric cardiac epithelium. However, the degree of nuclear atypia can help in differentiating dysplastic epithelium from reactive gastric mucosa.

Less frequently, dysplastic epithelium may secrete [excessive mucus](#) and once again may be confused with gastric cardiac epithelium. Careful examination of the nuclei in this pattern of dysplasia reveals prominent atypism with indentations in the nucleus produced by the mucin. The presence of obviously dysplastic epithelium elsewhere within the biopsy will help characterize this pre-malignant phase of Barrett's esophagus.

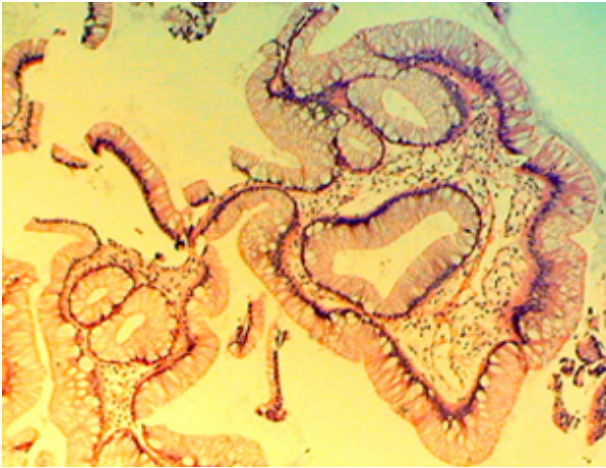
Clues to the Diagnosis of Dysplasia

Areas with mucin depletion

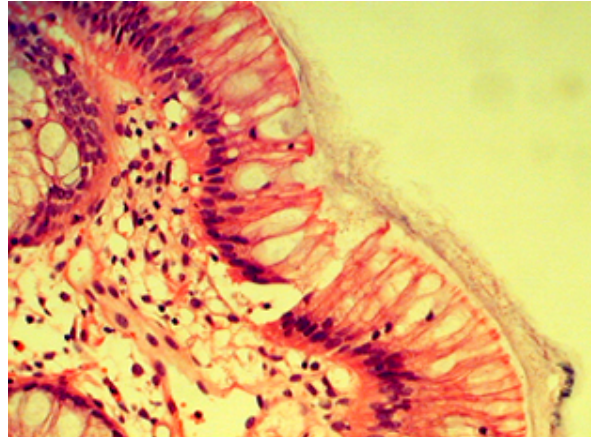


Lower power view will allow detection of areas with mucin depletion.

Areas with abundant mucin production



Areas involved by Barrett's metaplastic epithelium with abundant mucin production should alert the pathologist to look carefully for dysplastic nuclei.



The hypermucinous areas may resemble colonic mucosa. Based on the nuclear features, a diagnosis of "indefinite for dysplasia" or "low-grade dysplasia" may be warranted in this case.

Features of Reactive Barrett's Epithelium

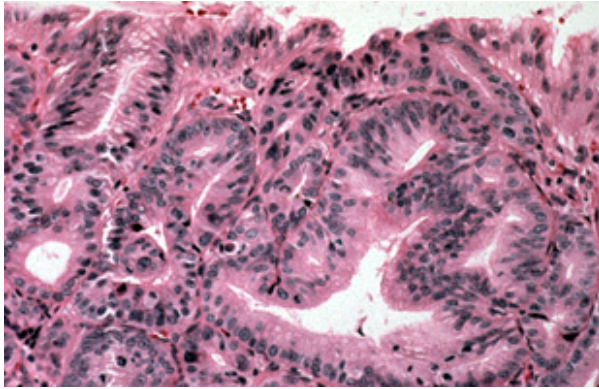
One feature that is commonly seen in non-dysplastic epithelium is the presence of apical mucin. We hesitate to make a diagnosis of dysplasia when apical mucin persists and usually make the diagnosis of negative or indefinite for dysplasia, depending on the nuclear features.

Reactive metaplastic columnar epithelium shows atypism; but the nuclei are uniformly enlarged with little hyperchromatism, and they maintain a basal orientation. It is the uniformity and lack of pleomorphism that indicate a reactive, rather than a neoplastic, process.

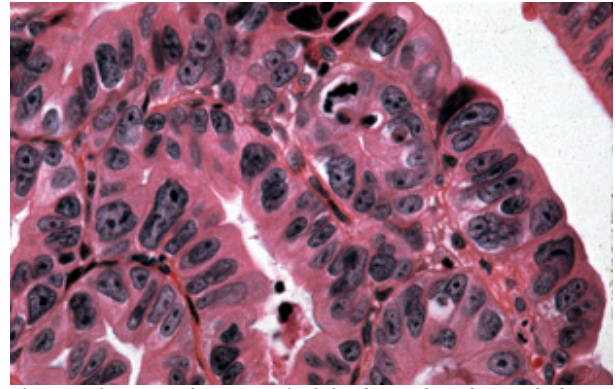
High-grade dysplasia: The accurate diagnosis of high-grade dysplasia is critically important because therapeutic intervention of some form, and often esophagectomy, may be initiated based on this diagnosis. At low power, distortion of glandular architecture usually is present and may be marked; it is composed of branching and lateral budding of crypts, a villiform configuration of the mucosal surface, or intraglandular bridging of epithelium to form a cribriform pattern of "back-to-back" glands. Most importantly, there should be dysplastic epithelium on the mucosal surface with **loss of nuclear polarity**, characterized by "rounding up" of the nuclei, and absence of a consistent relationship of nuclei to each other, before rendering the diagnosis of high-grade dysplasia.

Images of Barrett's Esophagus with High-grade Dysplasia

Diagnosing high-grade dysplasia is very important as many invasive procedures are initiated based on this diagnosis. We like to see loss of nuclear polarity ("rounding up" of nuclei) before making this diagnosis.

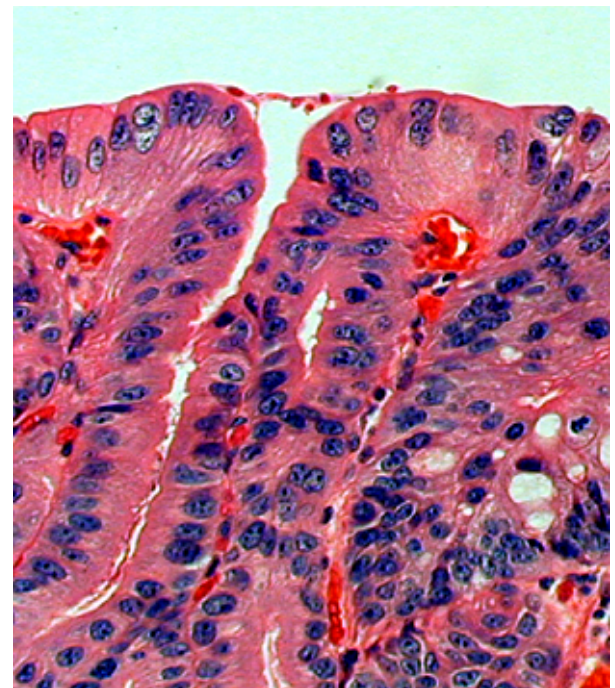
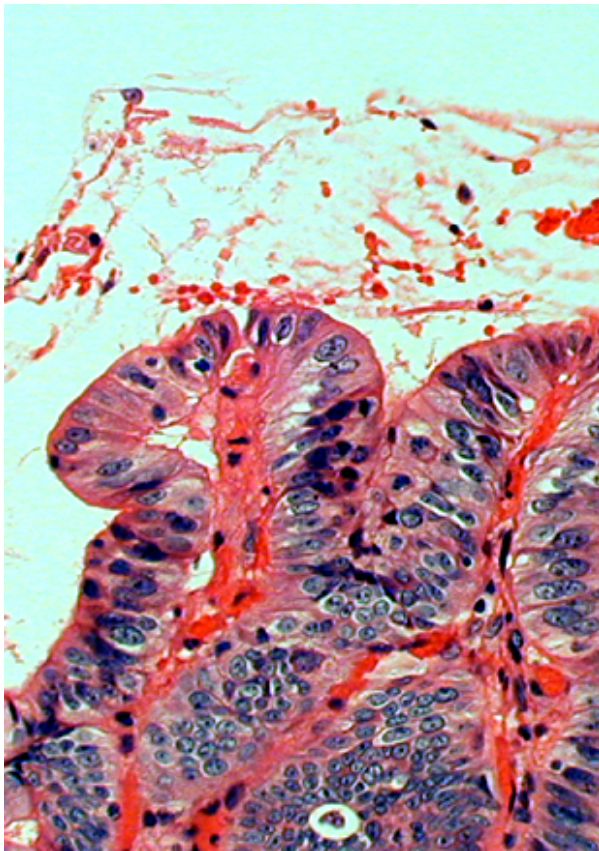


Low power view of disortion of crypt architecture.



The most important feature we look for: **loss of nuclear polarity**.

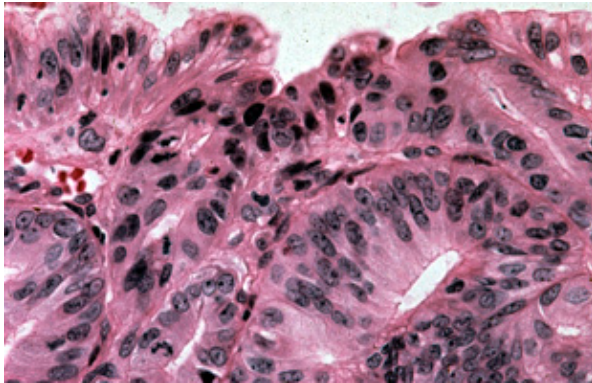
Additional examples we would interpret as high-grade dysplasia.



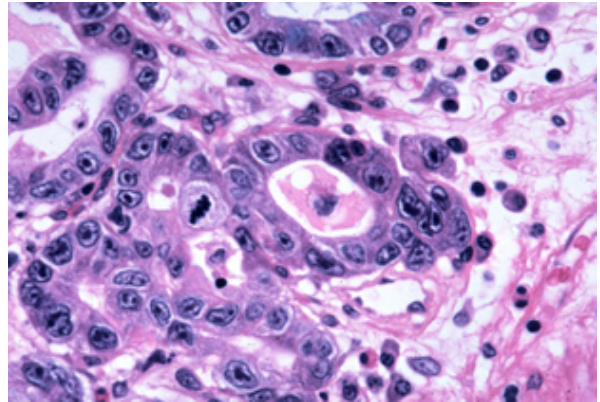
Intramucosal adenocarcinoma: Glandular architecture can be highly complex in high-grade dysplasia. This complexity often makes it difficult to exclude the diagnosis of intramucosal adenocarcinoma. Before making the diagnosis of invasive carcinoma, we require the presence of **individual cytologically malignant cells or abortive glands infiltrating the lamina propria**. Typically, the desmoplastic stroma often present in carcinomas invading the submucosa is absent when invasion is limited to the lamina propria.

Images of Barrett's Esophagus with Intramucosal Adenocarcinoma

We like to see individual malignant cells in the lamina propria before rendering the diagnosis of intramucosal adenocarcinoma. A low power impression of marked glandular crowding makes us suspicious of invasion.

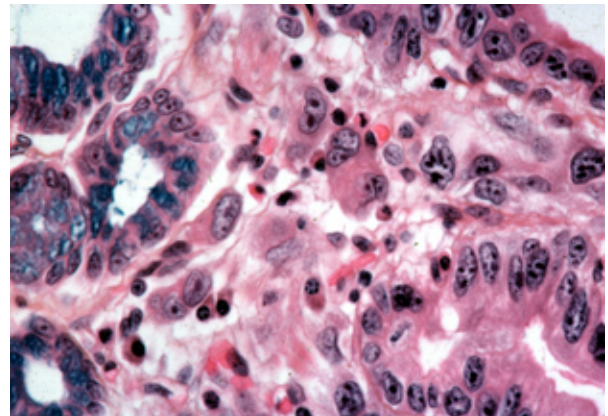
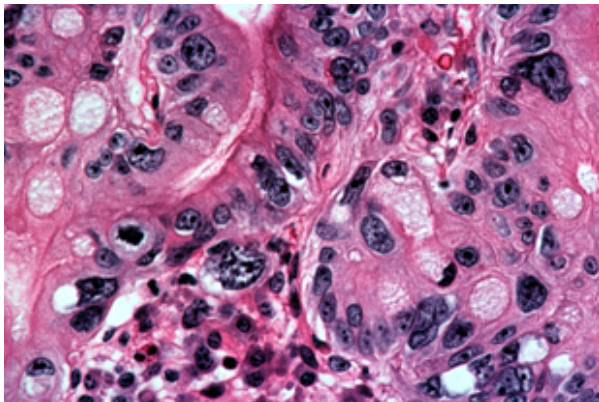


Complex glandular architecture that can make it difficult to see invasion.



An individual malignant cell in the lamina propria is adjacent to the gland in the center of this image.

Additional examples we would interpret as intramucosal adenocarcinoma.



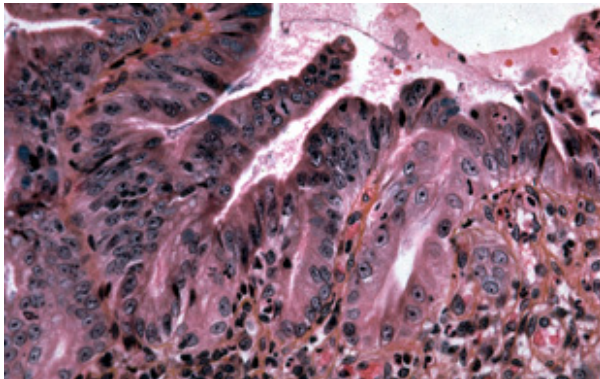
PITFALLS IN THE DIAGNOSIS OF DYSPLASIA

The pathologist must be aware of situations in which reactive epithelial alterations may mimic dysplasia in order to avoid its over-diagnosis.

Ulcer/Erosion with marked active inflammation: Active inflammation may cause nuclear changes that mimic high-grade dysplasia. One should be cautious when numerous neutrophils infiltrate the overlying epithelium; however, the **degree** of inflammation is important to note. Barrett's esophagus with high-grade dysplasia may be associated with a few neutrophils in the overlying epithelium, but the nuclear changes are so dramatic that the diagnosis of high-grade dysplasia can be made. If numerous neutrophils or an adjacent ulcer are present, we avoid the diagnosis of dysplasia and use the category of "indefinite for dysplasia." Chronic inflammatory cells do not cause the nuclear abnormalities associated with active inflammation.

Pitfalls in the Diagnosis of Dysplasia - Ulcer/Erosion with Marked Active Inflammation

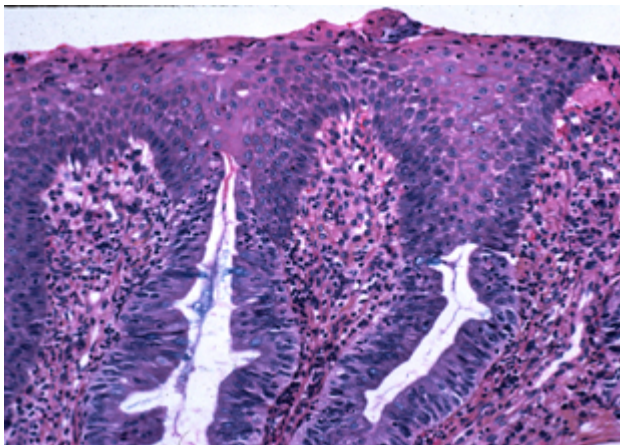
Marked active inflammation causing changes mimicking dysplasia.



This biopsy is from an ulcer edge. It displays changes mimicking high-grade dysplasia.

Metaplastic columnar epithelium underlying squamous epithelium: Use of proton-pump inhibitors may cause caudad migration of the squamo-columnar junction, or squamous islands may develop within the Barrett's segment. In either case, Barrett's metaplastic epithelium may still present underneath the squamous epithelium on the surface (squamous overgrowth). Because dysplasia and adenocarcinoma may develop within the metaplastic columnar epithelium underneath the squamous surface, the endoscopist must biopsy these squamous islands. Unfortunately, since no overlying columnar epithelium is present for evaluation (being completely replaced by squamous epithelium) the criterion of mucosal surface involvement by atypical epithelium cannot be used to make the diagnosis of dysplasia. We look for marked nuclear atypia in combination with architectural distortion before raising the possibility of dysplasia. We are hesitant to make the diagnosis of low-grade dysplasia based on the deep glands; but we think that a diagnosis of high-grade dysplasia can be rendered if the nuclear features (loss of nuclear polarity, hyperchromatism, pleomorphism) are consistent with high-grade dysplasia.

Pitfalls in the Diagnosis of Dysplasia - Metaplastic Columnar Epithelium Underlying Squamous Epithelium



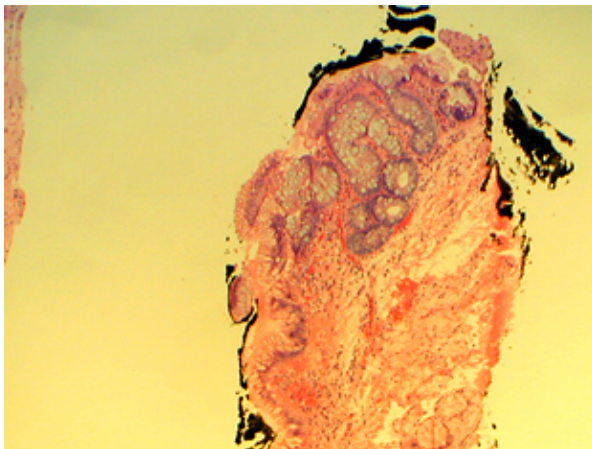
Metaplastic columnar epithelium adjacent to a squamous island: Frequently the columnar epithelium immediately adjacent (1 to 2 glands) to a squamous island displays atypical nuclear features that are present on the mucosal surface. We are hesitant to make the diagnosis of dysplasia in this context. We like to see the nuclear atypia involve the surface epithelium in areas several crypts away from the squamous island before making the diagnosis of dysplasia. The question arises, "How far is far enough?" We believe that in Barrett's esophagus negative for dysplasia, the epithelium on the mucosal

surface should appear normal 2 or 3 glands away from the squamous island. Abnormal nuclear changes beyond this point probably indicate dysplasia.

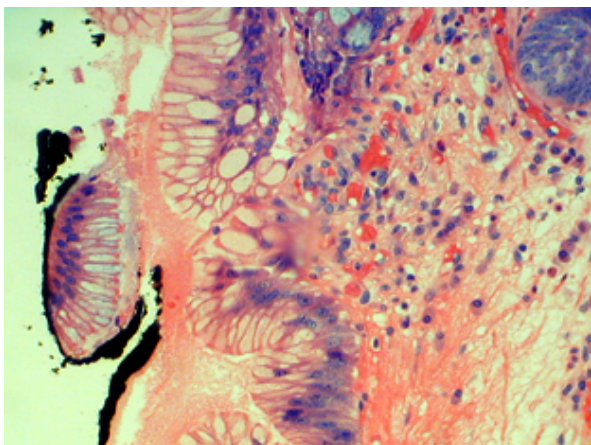
Detached fragments of atypical epithelium: The surface epithelium in Barrett's esophagus may become detached from the lamina propria and these detached fragments may display features suggesting dysplasia. For reasons that are not clear, but possibly due to the trauma that removed them from the surface, the nuclei of the cells within these strips of detached atypical epithelium may appear highly atypical when there is no dysplasia. We hesitate to make the diagnosis of dysplasia based on these fragments if no dysplastic epithelium is present within the intact biopsy. Almost as a rule, we do not diagnose high-grade dysplasia based on detached fragments alone. If the nuclear changes are highly atypical, we would consider the diagnosis of indefinite for dysplasia or, possibly, dysplasia, without assigning a grade.

Reactive gastric cardiac mucosa: Reactive gastric cardiac mucosa displays nuclear atypia that may be misinterpreted as dysplastic metaplastic epithelium. The absence of goblet cells may be an important clue; but it must be remembered that in dysplastic epithelium, goblet cells may not be seen on biopsy specimens. Dysplastic epithelium lacking goblet cells will display greater nuclear atypia than seen in reactive gastric cardiac epithelium.

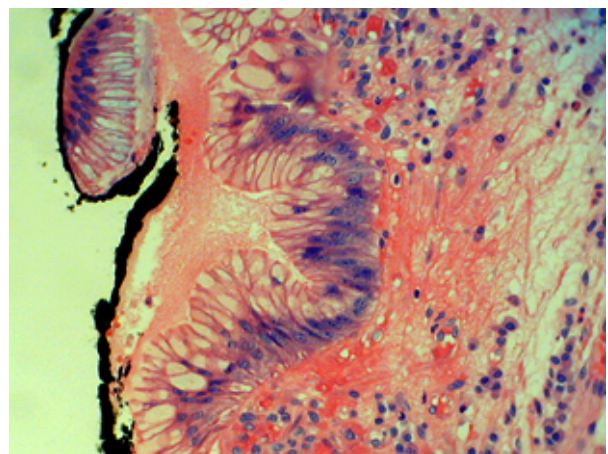
Pitfalls in the Diagnosis of Dysplasia - Reactive Gastric Cardiac Mucosa



Metaplastic columnar epithelium is present adjacent to gastric cardiac mucosa.



The gastric cardiac mucosa from the case above demonstrates reactive nuclear atypia that may be misinterpreted as dysplasia.



Pseudogoblet cells in the gastric mucosa may contribute to the misinterpretation of dysplasia in this case.

PROBLEMS WITH GRADING OF DYSPLASIA IN BARRETT'S ESOPHAGUS

Two principle problems interfere with the diagnosis and grading of dysplasia in Barrett's esophagus: fixation and orientation.

Formalin is not the ideal fixative for nuclear detail, and we rely heavily on nuclear features for the diagnosis and grading of dysplasia. We use Hollande's fixative, which is a modification of Bouin's solution, for our biopsy material. We have had excellent results with this fixative, and if you compare the nuclear detail achieved with Hollande's solution as compared to that achieved with formalin, the differences become obvious.

Another important element is proper orientation of the specimen. Surface epithelial involvement by atypical epithelium is an important criterion for the diagnosis of dysplasia. Improperly oriented specimens make it difficult to evaluate the surface epithelium and often result in the diagnosis of indefinite for dysplasia. Ideally, the endoscopist or an assistant should orient the biopsy onto a substrate, such as monofilament mesh, by teasing it out of the biopsy forceps and onto the tip of the finger. The biopsy can then be carefully flattened out on the fingertip, mucosal surface down, with the aid of the side of a dissecting needle, and can subsequently be transferred to the selected substrate with the mucosal surface up.

The use of the larger 3.4 mm forceps results in larger biopsies than the standard 2.4 mm biopsy forceps, and they are therefore best for diagnostic purposes. The larger specimens obtained with these forceps are easier to orient and have proportionately less crush artifact. The use of the large forceps is not associated with a higher risk of complications. In clinical research at the University of Washington, over 100,000 biopsies have been taken with the larger forceps without any increase in complications beyond that expected for the smaller forceps.

Please send comments or suggestions to the GI & Hepatic Pathology Fellow: Dan Toweill, MD

Gastric Cancers

Melissa Upton, MD

SURGICAL PATHOLOGY REPORT FORM

APPROACH TO THE GROSS EXAMINATION:

1. Ink the proximal and distal margins carefully, avoiding the mucosa.
2. Open the specimen along the greater curvature and note the composition of the proximal and distal margins, whether esophageal or duodenal tissue is incorporated into the specimen.
3. The stomach is photographed prior to fixation, with care taken not to handle the mucosa, as it abrades and denudes easily.
4. The specimen is pinned flat and fixed in formalin overnight. Adventitial soft tissue is removed except at the deep margins of lesions.
5. Soft tissue is dissected fresh, and all lymph nodes identified are submitted. Nodes should be separated into those located within 3 cm of the primary tumor and those more than 3 cm from the primary tumor.
6. Page the attending to offer a chance to review the gross specimen together prior to sectioning.
7. Review the patient medical record online for clinical history prior to taking final microscopic sections.

THE GROSS DESCRIPTION SHOULD COMMENT ON THE FOLLOWING:

- Length of esophageal and gastric (greater & lesser curvatures) segments, with precise anatomic location of all gross lesions.
- Tumor measurements in 3 dimensions.
- Apparent depth of invasion.
- Distance to mucosal and radial margins; note importance of inking margins.
- Presence of additional lesions (polyps, large folds, ulcers).
- Comment on the outer surface of the stomach for evidence of tumor invasion through the wall, whether the serosa is glistening, dull, retracted, nodular, or indurated.
- Comment on size and number of lymph nodes

THE FINAL DIAGNOSIS SHOULD INCORPORATE THE FOLLOWING:

- Classification of histologic type (adenocarcinoma, diffuse or intestinal or mixed).
- Grade (well, moderately, poorly differentiated, or undifferentiated).
- Depth of invasion:

TX	Tumor cannot be assessed
T0	No evidence of primary tumor.
Tis	Carcinoma in situ: intraepithelial tumor without invasion of lamina propria.
T1	Tumor invades lamina propria or submucosa.
T2a	Tumor invades muscularis propria.
T2b	Tumor invades subserosa.
T3	Tumor penetrates serosa (visceral peritoneum) without invasion of adjacent structures.
T4	Tumor invades adjacent structures (direct invasion may occur by extension to spleen, transverse colon, liver, diaphragm, pancreas, abdominal wall, adrenal gland, kidney, small intestine, and retroperitoneum).
AJCC Cancer Staging Manual, Sixth Edition, 2002	

- Presence of angiolymphatic invasion.
- Status of nodes (No. positive/No. present) * Per AJCC Cancer Staging Manual, Sixth Edition (2002), a regional lymphadenectomy from a gastric resection should contain 15 or more lymph nodes. Regional lymph nodes are considered the nodal groups comprising the perigastric nodes found along the greater and lesser curvatures and the nodes along the left gastric, common hepatic, splenic or celiac arteries. Involvement of other intra-abdominal lymph nodes, such as the hepatoduodenal, retropancreatic, mesenteric, and par-aortic nodes, are considered and classified as distant metastases.

NX	Regional nodes cannot be assessed.
N0	No regional lymph node metastasis.
N1	Metastasis to 6 or fewer regional lymph nodes.
N2	Metastasis to 7-15 regional lymph nodes.
N3	Metastasis to > 15 regional lymph nodes.
AJCC Cancer Staging Manual, Sixth Edition, 2002	

- Status of mucosal and radial margins.
- Presence of additional lesions (gastritis, intestinal metaplasia, dysplasia, polyps, H. pylori).

MICROSCOPIC SECTIONS:

- Neoplasm: <4 sections, including the deepest aspect, and radial sections of any ulcers.
- Margins: Represent the proximal, distal and deep margins. If the proximal margin is the esophagus, take a complete en face margin. If the neoplasm is close to the gastric margin, take sections perpendicular to the margin, including the neoplasm. If the neoplasm is far from the gastric distal margin, take an en face margin.
- Stomach: Representative sections of cardia, fundus, and antrum, if not incorporated into other sections.
- Lymph Nodes: Submit all.

- Adjacent or Contiguous Organs: Document neoplastic involvement.
- Cassette Number: The average gastrectomy specimen will require 8 cassettes from the stomach plus any lymph node cassettes. If the total number of cassettes for the stomach specimen (without nodes) exceeds 10 cassettes, consult the attending pathologist.

ANCILLARY STUDIES (IF DONE):

- o Flow cytometry
-

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Appendix

Mary Bronner, MD

PROCEDURE

- INK THE STUMP MARGIN—ALWAYS.
- IF TUMOR IS PRESENT, INK SEROSAL MARGIN OVER TUMOR AS WELL.
- Measure the organ (length and greatest diameter).
- Divide the last 2 cm of the tip in half longitudinally (see figure below).
- Cross-sectionally breadloaf the remaining proximal appendix from the inked stump margin at 0.5 cm intervals (see figure below).

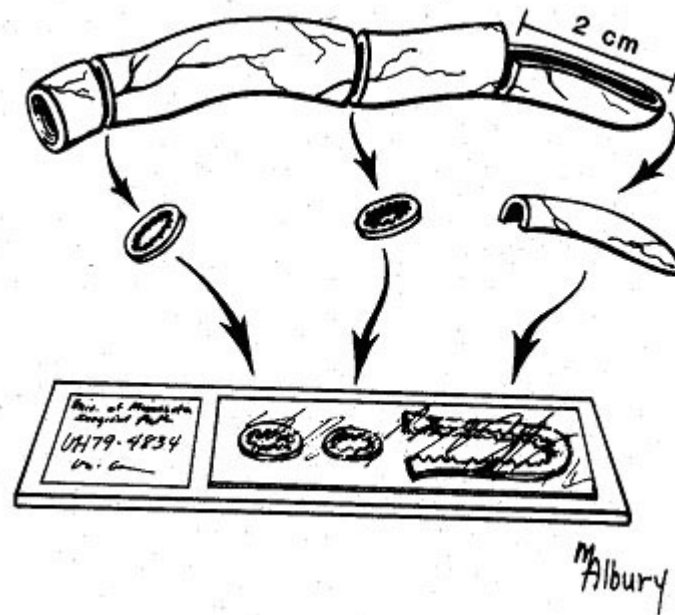
DESCRIPTION

- Length and greatest diameter.
- External surface: fibrin? pus? hemorrhage? hyperemia? perforation?; appearance of mesentery?.
- Wall: any discrete lesions?—if so measure and describe. Does the wall look diffusely thickened (normal =approximately 2-3 mm)?
- Lumen: obliterated? dilated?; Content: fecaliths? mucus? tumors?

SECTIONS FOR HISTOLOGY

- IF NO GROSS ALTERATIONS PRESENT:
 - ONE BLOCK ONLY containing--proximal tip (one longitudinal section), inked surgical stump margin (one cross section) and mid appendix (one cross section)—SEE FIGURE BELOW.
- WHEN TUMOR IS PRESENT:
 - If cystic, liberally sample cyst wall (up to 1 block per cm of cyst diameter) and especially sample any areas with solid fleshy lesions within cyst lining.
 - If solid, take up to 5 blocks to sample grossly heterogeneity in tumor composition.
 - BE SURE YOU HAVE INKED AND SUBMITTED STUMP MARGIN AND DESCRIBE HOW CLOSELY THE TUMOR APPROXIMATES THE MARGIN GROSSLY OR IF IT

GROSSLY INVOLVES IT!!



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CAP Cancer Protocols and Checklists

Gastrointestinal Tract

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Ampulla of Vater	Checklist	Full Protocol
Anus	Checklist	Full Protocol
Colon and Rectum	Checklist	Full Protocol
Esophagus	Checklist	Full Protocol
Small Intestine	Checklist	Full Protocol
Stomach	Checklist	Full Protocol

[Back to GI Tract Menu](#)

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Liver

Section 1 - Reporting of Chronic Liver Disease

Author: Matthew M. Yeh, MD PhD

Section 2 - Liver Explant and Hepatectomy for Hepatocellular Carcinoma (HCC)

Author: Matthew M. Yeh, MD PhD

Section 3 - Evaluation of Donor Liver for Transplantation

Author: Matthew M. Yeh, MD PhD

Section 4 - Liver Biopsies After Transplantation

Authors: Matthew M. Yeh, MD PhD

Section 5 - CAP Cancer Protocols and Checklists

Including: Liver (Including Intrahepatic Bile Ducts)

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Reporting of Chronic Liver Disease

Matthew M. Yeh, MD PhD

CHRONIC HEPATITIS

Any report for a liver biopsy with chronic hepatitis should include the following:

- Degree of inflammatory activity (grade).
- Degree of fibrosis, if any (stage).
- Etiology (i.e. hepatitis B, hepatitis C, etc.).
- Semiquantitative score for grade and stage.

SAMPLE REPORT

Chronic hepatitis with mild activity and periportal fibrosis, consistent with hepatitis C-induced disease; grade 2, stage 2 ([Batts and Ludwig](#)).

The purpose of the semi-quantitative scoring system is to help monitor response to therapy, particularly when the patient is enrolled in a clinical drug trial. There are separate systems used for hepatic and biliary disease processes. For the **hepatic diseases** (viral or autoimmune hepatitis), the scoring system we use is that of Batts and Ludwig (see [tables and diagrams](#) below for scoring criteria). In this system, two scores are assigned: one score for the degree of inflammatory activity (grade) and a second score for the amount of fibrosis (stage), the Batts-Ludwig system uses only the piecemeal necrosis and the lobular inflammation/necrosis to evaluate the degree of inflammatory activity. This scoring system should also be applied to those cases of chronic hepatitis recurring post-transplant.

Grading of Disease Activity in Chronic Hepatitis				
Grading Terminology		Criteria*		Figure 1 - Grading of chronic hepatitis, schematic diagram (Am J Surg Pathol Vol. 19, No. 12, 1995)
Semiquantitative	Descriptive	Piecemeal Necrosis (interface hepatitis)	Lobular Inflammation and Necrosis	Click to open thumbnail.
0	Portal inflammation only; no activity	None	None	
1	Minimal	Minimal, patchy	Minimal; occasional spotty necrosis	
2	Mild	Mild; involving some or all portal tracts	Mild; little hepatocellular damage	
3	Moderate	Moderate; involving all	Moderate; with noticeable	

		portal tracts	hepatocellular damage	
4	Severe	Severe; may have bridging necrosis	Severe; with prominent diffuse hepatocellular damage	

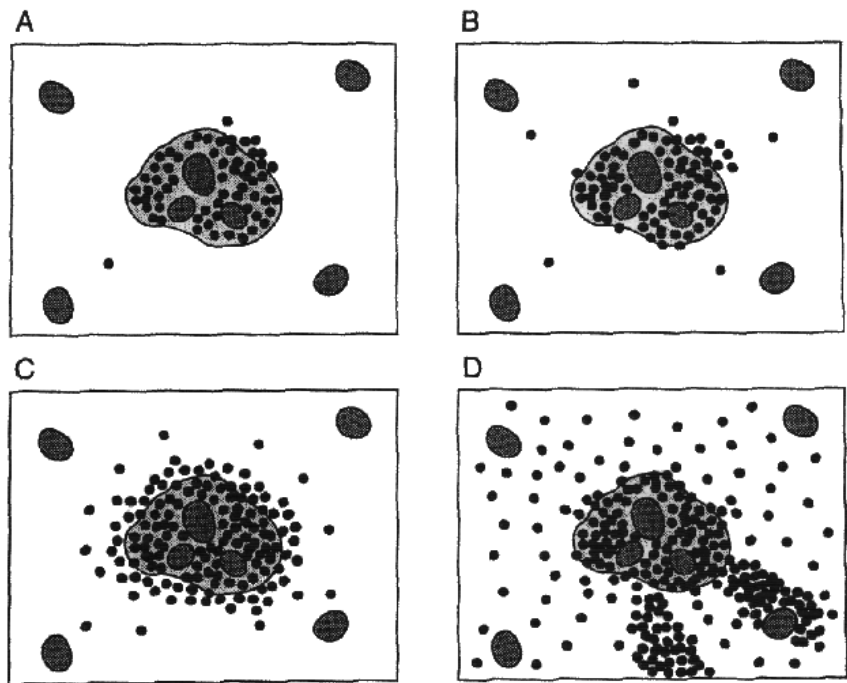


FIG. 2. Grading of chronic hepatitis, schematic diagram. **A:** Minimal activity (grade 1) with mild portal inflammation but scant piecemeal necrosis and no lobular necrosis. **B:** Mild activity (grade 2) with mild portal inflammation, piecemeal necrosis, and scant lobular spotty necrosis. **C:** Moderate activity (grade 3) with moderate portal inflammation, piecemeal necrosis, and lobular spotty necrosis. **D:** Severe activity (grade 4) with marked portal inflammation, brisk piecemeal necrosis, considerable spotty necrosis, and areas of confluent necrosis resulting in bridging. When discrepancies exist between piecemeal and lobular necrosis, the more severe lesion should determine the grade.

Staging of Chronic Hepatitis			
Semiquantitative	Descriptive	Criteria	Figure 2 - Staging of chronic hepatitis, schematic diagram (Am J Surg Pathol Vol. 19, No. 12, 1995)
0	No fibrosis	Normal connective tissue	Click to open thumbnail.
1	Portal fibrosis	Fibrous portal expansion	
2	Periportal fibrosis	Periportal or rare portal-portal septa	
3	Septal (bridging) fibrosis	Fibrous septa with architectural distortion; no obvious cirrhosis	
4	Cirrhosis	Cirrhosis (bridging fibrosis with regenerative nodules)	

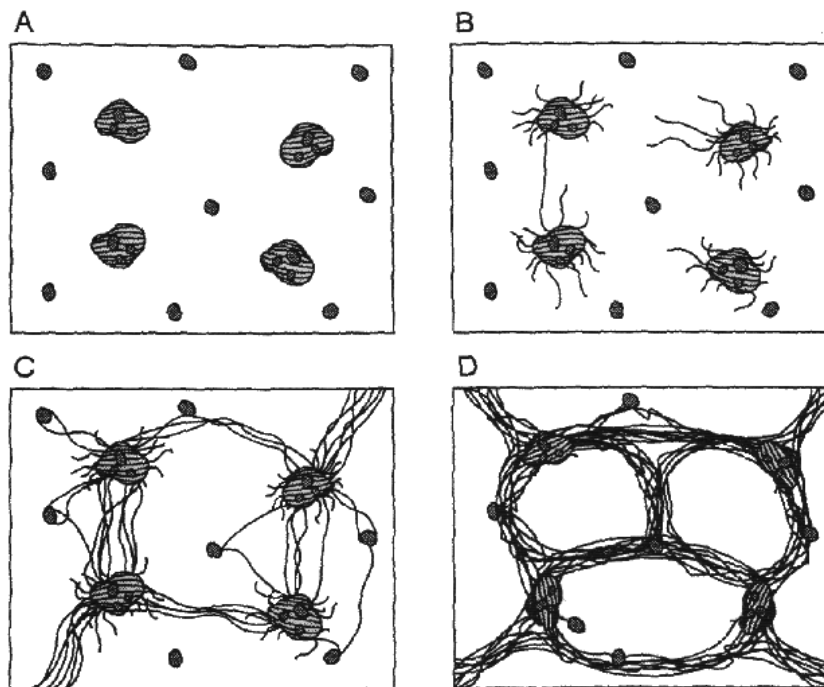


FIG. 3. Staging of chronic hepatitis, schematic diagram. **A:** Portal fibrosis (stage 1) characterized by mild fibrous expansion of portal tracts. **B:** Periportal fibrosis (stage 2) showing fine strands of connective tissue in zone 1 with only rare portal-portal septa. **C:** Septal fibrosis (stage 3) manifested by connective tissue bridges that link portal tracts with other portal tracts and central veins, minimally distorted architecture, but no regenerative nodules. **D:** Cirrhosis (stage 4) showing bridging fibrosis and nodular regeneration.

NON-ALCOHOLIC STEATOHEPATITIS (NASH)

For the **non-alcoholic steatohepatitis (NASH)**, a scoring system (Brunt system; [see criteria below](#)) is applied that uses a combination of features to assign a grade and stage. Grade indicates disease activity and stage reflects the extent of fibrosis. Again, the purpose of the semi-quantitative scoring system is to help provide information as to the decision of clinical management and prognosis, particularly when the patient is enrolled in a clinical trial. A *sample report* for a biopsy from a patient with NASH might read as follows:

SAMPLE REPORT

Steatohepatitis with moderate activity and bridging fibrosis, grade 2, stage 3 (Brunt system).

Steatohepatitis: Grade			
Grade	Steatosis	Ballooning	Inflammation
Mild Grade 1	1-2 (up to 66%)	Minimal	L: 1-4/20X field P: None-Mild
Moderate Grade 2	2-3 (>33%; may be >66%)	Present	L: 2-4/20X field P: Mild-Moderate
Severe Grade 3	3<	Marked	L: >4/20X field P: Mild-Moderate
Steatosis Grade 1: $\leq 33\%$; Grade 2: $>33\%$ $<66\%$; Grade 3: $\geq 66\%$ L = lobular inflammatory foci; P = portal			
Brunt EM, et al: Nonalcoholic steatohepatitis: a proposal for grading and staging the histological lesions. <i>Am J Gastroenterol</i> 1999; 94:2467-74.			

Steatohepatitis: Stage				
Stage	Zone 3 perisinusoidal	Portal-based	Bridging	Cirrhosis
Mild 1	Focal or extensive	0	0	0
2	As above	Focal or extensive	0	0
3	Bridging septa	Bridging septa	+	0
4	+/-	+/-	Extensive	+
Brunt EM, et al: Nonalcoholic steatohepatitis: a proposal for grading and staging the histological lesions. <i>Am J Gastroenterol</i> 1999; 94:2467-74.				

CHRONIC BILIARY DISEASE

For the **biliary disease** (primary biliary cirrhosis and primary sclerosing cholangitis), a scoring system (again by Ludwig; see criteria below) is applied that uses a combination of features (primarily the amount of fibrosis) to assign a stage. Generally, however, a statement is made in the final diagnostic line as to the degree of inflammatory activity. Thus, a *sample report* for a biopsy from a patient with primary biliary cirrhosis might read as follows:

Histologic changes consistent with primary biliary cirrhosis with moderate activity and bridging fibrosis, Ludwig stage III.

Ludwig Staging System for Biliary Tract Diseases		
Stage	Designation	Criteria
1	Portal stage	Inflammation confined to portal tract (florid duct lesion); no fibrosis
2	Periportal stage	Piecemeal necrosis, bile ductular proliferation, fibrous portal expansion
3	Septal stage	Bridging fibrosis
4	Cirrhosis	Cirrhosis

Note: Microscopic descriptions should accompany reports for all medical (non-transplant) liver biopsies.

REFERENCES

-  [Batts KP, Ludwig J:](#) Chronic Hepatitis: An Update on Terminology and Reporting. *Am J Surg Pathol* 1995;19:1409-17.
-  [Brunt EM, et al:](#) Nonalcoholic steatohepatitis: a proposal for grading and staging the histological lesions. *Am J Gastroenterol* 1999; 94:2467-74.
-  [Kleiner DE, et al:](#) Design and validation of a histologic scoring system for nonalcoholic fatty liver disease (NAFLD). *Hepatology* 2005; 41:1313-21.

Liver Explant and Hepatectomy for Hepatocellular Carcinoma (HCC)

Matthew M. Yeh, MD PhD

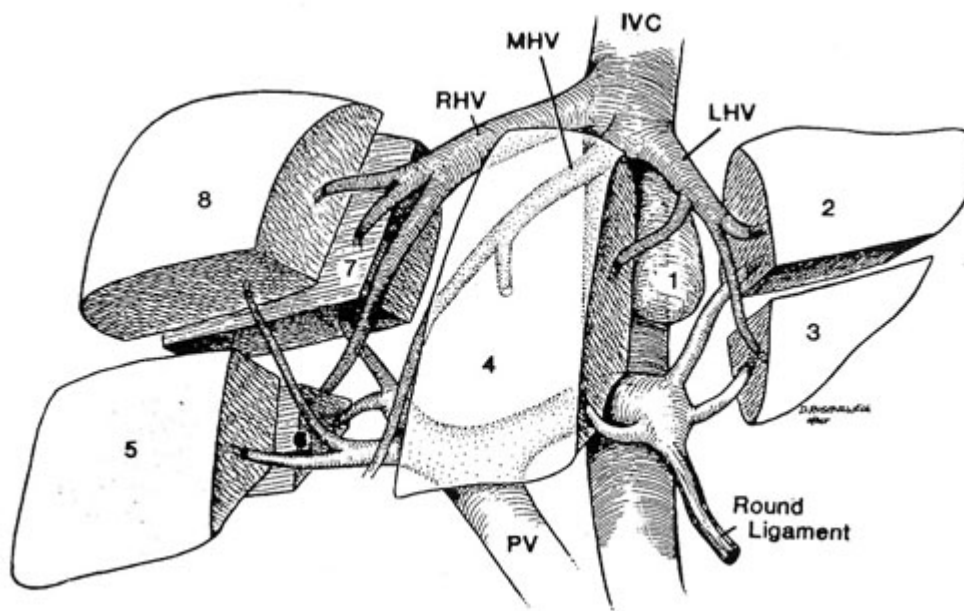
Hepatectomy specimens are received as either an entire explanted liver in a transplantation procedure, or partial hepatectomy for tumor resection. The former may include an attached gallbladder.

EXPLANTED LIVER

In handling an explanted liver, use the following procedures:

FIXATION AND GROSS PROCESSING

- **Infectious precautions have to be strictly practiced. Bear in mind that hepatitis C is the most common indication for liver transplantation and if one is accidentally infected by careless gross handling procedures, there is a >80% likelihood that one will get chronic hepatitis and even cirrhosis or hepatocellular carcinoma.**
- Weigh and measure.
- Section liver into 1.0 cm thick slabs in the transverse plane from superior to inferior, fix in formalin, using at least a volume ratio of 2:1 (formalin:liver) (put paper between slabs to aide fixation).
- Describe cirrhotic nodules, indicating the overall color and **nodule size range**. Specifically mention and sample nodules **0.8 cm in size or greater**, or any nodules that **differ in color** from the overall liver. Describe unusual features of large nodules (color change, necrosis, hemorrhage, and possible invasion). If obvious hepatocellular carcinoma is identified, follow the grossing procedure for HCC described [below](#). Carefully examine if there is any gross evidence of vascular invasion. **Gross photographs of these suspicious nodules and frank HCC including large vessel invasion should be obtained and their anatomic locations should be documented** (see [diagram](#) of segmental anatomy of the liver). The rationale for these descriptions is based on their association with increased probability for hepatocellular carcinoma and their correlation with image findings.
- Gallbladder: usual description mentioning size, serosa, wall thickness, mucosa, and stones/sludge/bile contents.
- Sections to submit:
 - o A Masson trichrome, reticulin, PAS/D and an iron stain are performed routinely on one representative block of all **resected native livers** for transplantation (**not** TP biopsies). To accomplish this, histology performs these two special stains routinely on the **first block** of each resected liver. Thus, residents must ensure that a representative portion of liver is put in the **first block** on each resected liver.
 - o 1 block of porta hepatis (to study large ducts and vessels).
 - o 4-5 blocks of cirrhotic liver if uniform.
 - o 1 block (at least) of any nodule greater than 0.8 cm in size, sampling all unusual gross features of large nodules as described above.
 - o 1 block of native gallbladder with representative sections of neck, fundus, and body and any lymph nodes; all should fit in one cassette; also sample any lesions if present (may rarely need an additional block).



MICROSCOPIC DIAGNOSIS

In general, the following format may be used and modified as needed:

"Native liver and gallbladder, explanation: Cirrhosis with _____ (minimal, mild, moderate, marked) hepatitis activity or inactive; consistent with clinical history of _____ (hepatitis C-induced disease, etc.)", Batts and Ludwig, grade _____, stage 4.

It is **mandatory** to include clinical and pathologic information on etiology, as the subsequent allograft biopsy interpretations are often dependent on knowing what the primary disease was. A permanent notebook of patient clinical data for all liver and pancreatic transplant patients is maintained in the file room and is alphabetized by patient surname. Also, always include a mention of the results of the Masson trichrome, reticulin, PAS/D and iron stain with controls.

HEPATECTOMY FOR HCC

The gross description of HCC specimens is critical, as a 1.0 cm margin has been determined to be an important prognostic factor for recurrence. Thus, initially the friable, cauterized, and irregular resection margin should be inked, following which the specimen should be serially sectioned perpendicular to the inked surgical margin at approximately 1 cm intervals. The distance to the closest gross surgical margin should then be carefully measured and documented within the report, particularly if it is less than 1.0 cm.

Gross photographs of the tumor should be obtained and its anatomic location should be documented (see [diagram](#) of segmental anatomy of the liver). Optimally, inking and taking measurements should be done prior to fixation, to avoid introduction of fixation shrinkage artifact regarding margin measurements. Special infectious precautions should be utilized when cutting any fresh hepatic specimen, due to the high likelihood of Hepatitis B virus, Hepatitis C virus, or other highly infectious agents. After inking, sectioning, freezing, description and photography, the specimen should be fixed overnight in at least two volumes of formalin relative to the specimen size. To aid formalin fixation of the main specimen, paper towels should be placed between the slabs of liver.

FEATURES TO BE INCLUDED IN THE GROSS DESCRIPTION

1. Closest gross surgical margin as discussed above (1 cm is an important threshold).
2. Three dimensional tumor size.

3. Tumor color and texture along with descriptions of necrotic areas or other abnormalities.
4. Evidence of gross vascular invasion.
5. Gross evidence of satellitosis (= separate nodules of tumor).
6. The appearance of the non-tumor liver, particularly regarding whether it is **cirrhotic** or non-cirrhotic. As with any cirrhosis, the **range in size** of the cirrhotic nodules should be described, and **any nodule greater than 0.8 cm should be carefully described and sampled for histology** (the rationale is the increased risk for HCC in such nodules).

SECTIONS FOR HISTOLOGY

1. One or two sections of the closest inked surgical margin (and adjacent tumor, if it fits into one block).
2. Representative sections (4 to 6 or more if needed) sampling gross features of the tumor as described above and 1 or 2 blocks demonstrating tumor and adjacent non-tumor liver.
3. Sections demonstrating areas of grossly evident or potential vascular invasion.
4. Two or three sections of non-tumor liver away from the HCC, including any cirrhotic nodule(s) greater than one centimeter.

Definition of TNM - Primary Tumor (T)	
AJCC, 2002	
TX	Primary tumor cannot be assessed.
T0	No evidence of primary tumor.
T1	Solitary tumor without vascular invasion.
T2	Solitary tumor with vascular invasion or multiple tumors none more than 5 cm.
T3	Multiple tumors more than 5 cm or tumor involving a major branch of the portal or hepatic vein(s).
T4	Tumor(s) with direct invasion of adjacent organs other than the gallbladder or with perforation of visceral peritoneum.

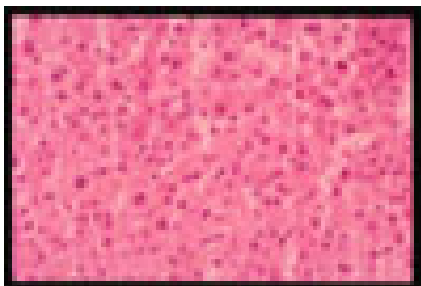
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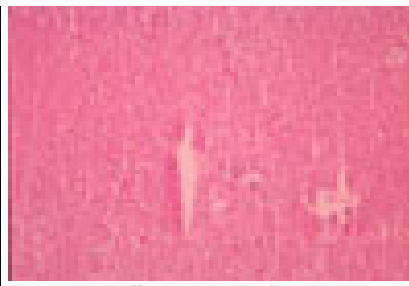
Evaluation of Donor Liver for Transplantation

Matthew M. Yeh, MD PhD

Livers being considered for transplantation may be histologically assessed for fat content and other disease. If clinically indicated, a frozen section will have been done at the center where the liver was collected; this section will accompany the liver. A second frozen section will rarely be requested at UWMC. **If the fat exceeds approximately 40%** of liver volume in the biopsy specimen, the probability that the liver will function in the recipient is diminished and the liver will probably not be grafted. This is a low power overall volume % fat, and not a % of cells with fat and is based on H&E stains only (not special fat stains). **Fat percentage estimates are only necessary to include in reports of the first allograft biopsy.**



liver FS no fat



liver FS no fat



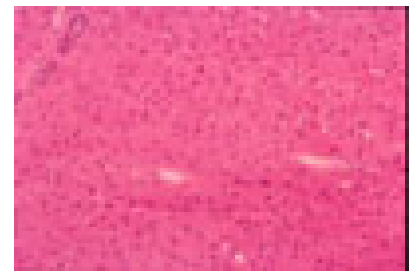
liver FS knife artifact not fat



liver FS knife artifact not fat



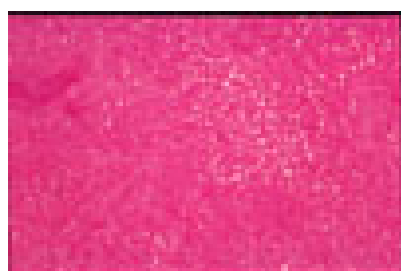
scant fat <5%



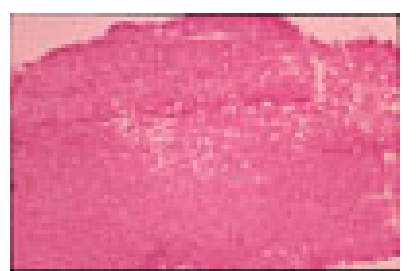
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10-20% fat



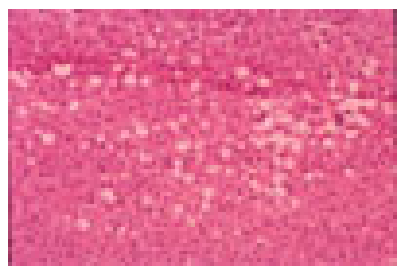
10-20% fat



10-20% fat



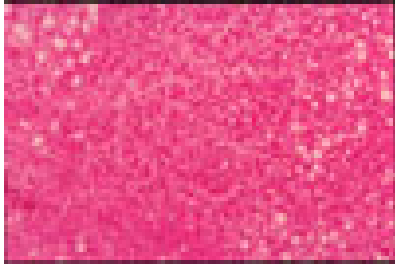
30-40% fat



30-40% fat



>50% fat



>50% fat

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Liver Biopsies After Transplantation

Matthew M. Yeh, MD PhD

GENERAL CONSIDERATIONS

Liver transplant biopsies should be routinely signed out with the general Surgical Pathology daily sign out attending once the slides are ready (routine stains: 3 H/E and 1 Masson trichrome stained slides).

- For the consistency of formatting histologic diagnoses and conveying such results to the transplant team, we recommend using the criteria below for the diagnosis and grading of rejection in allograft liver biopsies.
- Always remember to document the post transplant time interval for allograft biopsy reports, to facilitate weekly conference (every Tuesday afternoon at 4:00 pm) organization and clinical utility. (Example: Liver allograft, core needle biopsy, 1 month post transplant: Diagnosis)
- When signing out native livers, please include the clinical etiologic information in the diagnosis (it may be necessary to call clinicians and add to clinical history section of report as well); (Example: consistent with clinical history of hepatitis C-induced disease {or primary biliary cirrhosis}; etc.) Note that a notebook with all listed transplant patients' clinical primary disease work up is kept in the slide file room with the slide files.
- Finally, to the residents and fellows, please bring the printout of the patient's previous diagnoses and that patient's previous relevant transplant biopsy slides (it is encouraged that residents review series of transplant liver biopsies in order to be familiarized with the post-transplant course) to each new biopsy sign out with attending (each patient has their own slide file in slide file room, filed in slide drawers, alphabetized by patient surname). These drawers are in a specially designated file in the slide file room. After the cases have been signed out, please place the slides on the shelf designated "liver transplant" (right top shelf) in the resident room or hand them to the GI pathology fellow for the upcoming weekly liver transplant conference.

CUTOFF TIME, GROSS, PROCESSING AND REPORTING ISSUES

- A "rush" biopsy is an urgent clinical case that requires a same-day diagnosis which is delivered to the Pathology Lab by noon. A diagnosis should be called to the submitting clinician by 5-6 p.m. the same day. The clinicians will label these as "rush" on the accession form.
- As the next most rapid option, urgent clinical cases that cannot be delivered to Pathology by noon will still be expedited by Pathology and called back to the submitting clinician early the following morning (to be called back by 12 noon). The clinicians will indicate the need for an early morning next day report on the accession form. These must be received by 6 PM the day of the biopsy.
- All rejection diagnoses should be called to the clinical team (page the submitting hepatologist or fellow, transplant surgeon or fellow, or the transplant nurse coordinator). If residents preview transplant cases that were submitted without a request for urgent diagnosis and they think there might be rejection, they should expedite signing it out on their review day by bringing it to the attending early.
- All diagnoses of rejection and diagnoses from rush and next day cases must be called to the clinicians. This call should be documented in the comment section of the pathology report, including the date, time and person called.
- If recurrent viral hepatitis (C or B) or autoimmune hepatitis have been established in the previous post-transplant biopsies, it is required to assign a histologic grading and staging, i.e., Batts and Ludwig scoring system, to each subsequent biopsy, in order to record the disease progression and to facilitate clinical decision. Same rule applies to other recurrent diseases such as steatohepatitis (Brunt scoring system), PBC and PSC (Ludwig), etc.

DIAGNOSIS AND GRADING OF REJECTION

- Biopsy adequacy requires at least 3-4 portal tracts for review.
- Cellular Rejection without bile duct loss requires at least two out of three of the following (Snover's triad, defined below): rejection infiltrate in portal tracts, lymphocytic cholangitis, and endothelitis (endothelialitis).
 - o Focal Mild Cellular Rejection: Rejection present in less than 20% of portal tracts.
 - o Mild Cellular Rejection: Rejection involving greater than 20%, but not a majority of portal tracts.
 - o Moderate Cellular Rejection: Rejection involving most or all of portal tracts.
 - o Severe Cellular Rejection: Features of moderate cellular rejection with spillover into periportal areas and central vein endotheliitis, with centrilobular hepatocyte dropout.
- Ductopenic Rejection
 - o Defined as interlobular bile ducts* remaining in less than 50% of portal tracts, calculated over at least 20 portal tracts (often requiring serial biopsies).
 - o Comment on associated findings, including: centrilobular canalicular cholestasis, central perivenular sclerosis, centrilobular hepatocellular swelling, or centrilobular necrosis/dropout. Note that these are often the first findings, predating duct loss. Whenever a suspicion for ductopenic rejection is raised, a formal count of interlobular bile duct* should be performed and the results documented in the report.
 - o Indeterminate ductopenia--defined as follows: interlobular bile ducts* present in 50-80% of portal tracts, calculated over at least 20 portal tracts (often requiring serial biopsies)
 - o Normal interlobular bile duct numbers should be confirmed in each liver TP biopsy (though not necessarily reported unless requested), as ductopenia may develop as early as < 6 weeks post transplant. Normal is defined as interlobular ducts present in 80-100% of portal tracts.

*Interlobular bile ducts need to be distinguished from proliferating ductules. True interlobular ducts may be identified by virtue of having a lumen, well-defined basal lamina (best seen on PAS-D staining), and having a similar diameter as the corresponding hepatic artery. They are also generally located one artery diameter away from the artery.

Rejection Infiltrate:

Polymorphous lymphocytic infiltrate including mature and large activated/transformed lymphocytes, and plasma cells. Eosinophils are generally conspicuous but still comprise a minority of the cellular infiltrates. (Note: Eosinophils may be diminished with triple rejection therapy).

Lymphocytic Endotheliitis:

Subendothelial lymphocytes between the endothelial cells and their basement membranes in association with endothelial cell swelling and damage and occasional attachment of luminal lymphocytes along endothelial cell surfaces. The endothelial surface is usually lifted up and even disrupted with lymphocytes underneath.

Lymphocytic Cholangitis:

Intraepithelial lymphocytes within duct basement membrane with associated ductal epithelial damage manifested by decreased epithelial cytoplasm, cytoplasmic vacuolization, reactive nuclear atypia and/or epithelial sloughing.

In patients with a history of HCV:

A diagnosis of rejection in general is difficult to establish with certainty, for the histologic features of cellular rejection and recurrent HCV are very similar, including portal infiltrates, lymphocytic cholangitis and endotheliitis in both conditions. In these cases, the presence of lobular hepatitis (lobular infiltrates, hepatocytolysis, and acidophil bodies), later onset of findings without a change in the immunosuppressive protocol (generally >6 months), and a less activated appearing lymphoid infiltrate generally without eosinophils, with associated interface hepatitis and fibrosis all favor recurrent HCV. Unfortunately, none of these features are definitively diagnostic of recurrent HCV, and reports should comment to this effect (i.e. state in a comment that the features favor rejection or recurrent HCV but are not definitive).

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CAP Cancer Protocols and Checklists

Liver

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Liver (Including Intrahepatic Bile Ducts)	Checklist	Full Protocol

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Gall Bladder & Pancreas

Section 1 - Pancreatic Transplant Biopsies
Author: Shari L. Taylor, MD

Section 2 - CAP Cancer Protocols and Checklists
Including: Extrahepatic Bile Ducts, Gallbladder,
Pancreas (Endocrine), Pancreas (Exocrine)

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Pancreatic Transplant Biopsies

Shari L. Taylor, MD

GENERAL REQUESTS

In general, pancreas transplant biopsies should be signed out with the general Surg Path daily sign out attending.

- In order to facilitate uniformity of histologic diagnoses, please use the criteria indicated below for the diagnosis and grading of rejection in pancreatic allograft tissue.
- Please also state the **post transplant time interval** for allograft biopsy reports, to aid weekly conference organization and clinical utility. (**Example: Pancreas allograft biopsy, 1 month post transplant: Diagnosis**)
- Finally, to the residents, please bring the printout of the patient's **previous diagnoses** and that patient's **transplant biopsy slide box** to each new biopsy sign out with attending (each patient has their own black slide box in slide file room, filed on shelves, alphabetized by patient surname). Note: Slides from the earliest years, beginning in 1990, are now filed in slide drawers, alphabetically by patient's last name, to conserve space. These drawers are in a specially designated file in the slide file room.

TRANSPLANT BIOPSY CUTOFF, GROSS, PROCESSING AND REPORTING ISSUES

- A "rush" biopsy is an urgent clinical case that requires a same-day diagnosis **and** which is delivered to the Pathology Lab by noon. A diagnosis should be called to the submitting clinician by 5-6 p.m. the same day. The clinicians will label these as "rush" on the accession form.
- As the next most rapid option, urgent clinical cases that cannot be delivered to Pathology by noon will still be expedited by Pathology and called back to the submitting clinician early the following morning (to be called back by 12 noon). The clinicians will indicate the need for an early AM next day report on the accession form. These must be received by 6 PM the day of the biopsy.
- All other diagnoses should be available on the afternoon of the third working day (counting the day of the biopsy as day one).
- **All rejection diagnoses should be called to the clinical team (page the transplant fellow for whatever organ you are dealing with or the organ's transplant nurse coordinator). If residents preview transplant cases that were submitted without a request for urgent diagnosis and they think there might be rejection, they should expedite signing it out on their review day by bringing it to the attending early.**
- **All diagnoses of rejection and diagnoses from rush and next day cases must be called to the clinicians.** This call should be documented in the comment section of the pathology report, including the date, time and person called.

PANCREATIC REJECTION

- Tissue adequacy requires at least one core biopsy that spans a 10X by 10X microscopic field
- Criteria:
 - Lymphocytic endotheliitis, as defined above in liver*
 - Acinar intraepithelial lymphocytic infiltration*

- o Ductal intraepithelial lymphocytic infiltration
 - * **Both are required for a diagnosis of rejection**
- Grading:

Focal Mild Cellular Rejection	Mild rejection (see below) involving <50% of lobules
Mild Cellular Rejection	Acinar infiltrates spanning less than a 40X by 10X microscopic field in >50% of lobules + endotheliitis +/- ductal infiltration
Moderate Cellular Rejection	Acinar infiltrates spanning more than a 40X x 10X microscopic field + endotheliitis +/- ductal infiltration (this process will virtually always have more than one focus of inflammation; if there is only one focus in an adequate biopsy, interpret it as "focal moderate rejection").
Severe Cellular Rejection	Diffuse panacinar destructive lymphocytic infiltration + endotheliitis +/- ductal infiltration; or arteritis with or without any of the above (i.e., items 1-3)

DUODENAL REJECTIONS ACCOMPANYING PANCREATIC BIOPSIES

- Tissue adequacy requires at least mucosa and submucosa, unless prominent features (see below) are present in lesser tissue (note: duodenal tissue is usually present incidentally along with the pancreatic tissue, and is only rarely specifically and separately biopsied currently).
- Criteria:
 - o Mucosal cryptal apoptosis (normally none present in basal crypts).
 - o Mucosal intraepithelial lymphocytes (normally, should be less than 1 lymphocyte/10 epithelial cells).
 - o Mucosal lamina propria basal lymphoplasmacytosis expanding lamina propria between crypt bases and muscularis mucosae.
 - o Submucosal endotheliitis.
 - o Brunner gland intraepithelial lymphocytic inflammation.
 - o Muscularis propria chronic inflammation.
- Grading:

Focal Mild Cellular Rejection	Mild rejection (see below) involving <50% of lobules
Mild Cellular Rejection	Acinar infiltrates spanning less than a 40X by 10X microscopic field in >50% of lobules + endotheliitis +/- ductal infiltration
Moderate Cellular Rejection	Acinar infiltrates spanning more than a 40X x 10X microscopic field + endotheliitis +/- ductal infiltration (this process will virtually always have more than one focus of inflammation; if there is only one focus in an adequate biopsy, interpret it as "focal moderate rejection").
Severe Cellular Rejection	Diffuse panacinar destructive lymphocytic infiltration + endotheliitis +/- ductal infiltration; or arteritis with or without any of the above (i.e., items 1-3)

- Grading Criteria not yet established. For now please diagnose one of the following: inadequate tissue present; no evidence of rejection; minimal changes insufficient for diagnosis of rejection when only focal minimal findings of one feature present; or positive for rejection if one or more features definitively present.

CAP Cancer Protocols and Checklists

Gallbladder & Pancreas

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Extrahepatic Bile Ducts	Checklist	Full Protocol
Gallbladder	Checklist	Full Protocol
Pancreas (Endocrine)	Checklist	Full Protocol
Pancreas (Exocrine)	Checklist	Full Protocol

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Urinary Tract

Section 1 - Radical Nephrectomy

Author: Larry True, MD

Section 2 - Kidney Cancer Immunotherapy

Author: Larry True, MD

Section 3 - After-Hours Renal Biopsies

Author: Kelly Smith, MD PhD

Section 4 - Radical Cystectomy

Author: Larry True, MD

Section 5 - Urinary Bladder Biopsy Specimens

Author: Larry True, MD

Section 6 - CAP Cancer Protocols and Checklists

Including: Kidney, Urinary Bladder, Renal Pelvis,
Ureter

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Radical Nephrectomy

Larry True, MD

PROCEDURE

If you are called to the OR to cut the specimen to obtain fresh tissue, cut into the tumor from a side of the specimen where the tumor appears to be remote from the surgical margin. Below is the procedure for examining the specimen.

1. Weigh and measure the outside dimensions of the specimen and the attached ureter and vessels.
2. Palpate to locate the tumor. Apply India ink to the surface over the tumor only if fat appears to adhere to tumor (otherwise, don't ink).
3. Hemisect the kidney through the tumor, extending your cut to the hilum.
4. Photograph the cut surface
5. Measure the thickness of fibrofatty tissue around the nephrectomy.
6. Section at 0.5 to 1.0 cm intervals, parallel to the initial section.
7. Examine the soft tissue from the hilum for lymph nodes and the supra-renal tissue for the adrenal gland. Look for the renal vein and/or vena cava. Open the vein(s) longitudinally to identify thrombus and/or tumor.

DESCRIPTION

- Weigh and measure overall specimen dimensions and dimensions of the kidney.
- Length and any gross structural abnormality of ureter, artery and vein.
- Location of tumor, including distances to surgical margins, capsule, hilum, and renal pelvis and calyces.
- Describe tumor - size, nature of tumor border (i.e. sharply defined, infiltrative), color and texture, presence of hemorrhage, necrosis and/or cystic change.
- Describe uninvolved kidney - scars? nodules?
- Presence, number, size of lymph nodes (typically, no nodes are found).

Sections	# Sections
Tumor (1 section/cm diameter of tumor, include areas of necrosis/hemorrhage)	1-10+
Interface of tumor/normal renal parenchyma, and random section (1) of kidney	2-4
Relationship of tumor to the soft tissue surgical margin or to the renal capsule, and to the hilum	2-4
Venous and ureteral margins	1
If there is a venous thrombus, section the thrombus for tumor and vein wall invasion	0-2

DIAGNOSTIC REPORT

Kidney, (right) (left), radical nephrectomy: Renal cell carcinoma, with the following features:

- ____ x ____ x ____ cm tumor in the (upper/mid/lower) portion of the kidney.
- The histologic type is clear cell/chromophobe/papillary/collecting duct/urothelial cell.

- Nuclear grade ____ of 4 ([Fuhrman system](#)).
- (No) invasion through the capsule into perinephric fibroadipose tissue.
- If tumor invades perinephric fat, report whether tumor extends to the soft tissue surgical margin (see block(s) ____).
- (No) macroscopic tumor thrombus within the renal vein and/or inferior vena cava.
- (____ of ____) hilar nodes contain tumor.
- The adrenal gland (contains/lacks) tumor.
- The ureteric margin is free of tumor.
- The renal vein (is free of/is positive for) tumor which [does/does not] extend to the margin.
- Sections reveal (no) additional renal cell tumor(s) of ____ x ____ x ____ cm size.
- The uninvolved kidney shows _____ (no significant histologic abnormalities.)

Of note, oncocytomas are not graded. If the tumor is a transitional cell carcinoma, follow above protocol, report per [Urinary Bladder](#) guidelines. Report the extent of a carcematoid component, if any is present. Be sure to evaluate for invasion of perinephric fat in the hilum, in addition to the perinephric fat around the exterior aspect of the kidney.

Comment: "Consistent with stage pT_ (AJCC, 2002)."

Definition of TNM - Primary Tumors (T) AJCC, 2002	
TX	Primary tumor cannot be assessed.
T0	No evidence of primary tumor.
T1	Tumor 7 cm or less in greatest dimension, limited to the kidney.
T1a	Tumor 4 cm or less in greatest dimension, limited to the kidney.
T1b	Tumor more than 4 cm but not more than 7 cm in greatest dimension, limited to the kidney.
T2	Tumor more than 7 cm in greatest dimension, limited to the kidney.
T3	Tumor extends into major veins or invades adrenal gland or perinephric tissues but not beyond Gerota's fascia.
T3a	Tumor directly invades adrenal gland or perirenal and/or renal sinus fat but not beyond Gerota's fascia.
T3b	Tumor grossly extends into the renal vein or its segmental (muscle-containing) branches, or vena cava below the diaphragm.
T3c	Tumor grossly extends into vena cava above diaphragm or invades the wall of the vena cava.
T4	Tumor invades beyond Gerota's fascia.

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Kidney Cancer Immunotherapy

Larry True, MD

Some nephrectomies are done to obtain immune cells (lymphocytes, dendritic cells, NK cells) for development of patient-specific immune therapy, and for tumor debulking in patients with known renal cell carcinoma metastases. Although this protocol requires that large portions of the tumor be submitted as rapidly as possible for cell retrieval and culture, histologic confirmation that the tumor is a renal cell carcinoma is important.

You may be called to the OR to cut the specimen to obtain fresh tissue. The protocol requires no more than documentation that the tumor is a renal cell carcinoma. However, additional pathologic information may be sought on some patients. To not compromise the pathologic data, cut into the tumor from a side of the specimen where the tumor appears to be remote from the surgical margin. Talk with the surgeon concerning the pathologic information that will be needed on the patient and base your tissue handling on this information.

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After-Hour Renal Biopsies

Kelly Smith, MD PhD

Procedure for residents and attendings who receive renal biopsy requests after hours:

1. If this is a rush case, contact the renal pathology attending on call and the histologist on call (Pager 663-8098)
2. If this is a non-rush case follow the recommendation below; these recommendations and additional information can also be found on the web at http://www.pathology.washington.edu/clinical/renal_biopsy/

GENERAL RECOMMENDATIONS FOR SPECIMEN HANDLING

Specimen Preparation

- I. Three vials needed for each biopsy
 1. Light Microscopy (LM): Sorenson's fixture
 2. Electron Microscopy (EM): 1/2 strength Karnovsky's fixative
 3. Immunofluorescence (IF): Michel's Transport Medium.

Discard any vials with ppt.
Label each with name of patient and date of surgery.
Fill out Pathology Service Request Form.
- II. Immediately after the biopsy is obtained:
 1. Place biopsy cores in each of the three specimen bottles.
 2. If only a single core is obtained, and if IF and/or EM will be essential for establishing the diagnosis, divide in three parts with clean, sharp blade as indicated in diagram.
 3. If wedge biopsy, cut in 1-2 mm blocks. Handle all pieces carefully. Avoid crushing.
 4. Place pieces in containers, as indicated by diagram, as quickly as possible. Priority should be given to a) light microscopy, b) immunofluorescence, c) electron microscopy.

Shipping:	Deliver as soon as possible. Do not freeze the specimens or ship on dry ice.
Pathology Service Request Form Required:	Send with the specimen, and include relevant clinical data.
Renal Pathologists:	Charles Alpers, M.D., (206) 548-6409 Pager: (206) 344-0570 Email: calp@u.washington.edu Jolanta Kowalewska, MD (206) 543-6746 Pager: (206) 645-0998 Email: jkowal@u.washington.edu Roberto Nicosia, M.D., (206) 764-2284 Pager: (206) 699-2313 Email: Roberto.Nicosia@med.va.gov Kelly D. Smith, M.D., Ph.D., (206) 598-7860 Pager: (206) 986-4956 Email: kelsmith@u.washington.edu

Director of Renal Pathology:	<i>Contact for interpretation assistance:</i> Charles Alpers, M.D., (206) 598-6409 Pager: (206) 344-0570 Email: calp@u.washington.edu
Renal Biopsy Laboratory:	<i>Location:</i> University of Washington Medical Center, Room BB240 <i>Contact for technical assistance:</i> Richard King, Renal Biopsy Laboratory (206) 598-6061 Email: dick@u.washington.edu
Electron Microscopy Laboratory:	<i>Location:</i> University of Washington Medical Center, Room BB-240 <i>Contact for technical assistance:</i> Chiyen Miller, Electron Microscopy Supervisor (206) 598-6411 Email: chiyen@u.washington.edu

Please do not ship for weekend or holiday delivery without prior notification. Instructions, vials with fixatives and solutions are available from the Renal Biopsy Laboratory, (206) 598-6061.

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Radical Cystectomy

Larry True, MD

PROCEDURE

- Weigh and measure the specimen.
- Verify that the surgical margins of the ureters have already been submitted as separate parts.
- Palpate to locate the tumor mass; ink the external surface over the tumor.
- If no palpable tumor, do not ink.
- First take an enface section of the distal urethral margin.
- Then open the anterior bladder with a Y-shaped incision.
- Describe the bladder (mass, ulcer, area of induration, trabeculations).
- Remove attached fibrofatty tissue (leave intact tissue that appears to be invaded by tumor and examine it for lymph nodes; typically no nodes are found in the perivesical soft tissue).
- Pin out and fix overnight.
- If a prostate is included, obtain approximate external dimensions.

Section	# of blocks
Tumor - 1 section per cm of diameter of each tumor; to characterize depth of invasion	1+
Ulcer - sections of all of ulcer	
Random sections of mucosa (these need not be full thickness of bladder wall, but only of mucosa, i.e. "wedge" sections - lateral, posterior & anterior walls, trigone, (2 from each site))	3+
Any abnormal mucosa (granular texture, mottled, erythematous, puckered, indented)	0+
Urethral Margin (enface, as a donut)	1
Lymph Nodes (if any)	0+
Ureter Margins (only if they are not submitted as separate parts)	0+
Prostate (if present, section any abnormalities, or 4 quadrants of one cross-section)	0-4

DIAGNOSTIC REPORT

The report for urinary bladder, radical cystectomy should include:

- Carcinoma, (papillary), (histologic type, i.e. transitional cell carcinoma), with the following features:
 ____ x ____ x ____ cm tumor located in the ____ (region) of the bladder.
- Invasion extends into the (submucosa) (inner/outer half of muscularis propria) (subserosal soft tissue), (or there is no invasion.)
- Grade (low-grade vs high-grade).
- (Focal) (multifocal) carcinoma-in-situ is present.
- Urethral margin is (free of) (contains) carcinoma.
- Tumor approaches to within ____ mm/cm of the lateral soft tissue surgical margin (see block ____).
- Ureteric margins are (free of/ positive for [specify laterality] carcinoma).

- Comment: There is (squamous/glandular) metaplasia. There (is/is not) a papillary component to the tumor. Additional invasive transitional cell carcinomas (are/are not) present. Tumor (does/does not) involve the prostate.

If the specimen is a cystoprostatectomy, report findings in the prostate (40% of cystoprostatectomies have a prostate cancer, which usually is pT1 in stage). If there is a prostate cancer, and if it is voluminous, i.e. within 2+ blocks, stage it by assessing the seminal vesicles at their junction with the prostate and the lateral surgical margin of the prostate.

Report pathologic stage as a comment: "Consistent with stage T_ (AJCC, 2002)."

Definition of TNM - Primary Tumor (T)	
<u>AJCC, 2002</u>	
TX	Primary tumor cannot be assessed.
T0	No evidence of primary tumor.
Ta	Non-invasive papillary carcinoma.
Tis	Carcinoma <i>in situ</i> : "flat tumor".
T1	Tumor invades subepithelial connective tissue.
T2	Tumor invades muscle.
pT2a	Tumor invades superficial muscle (inner half).
pT2b	Tumor invades deep muscle (outer half).
T3	Tumor invades perivesical tissue.
pT3a	Tumor invades perivesical tissue microscopically.
pT3b	Tumor invades perivesical tissue macroscopically (extravesical mass).
T4	Tumor invades any of the following: prostate, uterus, vagina, pelvic wall, abdominal wall.
T4a	Tumor invades prostate, uterus, vagina.
T4b	Tumor invades pelvic wall, abdominal wall.

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Urinary Bladder Biopsy Specimens

Larry True, MD

BLADDER BIOPSIES ARE MOST COMMONLY OF FOUR CLINICAL CATEGORIES

- A transurethral resection of a bladder tumor (TURB).
- A biopsy of bladder mucosa of a patient with a previous transitional cell carcinoma. This may be either random or directed toward a mucosal abnormality.
- A biopsy of the bladder neck/prostatic urethra, to stage the lower urinary tract of a patient with a history of bladder cancer.
- A biopsy of a patient with the clinical syndrome of interstitial cystitis.

< for sampled be should tissue biopsy all situations,>

IF THERE IS A TUMOR, THE REPORT SHOULD INCLUDE:

- Histologic type of tumor, i.e. (papillary) transitional cell carcinoma, adenocarcinoma.
- Absence/presence of invasion, and if invasion is present, deepest level of invasion (superficial stroma ["lamina propria"] vs. muscularis mucosae vs. muscularis propria).
- Grade of tumor (low-grade vs high-grade).
- Absence/presence of a papillary component.
- Absence/presence of angiolymphatic invasion.
- Absence/presence of concomitant squamous and/or glandular differentiation.
- Characterization of the adjacent flat mucosa, e.g., is it histologically normal or does it exhibit "dysplasia" or "carcinoma in situ"?
- Absence/presence of muscularis propria in the tissue.
- Comment on associated lesions, i.e. granulomas.

IF THERE IS NO TUMOR MASS, THE REPORT SHOULD INCLUDE:

- Absence/presence of carcinoma. (A diagnosis of "dysplasia" is applied to urothelial atypia which is interpreted as being too severe to be reactive but is insufficiently atypical to be carcinoma).
- Absence/presence of muscularis propria in the biopsy tissue.

Report pathologic stage as a comment: "Consistent with stage T_ (AJCC, 2002)."

Definition of TNM - Primary Tumor (T)	
AJCC, 2002	
TX	Primary tumor cannot be assessed.
T0	No evidence of primary tumor.
Ta	Non-invasive papillary carcinoma.
Tis	Carcinoma <i>in situ</i> : "flat tumor".
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T2	Tumor invades muscle.

pT2a	Tumor invades superficial muscle (inner half).
pT2b	Tumor invades deep muscle (outer half).
T3	Tumor invades perivesical tissue.
pT3a	Tumor invades perivesical tissue microscopically.
pT3b	Tumor invades perivesical tissue macroscopically (extravesical mass).
T4	Tumor invades any of the following: prostate, uterus, vagina, pelvic wall, abdominal wall.
T4a	Tumor invades prostate, uterus, vagina.
T4b	Tumor invades pelvic wall, abdominal wall.

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CAP Cancer Protocols and Checklists

Urinary Tract

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Kidney	Checklist	Full Protocol
Urinary Bladder, Renal Pelvis, Ureter	Checklist	Full Protocol

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Male Reproductive System

Section 1 - Radical Prostatectomy

Author: Larry True, MD

Section 2 - Prostate Needle Biopsies

Author: Larry True, MD

Section 3 - Transurethral Resection of the Prostate - TURP

Author: Larry True, MD

Section 4 - Recurrent Germ Cell Tumor of Testis

Author: Larry True, MD

Section 5 - Testis with Tumor - Radical Orchiectomy

Author: Larry True, MD

Section 6 - CAP Cancer Protocols and Checklists

Including: Prostate Gland, Testis

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Radical Prostatectomy

Larry True, MD

Contact Dr. True (598-4027; beeper 344-0584) or the tissue acquisition technician (Urology Research Lab 543-1461) who obtains fresh tissue for research. Unfixed portions of both cancer and non-cancer tissue are obtained quickly to prepare mRNA and culture cells. Dr. True will microdissect these tissues and confirm their composition by frozen sections.

PROCEDURE

- Weigh
- Ink the surface (right anterior - black, right posterior - green, left anterior - blue, left posterior - yellow)
- Obtain fresh tissue (per relevant research protocol)
- Section, either fresh or after overnight fixation (fix by injecting with and immersing in formalin)
- First, obtain donuts of apex and base. Submit these as serial sagittal sections. Section as parallel transverse sections from distal (apex) toward the bladder neck.
- Submit sections as follows:
 - o apex (block 1)
 - o bladder neck (block 2)
 - o seminal vesicles (final sections)
 - o then, each half or quadrant of each whole section
- Number, sequentially, right anterior (odd #), left anterior (even #), right posterior (odd #), and left posterior (even #) through the seminal vesicles at their junction with the prostate. Nodes are submitted as separate parts.

DESCRIPTION

- Weight of prostate specimen and presence, size, and location of carcinoma if visible, BPH nodules, or other lesions.
- Nature of seminal vesicles and of vas deferens, i.e., attached? fragmented?

Currently, the research technician, who works with me and under my supervision, prepares the nodes and prostate, and completes a written template of both types of specimens. This completed template, which includes the amount of prostate tissue removed for research studies, provides information for your gross dictation. The technician and I also indicate on a clear acetate sheet location and relative volume of cancer in the blocks of frozen tissue. When you work up the case, add the volume of cancer removed for research studies to the amount in the permanent sections. And, indicate on the clear acetate form the location and relative volume of cancer in the permanent sections.

SECTIONS	# of blocks
Apex (as sagittal and parasagittal sections)	1
Bladder neck (as sagittal and parasagittal sections)	1
Seminal vesicles, at junction with prostate	2
Prostate (as quadrants or halves; right - odd; left - even; anterior before posterior)	8-24+
Methacarn-fixed tumor tissue (optional)	1

DIAGNOSTIC REPORT

Adenocarcinoma (or, histologic subtype) of a ____ gm prostate, with the following features:

- Gleason's grade () + () = () of 10.
- Estimated tumor volume is ____ cc. (To measure the volume, outline cancer on the slides with ink. Estimate the area of cancer (in cm²) on each slide. A penny is equivalent to approximately 1 cc of 3 mm thick tissue. The clinically significant volume thresholds are <1.0 cc, 1-5 cc, and >5 cc.)
- If there is a third pattern that is pattern 5, report it as a comment and estimate the percent of pattern 5.
- Report whether tumor is unilateral or bilateral.
- Apex (free of) (positive for) tumor, which does (not) extend to the inked surgical margin.
- Bladder neck (free of/positive for) tumor, which does (not) extend to the inked surgical margin.
- Seminal vesicle(s) (free of/positive for) tumor. (If positive, characterize per Ohori '95).
- Tumor (doesn't/focally/multifocally) involves the lateral surgical margin (block ____). (If tumor is not at the margin, report the margin as negative.)
- Tumor (does not/does..focally/multifocally) invade periprostatic fibroadipose tissue, where it approaches to within mm of/extends to the surgical margin (see section ____).

Status of lymph nodes (# with tumor, total # of nodes dissected, size of largest nodal metastasis).

Comment: "Consistent with stage T_ (AJCC, 2002)." Subtypes of carcinoma include endometrioid, mucinous, signet ring cell, neuroendocrine, small cell, transitional cell, squamous, sarcomatoid); the location of the tumor (unilateral vs. bilateral) and zonal distribution - central, transition zone, or peripheral, whether the tumor is multifocal and (optionally) upon presence of PIN.

Definition of TNM - Primary Tumor (T)	
AJCC, 2002	
TX	Primary tumor cannot be assessed.
T0	No evidence of primary tumor.
T1	Clinically inapparent tumor neither palpable nor visible by imaging.
T1a	Tumor incidental histologic finding in 5% or less of tissue resected.
	Tumor incidental histologic finding in more than 5% of tissue resected.
T1c	Tumor identified by needle biopsy (e.g., because of elevated PSA)
T2	Tumor confined within prostate. (Note: Tumor found in one or both lobes by needle biopsy, but not palpable or reliably visible by imaging, is classified as T1c.)
T2a	Tumor involves one-half of one lobe or less.
T2b	Tumor involves more than one-half of one lobe but not both lobes.
T2c	Tumor involves both lobes.
T3	Tumor extends through the prostate capsule. (Note: Invasion into the prostatic apex or into (but not beyond) the prostatic capsule is classified not as T3 but as T2.)
T3a	Extracapsular extension (unilateral or bilateral).
T3b	Tumor invades seminal vesicle(s).
T4	Tumor is fixed or invades adjacent structures other than seminal vesicles: bladder neck, external sphincter, rectum, levator muscles, and/or pelvic wall.

Definition of TNM - Regional Lymph Nodes (N)	
AJCC, 2002	
NX	Regional lymph nodes were not assessed.
N0	No regional lymph node metastasis.
N1	Metastasis in regional lymph node(s).

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Prostate Needle Biopsies

Larry True, MD

PROCEDURE

- Wrap in paper and submit each biopsy separately, after describing, i.e.
Received as "right apex" is a 1.2 cm long, 2 mm diameters tan core of tissue. Submitted in toto.
- Ensure that 3 levels are ordered.

DIAGNOSTIC REPORT

Prostate, (right apex), needle core biopsy:

- Report the tissue, i.e. prostatic parenchyma, seminal vesicle, skeletal muscle.
- If adenocarcinoma, include the following features in the report:
 - Combined Gleason's score is () + () = () of 10 involving a ___ mm long segment of the ___ mm long biopsy. (Report perineural invasion, if present).
- If there is a third pattern that is pattern 5, report it as a comment and estimate the percent of pattern 5.
- If there is PIN (prostatic intraepithelial neoplasia and/or angiolymphatic) that is at least PIN II in grade, report its: PIN grade_ (II vs. III).
- Report multifocality, if present, in a biopsy.

HISTOLOGIC CRITERIA FOR GRADING OF PIN	
PIN I	There should be a prominent increase in nuclear size and variation in size . Additional features include cell crowding, irregularity of cell spacing, multilayering of cells, infrequent small but prominent nucleoli, cytoplasmic eosinophilia, but a normal chromatin pattern.
PIN II	In addition to PIN I features (nuclear enlargement and size variability and cell crowding with irregularity of cell spacing), there should be increased heterochromatin , which is finely granular. Furthermore, nucleoli are more numerous and more prominent and the cytoplasm of most cells is deeply eosinophilic.
PIN III	In addition to accentuation of PIN II features (where cell crowding may lead to occasional luminal bridging), the cardinal feature is large, prominent nucleoli in most nuclei and a marked prominence in chromatin.

In our study, degree of observer concordance was "excellent" for PIN 3 (kappa .81) but "poor" for PIN of lower grades (the kappa statistic evaluates agreement, controlling for chance concordance). Since a 1989 Workshop concluded that PIN 2 and 3 should be considered "high grade PIN" and monitored closely, the "poor" concordance for PIN 2 is of concern.

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- [ImmunoQuery](#)

Transurethral Resection of the Prostate - TURP

Larry True, MD

PROCEDURE

- Weigh or estimate aggregate volume, or dimensions.
- Submit ≤ 8 cassettes (~13 gm) of randomly sampled tissue; the cassettes should be filled, but not stuffed, with chips. ("All" stage T1b tumors will be identified by this sampling scheme. Conversely, only by sampling all tissue will all T1a tumors be found).

If cancer is found in these initial blocks of a TURP, there is no need to submit additional tissue since neither grade nor pathologic stage will be altered.

DIAGNOSTIC REPORT

Prostate, transurethral resection:

- Report the tissue.
- If adenocarcinoma, include the following features in the report:
 - o Combined Gleason's score is () + () = () of 10.
 - o Involving ___ of ___ chips (___ % of sampled specimen).
- If there is PIN (prostatic intraepithelial neoplasia) that is at least PIN II in grade, report as "PIN grade_" (II vs. III).
- Extent (number of foci/ number of tissue chips).

Definition of TNM - Primary Tumor (T)	
AJCC, 2002	
TX	Primary tumor cannot be assessed.
T0	No evidence of primary tumor.
T1	Clinically inapparent tumor neither palpable nor visible by imaging.
T1a	Tumor incidental histologic finding in 5% or less of tissue resected.
<T1B< FONT>	Tumor incidental histologic finding in more than 5% of tissue resected.
T1c	Tumor identified by needle biopsy (e.g., because of elevated PSA).
T2	Tumor confined within prostate. (Note: Tumor found in one or both lobes by needle biopsy, but not palpable or reliably visible by imaging, is classified as T1c.)
T2a	Tumor involves one-half of one lobe or less.
T2b	Tumor involves more than one-half of one lobe but not both lobes.
T2c	Tumor involves both lobes.
T3	Tumor extends through the prostate capsule. (Note: Invasion into the prostatic apex or into (but not beyond) the prostatic capsule is classified not as T3 but as T2.)
T3a	Extracapsular extension (unilateral or bilateral).
T3b	Tumor invades seminal vesicle(s).

T4	Tumor is fixed or invades adjacent structures other than seminal vesicles: bladder neck, external sphincter, rectum, levator muscles, and/or pelvic wall.
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NX	Regional lymph nodes were not assessed.
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N1	Metastasis in regional lymph node(s).

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Recurrent Germ Cell Tumor of Testis

Larry True, MD

AS A METASTASIS AND/OR NODAL DISSECTION OF METASTATIC TESTIS CANCER (Retroperitoneal, Mediastinal, Pulmonic, etc.)

PROCEDURE

- Measure size of resection specimen.
- Section at 1 cm intervals.
- Photograph one or more sections.

DESCRIPTION

- Size of specimen, including, if grossly apparent, size of tumor mass and of grossly tumor-free attached tissue.
- Describe the specimen, i.e., solid? cystic? necrotic? hemorrhagic? variegated?

Sections	# of blocks
Sections of tumor mass, including grossly distinctive areas, i.e. necrosis, cystic	3-many

DIAGNOSTIC REPORT

Tumor Resection, Retroperitoneum

- Report histologic composition of the resection mass, i.e. (germ cell tumor), necrosis (give histology of necrotic tumor, if possible), fibrosis.
- Report the histologic composition of any histologically intact tumor, especially distinguishing embryonal carcinoma from teratoma.

With Respect to Nodes, Report

- Number of nodes involved with tumor.
- Size of largest node containing tumor (2 cm maximum dimension is a threshold value).
- Whether tumor invades outside the node into perinodal soft tissue.
- Status of the surgical margin.

Definition of TNM - Pathologic Regional Lymph Nodes (pN)	
AJCC, 2002	
pNX	Regional lymph nodes cannot be assessed.
pN0	No regional lymph node metastasis.
pN1	Metastasis with a lymph node mass 2 cm or less in greatest dimension and less than or equal to

	5 nodes positive, none more than 2 cm in greatest dimension.
pN2	Metastasis with a lymph node mass more than 2 cm but not more than 5 cm in greatest dimension; or more than 5 nodes positive, none more than 5 cm; or evidence of extranodal extension of tumor.
pN3	Metastasis with a lymph node mass more than 5 cm in greatest dimension.

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Testis with Tumor - Radical Orchiectomy

Larry True, MD

PROCEDURE

- Weigh specimen and measure testis and length of spermatic cord.
- Section cord (surgical margin and random sections) and epididymis before cutting tumor to avoid "contamination" by tumor cells.
- Bivalve testis through the hilum (rete testis) and tumor.
- Photograph the half that best exhibits the tumor and its location; avoid a "butterfly" photo.
- Cut serial slices, parallel to the initial section, of the testis/tumor.

DESCRIPTION

- Weight of specimen and dimensions of testis and length of spermatic cord.
- Size of gross tumor mass and apparent distance between tumor and tunica albuginea and hilum.
- Describe the tumor, i.e., color (variegated, uniformly white?), necrotic? hemorrhagic? cystic?

Sections	# of blocks
Spermatic cord - sections of the margin and of the midsection of the cord	1
Epididymis - one section	1
Tumor, at least 1 block/cm of tumor diameter. Include sections of all grossly different areas, including hemorrhagic, necrotic, and solid areas. Sections should also show the relationship of the tumor to the uninvolved testis, to the hilum, and to the tunica albuginea.	2-many
Uninvolved testis - one section	1

DIAGNOSTIC REPORT

Testis, (right/left), (radical) orchiectomy: (Type of malignant germ cell tumor, i.e. classical seminoma, or mixed germ cell tumor) , with the following features:

- Report the histologic elements, and their ratios as a percentage of the tumor mass, i.e. classical seminoma, embryonal cell carcinoma, teratoma, yolk sac tumor and/or choriocarcinoma.
- Size of tumor.
- (Focal/multifocal) vascular invasion (is/is not) present (see block _____).
- Tumor (does/does not) extend into the rete testis.
- Tumor (does/does not) extend into the epididymis.
- Tumor (does/does not) involve the spermatic cord.
- Tumor (does/does not) involve the tunica albuginea.

Comment: "Consistent with stage pT_ (AJCC, 2002)."

Definition of TNM - Primary Tumor (T)	
The extent of primary tumor is usually classified after radical orchiectomy, and for this reason, a <i>pathologic</i> stage is assigned. AJCC, 2002	
pTX	Primary tumor cannot be assessed. (Note: Except for pTis and pTr, extent of primary tumor is classified by radical orchiectomy. TX may be used for other categories in the absence of radical orchiectomy.)
pT0	No evidence of primary tumor (e.g., histologic scar in testis.)
pTis	Intratubular germ cell neoplasia (carcinoma <i>in situ</i>).
pT1	Tumor limited to the testis and epididymis without vascular/lymphatic invasion; tumor may invade into the tunica albuginea but not the tunica vaginalis.
pT2	Tumor limited to the testis and epididymis with vascular/lymphatic invasion, or tumor extending through the tunica albuginea with involvement of the tunica vaginalis.
pT3	Tumor invades the spermatic cord with or without vascular/lymphatic invasion
pT4	Tumor invades the scrotum with or without vascular/lymphatic invasion.

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CAP Cancer Protocols and Checklists

Male Reproductive System

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Female Reproductive System

Section 1 - Cervical Carcinoma

Author: Rochelle Garcia, MD

Section 2 - Endometrium & Endometrial Carcinoma

Author: Rochelle Garcia, MD

Section 3 - Vulvar Carcinoma

Author: Rochelle Garcia, MD

Section 4 - Ovarian Carcinoma

Author: Rochelle Garcia, MD

Section 5 - Placenta

Author: Corinne Fligner, MD

Section 6 - CAP Cancer Protocols and Checklists

**Including: Endometrium, Fallopian Tube, Ovary,
Trophoblastic Tumors, Uterine Cervix, Vagina, Vulva**

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Cervical Carcinoma

Rochelle Garcia, MD

Here are some tips on handling and items to be addressed in reports that may be helpful to clinicians in patient management, i.e., staging and need for adjuvant therapy. N.B. *All* large gyn specimens should be photographed (i.e., greater than biopsies).

"WEDGE" AND "CONE" BIOPSIES OF THE CERVIX

Although many will insist that the diagnosis of "carcinoma" implies "invasion" - this is not universally understood or accepted. Therefore, it is preferable to use the CIN terminology (not carcinoma in-situ) but to avoid misunderstanding always specify whether "invasive" or "cannot evaluate the presence of" due to artifacts, fragmentation, etc. Note presence or absence of CIN and/or *invasion at surgical margins*. "Microinvasive cervical carcinoma" has a different definition at each major institution. At the University of Washington this is used as a "guide":

- Within 5 mm deep and not longer than 7 mm lateral extent of nearest definable basement membrane (gland or surface).
- No lymphatic/vascular space invasion.
- Stage 1A - ≤ 3 mm, no lymph or vascular invasion ([per AJCC, 2002](#))

As it is difficult to apply these criteria except in the most minimal invasion, it is best **to avoid using the term altogether**. Instead, describe carefully the numbers or extent of foci of invasion if "early"; i.e., their distance from a reference point such as overlying disrupted surface. If there is lymphatic/vascular invasion describe approximate extent or numbers of these foci and their relationship to rest of invasive tumor. If a biopsy is too distorted to evaluate for invasion, comment that it is worrisome for invasive carcinoma. **Do not** use microinvasion in the diagnosis.

"Cervix cone biopsies for pick-up only" are brought to the Frozen Section Room by the OR staff, and the Anatomic Pathology Front Office is notified at the same time. A representative will be sent from the Histology Lab to pick up the specimen. The Histology Lab will notify the biopsy resident or the pathology assistant.

RCH memo of Aug 16, 1994

CERVICAL ADENOCARCINOMA IN SITU (high grade *in situ* glandular neoplasia)

There is no acceptable category for "microinvasive adenocarcinoma" and early invasion can be very difficult to evaluate in a small biopsy. "In situ adenocarcinoma" must show normal glandular contours, be well within layer of normal adjacent glands and show no definite stromal desmoplasia around glands. Glands considered invasive are irregular "crab claw like", or excessively complex, or are significantly deeper than normal glands.

RADICAL HYSTERECTOMY FOR CERVICAL CARCINOMA

Note: you **must** comment whether a uterus is from a simple hysterectomy, modified radical hysterectomy, or radical hysterectomy. **Ask** if you do not know!

Includes a vaginal cuff and the parametrial/cervical soft tissue. The latter should be well sampled (one cassette per side if no gross nodes) with particular attention to any small lymph nodes sometimes found

in this region. The specimen should be inked on all paracervical nonserosal soft tissue surgical margins, then bivalved and fixed overnight. If the vaginal cuff is entirely normal, it can be trimmed off and only the distal margin should be submitted as a "ring" parallel to margin (accommodated in 2 cassettes).

Figure 1.

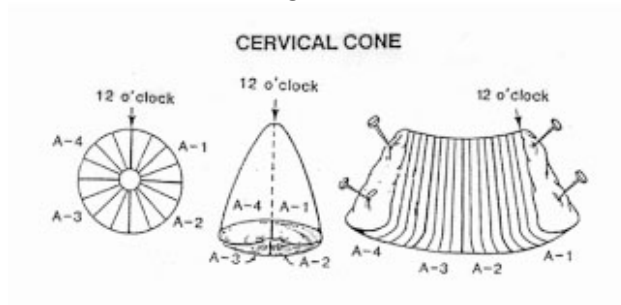
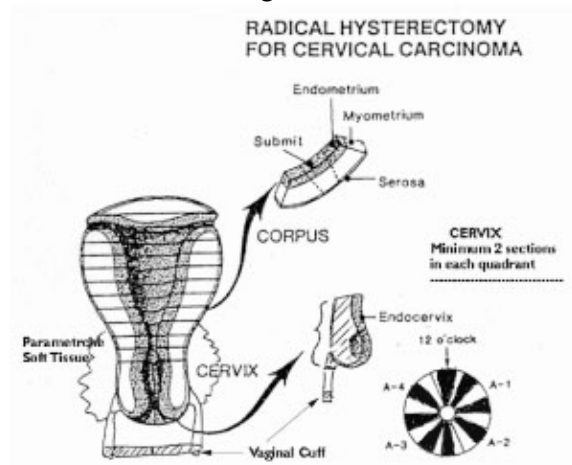


Figure 2.



If the vaginal cuff has any abnormality or close proximity to possible neoplasm, take representative sections in this region perpendicular to inked margin. Sample cervix, including any mass, as much as can be accommodated in a cassette in the same planes as a cone biopsy, but include the paracervical-inked margin. If obvious mass, submit at least two sections in each quadrant and include planes at 12, 3, 6 and 9 o'clock (Fig. 2) - the lateral planes are the most critical, as these have the closest proximity to lymphatic drainage outside cervix.

If there is no obvious mass, more sections should be submitted, or the whole cervix, if relatively small. AGAIN - ask if unsure.

POST RADIATION HYSTERECTOMY FOR CERVICAL CARCINOMA (Frequently the clinical history will say Adjunct Hysterectomy.)

Specimens usually have a small ragged cervix with a poorly defined or absent endocervical canal. In such cases ink and embed entire cervix to best demonstrate distal and paracervical surgical margins.

FORMAT OF REPORT FOR CERVICAL CARCINOMA

EARLY (MICRO) INVASIVE CERVICAL CARCINOMA

- Depth in mm from nearest definable basement membrane (or surface if cannot define basement membrane).
- Growth pattern, i.e., few "tongues"/"fingers" or "confluence".
- Lymphatic/vascular invasion? - focal or multifocal
- Relationship to surgical margins.

(It is not necessary to "diagnose microinvasive"; surgeons will make this decision based on detailed description. It is important to measure depth, or say it can't be done or a phone call will result)

(FRANKLY) INVASIVE CERVICAL CARCINOMA

- Histologic type: squamous, adeno, -special features "glassy cell", "small cell", etc.
- Differentiation grade. (**Optional**, is actually not shown to be important.)
- Proportionate depth of invasion, "%:", or "inner 1/2 stroma", (e.g., "maximum depth of invasion is ____% of the ____cm thick wall). Best to specify in cm. Example: x cm invasion of x cm wall.
- Parametrial soft tissue extension?
- Surgical margins? (If close, define number of mm.)
- Lymphatic/vascular extension? (location and extent. They want to know, but is of questionable value.)

A summary comment emphasizing specific aspects is useful particularly in a complex case. Bad actors in cervical carcinoma include "small cell" (similar to a lung small cell) and (some believe) "glassy cell" carcinoma. Glassy cell is a large cell undifferentiated, often bulky exophytic rapidly growing lesion. Eosinophils are often very prominent in a stromal inflammatory response to this neoplasm.

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Endometrium & Endometrial Carcinoma

Rochelle Garcia, MD

ENDOMETRIAL BIOPSY FOR INFERTILITY

Curettage biopsies for dating are characterized by post-ovulatory histologic stage (usually as a range of 2 days). Done infrequently; however, it is crucial to have the ability to recognize normal in order to recognize abnormal.

Post Ovulatory Day	Histologic Features
2	Subnuclear vacuolization; mitoses frequent.
3	Subnuclear vacuolization; mitoses sparse.
4	Luminal secretion vacuoles.
5	Cytoplasmic vacuoles infrequent.
6	Glandular secretion prominent.
7	Stromal edema becomes prominent.
8	Maximal edema.
9	Spiral arteries and predecidualization periarterial stroma.
10	Thick periarterial cuffs of predecidua.
11	Scattered islands of predecidualization.
12	Multifocal coalescence of predecidualization islands.
13	Solid predeciduum.
14	Interstitial hemorrhage.

ENDOMETRITIS

Usually a mixed inflammatory reaction with neutrophils, histocytes, plasma cells and lymphocytes. Rare plasma cells alone are not endometritis.

ENDOMETRIAL HYPERPLASIA

- Simple - likely non-neoplastic, crowded, but not disorganized or irregular glands and without significant cytologic atypia (which means you do not have to hunt for it); is not treated aggressively. Synonym (to some): Disordered Proliferative.
- Complex - neoplastic, crowded and disorganized glands. Atypia, is poorly reproducible, "clonal" pop that looks different than rest or marked nuclear size, "clearing" and nucleoli.

ENDOMETRIAL CARCINOMA

ENDOMETRIAL BIOPSIES (OFFICE BIOPSIES)

The FIGO grade is often difficult to evaluate accurately in these small and often fragmented specimens but some comment should be made about the "FIGO grade". If the term "papillary" is used as an adjective in the diagnosis it should be specifically addressed whether this belongs in the high grade "papillary serous variant" category. This variant often has a very organized architecture and **cannot** be graded accurately according to the FIGO system, as it is in a category by itself; i.e. always aggressive! It must have a high nuclear grade. Similarly, clear cell carcinoma IS NOT GRADED.

Endometrial CA (GOG Modification of FIGO) - Grading	
Grade I	5% or less of a nonsquamous nonmorular solid growth pattern
Grade II	Between 5% and 50% solid growth pattern
Grade III	More than 50% solid growth pattern
Notable nuclear atypia in Grade I or II raises the grade by one. Do not FIGO grade papillary serous clear cell carcinoma or carcino-sarcoma (mixed Mullerian neoplasm). Ref: Blaustein's Pathology of the Female Genital Tract	

ENDOCERVICAL CURETTINGS

Specify whether any carcinoma fragments are separate from benign endocervical fragments. Only unequivocal endocervical stromal invasion by neoplasm is regarded as a "+ve E.C.C." clinically. Neoplastic fragments may be contaminated from above.

HYSTERECTOMY FOR ENDOMETRIAL CARCINOMA

These specimens often have a request to be opened for inspection at the time of surgery to evaluate myometrial invasion, although this is quite inaccurate. Be as non-specific as possible! After bivalving, specimen is fixed overnight. Appropriate sections should be taken to evaluate extent of involvement of endometrial cavity, **including lower uterine segment** (lower 1/3), and cervix (2 sections minimum, if normal). **Take 1 section as longitudinal sections from cervix to body of uterus.**

Figure 1.

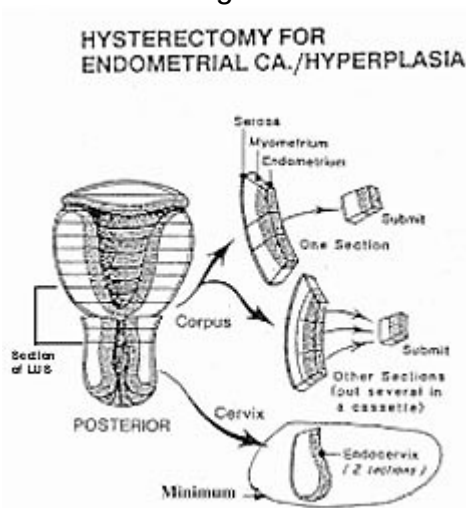
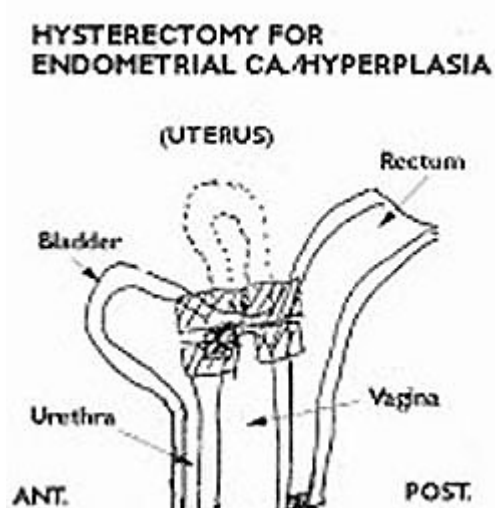


Figure 2.



Final diagnosis and or comment should address:

- Proportionate depth of myometrial invasion by carcinoma measured from normal endo-myometrial interface
- Inner 1/3, 1/2, etc., measured in cm, including extent of this process.
- FIGO grade.
- Lymphatic/vascular invasion +/-.
- Involvement of surface lining and myometrial invasion in lower uterine segment and cervix.

FORMAT OF REPORT FOR ENDOMETRIAL CARCINOMA

- Type of hysterectomy; usually simple, but sometimes radical if cervical involvement is documented pre-operation.
- Weight of uterus.
- FIGO grade and/or histologic pattern; "papillary serous", "clear cell", etc.
- If squamous differentiation, benign metaplasia, "atypical" or adenosquamous CA?
- Myometrial invasion, depth (proportionate) extent, ? serosa involved.
- Lower uterine segment (lower 1/3) involved? (Surface + myometrial invasion)
- Cervical involvement?
- Lymphatic/vascular involvement?
- Surgical margins? Serosa is not a margin.
- Submit representative sections to address above parameters. Also try to make an estimate of size or volume of tumor projecting into endometrial cavity. The parametrium (paracervical soft tissue containing large vessels) is not removed in endometrial cancer, unless there is gross cervical extension by tumor.

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Vulvar Carcinoma

Rochelle Garcia, MD

VULVAR BIOPSIES

These may be "incisional" or "excisional" for neoplasia, most often VIN III. Make comment on "apparent" surgical margin involvement if specimen is not inked. Larger "excisional" biopsies are usually labeled as such. These should be inked and oriented (with help of surgeon), then pinned out, fixed, serially sectioned and totally submitted if small to medium sized (e.g., ~1 x 3 cm). **If larger, partial vulvar resections** including "skinning vulvectomies" for C.I.S., ask advice from attending or Dr. Garcia. Questions to be answered: extent of disease? involved margins? invasion? For evaluation of the latter, take representative sections of the thickest palpable regions (if not totally submitted specimen).

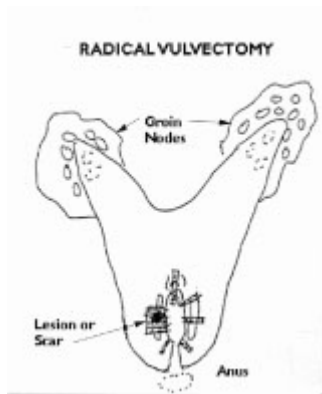
In microscopic final reports where there is invasive carcinoma, the extent should be addressed. Avoid the term "microinvasive" carcinoma, but rather describe in detail:

- The depth of invasion as measured from overlying/adjacent surface epithelial basement membrane or ulcer base, etc., - or if it cannot be evaluated (malorientation). Microinvasion defined as < 1mm from nearest basement membrane.
- Involvement of surgical margin.
- Lymphatic/vascular space involvement present, absent, suspicious, how many foci, etc.
- "Spray pattern" of invasion present: (Small groups or "droplets" of high-grade carcinoma.)
- Associated VIN, or associated epithelial hyperplasia.

There are many "shades of gray" in making the decision between a local excision for early invasive carcinoma and a radical or modified radical vulvectomy. The surgeon, based on a very detailed description, makes this decision. Most cases of even early small invasive vulvar carcinomas used to be treated by radical vulvectomy. There is now a trend toward more conservative excisions for small lesions. Invasive carcinoma cases exceeding 1 mm in depth below the adjacent or overlying epithelial basement membrane, as measured above, will usually receive groin node sampling.

RADICAL VULVECTOMY (Rarely performed anymore.)

This may be bilateral, partial or unilateral and includes subcutaneous fat and groin nodes sometimes in continuity with "skin bridge" (to include lymphatics). Ink vulvar introital and deep margins, including any surgical margins close to tumor. Groin nodes (all) can be dissected and placed in cassettes; fix over night if they are not well fixed. Be sure to count at **gross** bench. Then pin specimen and fix overnight. Open posterior fourchette after inking if this allows for better positioning of tissue in relation to residual tumor. Often the invasive carcinoma has been previously excised and only a scar remains. This area should be blocked out and totally submitted.



The vulvar introital margin is usually closest to any residual tumor, - take multiple representative sections perpendicular to margin to include tumor and deep soft tissue. There is no one best way to do this, use common sense, i.e., sections showing extent of tumor and relationship to closest margins. Also submit a few representative sections anterior, lateral, posterior, "normal" vulva perpendicular to introitus. Lateral skin margins do not need to be sampled unless there is an abnormality. Sample any other additional abnormalities in specimen, e.g., palpable nodules.

FORMAT OF REPORT FOR VULVAR CARCINOMA

INVASIVE VULVAR CARCINOMA (VULVECTOMY)

- Location on vulva.
- Relationship to surgical margins.
- Differentiation/cytological grade (optional).
- Lymphatic/vascular involvement? - focal, multifocal.
- Special features, i.e., "spray pattern" of invasion, associated epithelial hyperplasia.
- Groin lymph node involvement by neoplasia?

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Ovarian Carcinoma

Dr. Rochelle Garcia

OVARIAN MASSES

Include gross description of outer surface, i.e., smooth, lobulated, tumor excrescences, etc. General guideline: **one sample** per 1 cm diameter of mass (whether cystic or solid), 3 or more small samples can be put in one cassette. Sample the most "solid" fleshy areas if any; avoid grossly hemorrhagic or obviously necrotic areas. This is a rough guide; not necessary if metastatic disease (e.g. by fs) is already documented.

Omentectomy is part of the "staging" procedure for genital tract malignancies. If omentum has obvious involvement by neoplasm, a few representative samples in one or two cassettes are sufficient. If there is **no** obvious gross neoplasia, submit **one sample per 1 cm diameter** of omentum "balled" (same as in ovary); this is for detection of microscopic tumor spread. In neoplasms which may have a spectrum from benign to borderline to focal carcinoma, estimate relative quantities of these elements, i.e. in percentage of whole neoplasm. This may influence further treatment, e.g., a largely benign stage IA mucinous neoplasm with focal carcinoma would receive no further treatment if well staged.

FORMAT OF REPORT FOR OVARIAN CARCINOMA

OVARIAN NEOPLASMS

- Type.
- Maximum diameter (weight if possible).
- Serosal surface involvement? (don't need if there is metastatic disease)
- Differentiation /grade.
- In "borderline" or focally malignant mucinous neoplasms specify approximate relative quantities (% all) of these components.

PELVIC EXENTERATION

(for post-radiation recurrence of vaginal, cervical or uterine malignancy)

Unless you have had experience in handling these specimens always **call attending** and/or Dr. Garcia for help in orientation and instructions for dissection. These specimens may include rectum, anus, vulva, vagina, uterus, bladder and urethra, or any combination of these. Lateral surgical "soft tissue" margins are the most critical for evaluating proximity-associated residual neoplasm in the often dense, associated fibrosis. These ragged margins should be inked liberally (blue or black). The whole specimen should then be sagittally sectioned, initially only partly, to allow formalin fixative into the hollow organs; i.e., the bladder, vagina and rectum (including uterus). Stuff these loosely with gauze to retain shape, then fix overnight. Complete the sagittal section and photograph the one most representative cut surface. Take representative sagittal sections best demonstrating residual neoplasm in all directions and relationship to organs removed; i.e., bladder/vagina/cervix; recto/vaginal septum; relationship to pelvic or cul de sac serosa, including some normal tissue at edges of neoplasm. It is not necessary to sample obviously normal rectum or bladder, etc. away from neoplasm. Most important, take bilateral multiple (minimum 2-3) sections perpendicular to inked lateral margins in the horizontal plane, showing closest distance of residual tumor to margin (most often in the region of the vaginal apex or cervix). There are no lymph nodes expected in this radiated region.

An "exenteration" for ovarian carcinoma is a tumor debulking procedure and does not require the same care/attention to margins but just documentation that carcinoma is present.

SPECIAL STUDIES ON GYNECOLOGICAL TUMORS

- Flow cytometry has not been routinely done - only in cases selected by pathologist or surgeon.

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Handling Placentas in UWMC Anatomic Pathology

Dr. Corinne Fligner

1. Placenta specimens and corresponding PCR's are picked up Monday through Friday by Surgical Pathology (SP) staff, by 0900 in the two Labor and Delivery (L&D) refrigerators (EE 607 in East wing of L&D and EE615 in the south wing of L&D). If no PCR is attached to a specimen, write down the name and hospital number from the specimen, and call the charge nurse on L and D (598-4616) to request that a PCR be completed (should be done by one of the PA's or the Autopsy coordinator). If no attending is listed, accession to Eschenbach, and circle absent attending box on PCR.
2. Placentas are sorted in Surgical Pathology by SP staff. If the PCR is equivocal in terms of whether an examination is requested, the specimen should be accessioned, or if time permits, contact the Autopsy Coordinator, Autopsy Lead, or Placenta Attending of the Day for assistance. Placentas which are not to be examined are stored for 7 days in the appropriate bin in the Surgical Pathology refrigerator. Placentas are accessioned to Dr. Fligner (attending) and Janet Miller (resident). Accessioned placentas to be examined are placed in the Autopsy refrigerator in BB250 (small autopsy room).
3. Placentas are generally examined twice a week, on Mondays (SP resident on gross) and Thursdays (first year resident on Autopsy), preferably in mornings, at a mutually agreeable time. Alterations in this schedule can be made by the placenta attending, depending on workload and staffing needs. Ideally, cassetting of placentas should be done the same afternoon, with sections submitted the same day, but this activity should be done no later than the following day. Liberal fixation of whole placentas prior to sectioning is encouraged, for ideal examination, and the following placentas should generally be fixed prior to sectioning: 1) Small immature placentas; 2) Placentas with multiple (more than 3) infarcts; 3) Placentas with grossly identifiable hematomas, or when there is a question of hematoma; 4) Placentas which are extremely lacerated, 5) Placentas where there has been IUFD, recurrent loss, or significant growth retardation.
4. Placentas:
 - o Routine: 2 sections of umbilical cord, 1 section of membrane roll, and 2 sections of representative (most normal) central sections of placental disc.
 - o Representative abnormalities should be submitted, to document lesions.
 - o For twins, dividing membrane should be submitted.
 - o For IUFD or diffuse abnormalities, more sections of disc (or involved area, such as cord thrombosis) should be submitted.
 - o During examination, untrimmed and trimmed weights should be written on PCR.
5. After initial examination of placentas, support staff should write initials of person (resident or attending) to receive slides on top of PCR.
6. Cassettes are taken to Histology (to the Gross Room) along with all the PCR's and the cassette QC list. Before taking cassettes to Histology, Tamtron should be checked, and the assigned attending and resident changed as appropriate. If this is not done, the wrong person will receive the case, and the case may be "lost" for a prolonged period of time.
7. Slides are distributed to the person whose initials are on the PCR. If no initials are present, slides are distributed as indicated in Tamtron (first to the listed resident, then to the listed attending). If case is accessioned in Tamtron to Miller/Fligner, slides are brought to BB-250 (Autopsy) for their

distribution to the appropriate pathologist. Distribution should be done on the day slides received in Autopsy.

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Breast

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Author: Tom Lawton, MD

Section 2 - Sentinal Lymph Node Sampling

Author: Tom Lawton, MD

Section 3 - Risk Assessment and Prognostic Factors in Breast Cancer

Author: Tom Lawton, MD

Section 4 - TNM Classification

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Section 5 - CAP Cancer Protocols and Checklists

Including: Breast

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Breast Biopsies and Mastectomy

Tom Lawton, MD

GENERAL PRINCIPLES

The most important pieces of information to be conveyed back to the medical, surgical, and radiation oncologists regarding breast cancer specimens are:

- the size of the mass (be sure to correlate gross and microscopic and use what appears most accurate)
- the important histologic features of the neoplasm
- the status of individual surgical margins
- phenotypic characteristics of the neoplasm which have important prognostic and therapeutic implications, e.g., expression of estrogen receptor (ER), progesterone receptor (PR), etc.

In many cases, it is also important to document that microcalcifications identified in the mammogram are present in the specimen. The time period between when the tumor is removed from the patient and when the tumor is immersed in fixative is critical; prolonged intervals of over one hour can have serious deleterious effects upon the retention of immunohistochemically detectable ER and PR. It is also important to remember that fat fixes very slowly, and it is important that large breast specimens fix overnight before they are grossed in.

HANDLING AND ALLOCATION OF TISSUES

Needle Biopsies

The entire specimen is submitted in formalin. While margins and tumor size are not an issue, it is still possible to perform immunohistochemical studies to ascertain ER and PR status.

Excisional Biopsies

These may represent palpated masses, mammographically-detected masses (e.g., sites of microcalcification), or blind biopsies (e.g., of a contralateral breast). Frozen sections should not generally be performed on this tissue, as the distinction of carcinoma from, e.g., sclerosing adenosis, can be extremely difficult. It is rare that the decision to perform a mastectomy will hinge upon the results of a frozen section. Furthermore, freezing and thawing can adversely affect the final histology as well as the antigenicity of the tissue.

- **Radiographing specimens:** In cases where the surgeon requests that identification of microcalcifications be made, the specimen can be radiographed, either in radiology (they frequently do this) or in pathology – talk to Lindy and/or Janet Miller.
- **Inking specimens:** It is important, for optimal care of the breast cancer patient, that all excisional breast biopsies be inked in a standard fashion to permit identification of involved margins which are critical given current interest in breast conservation treatments. To address this, all breast biopsies will be treated as "cubes" with all six faces inked according to the following scheme; (this is usually done by the surgeon):

Breast Cube Face	Color
Superior	BLACK
Inferior	BLUE
Anterior	ORANGE
Posterior	RED
Medial	YELLOW
Lateral	GREEN

For re-excisions (same or subsequent procedure), the same inking protocol will be followed. (Thus, ink on the re-excision marks the new, fresh margin(s) with the same color scheme.) The surgeon in the operating room will perform the inking, and the specimen will be received by Pathology with the inking already performed.

It is advisable to submit the entire biopsy, making sure to identify, in your gross description, which margins correspond to which colors, and to identify which margins are in which cassettes. Often a drawing is a more efficacious approach. In large biopsy specimens, after inking, the specimen can be "breadloafed", and if a discrete mass is present grossly clear of the margins, representative sections of individual margins, as with any large specimen, may be submitted. Please orient gross lesions with respect to relationship to margins and not just the 'slice' that the lesion is in.

Mastectomies

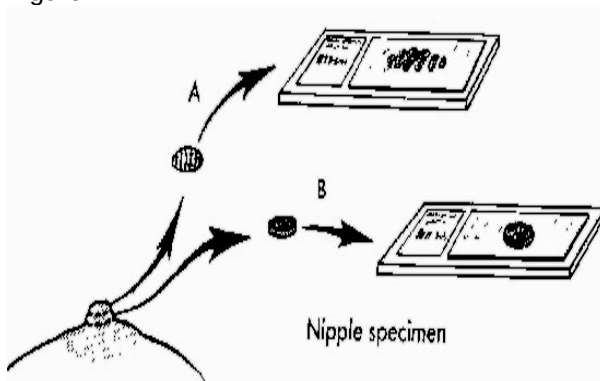
In the gross description, note the side (left or right), the type of mastectomy (modified radical, simple, etc.), and what tissues accompany the specimen (e.g., skin, nipple, muscle, etc.). If axillary fat is attached, it should be separated; weigh the specimen and note the presence of scars or biopsy sites in the breast tissue. A slightly different inking pattern is used for mastectomy specimens, according to the following scheme. In the case of mastectomies, the resident performs the inking:

Mastectomy Margin	Color
Superior superficial	BLACK
Inferior superficial	BLUE
Deep	ORANGE

The line between the superior and inferior portions will generally be that defined by the skin ellipse. If in doubt, the surgeon will be happy to help with identification.

Remove the nipple and areola with a scalpel and forceps, according to Figure 1:

Figure 1.



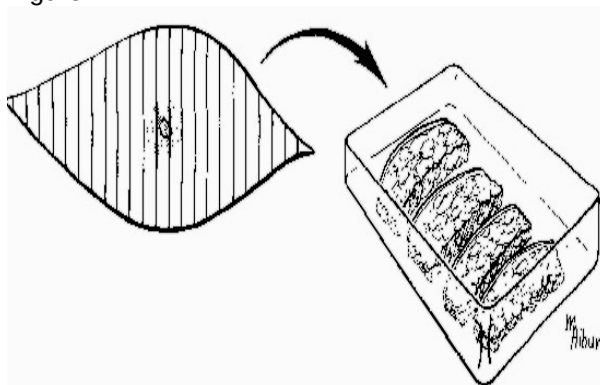
Ackerman's Textbook of Surgical Pathology ([J. Rosai, ed.](#))

One of the most important tasks of the surgical pathologist is in the determination of the location and size of the tumor mass, or, if there are multiple masses, the sizes of these masses and their relationship to one another (e.g., are they contiguous?).

Using a long knife, cut the breast longitudinally into 2 cm thick slides; you may keep the anterior surface of the breast together like the spine of a book or line up the portions of tissue according to the following diagram, and let fix overnight in formalin. Gross description should comment on which quadrant or 'o'clock' lesions are, NOT just what slice they are in. Also if there are multiple lesions, their relationship to each other should be noted.

Remove the nipple and areola with a scalpel and forceps, according to Figure 2:

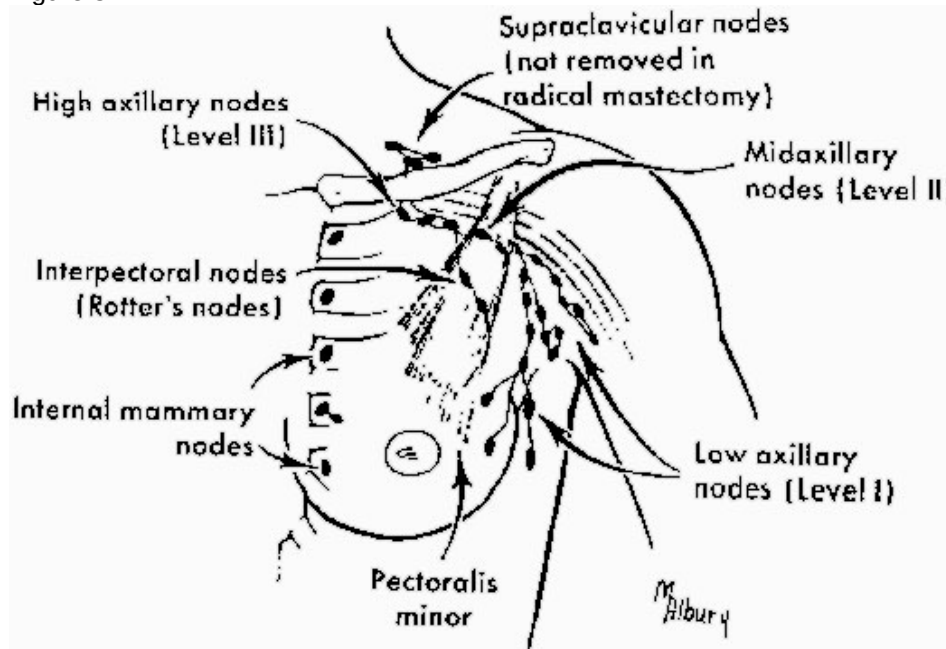
Figure 2.



Ackerman's Textbook of Surgical Pathology ([J. Rosai, ed.](#))

Lymph nodes obtained from a modified radical mastectomy will generally not correspond to the Level I, II and III nodes as outlined in Figure 3; most of the nodal tissue excised will correspond to Levels I and II (which you may designate as "lower" and "upper"). Carefully dissect out the lymph nodes from the fat and submit from lowest to highest, dictating the cassette arrangement. You should find at least 15-20 lymph nodes. If you bisect any, ink them and be sure to count at the gross bench.

Figure 3.



Ackerman's Textbook of Surgical Pathology ([J. Rosai, ed.](#))

Taking Sections

Take at least three sections of the main tumor, and sample all other lesions noted grossly. If normal, take one representative section from each quadrant. Sections should be taken liberally to permit determination of the relationship of the tumor to the deep margin(s). Sections of the nipple and areola should always be made and examined for involvement by tumor.

You should generally alert the IHC Lab that a breast cancer specimen has arrived, as arrangements can be made at that time for immunohistochemical marker studies.

WHAT TO INCLUDE IN THE DIAGNOSIS SECTION OF THE SURGICAL PATHOLOGY REPORT

The following sample report highlights the important features that need to be addressed:

NOTE: IF only DCIS is present in any of the biopsies, including the excision, need to order ER only

Final Diagnosis

Breast, (Right/Left), (Type of procedure: Excisional biopsy, core needle biopsy, needle-localization biopsy, modified radical mastectomy with/without lymph node dissection):

Infiltrating () carcinoma with:

1. **Size:** [maximum dimension in cm].
2. **Nottingham grade** [I, II or III or III] derived as follows: tubule formation [1, 2, or 3], nuclear pleomorphism [1, 2, or 3], mitotic activity [1, 2, or 3], where 1 is "most benign" (see below).

3. **Status of margins:** positive [qualify: widely, or focally positive, be sure to identify which margin is involved; see below] (do not need to measure if >0.5 cm)
 4. **Angiolymphatic space invasion by tumor:** [present/absent] DO NOT COMMENT ON IF THERE ARE POSITIVE LYMPH NODES
 5. **Marker studies:*****
 - a. ER/PR
 - b. c-erbB-2 [negative, intermediate, or high overexpression]; p53 [negative/positive for overexpression if less or more than 50% of cells positive]
 - c. Ki-67-defined cell proliferation rate: Low [.10%], Intermediate [10-20%], or High [.20%] proliferation rate.
 - d. others [myoepithelial markers, BCL-2, mdm-2, topoisomerase II, etc.]
 - e. **Lymph node status:** TOTAL number of positive nodes (including sentinel or intramammary nodes, if present); note presence or absence of extranodal extension.
 - f. **Associated DCIS:** (less detail required if there is invasive as opposed to In-situ carcinoma)
 - a. *Size:* if tumor forms discrete mass, indicate the greatest dimension. If tumor does not form a discrete mass, estimate the longest distance between two foci of DCIS.
 - b. *Nuclear grade:* low, intermediate, or high grade.
 - c. *Presence of necrosis:* focal, or marked.
 - d. *Margin status:* positive, close [measure the distance in mm], widely free [if >1cm].
 - g. **Associated changes:** - one brief comment, particularly about biopsy cavity and presence or absence of microcalcifications within/outside tumor nests.
-

* Histologic types include ductal, lobular, mucinous [colloid], cribriform, medullary, papillary. Note there is no such thing as a breast 'adenocarcinoma'.

** Nottingham Grade is a modification of the Bloom-Richardson grading scheme. Individual scores of 1-3 are given for each of the following factors: nuclear pleomorphism, tubule formation, and mitotic index. The individual scores are summed to give the total Nottingham score. It is best to report the total score along with each of the components. For further information regarding the Nottingham Grade see [Elston CW and Ellis IO](#) and [Frierson HF et al.](#)

Tubule formation	>75% = 1 10-75% = 2 <10% = 3
Nuclear pleomorphism	Small, regular nuclei = 1 Moderate increase in size and variability = 2 Marked variation = 3
Mitotic counts	Graph of mitotic counts by field diameter Reference:

The individual scores are summed to give the total Nottingham score:

Score: 3-5 = Grade I
6-7 = Grade II
8-9 = Grade III

A score of 3-5 qualifies as a Grade I tumor, a score of 6-7 qualifies as a Grade II tumor, and a score of 8-9 qualifies as a Grade III tumor. It is probably wise to include the individual score components along with the total Nottingham Grade.

*** Based on immunohistochemical studies. Usually immunohistochemistry studies are completed the day following the return of H&E-stained slides from the Histology Lab. If possible, include these data in the final report; alternatively, report as an Addendum.

When describing the presence or absence of carcinoma at surgical margins, identify margins by location, not color, e.g., do not describe tumor present the "green" margin. The preferred approach is to identify the margin as "medial" or "lateral" and omit color designations. (It is also advisable to include the block number containing the positive margin, as this facilitates review of slides at conferences, etc.) This is important because in situations (i.e., computer searches or printouts of old records) where the gross description of the specimen is not available (in which identification of colored margins should appear), correct identification of involved margins would not be possible.

If microcalcifications were noted on the specimen mammogram and not identified in the microscopic sections, it may be necessary to X-ray the paraffin blocks and get microscopic levels on the positive block(s) to help identify them.

Until recently, the only accepted treatment of breast cancer in most treatment centers in the world consisted of radical surgical excision. This was followed by a gradual introduction of chemotherapy and hormonal therapy. More recent studies showed that there is no significant survival advantage in breast cancer patients who are treated with mastectomy compared to those who are treated with excision alone and radiation therapy. Moreover, the introduction of mammography as a screening tool has led to the

detection of small non-palpable early cancers, which reduced the need for radical surgery even further. The increased use of conservative surgery was accompanied by an increased trend to use adjuvant chemotherapy, hormonal therapy and radiation therapy.

The evolution of breast cancer treatment was paralleled with the availability of newer techniques of sampling the breast tissue. Fine needle aspiration biopsies provide a quick means to establish a diagnosis in the presence of a palpable mass. The diagnostic limitations include inability to distinguish between invasive and non-invasive cancers. It also requires expertise in interpretation. With the wide use of mammography, needle-localization biopsy technique was introduced in an attempt to ensure the removal of the mammographically abnormal area by inserting metal wires under mammographic examination into the area that contains the abnormality. More recent techniques include the "mammotome" which is a stereotactic single pass core biopsy that rotates and cuts tissue under vacuum suction, and the "ABBI" device which allows the examiner to obtain cores of tissue as large as 2.0 cm in diameter.

Stereotactic core needle biopsy procedure under mammographic examination was introduced to minimize the need for wide and sometimes unnecessary removal of benign tissue. However, the small biopsy size often created problems in interpretation, leading to false-positive or false-negative diagnoses. With time, the pathologists have gained experience interpreting small core needle biopsies.

When the pathologist makes a diagnosis of cancer, it is insufficient to simply call a neoplasm malignant without addressing some important details about the **histologic grade**, status of excisional **margins** in relation to neoplasm, the involvement by **lymphatics** or vessels by neoplasm, and finally the **number of lymph nodes** involved by the neoplasm. These data can help predict the prognosis, risk of recurrence and response to adjuvant therapy. For this reason, there was a growing need among breast cancer specialists to adopt a universally acceptable reporting system that is reproducible and easy to apply at the same time. It is now acceptable among many breast cancer experts that the Nottingham grading system, which is a modification of the Bloom-Richardson grading system, is currently the best reporting system available for invasive carcinoma. [Table-1](#) addresses the Nottingham grading system in details.

TABLE 1: THE NOTTINGHAM GRADING SYSTEM			
Score	1	2	3
Nuclear Grade	small uniform	slightly larger	very pleomorphic
Tubular Formation	<75% tubules	10-75% tubules	<10% tubules
Mitotic Count	<5 in 10 high power fields	5-9 in 10 high power fields	>10 in 10 high power fields

Grade I = score 3-5

Grade II = score 6-7

Grade III = score 8-9

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Sentinel Lymph Node Sampling

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According to the Radiation Safety Officers at the UWMC, the amount of radiation emitted from the sentinel lymph node specimen is negligible.

BREAST CANCER

Bisect the lymph node and submit both halves in one block. The histology laboratory will make 3 H&E level sections. If the surgeon request a frozen, freeze one half ONLY or do a touch prep. Be sure to speak to the attending pathologist about their comfort level if the surgeon requests a touch prep only. Do not order IHC except if the primary growth pattern is lobular.

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MELANOMA

Bisect the lymph node and submit both halves in one block (more than one node can go in a block, but must be inked). The histology laboratory will make 3 H&E level sections. If there is no metastatic neoplasm in the H&E stained slides, you must order IHC on all blocks that contain lymph node tissue (feel free to have attending preview the slides).

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Risk Assessment & Prognostic Factors

Tom Lawton, MD

The risk of subsequent cancer in patients who had biopsies that showed benign breast disease has been recently addressed by three long-term follow-up studies, which showed that women who had non-proliferative disease did not have an increased risk of breast cancer as in contrast to women who had proliferative disease either without, or with cytologic atypia. Results are shown in Table 1. Note that the number in parenthesis represent the relative risk in case of history of breast cancer in first-degree relatives.

Table 1: Relative Risk of Breast Cancer According to Subtype of Benign Breast Biopsy in the Nashville study, Nurses' Health Study (NHS) and Breast Cancer Detection and Demonstration Project (BCDDP)			
	Non-Proliferative Disease	Proliferative Disease Without Atypia	Atypical Hyperplasia
Nashville	1 (1)	1.9 (2.7)	5.3 (8.9)
NHS	1 (1)	1.7 (4.5)	3.5 (7.3)
BCDDP	1 (1)	1.3 (2.6)	4.3 (22)

Non-proliferative changes include normal breast tissue, cysts, apocrine metaplasia, and mild duct hyperplasia. Proliferative changes without atypia include papillomas, sclerosing adenosis, fibroadenoma, and moderate to florid duct hyperplasia. Atypical hyperplasia can be either of the ductal or lobular type. Women with fibroadenomas with complex changes (cysts, sclerosing adenosis, apocrine changes) have a relative cancer risk of 3.1 compared to 1.9 for patients with fibroadenomas without complex changes. The elevated risk in women with atypical hyperplasia appears to decrease after menopause.

Note that the relative cancer risk for both atypical ductal and atypical lobular hyperplasia is equal in both breasts. On the other hand, only lobular carcinoma in situ is associated with 10 times increased risk in both breasts compared to 10 times increased cancer risk in ductal carcinoma in situ only in the same breast.

Remember that the association of proliferative breast disease (with and without cytologic atypia) with increased cancer risk represents only a small component of the risk of subsequent cancer.

When a breast biopsy is obtained and a diagnosis of invasive carcinoma is established, many critical questions should be addressed. These include:

- Are there risk factors that predict local recurrence?
- Are there any prognostic factors that can provide information on clinical outcome?
- Are there any predictive factors that can provide information on the likelihood of response to a given therapeutic modality?

Factors that predict local recurrence can be summarized in two main items: 1. closeness of tumor to the surgical margins of excision, and 2. presence of extensive ductal carcinoma in situ.

Extensive ductal carcinoma in situ is defined as simultaneous presence of DCIS within and outside the invasive tumor which comprises >25% of the tumor mass. This is associated with higher risk of local recurrence. The risk of local recurrence increases further when the invasive tumor is very close to the

excisional margins. In fact, the presence of extensive DCIS is not an independent predictor of local recurrence when the microscopic margin status is taken into consideration.

Currently, the most important prognostic factor for patients with invasive breast cancer is the status of axillary lymph nodes. In addition, the tumor size is an important prognostic factor, independent from the lymph node status. Tumor histologic type and grade are also important histologic prognostic factors. The best assessment of tumor grade is currently the Nottingham grading system. Finally, in patients with no evidence of metastatic carcinoma to the lymph node, the detection of tumor nests within lymphatic vessels is an independent prognostic indicator.

Although the status of estrogen and progesterone receptors in tumor cells has not yet been established as an independent prognostic factor, it is very useful in predicting response to hormonal therapy. In addition, overexpression of Her-2/neu (c-erbB-2) has been shown to correlate not only with worse prognosis, but also with response to Adriamycin-based chemotherapy.

The above factors are currently the most important ones to investigate in order to determine the likelihood of local recurrence, distant metastasis and response to adjuvant therapy.

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TNM Classification

Tom Lawton, MD

The following TNM Classification scheme appears for your reference only, highlighting the type of information that is necessary for clinical evaluation of breast cancer. It is generally not advised that you include a TNM stage in the report, as this determination is made on the basis of the pathology report as well as other clinical data of which you may not be aware.

Definition of TNM - Primary Tumor (T)	
<u>AJCC, 2002</u>	
TX	Primary tumor cannot be assessed.
T0	No evidence of primary tumor.
Tis	Carcinoma <i>in situ</i> .
Tis (DCIS)	Ductal carcinoma <i>in situ</i> .
Tis (LCIS)	Lobular carcinoma <i>in situ</i> .
Tis (Paget's)	Paget's disease of the nipple with no tumor Paget's disease associated with a tumor is classified according to the size of the tumor.
T1	Tumor 2 cm or less in greatest dimension.
T1mic	Microinvasion 0.1 cm or less in greatest dimension.
T1a	Tumor more than 0.1 cm but not more than 0.5 cm in greatest dimension.
T1b	Tumor more than 0.5 cm but not more than 1 cm in greatest dimension.
T1c	Tumor more than 1 cm but not more than 2 cm in greatest dimension.
T2	Tumor more than 2 cm but not more than 5 cm in greatest dimension.
T3	Tumor more than 5 cm in greatest dimension.
T4	Tumor of any size with direct extension to (a) chest wall or (b) skin, only as described below.
T4a	Extension to chest wall, not including pectoralis muscle.
T4b	Edema (including peau d'orange) or ulceration of the skin of the breast, or satellite skin nodules confined to the same breast.
T4c	Both T4a and T4b.
T4d	Inflammatory carcinoma.

Definition of TNM - Regional Lymph Nodes (N)	
AJCC, 2002	
NX	Regional lymph nodes cannot be assessed (e.g., previously removed).
N0	No regional lymph node metastasis.
N1	Metastasis to moveable ipsilateral axillary lymph node(s).
N2	Metastasis in ipsilateral lymph nodes fixed or matted, or in clinically apparent* ipsilateral internal mammary nodes in the <i>absence</i> of clinically evident axillary lymph node metastasis.
N2a	Metastasis in ipsilateral axillary lymph nodes fixed to one another (matted) or to other structures.
N2b	Metastasis only in clinically apparent* ipsilateral internal mammary nodes and in the <i>absence</i> of clinically evident axillary lymph node metastasis.
N3	Metastases to ipsilateral infraclavicular lymph node(s) with or without axillary lymph node involvement, or in clinically apparent* ipsilateral internal mammary lymph node(s) and in the <i>presence</i> of clinically evident axillary lymph node metastasis; or metastasis in ipsilateral supraclavicular lymph node(s) with or without axillary or internal mammary lymph node involvement.
N3a	Metastasis in ipsilateral infraclavicular lymph node(s).
N3b	Metastasis in ipsilateral internal mammary lymph node(s) and axillary lymph node(s).
N3c	Metastasis in ipsilateral supraclavicular lymph node(s).
(*Note: <i>Clinically apparent</i> is defined as detected by imaging studies (excluding lymphoscintigraphy) or by clinical examination or grossly visible pathologically.)	

Definition of TNM - Distant Metastasis (M)	
AJCC, 2002	
MX	Distant metastasis cannot be assessed.
M0	No distant metastasis.
M1	Distant metastasis.

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CAP Cancer Protocols and Checklists

Breast

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Lymph Nodes & Spleen Hematopathology

Section 1 - Lymph Nodes

Authors: Brent Wood, MD PhD, Harvey Greisman MD PhD, Jonathan Fromm MD PhD, Sindhu Cherian MD & Dan Sabath, MD PhD

Section 2 - CAP Cancer Protocols and Checklists

Including: Bone Marrow, Gastrointestinal Lymphomas, Hodgkin Lymphoma, Non-Hodgkin Lymphoma

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Lymph Nodes

Brent Wood, MD PhD, Harvey Greisman MD PhD, Jonathan Fromm MD PhD, Sindhu Cherian MD & Dan Sabath, MD PhD

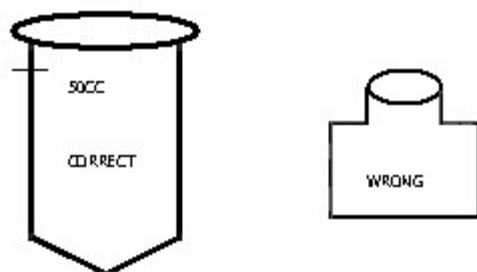
Lymph nodes (LN) are commonly received as fresh specimens from the ORs or clinics. Appropriate handling is necessary to obtain the clinically relevant information.

GROSS DESCRIPTION: NUMBER, SIZE AND APPEARANCE (NECROSIS, NODULES, ETC.)

When the LN is received, obtaining the clinical history is critical. For example, unless there is a reason to suspect lymphoma, an LN biopsy from the axilla in a woman with breast carcinoma **does not** require hematopathology (HP) evaluation and should be submitted only for routine histology, as should a cervical lymph node from a patient with carcinoma of the head and neck.

For cases in which the clinical history is "rule out lymphoma" or the frozen section/touch prep appearance is suggestive of lymphoma, do the following: (Note that a similar procedure should be used for other tissues in which the history is "rule out lymphoma", e.g., spleen.)

- **Submit tissue for flow cytometry.** Representative pieces (at least two small pea-sized selections from different areas of the node) should be placed in cell surface marker (RPMI) media. RPMI media comes in the 50cc conical tubes and will preserve cell viability for flow cytometric evaluation.
 - **DO NOT** use the small glass vials containing DNA flow cytometry media, which will compromise the specimen (see figure).



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- **Perform touch preparations by imprinting the cut surface of the lymph node (or other tissue) on a glass slide**, and allow at least one of these to air-dry for Wright-Giemsa staining in the HP lab (NW225).
- **Submit thinly-sliced, well-fixed tissue for routine histology at the same time.** The flow cytometric results are available within several hours and, thus, the inability to get sections through on the day the node is received slows down the HP work flow and unnecessarily delays diagnosis. A single, thin pilot section may be submitted if the specimen is received late (i.e., after 12PM) and fixation is a concern.
- **Extra tissue.** For large biopsy specimens or resections, where more diagnostic tissue is available than is needed for paraffin sections, place one or more fragments of extra tissue in a second tube of RPMI. This tissue will be cryopreserved in the HP lab and will be used for additional clinical/diagnostic testing.

Cases in which the clinical history is uncertain or unavailable should be handled as follows:

- **The sample in RPMI media should be promptly delivered to HP (NW225)** and the fellow/attending notified that the specimen is to "set up & hold."
- **Touch Preparations - air dried and formalin or alcohol fixed - should be evaluated.** Deliver the unstained air dried slides to HP for Wright-Giemsa staining. Evaluate the H&E stained fixed Touch Preps at this time with the fellow/attending in HP. The cytologic features may prompt them to evaluate the specimen by flow cytometry or to determine that the process is non-hematopoietic and cancel the work up.
- **Prepare one block for processing on the day the specimen is received.** Place the thinly sliced tissue that will be adequately fixed in a green cassette (RUSH). The slides should come out first thing the next morning and be promptly delivered to HP. For "set up and hold" cases, a decision as to whether or not to perform flow cytometry on the specimen can be made. If fixation is a concern (on specimens received after 12PM), a single, thin pilot section may be submitted.

ADDITIONAL CONCERNS

- Needle biopsies should be evaluated by HP if the specimen is too scanty for triage in the usual fashion.
- Molecular studies can be performed on the tissue submitted for flow cytometry or from paraffin-embedded tissue, although the tissue submitted for flow cytometry is preferred. (Routine submission of fresh tissue to be frozen is usually unnecessary.)
- Cases inappropriate for flow cytometric/cell surface marker work up include:
 - Granulomatous disease, where the lymphoid component appears clearly reactive.
- Note that non-hematopoietic neoplasms were inappropriate for flow cytometry until recently, but now some may be identified by flow.
- Some laboratories prefer B5 fixation for lymph nodes. However, B5 contains heavy metals and represents a medical waste disposal problem, and the quality of histology is generally not superior to well prepared formalin-fixed sections. In addition, B5 fixed tissue is not appropriate for most molecular studies. Consequently, there is no need to submit tissue in B5 fixative.

REPORTS

- If flow cytometry is performed, HP will generate a report. The H&E slides on these cases should be reviewed with the HP fellow/attending prior to signing out the case. The surgical pathology (SU-) report should give the diagnosis and reference the HP case number.
- If flow cytometry is not performed, the report needs a microscopic description and a detailed comment. Deliver the report to HP fellow for further modifications prior to delivery to the attending. IHC studies also may be required. Contact the HP fellow/attending on service to determine whether additional studies are needed and for guidance on preparing the final report. If HP will sign out the case, arrange to review the case with the HP attending.
- Note that in the UW Hematopathology Laboratory, classification of lymphoid and myeloid neoplasms is done according to the WHO classification system. (Jaffe, ES, et al. *Pathology and Genetics of Tumours of the Hematopoietic and Lymphoid Tissues*. IARC Press, Lyon, 2001)

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Hematopathology

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Bone & Soft Tissue

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Section 3 - Bone & Joints

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Section 4 - Revision Total Joint Arthroplasty

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Processing & Reporting Bone & Soft Tissue Tumors

Brian Rubin, MD PhD

GROSS DESCRIPTION AND PROCESSING OF SPECIMENS

- Note whether specimen was received fresh or in formalin when it arrived in pathology.
- Note location of lesion.
- Do your best to determine the type of procedure (excisional biopsy, simple or local excision, wide local excision, radical excision, amputation, etc.).
- Take gross photographs (and radiographs of any specimen with bone) for each tumor. It will probably be necessary to take photographs after the specimen is cut so that the relation of tumor to gross structures can be demonstrated. **Gross photographs are an essential part of pathologic documentation and are also necessary for teaching. Please, please, please take good gross photographs.**
- Note the appearance and texture of the cut surface, e.g. homogeneous or heterogeneous, color, firm/soft, fatty, gelatinous, necrotic, calcified, hemorrhagic, etc. Section the tumor at 1 cm intervals. Please place at least one, preferably a couple, of thin sections in a separate container of formalin immediately upon sectioning. These are the "quick fix" specimens -- see below. This is also the time to take tissue for cytogenetics and electron microscopy -- [see below](#). Prior to submitting any sections for histological analysis, please fix all well differentiated fatty lesions in a large volume of formalin for 24 hours after sectioning at 1 cm intervals. This will make it easier to cut thin sections for processing and the tissue will look better under the microscope. It's best if the sections can sit in cassettes in formalin for several hours before processing. **Please try to keep the specimen in one piece or in a couple of large pieces; cut in the same plane of section as much as possible**, such that the specimen can be reconstructed if necessary if there are questions/concerns about inaccurate/incomplete gross documentation. Diagrams are often useful to document complex specimens and can be used to designate the location of tissue blocks.
- Note all components of the specimen (skin, subcutaneous tissue, muscles, bones, organs, neurovascular bundles, and the relationship of each of these components to the tumor/lesion).
- Note the depth of the tumor (dermal, subcutaneous, fascial, subfascial, intramuscular, visceral).
- **Measure the size of the tumor in centimeters in three dimensions.**
- Note the presence or absence of apparent gross necrosis and the approximate percentage of the lesion that is involved.
- Note the presence or absence of previous biopsy scar, with dimensions and relationship to present resection margins.
- Note involvement or invasion of major structures, e.g. nerve, bone, major blood vessels, organs.
- Note the presence of satellite nodules and their size, relationship to the main mass and margins.
- Note the presence and number of any lymph nodes.
- Measure the minimal distance to all margins and note the quality of the margin (infiltrative or circumscribed/encapsulated). All margins less than 2 cm should be specified in the gross report. Most specimens have six margins: superficial/deep, proximal/distal, and medial/lateral. If a margin consists of a fascial layer, periosteum, or other anatomical barrier, eg. diaphragm, this should be specified in the gross report. It is sufficient to say that the distance of the tumor from the margin is greater than 2 cm if this is true.

Sections: in general, bone and ST specimens can be submitted in a dozen cassettes or less. **If you are planning to submit more than 20 cassettes, please page an attending pathologist before doing so.**

- o One section of the biopsy scar
- o Approximately one section of tumor/cm for tumors < 4 cm; one section of tumor/2 cm for tumors > 4 cm (minimum of 5 sections for tumors > 4 cm). **Sample all areas of tumor that look different grossly.** Conversely, if the tumor all looks the same, use common sense -- there's no need to submit 20 sections of a completely homogeneous 40 cm liposarcoma (6-8 would be fine; alternatively, put 4 small sections from different parts of the tumor in each of 5 cassettes). Submit one section demonstrating transition/invasion by tumor of all normal tissues including bones and parenchymal organs. **Important -- Please try and process quick fix section the day the specimen arrives. Show it to an attending as soon as possible so immunoperoxidase studies can be ordered so that they will be ready for signout. This will help in avoiding delayed signouts.** Also, please submit a section of tumor adjacent to the tumor submitted for cytogenetic analysis, electron microscopy, etc. and designate it as such in the section key.
- o One section of satellite nodules if present -- not necessary to sample all of them if there are many.
- o One section of tumor involved by gross necrosis (with transition from viable to necrotic tissue). For obvious reasons, never submit more than one block of gross necrosis. On occasion, a tumor is subtotally necrotic and is usually surrounded by a fibrous capsule or there is just a biopsy cavity. In this situation, it may be necessary to submit a half dozen blocks of the capsule to try and identify residual/viable tumor.
- o If present, one section of each grossly uninvolved lymph node should be submitted for histology. Multiple lymph nodes (up to four) can be placed in each cassette.
- o All margins less than 5 cm from the tumor should be sampled as **perpendicular margins** where the tumor comes closest to the margin. **Never take an en face margin with a bone or ST tumor.** Always include tumor in the margin section when possible. If tumor is included in the margin section, one section can be subtracted from the tumor sampling above. **Note** -- if the tumor is angiosarcoma or epithelioid sarcoma, then all margins, including those 5 cm and greater from any apparent tumor, should be sampled since these tumors can be inapparent grossly.

SPECIAL STUDIES (CYTOGENETICS, EM, DNA FLOW CYTOMETRY, AND RESEARCH TISSUE)

Cytogenetics: Take tissue for cytogenetics for all bone and ST tumors. **Using a clean (new) scalpel blade,** submit a small section of tumor (about 0.5 cm³) and cut into smaller pieces and place in cytogenetics medium. Note the differential diagnosis and whether or not the tumor has had either radiation or chemotherapy on the cytogenetics form. On occasion, there may be two grossly distinct areas in a tumor (e.g., a dedifferentiated nodule in a dedifferentiated liposarcoma) and it is important to submit both areas for cytogenetic analysis; accurately labeled so correlation can be made between the karyotype and the histology.

Electron Microscopy: Take tissue for electron microscopy for all poorly differentiated bone and ST tumors; i.e, those tumors that are not obviously well-differentiated fat or cartilage, etc. Have the specimen held in the EM lab until after immunohistochemistry is performed. Please take only a tiny (about 0.3 cm³) portion of tumor, cut into tiny cubes (0.05 cm³), and place immediately in EM fixative (should be available from the pathology assistant). **Don't ever submit large chunks of tumor for EM -- rapid fixation is absolutely essential for good results.**

DNA Flow Cytometry: It is not necessary to take fresh tissue for DNA flow cytometry unless explicitly asked for by the submitting physician. A small piece of tissue (0.1 cm³) should be taken and placed in the appropriate medium (DNA flow medium not cell surface flow medium).

Frozen Tissue (special studies): Please call (8-5024) or page (989-7207) for all bone and soft tissue tumors. He will come and assist in snap freezing lesional tissue.

Important: Any tissue taken for special studies should be taken from the best preserved portion of the tumor away from capsule or any tumor necrosis and uninked, if possible. Any tissue taken for special studies/research should be documented in the gross report e.g.: "A portion of tumor was taken for cytogenetics (0.5 cm³), EM (0.3 cm³), and snap freeze (1 cm³)".

SPECIAL PROCEDURES FOR PROCESSING BONE SPECIMENS

Any bone that is involved by tumor should be radiographed (in the autopsy room) prior to sectioning. This is to determine the best plane of section to cut the specimen. If there is no evidence of extra-osseous extension, the soft tissue can be dissected free. If there is extraosseous extension, then all of the soft tissue except in the area of tumor involvement is dissected free. The specimen can be fixed for a few hours to firm up the soft tissue prior to cutting on the bandsaw. If there is no evidence of extension across the joint space grossly, or radiographically, the joint space may be cut through. If the tumor does involve the joint space, leave the joint intact and cut across the adjacent bone in an uninvolved area. The center of tumor (epiphysis, metaphysis, diaphysis, intramedullary, periosteal), erosion of cortex, extension into soft tissue (compression or true invasion), extension through epiphyseal plate, extension into or across joint space, vascular involvement, skip metastases, distance from each margin should be noted.

The pathology assistant will help everyone cut the bone specimens and has equipment to do this. Residents are welcome to cut bones themselves but check with the pathology assistant first, to get oriented with the equipment. The general principle is to cut the specimen into thin pieces, fix them overnight, and then cut them into even smaller, cassette size pieces, which are then placed in decal solution. Never decalcify large specimens in their entirety. All tumors should be sectioned in three planes (X, Y, and Z) to determine the maximum extent of involvement by tumor in each plane of section. The thin sections are good for gross photography since the tumor can be seen well. In addition, the thin sections can be placed on plastic wrap and photocopied, and /or radiographs can be taken. Sections can be documented directly (draw grid) on the photocopies or radiographs and then stored permanently or incorporated into the gross reports

- The histology lab will help decalcify the specimens but **it is the resident's responsibility to know when they are submitted and determine the correct sectioning of the specimen.** Most bone specimens should be decalcified in 24-48 hours. If it has taken longer than 1 week to process and signout a bone specimen, then it has taken too long. On occasion, specimens with dramatic cortical thickening might take a bit longer to decalcify.
- **Important:** Please try and process at least one section of tumor that has received minimal or no decalcification. This is for immunoperoxidase studies, since decalcification can result in loss of immunogenicity. The section need not be big (0.5 cm is large enough) and a soft area can be identified by probing around lightly with a scalpel blade. If the entire specimen is rock hard/calcified, then it is most likely that immunoperoxidase studies won't need to be done anyway. Show the section to an attending as soon as possible so immunoperoxidase studies can be ordered, if necessary, so that they will be ready for signout.

SPECIAL NOTES ABOUT BIOPSY SPECIMENS

The trend in pathology is to try and do more with less which is particularly a problem with bone and ST specimens. Ideally, there will be sufficient tissue to divide each biopsy for H&E, immunoperoxidase studies, cytogenetics, and EM. This means that there should be at least two cores of tissue to divide for the different studies.

- Always take at least one core for H&E/immunoperoxidase studies. If there is tissue left, please trim about 1/3 of a core for EM and 2/3 of a core for cytogenetics. No core biopsies will be submitted to the tumor bank.
- At the time of processing, please order three H&E levels and 12 unstained slides for immunoperoxidase studies. This is to promote rapid turn around time as well as minimize tissue waste.
- Bone biopsies should be fixed for 2-3 hours in formalin and then decalcified before processing (usually overnight is enough for biopsies). For bone biopsies, determine whether the specimen is a core or curettings.
- If a bone biopsy has been submitted for metabolic or morphometric studies, don't do anything with it and page Brian Rubin immediately (beeper 989-7207). These specimens require special care.

SAMPLE DICTATION FOR BIOPSY

Received fresh labeled with the patient's name and unit number and "femur lesion" are multiple irregular fragments of tan/brown tissue with minute areas of irregular bone, measuring in aggregate 1 x 1 x 0.5 cm (the largest fragment measuring 0.4 cm in size). Frozen section examination is performed on a representative section. Tissue is apportioned for snap freezing, electron microscopy, and cytogenetics. The remainder of the tissue is fixed in formalin and then decalcified.

Cassette 1: Frozen section remnant, entirely submitted.

Cassette 2 - 3: Remainder of specimen, entirely submitted.

SAMPLE DICTATION FOR BIGS SPECIMEN

Received fresh labeled with the patient's name and unit number and "thigh mass" is a 15 x 10 x 9 cm complex resection specimen. There are two attached sutures designated "proximal" and "lateral". The superficial surface is covered by a skin ellipse (15 x 10 cm) with a centrally located, well-healed 5 cm surgical scar. The deep portion of the specimen consists of skeletal muscle (15 x 10 x 6 cm) bounded by fascia. 2 cm deep to the surgical scar is a well-demarcated fleshy, tan mass (6 x 6 x 4 cm) that is centered within the skeletal muscle but also involves the subcutaneous adipose tissue. The tumor extends to within 1.5 cm of the deep margin, 2 cm of the lateral margin, 2 cm of the medial margin, 3 cm of the proximal margin, and 3 cm of the distal margin. The tumor is focally hemorrhagic and approximately 20% of the tumor is grossly necrotic and cystic. A portion of tumor was taken for cytogenetics (0.5 cm³), EM (0.1 cm³), and special studies (0.1 cm³).

Cassette #1: Tumor, quick fix, representative sections

Cassette #2: Tumor adjacent to area submitted for EM, cytogenetics, and special studies, 1 fragment

Cassette #3: Tumor, representative sections including transition to grossly necrotic area, 2 fragments

Cassette #4: Tumor with transition to skeletal muscle, representative section, 1 fragment

Cassette #5: Tumor with transition to subcutaneous adipose tissue, representative section, 1 fragment

Cassette #6: Skin with scar, representative section, 1 fragment

Cassette #7: Proximal margin, perpendicular section, 1 fragment

Cassette #8: Distal margin, perpendicular section, 1 fragment

Cassette #9: Medial margin, perpendicular section, 1 fragment

Cassette #10: Lateral margin, perpendicular section, 1 fragment

Cassette #11: Deep margin, perpendicular section, 1 fragment

SAMPLE DICTATION OF BONE TUMOR

Received fresh labeled with the patient's name, unit number, and "left distal femur" is an above the knee amputation with disarticulation of the knee (12 x 9 x 7 cm) . The distal femur is 12 cm in length and surrounded by skeletal muscle. Centered within the metaphysis is a tan/yellow tumor (7.8 x 7 x 7 cm) that occupies the majority of the medullary cavity. The tumor appears to be entirely viable without gross areas of necrosis or hemorrhage. The tumor invades through the cortex medially, laterally, anteriorly, and posteriorly, and extends into soft tissue medially to form a soft tissue mass (2 x 1.8 x 0.4 cm). The tumor does not grossly involve the joint space. The tumor is located 3.5 cm from the proximal surgical resection margin, 0.4 cm from the posterior and lateral margins, and 0.1 cm from the anterior and medial margins. The tumor is 1 cm from the distal resection margin which consists of the grossly unremarkable cartilage surface of the distal femur. There is an attached skin ellipse over the anterior/medial portion of the specimen, measuring 9.3 x 1.1 cm, with a centrally located well-healed surgical scar measuring 7.5 cm. There is a hemorrhagic biopsy cavity (1 x 1 x 0.6 cm) located 4.5 cm deep to the skin surface and adjacent to the tumor. The femoral artery and accompanying nerves and vein are not present. The specimen is radiographed. A diagram is prepared with the location of sections marked. Sections containing bone are fixed and decalcified prior to submission.

Cassette 1-10: Complete cross section of tumor including relationship to cortex, submitted from proximal to distal, representative section(s)

Cassette 11: Tumor and medial margin including soft tissue extension, perpendicular

Cassette 12: Tumor and lateral margin, perpendicular section

Cassette 13: Tumor and posterior margin, perpendicular section

Cassette 14: Tumor and anterior margin, perpendicular section

Cassette 15: Bone at proximal margin, perpendicular section

Cassette 16: Bone and cartilage at distal margin, perpendicular section

Cassette 17: Soft tissue at proximal margin, perpendicular section

Cassette 18: Soft tissue at proximal margin, perpendicular section

Cassette 19: Skin with scar, representative section(s)

Cassette 20: Biopsy site, representative section(s).

Notes: Some specimens will be more complex but the approach is the same. Keep the gross description simple and include only the pertinent information. If you don't understand the specimen then don't cut it up. Call me or the surgeon who resected the specimen for orientation and advice on processing. Please let me know if any of the above is not clear. I am always available to go to the gross or frozen section rooms and I am happy to assist in selection of tissues for special studies, processing of specimens or whatever. I would prefer to see a specimen before it has been hacked to pieces. **It's probably a good idea for those of you with less experience to let me go over the specimen with you before it is processed.**

THE FOLLOWING INFORMATION SHOULD BE REPORTED IN THE FINAL DIAGNOSIS

- **Histologic type:** Use the WHO system when possible. Since it excludes a large number of specific tumor types, we will add these as necessary. I prefer the term unclassified sarcoma to MFH with the exception of MFH of bone, which is a distinct entity.
- **Maximal dimension of tumor (in cm)**
- **Histologic Grade:** For primary, untreated sarcomas, use the French Federation of Cancer Centers Sarcoma Group (FNCLCC) system for ST tumors. Grade in the FNCLCC system is based on three parameters: differentiation, mitotic activity, and necrosis. These can be summarized as follows:
 - *Tumor Differentiation* -- See [table 1](#) in the paper by [Guillou et al \(J Clin Oncol 15:350-62, 1997\)](#) to give you a feel for what is meant by tumor differentiation.
 - Score 1: Sarcomas closely resembling normal, adult mesenchymal tissue

- Score 2: Sarcomas of certain histologic type.
- Score 3: Synovial sarcomas, embryonal sarcomas, undifferentiated sarcomas and sarcomas of doubtful tumor type.
- o *Mitosis Count*: The count is made in the most mitotically active area in ten successive high power fields (HPFs) (a high-power field X 400 = 0.1734 mm²)(use the blue 40X objective). 10 high power fields in 5 different areas should be counted (50 fields total) and the highest count should be used.
 - Score 1: 0-9 mitoses per ten HPFs
 - Score 2: 10-19 mitoses per ten HPFs
 - Score 3: >20 mitoses per ten HPFs
- o *Tumor Necrosis*:
 - Score 0: no tumor necrosis on any examined slides
 - Score 1: less than 50% tumor necrosis for all the examined slides
 - Score 2: more than 50% tumor necrosis on the examined slides
- o *Grade* (based on the sum of all three scores from above):
 - Grade 1: a total of 2-3
 - Grade 2: a total of 4-5
 - Grade 3: a total of 6-8

Correct grading assumes that the tumor has been adequately sampled (see section on processing).

Bone specimens are more problematic to grade. In general, I follow the Mayo Clinic guidelines and combine their grades III and IV into grade III when applicable. These guidelines are in Dr. Dahlin's book, which is in the resident library. By far the most important consideration in bone tumors is to arrive at the right diagnosis/correct classification. Grading is usually not an important issue with the biggest exception being the grading of chondrosarcomas.

- **Histologic Evidence of a Precursor Lesion:** This is only seen in the case of a neurofibroma gone bad resulting in MPNST or an enchondroma gone bad resulting in chondrosarcoma. There are no other bone and ST precursor lesions that have been identified.
- **Lymph Node Status:** Rarely an issue.
- **Results of special studies:**
 - o *Immunohistochemistry*: Give raw results (+ve or -ve) of each antibody and you're your interpretation (e.g., consistent with the diagnosis of leiomyosarcoma)
 - o *Electron Microscopy*: The current system is to report the results in the section above the final diagnosis. I like to say something like, "The results of electron microscopic analysis support the above diagnosis (see separate section above for details)."
 - o *Cytogenetics and flow are reported separately.*
- **Mitotic Rate:** Expressed as above in grading: x mitotic figures/10HPF from the most mitotically active area of the tumor
- **Extent of Necrosis:** See grading above
- **Angiolymphatic Invasion:** When present
- **Treatment Response:** This is a difficult area but generally I comment on the approximate percentage of viable cells (e.g. – scattered, 10%, 25%, 50%, 75%, 100%). The resection specimen should always be compared with the pre-treatment biopsy.
- **Margins:** Any margin less than 2 cm from the tumor should be specified in terms of location and distance. Margins > 2 cm need to be specified as to location.

EXAMPLE

Smooth muscle actin -- diffusely and strongly positive
Desmin -- focally and strongly positive
S-100 protein -- negative

IHC Interpretation: Immunohistochemical studies performed on paraffin embedded sections reveal the tumor cells to be positive for smooth muscle actin and desmin, and negative for S-100 protein. These results support the above diagnosis of pleomorphic leiomyosarcoma.

FINAL DIAGNOSIS: Thigh, left, tumor, radical resection: **Pleomorphic Leiomyosarcoma**, 12.5 cm. The tumor grade is FNCLCC grade 3 of 3 (high-grade). Mitotic figures number up to 23/10 high power fields. Approximately 20% of the tumor is necrotic. Vascular invasion is identified. The tumor extends to within 1.5 cm of the superficial margin, 1.0 cm of the lateral margin (bounded by fascia), 0.5 cm of the deep margin, and is > 2cm from the proximal, distal, and medial margins.

REFERENCE

 [Guillou L, et al:](#) Comparative Study of the National Cancer Institute and French Federation of Cancer Centers Sarcoma Group Grading Systems in a Population of 410 Adult Patients with Soft Tissue Sarcoma. *J Clin Oncology* 1997; 15:350-362.

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Amputations & Large Resections

Brian Rubin, MD PhD

The most common reasons for amputations are peripheral vascular disease, trauma, and occasionally tumors. Some amputation specimens may be requested by the patient (e.g. some religions require burial of the limb).

GENERAL GROSS DESCRIPTION

The description of all amputations includes the following:

Structures Present	Left lower leg below the knee amputation, right foot, left index finger, etc. Dimensions of each structure (e.g. upper leg, lower leg, foot) including length and maximum circumference of limbs.
Type of Procedure	Disarticulation (cartilage covered joint surface present) vs. amputation (exposed bone surface present)
Type of Resection Margin	e.g. disarticulated femoral head, amputation of the third metacarpal, diaphysis of femur, 10 cm from distal surface of medial femoral condyle. Smooth (surgical) or irregular (traumatic) resection margin.
Soft Tissue at Resection Margin	Condition (e.g. grossly viable vs necrotic or ulcerated). Distance of skin and soft tissue from bony resection margin.
Skin	Color, lesions (ulcers, areas of discoloration, bruising, gangrene) or identifying marks (e.g. scars, tattoos).
Lesions	Bone fractures, blood vessels (atherosclerosis, thrombosis), osteomyelitis, tumor (if present), previous amputation sites.
Prior Surgical Procedures	Amputations, vascular grafts, etc.

TRAUMATIC AMPUTATIONS

Traumatic amputations may involve litigation and the pathologic examination may become legal evidence. It is helpful to photograph such specimens for documentation. Process as described for amputations for vascular insufficiency. The presence and extent of peripheral vascular disease may be of clinical value if present.

Digits – Non-Tumor

Fingers and toes are usually removed due to vascular insufficiency (toes) or trauma (usually fingers).

1. Describe including the features listed above.
2. Submit one section of soft tissue margin and an additional section of any skin lesions.
3. Fix entire specimen overnight. Decalcify the following day (N.B.: All decalcification procedures must be documented in the gross description). Take one section of bone at the resection margin and an additional section of bone if there is a question of osteomyelitis (e.g. bone below a deep ulcer bed).

Microscopic Sections

Skin and Soft Tissue	One section of margin and additional section(s) to evaluate any skin lesions
Bone	One section of the resection margin. Additional section(s) of bone beneath deep ulcers if there is a question of osteomyelitis.

Sample Dictation

Received fresh labeled with the patient's name and unit number and "toes" are two digits amputated through the first metatarsal bone with a smooth resection margin and measuring 2 x 2 x 1.5 cm and 1.5 x 1.5 x 1 cm. The larger digit has a deep ulcer on the plantar surface (1 x 1 cm) that grossly appears to extend to the underlying bone. The skin of the smaller digit has a purple/black color, but no ulceration is present. The nails are unremarkable. The resection margins consist of unremarkable bone and soft tissue. The bone is fixed and decalcified prior to submission.

Cassette #1: Larger digit, ulcer, representative section(s).

Cassette #2: Larger digit, skin at margin, representative section(s).

Cassette #3: Larger digit, bone below ulcer, representative section(s).

Cassette #4: Larger digit, bone at margin, representative section(s).

Cassette #5: Smaller digit, representative skin and soft tissue at tip, representative section(s).

Cassette #6: Smaller digit, skin at margin, representative section(s).

Cassette #7: Smaller digit, bone at margin, representative section(s).

Lower Extremity – Non-Tumor

Vascular Insufficiency

Vascular insufficiency is the most common reason for amputations. Often there will be prior amputations (e.g. several toes) and skin lesions (ulcers or frank gangrene). To document the disease process, dissect and examine the vessels of the leg.

Dissection of the Vessels of the Lower Extremity

1. Make a skin incision that starts just behind the medial malleolus and extends proximally in an oblique manner to reach the posterior aspect of the leg and thence straight upwards to the line of resection.
2. Identify the posterior tibial neurovascular bundle behind the medial malleolus. Sever the distal ends and proceed to strip the vessels upwards, dissecting the muscle and subcutaneous tissue away from the vessels. Stop when the junction of the posterior tibial and the popliteal arteries is reached at the interosseous membrane between the tibia and fibula.
3. Return to the ankle region and extend the original incision distally and then laterally to traverse the dorsum of the foot just distal to the ankle. Reflect the skin flap to expose the anterior compartment of the leg.
4. Identify the anterior tibial neurovascular bundle at the ankle (the anterior tibial artery becomes the dorsalis pedis artery and traverses the dorsum of the foot at this site). Sever the distal ends and reflect proximally as for the posterior tibial. When the interosseous membrane is reached, dissect bluntly around the vessel to free it. Then return to the posterior aspect of the leg and pull the anterior tibial vessels through the interosseous membrane.
5. Complete the removal of the vessels by continuing the reflection of the popliteal artery to the lines of resection.

Usually the vessels will be densely calcified and will require decalcification before cutting.

Processing the Specimen

1. Record the measurements and features described in the first section.
2. Dissect out the anterior and posterior vessels and any grafts if present (see above). If vein grafts are present, describe their anatomic relationships to other vessels, the status of the anastomosis (intact, patent, obstructed) and the presence or absence of thrombi.
3. Take skin and soft tissue sections from the margin and from any lesions present. Take a cross section of the soft tissue of one of the grossly normal toes to look for small vessel disease. Bone sections need not be taken if there are no gross lesions. If there is a suspicion of bone involvement (osteomyelitis) that section of bone is resected with the bone saw for fixation and decalcification. The metatarsal-phalangeal joint of the great toe is dissected open and examined for evidence of joint disease (see section on "Synovium" for gross differential diagnosis of joint disease). The marrow can be removed from the cut section of the bone and prepared as for a rib marrow squeeze if there is a clinical suspicion of disease involving the marrow.
4. Fix the tissue sections and blood vessels in small formalin containers with appropriate labels (e.g. "anterior vessels and margin," "posterior vessels and skin lesion"). The remainder of the specimen is kept unfixed but refrigerated.
5. The following day the soft tissue is submitted for processing (one cassette of margin, cassette(s) of lesion(s), cassette of soft tissue of toe). The vessels are decalcified.
6. The following day the vessels and grafts are serially sectioned. Record the location and extent of occlusions (calcified plaque, thrombosis). Submit multiple cross sections in two separate cassettes from the anterior and from the posterior vessels of the areas of greatest occlusion. If a graft is present, submit areas of obstruction and the vein-artery anastomotic site.

Microscopic Sections

Skin and Soft Tissue	One section of margin and additional section(s) to evaluate any skin lesions.
Cross Section of Toe	One cross section (to evaluate small vessel disease).
Bone	Only submit section(s) of bone if there is a question of osteomyelitis or if bony lesions are present. The margin need not be submitted.
Vessels and Grafts	Submit one cassette each of anterior and posterior vessels showing area(s) of greatest occlusion. Submit area of greatest occlusion of grafts and the vein-artery anastomotic site.
Bone Marrow	Only submitted if there is a clinical suspicion of disease affecting the bone marrow.
Joint	Only submitted if there is clinical suspicion or gross evidence of disease affecting the joints (e.g. gout).

Sample Dictation

Received fresh labeled with the patient's name and unit number and "leg" is a right lower extremity amputated through the tibia and fibula with a smooth resection margin (length of leg 37 cm; circumference of calf 40 cm; foot 26 x 9 cm). The fourth and fifth digits have been previously amputated. The skin is diffusely mottled purple and red. There are ulcerations present on the lateral aspect of the foot (3 x 1 cm) and on the plantar surface of the great toe (1 x 1 cm). The anterior vessels are diffusely calcified with luminal obstructions of up to 80%. The posterior vessels are diffusely calcified with luminal

obstructions of up to 50%. The metatarsal-phalangeal joint of the great toe consists of smooth glistening white cartilage and is grossly unremarkable. The bone and soft tissue at the resection margin are unremarkable. A cross section of the third digit is fixed and decalcified prior to submission.

Cassette #1: Skin, ulcers, representative section(s).

Cassette #2: Skin and soft tissue at margin, representative section(s).

Cassette #3: Cross section of third digit, representative section(s).

Cassette #4: Anterior vessels, representative section(s).

Cassette #5: Posterior vessels, representative section(s).

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Bone & Joint

Brian Rubin, MD PhD

Bones are common surgical specimens that may be submitted after reconstructive or joint replacement surgery, as part of a larger soft tissue resection, to diagnose metabolic bone disease, or after resection of tumors primary to bone.

TOTAL JOINT ARTHROPLASTY (HIPS AND KNEES)

Bone, cartilage, and adjacent soft tissues are removed during artificial joint replacements, usually due to degenerative joint disease but also for rheumatoid arthritis, osteonecrosis, traumatic fractures, and pathologic fractures. Specimens are submitted for documentation and to exclude clinically unsuspected diseases (e.g. hemochromatosis, rheumatoid arthritis, gout, and rarely tumors such as metastatic prostate carcinoma, or multiple myeloma).

Processing the Specimen

1. Describe the number of fragments of bone (estimate if many), size in aggregate, range of sizes. Describe any recognizable portions of bone: femoral head (see next section), tibial plateau, femoral condyles.
2. Describe articular surface including color (usually white, black if ochronosis, brown/green if hemochromatosis), crystalline deposits (both gout and chondrocalcinosis will produce chalky white deposits), erosions or pits, or eburnation (= bone which is markedly thickened and smooth (like ivory) due to complete loss of the overlying cartilage - do not mistake eburnated bone for cartilage!). Describe subchondral cysts or osteophytes if present.
3. Describe the number of fragments of soft tissue (estimate if many), size in aggregate, range of sizes.
4. Describe the color and consistency of the soft tissue:
 - o normal = white, delicate, villous
 - o hemochromatosis = brown/green
 - o β 2 microglobulin amyloidosis = tan/yellow, firm, and homogenous
 - o pigmented villonodular synovitis = red/brown and shaggy (delicate villi with small nodules may be appreciated if the tissue is floated in saline). Necrotic foci may appear yellow due to the presence of histiocytes.
 - o gout or chondrocalcinosis = chalk white crystalline material
See the separate section on "synovium" for a more complete description and special processing of unusual specimens.
5. The bone is separated from the soft tissue. Submit one section of soft tissue including synovium if possible. Normal synovium will look like a thin delicate membrane. Fix the bone overnight in formalin and decalcify the following day. All decalcification procedures must be documented in the gross description.
6. Serially section through the decalcified bone to find the best diagnostic areas. One fragment of bone should include the junction of normal and abnormal cartilage and the other fragment should be from the periphery to include exostosis and/or pannus. The sections should be about 2 x 1 cm in size with the short axis perpendicular to the cartilage surface including 5 to 10 mm of subchondral bone.

If osteonecrosis is suspected, the entire specimen must be serially sectioned to look for the characteristic gross findings (see below). Submit sections to document the interface of normal and abnormal bone. Radiography of the specimen may be helpful to identify the area of necrotic bone.

SPECIAL STUDIES

Crystal disease: Chalky white deposits in soft tissue may be due to urate crystals (gout) or calcium pyrophosphate dihydrate crystals (= calcium pyrophosphate dihydrate deposition disease (CPPD) = pseudogout = chondrocalcinosis). Tissue must be saved in absolute (100%) alcohol because these crystals are soluble in aqueous solutions. The tissue must be hand processed and stained with an aqueous Wright stain. Crystals can also be visualized in unstained sections. See also Section One under "Microscopy" for a description of polarization.

Crystals sometimes survive routine processing in aqueous solutions but are lost in the final staining steps. Look for preserved crystals in tissue folds if present. An unstained slide may also be requested and examined under polarized light after deparaffinizing.

Crystals can also be examined directly by smearing the unfixed crystals on a slide or suspending in absolute alcohol as necessary (remember that they will dissolve in water). If the crystals are viewed using a compensating first order red filter under polarized light, uric acid can usually be distinguished from CPPD crystals. The crystals are aligned parallel to the line on the compensating filter. If not available in the pathology department, most rheumatologists will have such a microscope available for examination of synovial fluids. Crystals will polarize in properly fixed and stained histologic sections, but positive and negative birefringence cannot be reliably performed on fixed tissue.

Uric acid	Needle shaped; strong negative birefringence, bright yellow
CPPD crystals	Rhomboid; weakly positive birefringence, less bright and blue

Calcium oxalate crystals can be seen in bone, articular cartilage, and bone marrow in patients with primary (familial) oxalosis or secondary oxalosis usually secondary to chronic renal failure. The crystals are needle shaped, refractile, and are in radially arranged clusters. The crystals are polarizable. They can dissolve in formalin, but only after several days. The type of crystal can be identified by chemical analysis, x-ray diffraction, or electron diffraction.

If there is a suspicion of metastasis: Determine from the clinical history if there is a known primary. If not, additional studies may be warranted (e.g. snap freezing, EM, immunohistochemistry). Remove as much soft tissue as possible to avoid exposing potential tumor to decalcification.

GROSS DIFFERENTIAL DIAGNOSIS

Degenerative Joint Disease: The cartilage surface shows fibrillation and loss over the center of the femoral head or over the tibial plateau. The exposed bone becomes thickened and smoothly polished ("eburnated" or "like ivory") and can be mistaken for a cartilage surface. Fractures through articular bone result in subchondral cysts and collapse of the bone. The femoral head is often flattened and misshapen. Osteophytes commonly form around the edge of the articular surface. The soft tissue is relatively unaffected and may be fibrotic.

Rheumatoid arthritis: Patients usually undergo arthroplasty after significant secondary degenerative changes have occurred. Thus, most will show the changes of degenerative joint disease and features of rheumatoid arthritis may be subtle or absent. Findings characteristic of rheumatoid arthritis are an edematous hyperplastic synovium with growth over the cartilage surface to form a pannus.

Gout or CPPD: Chalky white crystalline deposits are present in soft tissue, cartilage, and sometimes erode bone. The synovium becomes fibrotic, thickened, and hyperplastic and forms a pannus overlying cartilage. It is usually not possible to distinguish gout from chondrocalcinosis grossly in mid-sized joints in which both are common. However, CPPD crystals may preferentially be found within the cartilage and uric acid crystals in periarticular soft tissue. Gout is much more common in small joints of the foot and hand. Neither commonly affects the hip.

Usually joint replacement is performed after significant secondary degenerative changes have occurred (see above).

Crystals should be saved in alcohol (see "Special Studies").

Osteonecrosis (Aseptic necrosis, avascular necrosis): Osteonecrosis of bone is a common cause of joint disease (approximately 10% of joint replacements) and is often bilateral. Patients are younger than the typical patient with degenerative joint disease (55 vs 67 years) and often have predisposing conditions such as steroid use, sickle cell disease, or alcoholism. The pathogenesis is poorly understood but is thought to result from ischemic infarction of subchondral bone.

There is a characteristic wedge shaped area of pale yellow necrotic bone below the cartilage surface. A band of hyperemia is often present below this area. Usually the overlying cartilage will have separated away from the bone. The infarcted bone may collapse with distortion of the cartilage and resultant degenerative changes. Radiographs of bone slices can be helpful to look for areas of abnormal mineralization.

Metastatic Disease: A joint replacement is sometimes performed to repair a known or suspected pathologic fracture, generally within the femur. The metastatic tumor may be subtle and only apparent after histologic examination of numerous sections. The bone destruction observed radiologically is usually produced by soluble factors produced by the tumor cells and not replacement of bone marrow by tumor per se. Therefore, in such cases histologic sampling of the fracture site is necessary to evaluate the presence of tumor.

If a pathologic fracture is strongly suspected clinically or grossly, and the primary site is unknown, consider taking tissue for special studies (e.g. snap freezing, EM).

Microscopic Sections

Soft Tissue	One section including any grossly recognizable synovium. If a metastatic deposit is suspected, submit as much soft material from the bone marrow as possible that will not need decalcification.
Bone	One section including the junction of normal and abnormal cartilage and one from the periphery. If osteonecrosis is known or suspected, submit one to two sections of necrotic bone including interface with normal bone.
Crystals	If crystals are present, submit one section fixed in absolute alcohol for special anaqueous processing. Order one H&E, one anaqueous Wright stain, and one unstained slide.

Sample Dictation:

Received fresh, labeled with the patient's name and unit number and "left total knee" are multiple fragments of bone (in aggregate 5 x 5 x 3 cm, largest 2 x 1 x 1 cm) and soft tissue (4 x 3 x 2 cm, largest 3.5 x 2 x 1 cm). The bone fragments include recognizable portions of the tibial plateau and femoral condyles. The articular surface is markedly roughened with areas of cartilage loss and eburnation of the bony surface. The soft tissue is tan/pink and includes fragments of meniscus. The bone is fixed and decalcified prior to submission.

Cassettes #1: bone with articular surface, representative section(s).

Cassette #2: soft tissue, representative section(s).

SPECIMENS WITH INTACT FEMORAL HEADS

1. The femoral head is cut into thirds, parallel to the long axis, with the bone saw. The central section must be thin, approximately 0.5 cm in width.
2. Describe the femoral head including dimensions, shape (flattened, round), cartilage surface (smooth and glistening, erosions, pits, eburnation of bone surface, fibrillation of cartilage, pannus formation), detachment of cartilage (as in osteonecrosis), presence of exostoses. Describe the quality of the bone (osteoporotic, sclerotic, pale as in osteonecrosis) and subchondral cysts.
3. Describe the resection margin including surface (flat and smooth if surgical, jagged and with medullary hemorrhage if fracture), quality of adjacent bone (soft may indicate a metastasis, osteoporotic, sclerotic). If the fracture site is grossly or clinically suspicious for a pathologic fracture, save as much soft tissue from this site as possible in a cassette without bone (to avoid tissue alterations associated with decalcification) and consider taking tissue for special studies (see above).
4. Describe soft tissue (see description above) and submit one cassette including synovium if possible.
5. Fix the femoral head in formalin overnight and decalcify the following day.

Microscopic Sections

Soft Tissue	One section including any grossly recognizable synovium.
Bone	One section including the junction of normal and abnormal cartilage and one from the periphery.
Fracture Site	Two representative sections in one cassette from the fracture site. If sufficient soft tissue (i.e. possible tumor) is present, submit an additional cassette of nondecalcified tissue.

Sample Dictation - Hip Replacement for Degenerative Joint Disease:

Received fresh labeled with the patient's name and unit number and "left hip" is a 5 x 5 x 4 cm flattened femoral head and attached neck with a smooth resection margin. The articular surface is covered by irregularly surfaced cartilage with areas of cartilage loss and eburnation of the underlying bone. Multiple peripheral osteophytes are present. The bone is fixed and then decalcified. Also received are multiple fragments of pink/tan fibrous tissue measuring in aggregate 3 x 3 x 2 cm. The bone is fixed and decalcified.

Cassette #1: Joint surface, representative section(s).

Cassette #2: Soft tissue, representative section(s).

Sample Dictation - Hip Replacement After Fracture

Received fresh labeled with the patient's name and unit number and "right hip" is a 5 x 5 x 3 cm round femoral head with a smooth white cartilage surface. The femoral neck resection margin is irregular and hemorrhagic. There are multiple smaller fragments of irregular bone measuring in aggregate 3 x 3 x 1 cm. There are no areas of soft tissue within the bone. The bone trabeculae are markedly thinned. The bone is fixed and then decalcified. Also received are multiple fragments of pink/tan fibrous tissue measuring in aggregate 3 x 3 x 2 cm. The bone is fixed and decalcified prior to submission.

Cassette #1: Fracture site, representative section(s).

Cassette #2: Joint surface, representative section(s).

Cassette #3: Soft tissue, representative section(s).

Sample Dictation - Hip Replacement for Avascular Necrosis

Received fresh labeled with the patient's name and unit number and "right hip" is a 4.5 x 4 x 4 cm deformed flattened femoral head with a smooth resection margin. There is a wedge-shaped area of pale yellow bone immediately beneath the cartilage surface measuring 2 x 2 x 1 cm with a red/brown border. The overlying cartilage is intact but has pulled away from this area leaving a gap. The sliced section is radiographed. The bone is fixed and then decalcified. The remainder of the cartilage surface is smooth and unremarkable. Also received are multiple fragments of pink/tan fibrous tissue measuring in aggregate 3 x 2 x 2 cm. The bone is fixed and decalcified prior to submission.

Cassettes #1 - 2: Area of probable necrosis, representative section(s).

Cassette #3: Joint surface, representative section(s).

Cassette #4: Soft tissue, representative section(s).

REVISION TOTAL JOINT ARTHROPLASTY

About 5% of prosthetic joints fail, either from mechanical loosening or due to infection. It may be difficult to clinically distinguish between these two possibilities as the presentation may be similar and false positive and negative culture results are possible. Prosthetic joints that have failed mechanically may be removed and replaced in the same procedure. If infection is present, drainage or removal of the prosthesis may be indicated and replacement may be delayed until after treatment. The most common acute pathogens are *S. epidermidis* and *S. aureus* with Gram negative bacilli being more common in later infections. A frozen section evaluation of periarticular soft tissue may be requested if infection is suspected (see "Operating Room Consultations").

Processing the Specimen

1. The specimen usually consists of small fragments of unidentifiable bone, fibrous soft tissue, and often fragments of bone cement. Bone cement is usually light brown, homogeneous in appearance, hard, and may be difficult to distinguish from bone. The soft tissue may be gray or black due to metallic debris.
2. Describe the number of fragments of bone (estimate if many), size in aggregate, range of sizes. Bone may not be present.
3. Describe the number of fragments of soft tissue (estimate if many), size in aggregate, range of sizes, color, presence of necrosis. If infection is suspected clinically or by gross examination, and cultures have not yet been sent, send tissue for bacterial culture.
4. The explanted prosthesis is described including number of parts, hip or joint prosthesis, identification markings (e.g. serial numbers, brand names), and the presence of any marked abnormalities (e.g. broken metal components, erosions, ridges, or pits in the articular surfaces).
5. The bone is separated from the soft tissue. Submit one section of soft tissue including synovium if possible. Fix the bone overnight in formalin and decalcify the following day. All decalcification procedures must be documented in the gross description.

Gross Differential Diagnosis

Detritic synovitis: Occasionally there will be an exuberant papillary proliferation of synovium with hemosiderin deposition in response to foreign material that grossly mimics pigmented villonodular synovitis. However, unlike PVNS, there will be a history of an artificial joint, foreign material is present, and the process usually is superficial and does not extend deeply into soft tissue.

Foreign Material from Implants: Numerous types of foreign material derived from the implant can be found around failed prostheses and include bone cement (with barium to make the material radio-opaque), metal fragments, polyethylene, methylmethacrylate, silicone, and ceramic (see "Noncellular Material in Histologic Sections"). The tissue may be black due to deposits of oxidized metal.

Infection: The soft tissue from infected joints may be necrotic and purulent. Cultures should be sent either by the surgeon or the pathologist. Some infections may not be apparent grossly.

Microscopic Sections

Soft tissue	One section including any grossly recognizable synovium.
Bone	One section.

Sample Dictation:

Received fresh labeled with the patient's name and unit number and "left hip" are multiple fragments of soft tissue and bone. There are five bone fragments, measuring in aggregate 3 x 2 x 2 cm. No articular surfaces are present. The bone is fixed and decalcified prior to submission. There are approximately 20 fragments of tan/white fibrous soft tissue without recognizable synovium.

Also received is a joint prosthesis consisting of an acetabular component consisting of a white prosthetic socket (6 x 6 x 4 cm) inscribed with "ABDC" and femoral component consisting of a metallic ball attached to a stem (15 x 3 x 2 cm). A fragment of brown bone cement with a smooth outer surface is also present (4 x 2 x 2 cm).

Cassette #1: Bone, representative section(s).

Cassette #2: Soft tissue, representative section(s).

CORE BIOPSY FOR ASEPTIC (AVASCULAR) NECROSIS

Cores of bone may be submitted from patients with clinical and radiologic osteonecrosis. These cores are taken through the femoral head and into the area of necrosis in order to promote revascularization ("decompression") and are generally used for treatment and not diagnosis. There should be an area of osteonecrosis at one edge of the biopsy. These core biopsies are fixed in formalin and then gently decalcified. If the specimen will not fit in a cassette in entirety, section the specimen longitudinally.

Biopsy, Metabolic Bone Disease

Needle or core bone biopsies are sometimes submitted from patients with metabolic bone disease (osteomalacia, osteoporosis, hyperparathyroidism, effects of long-term hemodialysis, etc) with a request for metabolic bone studies. A good review is [Rosenberg, A](#), The Pathology of Metabolic Bone Disease, *Radiologic Clinics of North America*, 29(1):19-36, 1991.

The evaluation of metabolic disease requires sectioning of nondecalcified bone, special stains, and morphometry. These techniques are generally performed by a specialty laboratory. The specialty laboratory will provide instructions as to the fixation and transportation of these specimens.

Incidental Ribs

Portions of ribs are often removed to perform thoracotomies or nephrectomies. The rib is usually 2 to 5 cm long and is rarely of diagnostic importance.

Specimen Processing

Ribs resected from patients without malignant disease and without other clinical indication for examination (e.g. a known hematologic disorder) do not require histologic examination and are submitted

as "gross only" specimens. There are two methods for examining all other specimens.

Decalcification Method: This method should be used for all patients with a history of lymphoma or other hematologic disorder (treat as a diagnostic bone marrow biopsy, see "Lymph nodes, spleen, and bone marrow"), malignancies that frequently metastasize to bone marrow (e.g. small cell lung carcinomas), or ribs with grossly evident or clinically suspected lesions.

1. The rib is described (measurements, color, gross identification as portion of rib) and fixed in formalin. Cartilage may be present at one end if near the costochondral junction. It will be homogeneously pale white, will cut easily with a razor blade, and will not be visible on x-ray.
2. If a gross lesion is present that is suspicious for metastatic disease, the specimen is radiographed, serially sectioned, and any soft tissue (i.e. potential tumor) removed prior to decalcification.
3. The remainder of the bone is gently decalcified. Grossly normal bones can be submitted as multiple sections in one cassette. If gross or radiographic lesions are present, submit them in a separate cassette. Do not submit grossly benign cartilage.

Rib Squeeze Method: The disadvantage of this method is that metastatic tumors and lymphomas may not be easily expressed from the bone marrow due to accompanying marrow fibrosis. However, often bone marrow involvement will have been investigated clinically before surgery is performed and the finding of malignancy in incidental ribs is very rare.

The advantage of this method is that it provides better histologic preservation of the bone marrow elements and does not delay the rib in processing. Thus this is the preferred method with the exceptions noted above.

1. The rib is described as above.
2. The specimen must be fresh and unfixed. Use the bone saw to cut a portion about 2 cm in length with marrow present at both ends of the specimen. Use a pliers to squeeze until marrow is expressed from both ends. Collect the marrow in formalin. If very little marrow can be expressed, the bone should be fixed and decalcified as described above. Order one H&E. The remainder of the rib is cut longitudinally and examined for gross lesions. Submit any lesions seen. Document in the gross description that the bone was **not** decalcified.

MENISCUS

Menisci are usually removed because of traumatic tears that interfere with articular movement. Occasionally joint mice (= loose bodies) may be removed during the same type of procedure. These are fragments of cartilage free in the joint space and often become ossified. The meniscus can also be affected by CPPD, and ochronosis (see gross differential diagnosis under "Synovium").

Processing the Specimen

1. Describe the specimen including size, color (normally white and glistening), texture (smooth, fibrillated), presence of tears.
2. If chalky white deposits are present, a portion of the specimen is processed in absolute ethanol to preserve crystals (see also "Synovium").
3. Submit representative sections in one cassette.

SYNOVIUM

Synovium may be biopsied for diagnostic purposes (e.g. inflammatory arthritis) or removed for the treatment of disease (e.g. pigmented villonodular synovitis or dialysis related amyloidosis).

Processing the Specimen

1. Record the aggregate dimensions, size range, and approximate number of fragments.
Describe the color and consistency of the synovium:
 - o normal = white, delicate, villous
 - o hemochromatosis = brown/green
 - o β 2 microglobulin amyloidosis = tan/yellow, firm, and homogenous
 - o pigmented villonodular synovitis = red/brown and shaggy (delicate villi with small nodules may be appreciated if the tissue is floated in saline). Necrotic foci may appear yellow due to the presence of histiocytes.
 - o gout or chondrocalcinosis = chalk white crystalline material

If **infection** is suspected and fresh tissue is received, confirm that cultures have been taken. If not, send sterile tissue to microbiology.

2. Submit up to two cassettes and order one level (H&E). Order special studies as indicated below for specific cases. If the specimen is a small biopsy, submit all the tissue and order three levels.

SPECIAL STUDIES

Crystal disease: Chalky white deposits may be present in synovium and representative sections must be fixed in absolute alcohol. See "Total Joint Arthroplasty", "Special Studies".

Amyloidosis: All tissue can be fixed in formalin. Amyloid can be diagnosed using a Congo Red stain and polarized light. Immunohistochemistry can be used to identify the type of amyloid present. Dialysis related amyloidosis of joints is due to β 2 microglobulin.

Infection: Fresh sterile tissue may be sent for culture.

GROSS DIFFERENTIAL DIAGNOSIS

Normal synovium: Normal synovium is glistening white with delicate villous projections.

Gout or CPPD: Chalky white or crystalline deposits are present and must be fixed in absolute alcohol. See "Total Joint Arthroplasty", "Special Studies" for information on how to process.

Pigmented villonodular synovitis (PVNS): The synovium is a rusty red color due to extensive hemosiderin deposition. Coarse villi with occasional attached nodules are present. These areas become more apparent when floated in saline and can be photographed well in this manner. There may be an abundance of tissue with areas of fibrosis. Current therapy may involve total synovectomy followed by radiation therapy. Special studies are not required.

Detritic synovitis: (changes occurring around an artificial joint) can appear very similar to PVNS (see "Revision Total Joint Arthroplasty").

Dialysis-related amyloidosis: There are characteristic yellow/tan plaques that may be superficial, run along tendons, or form large homogeneous nodules.

Synovial chondromatosis: Multiple small nodules of cartilage are present within the synovial tissue. The cartilage may need to be decalcified.

Hemochromatosis: The synovium can become hyperplastic and brown in color due to dense hemosiderin deposition. The appearance can mimic PVNS, but nodules are not present. The cartilage takes on a characteristic greenish-black appearance.

MICROSCOPIC SECTIONS

Synovium	Up to two cassettes. If the biopsy is small (only enough tissue for one cassette), order three levels.
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Sample Dictation:

Received fresh labeled with the patient's name, unit number, and "synovium right knee" are multiple fragments of reddish brown soft tissue measuring in aggregate 5 x 4 x 1 cm. Delicate villous projections and small nodules are present.

Cassettes 1 and 2: representative section(s).

CARPAL TUNNEL RELEASE (TENOSYNOVIUM)

Most patients present with idiopathic carpal tunnel syndrome and only a small fraction of these patients will show evidence of amyloid on microscopic examination. However, in renal dialysis patients carpal tunnel syndrome is very common and $\beta 2$ microglobulin amyloidosis is often present.

These specimens consist of synovium and soft tissue from around the tendons and nerves of the carpal tunnel that are removed during a carpal tunnel release procedure. The specimens may be processed in the same manner as synovium but are examined with one level.

INTERVERTEBRAL DISC MATERIAL

These specimens are derived from operations on herniated discs and will consist of small fragments of bone, nucleus pulposus, annulus fibrosus, and ligamentum flavum. These specimens are rarely of diagnostic importance. The specimen is fixed, decalcified, and one representative section is submitted.

If there is a question of metastatic disease, any soft tissue is dissected away and submitted without decalcification. If the primary site is unknown, and there is sufficient tissue, then consideration should be given to special studies (frozen tissue, EM).

If there is a question of infection, any soft tissue is dissected away and submitted without decalcification. If there is sufficient tissue, consideration should be given to sending tissue for cultures. Special stains may be helpful. *Aspergillus* can invade into cartilage without an inflammatory response and may not be detectable without fungal stains.

The value of examining "routine" disc specimens has been questioned ([Daftari TK, Levine J, Fischgrund JS, Herkowitz HN](#) Is pathology examination of disc specimens necessary after routine anterior cervical discectomy and fusion? *Spine* 1996; 21:2156, and [Grzybicki DM, Callaghan EJ, Raab SS](#) Cost-benefit value of microscopic examination of intervertebral discs. 1998; *J Neurosurg* 89:378-381). In the latter study, if cases with significant clinical histories were excluded (i.e. any indication for surgery other than a benign noninfectious indication for laminectomy), only 3 of 1071 (0.3%) specimens yielded a clinically significant unsuspected diagnosis. All three cases were epidural abscesses which were also diagnosed clinically in the perioperative period. Of 38 cases with a significant clinical history, 21 (55%) resulted in a

clinically significant pathologic diagnosis. Thus, **if an adequate clinical history is provided**, it may not be necessary to examine such specimens histologically.

ABDOMINAL FAT PAD BIOPSY FOR THE DIAGNOSIS OF AMYLOIDOSIS

There are several methods of sampling tissues to establish the diagnosis of systemic amyloidosis. Rectal biopsies are reported to be the most sensitive (97%) followed by fine needle aspiration of the abdominal fat pad (75%), oral biopsy (64%), and biopsy of the abdominal fat pad (50%). These latter biopsies can be either excisional or by core biopsy.

The tissue can be fixed in formalin and stained with Congo Red. Both false positive and false negative results have been reported. If there is sufficient tissue, some could be saved for EM which may be helpful in confirming a diagnosis. Immunohistochemical studies can be used to identify subtypes of amyloid.

The abdominal fat pad biopsy technique is not helpful in the evaluation of dialysis patients with β -2 microglobulin amyloidosis as this type of amyloid is preferentially found near joints.

REFERENCE

-  [Daftari TK et al:](#) Is pathology examination of disc specimens necessary after routine anterior cervical discectomy and fusion? *Spine* 1996; 21:2156.
-  [Grzybicki DM et al:](#) Cost-benefit value of microscopic examination of intervertebral discs. *J Neurosurg* 1998; 89:378-381.
-  [Rosenberg AE:](#) The pathology of metabolic bone disease. *Radiol Clin North Am* 1991; 29:19-36.

Revision Total Joint Arthroplasty

Larry True, MD

It is clinically difficult to differentiate between septic and aseptic loosening of a prosthesis. At the time of surgery for revising a joint arthroplasty, it is important for the surgeon to know whether there is histologic evidence of infection to provide a basis for deciding whether to install a new prosthetic joint. The criteria for diagnosing infection at the time of frozen section is:

- Whether there are greater than 5 neutrophils per high powered microscopic field (40X objective) in at least 5 separate microscopic fields, choosing the most cellular areas of the tissue samples for evaluation.
- Debris due to nuclear fragmentation is excluded.

REFERENCE

- [Della Valle CJ et al](#): Analysis of frozen sections of intraoperative specimens obtained at the time of reoperation after hip or knee resection arthroplasty for the treatment of infection. *J Bone Joint Surg Am* 1999; 81:684-9.
- [Feldman DS et al](#): The role of intraoperative frozen sections in revision total joint arthroplasty. *J Bone Joint Surg Am* 1995; 77:1807-13.
- [Lonner JH et al](#): The reliability of analysis of intraoperative frozen sections for identifying active infection during revision hip or knee arthroplasty. *J Bone Joint Surg Am* 1996; 78:1553-8.
- [Pandey R et al](#): An assessment of the histological criteria used to diagnose infection in hip revision arthroplasty tissues. *J Clin Pathol* 1999; 52:118-23.

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Cardiovascular System

Section 1 - Cardiovascular Surgical Specimens

**Authors: Dennis Reichenbach, MD, Chuck Murry, MD
PhD, Michael Laflamme, MD PhD**

Section 2 - CAP Cancer Protocols and Checklists Including: Heart

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Cardiovascular Surgical Specimens

Dennis Reichenbach, MD; Chuck Murry, MD PhD;
Michael Laflamme, MD PhD

GENERAL COMMENTS

- Diagnostic cardiovascular pathology requires appropriate gross and histologic evaluation of the specimen. Unfortunately, perhaps because of their frequent fragmentary and/or calcified nature, cardiovascular surgical specimens have sometimes been "short-shrifted" in terms of their gross handling. Such mishandling can result in loss of useful or required gross details (details that may be destroyed in sectioning, etc); and, more commonly, incorrect sectioning and embedding of the tissue. In many instances, little or no useful histopathologic information can be obtained at signout if the specimen has been incorrectly sectioned and embedded, such as with a valve leaflet that is merely laid in a cassette or is sectioned along an incorrect axis.
- Photography, particularly of valves and unusual-appearing specimens, is strongly encouraged.
- Although not generally required, in rare instances (such as with suspected endovascular stents within an explanted heart or atherectomy, etc.), a scout roentgenogram of the specimen can provide useful information and guide its subsequent handling.
- Virtually all cardiovascular specimens require an elastin stain (such as a VVG stain) for proper microscopic evaluation, and the resident is therefore encouraged to request such studies "up front" to assist in timely sign out.
- It is current UWMC practice that the surgeon send tissue for indicated microbiologic culture on specimens, such as possibly infected cardiac valves, prior to receipt in Anatomic Pathology.

GROSS DESCRIPTION & PROCEDURE

Native valves

- Describe the total number of tissue fragments received, as well as either their aggregate weight or size range. In most cases, the in situ anatomic arrangement of the valve can be at least partially reconstructed, and this should be attempted. State whether the valve is semilunar or atrioventricular (i.e. cusps or leaflets with chordae). Briefly detail the apparent number of leaflets or cusps received (trileaflet, bileaflet, or unicommissural), as well as the greatest dimension of each. With semilunar valves, note whether the cusps appear equal or unequal in size. If they appear asymmetric, state whether a raphe is present. Unicommissural semilunar valves classically have an "exclamation point" configuration.
- Note the presence or absence of other features including opacification, increased translucency, fibrosis, lipid deposition, calcification, commissural fusion, vegetations, and increased/decreased apparent leaflet mobility. If enough of the valve is received intact, one may comment whether its gross appearance is suggestive of stenosis and/or regurgitation.
- Describe any associated valve structures, if applicable, such as chordae tendineae and or papillary muscles. In particular, note if these structures appear intact, ruptured, elongated, fused, scarred, etc.
- After decalcification if necessary, submit at least one section from each leaflet, taken along an axis extending from the base to the free edge of the leaflet, perpendicular to the apparent line of coaptation/apposition; and, if all leaflets appear approximately the same, these standard sections may be submitted together in a single cassette. Additional sections should be taken through any unusual structures such as fused commissures. In the dictation, the latter sections should be distinguished from the standard valve sections, and any unusual axis or plane of section should be noted.

- If chordal rupture or avulsion is suspected, these should be separately submitted for histology, usually with longitudinal embedding.
- Recall that the fibrous nodule (of Arantius) located in the middle of the free edge of a valve cusp is an anatomically normal structure. Further, small fenestrations may be present in the lunula (that portion of the valve surface located above the line of apposition) and have no functional significance.

Prosthetic valves

- Prosthetic valves can be divided into mechanical and tissue types. Mechanical valve replacements may be of the following types: ball-and-cage (Starr type), tilting disc (Bjork-Shiley type), or hinged bileaflet (St. Jude type). Tissue (bioprosthetic) valve replacements may be constructed out of porcine or human, valvular or pericardial tissue (see next paragraph), although this may not be grossly evident. In the case of either a mechanical or tissue prosthetic, its leaflets will typically reside within a man-made ring (either with or without struts) that is surrounded by Teflon or another fabric weave. The distribution of fibrin or neointima on the surface of this ring may be a clue for an abnormal or even paravalvular flow path.
- Bioprosthetic valves can be derived from donor tissue from another human, in which case they are termed a "homograft" (or, synonymously, an "allograft"), or from donor tissue from another species, e.g. a heterograft (or "xenograft"). Although glutaraldehyde-fixed heterografts are the most frequently encountered type of bioprosthetic valve (in particular the Carpentier-Edwards valve), in certain circumstances use of a homograft may be favored, such as in younger individuals, individuals with infectious endocarditis, and those for which anticoagulation is contraindicated. Homografts may be inserted fresh (preserved with antibiotics), or (most often) cryopreserved prior to use. Not surprisingly, the method of tissue preparation and the species from which it is derived may alter or distinguish its histological appearance (refer to first reference below for more details).
- Describe type and dimensions of received prosthetic valve as a whole, as well as whether it appears intact. Note mobility and intactness of leaflets, carefully describing position and size of any defects identified. Note presence or absence of thrombi, vegetations, or any other lesions.
- After decalcification if necessary, submit sections from bioprosthetic valve leaflets for histology, including both standard sections (as described with native valves above) as well as sections from any lesions. In the case of both mechanical and tissue prostheses, submit for histology any thrombi as well as any fibrous or otherwise abnormal tissue accumulations noted on the sewing ring or elsewhere.

Aortic tissue

- Describe the nature and the total number of the tissue fragments received, as well as either aggregate weight or size range of fragments. Note whether the tissue appears to consist of the complete thickness or a subset of the components of the vessel wall (e.g. intima, media, adventitia). If complete rings of aortic tissue are received, their diameter should be noted (normal aortic diameter is <2.5 cm for older individuals).
- Describe any grossly abnormal features of the vessel fragments received, including atherosclerosis, calcification, associated thromboembolus, dissection with intimal flap, aneurysmal dilatation, etc.
- If a dissection plane is detected, note its apparent position and extension within the vessel wall, whether the tract appears lined by a fibrinous or neointimal surface, and whether it contains hematoma. Describe the characteristics of the intimal flap (if present), as well as the appearance of the involved and surrounding intimal surface, attending to the presence of any intimal rents or tears, unusual texturing, etc.
- Tissue sections of both involved and normal-appearing (if any) vessel should be submitted for histology. If a medial dissection is present, at least one section should include the point of attachment of the intimal flap to the outer media and adventitia, thereby documenting

histologically that dissection has occurred. Vessels with significant calcific atherosclerosis may require decalcification prior to sectioning.

Other vessels/endarterectomies/arterectomies

- Following decalcification, if necessary, the vessel should be "breadloafed" perpendicular to its long axis at 1-2 mm. Gross description should include the dimensions of the received vessel, as well as the distribution and maximal occlusion of any segments by atherosclerosis. If thromboembolus is included within the vessel, it should be noted whether this is mural and whether it stenoses or occludes the vessel. If separately received, blood clot should be weighed.

Cardiac tumors

- Cardiac tumors are extremely rare and therefore necessitate excellent gross photography in all instances. In some instances (such as with a suspected papillary fibroelastomas), the resident may consider photographing the specimen following submersion in saline.
- Cardiac tumors should otherwise be handled as would any other neoplastic case (e.g. with attention to margins, if applicable, etc.). As with many soft tissue neoplasms, Dr. Brian Rubin may be interested in obtaining small amounts of fresh tissue for special studies and tissue banking; he should be contacted in this regard. Cardiac sarcomas (very rare!) should be handled as are other deep-seated soft tissue tumors (see pertinent section of guidelines).
- Although themselves fairly rare, atrial myxomata comprise the majority of cardiac tumors received in surgical pathology.

Medical devices

- In most cases, a brief gross description of the device as well as dictation of any identifying inscription (serial number, etc.) on it should complete a sufficient examination. In rare instances, the referring clinician may request that the specimen be retained for medicolegal reasons, etc.; watch for this request on the accompanying requisition.

Explant hearts

- Due to their inherent complexity and alterations resulting from research tissue acquisition, explant hearts are at present assigned to and grossed-in exclusively by the cardiovascular pathologists (typically Dr. Laflamme). Should any resident have particular interest in participating and/or viewing these specimens, special accommodations can be arranged.

Endomyocardial biopsies

- Exclusively the cardiovascular pathologists- Drs. Dennis Reichenbach, Chuck Murry, Kelly Smith, and Mike Laflamme- handle cardiac biopsies. Interested residents should contact Dr. Murry to arrange resident biopsy review. The International Society for Heart & Lung Transplantation (ISHLT) scale used for grading cellular rejection in cardiac allograft biopsies is as follows:

Grade		
1	A	Focal (pervascular/interstitial) infiltrate without necrosis
	B	Diffuse but sparse infiltrate
2		One focus only with aggressive infiltration and/or focal myocyte damage
3	A	Multifocal aggressive infiltration and/or focal myocyte damage
	B	Diffuse inflammation with necrosis
4		Diffuse aggressive polymorphous +/- edema, hemorrhage, and vasculitis, with necrosis

REFERENCES

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-  Silver, M.D., Gotlieb, A.I., & Schoen, F.J. Churchill (editors). *Cardiovascular Pathology* 3rd ed. Livingstone, Philadelphia, PA, 2001.
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CAP Cancer Protocols and Checklists

Cardiovascular System

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Heart	Checklist	Full Protocol

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Neuromuscular System

Section 1 - Neuropathology

Author: Don Born, MD PhD

Section 2 - Nerve Biopsy

Author: Don Born, MD PhD

Section 3 - Muscle Biopsy

Author: Don Born, MD PhD

Section 4 - CAP Cancer Protocols and Checklists Including: Brain/Spinal Cord

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Neuropathology

Don Born, MD PhD

The following are guidelines that work well for most cases falling into the categories below. If you have any questions prior to preparing frozen sections or in working up cases not described below, consult with the Neuropathology attending or one of the Neuropathology fellows.

INTRAOPERATIVE CONSULTATION

- Requests for diagnosis at the time of initial surgery are relatively common for Neurosurgical procedures (prior biopsy diagnosis is unusual).
- Touch preparations and smears in addition to frozen sections are frequently indicated (further comments on this under relevant sections below).
- During regular hours use the Pathology Office at UWMC and HMC for assistance in reaching the Neuropathologist on call. A notification of anticipated frozen section is sometimes (and always should be) issued by the Neurosurgeons; please make sure the office staff has alerted the Neuropathologist on call. As soon as you receive tissue, again make sure the office has paged the Neuropathologist (rather than waiting till sections are stained).
- After hours use the paging operator to reach the Neuropathologist on call.

TUMOR RESECTIONS

- Since many primary brain tumors are mixtures of cell types, it is usually reasonable to submit each part completely. Representative samples of CUSA (cavitron) may be submitted. Tissue removed from overlying tumors may be sampled (1 block/cm tissue).
- If the neurosurgeon submits many small pieces as margins, multiple frozen sections may be cut on one chuck by inking individual pieces with different colors and combining as many as 4. The thawed sections are then submitted separately.
- Occasionally tumors will be infectious lesions and the surgeon should be alerted that cultures need to be made in the operating room.

STEREOTACTIC BIOPSIES

- Many types of lesions are approached by stereotactic biopsy. It is generally sufficient to indicate that diagnostic tissue was obtained. The exception is for an infection, which needs to be cultured.
- To decide if diagnostic tissue is included, usually a touch and/or smear preparation and a frozen section are made. **It is important** to establish with the neurosurgeon whether a sample should be frozen and the rest saved for permanent sections (the more common situation) or if the whole specimen can be frozen sectioned.

PITUITARIES

- Adenomas may be small, mucoid, or variably mixed with non-tumor, fibrous tissue; thus, they may require extra care in handling the tiny quantity of tissue.
- Touch preparations are necessary (and frequently the best for diagnosis) in addition to frozen sections.
- Remaining frozen tissue and other parts are fixed in formalin fixative. Wrap small specimens in filter paper before submitting in cassettes. The tissues are processed in neuropathology.
- Submit some tissue, when possible, for electron microscopy.

EPILEPSY RESECTIONS

(Note that some patients with tumors have epilepsy and these notes apply to surgery for resection of an epileptic focus.)

- Submit all tissue received except when it was removed for access to underlying brain where sampling is indicated..
- Recognizable portions of cortex should be sectioned perpendicular to the pial surface.
- Special stains are prepared in the neuropathology lab.
- Hippocampus, when resected, will sometimes be sectioned and stained by the neuropathology lab. These will be sent from HMC on request.
- If you are sectioning a specimen designated "hippocampus", it should be cut in the coronal plane (usually perpendicular to the long axis); call for assistance, if needed.

VASCULAR MALFORMATIONS

- Arteriovenous malformations (AVM), cavernous malformations, telangiectasia and portions of aneurysms usually arrive in formalin. A Verhoeff-van Gieson (VVG) stain is usually indicated.

OTHER CASES

- Abscesses and other infections, skull and scalp are usually best considered on a case-by-case basis. Consult with one of the neuropathology fellows or the neuropathologist on call.

SIGN OUT

- You can see which faculty member is assigned a case in the Tamtron PP2K system.
- All cases will be signed out at HMC. Sign-out begins at 2:00 daily.

CONFERENCES

- Surgical cases received in neuropathology are reviewed at the HMC Tuesday morning multihead microscopic review conference (8:00-9:00 am, 2EH91). If you wish to participate in the discussion about your cases, come to the conference and let someone know which cases are yours. Come prepared to give your differential diagnosis. We will project the cases on a video monitor for demonstration.
- Cases from all Affiliated Hospitals are presented 2nd and 4th Wed. (8-9 am, Research & Training Building), with clinical and radiology information. This is an excellent way to get a complete "picture" of cases.

Nerve Biopsy

Don Born, MD PhD

The surgeon must be instructed that the nerve biopsy specimen should be at least 3 cm long (there is no reason to have a shorter specimen, nerve function is lost for any length sample). The surgeon should place the specimen on a tongue blade or stiff paper and cover the nerve with telfa or gauze moistened with saline. **The specimen must NOT be immersed in saline.**

DIVIDING THE NERVE SPECIMEN

The specimen will be divided in three parts:

- A. One piece for plastic thick sections and if needed electron microscopy (1 cm).
- B. One piece for teasing placed in formalin (1 cm)
- C. One piece for paraffin embedding placed in formalin

A. Sample for embedding in plastic and possible electron microscopy

From the 3 cm biopsy of nerve on the tongue blade or stiff paper cut off about 1.0 cm. Make sure it is not from a crushed end. We use a double edge razor blade broken in half to ensure a clean cut and do not damage the nerve while cutting it (the nerve is quite fragile and subject to crush artifact). Note: If sample is shorter than described, then you should still use at least 1.0 cm here. Place this 1.0 cm sample into EM fixative (Trump's, Karnovsky's or other glutaraldehyde containing EM fixative, note these fixatives should be stored in the refrigerator).

B. Sample for nerve fiber teasing using formalin fixation, osmication and glycerol

A portion of the nerve at least 0.5 cm and up to 1.0 cm should be placed in formalin fixative. The same care should be taken as for an ultrastructural study.

C. Sample for routine light microscopy using formalin fixation and paraffin embedding

Leave remaining piece of the nerve on the tongue blade or stiff paper and fix by immersion in buffered formalin.

During regular hours the fresh nerve biopsy specimen can be sent to the Harborview Neurohistology laboratory by placing the specimen in a container (e.g. Petri dish), placing it in a sealable bag and placing the bag on wet ice. Request help from the Histology/Gross room staff to arrange this.

Muscle Biopsy

Don Born, MD PhD

Instruct the surgeon that the muscle biopsy specimen should be a longitudinal piece of **muscle 0.8 to 1.0 cm in diameter** (just thicker than a pencil) and at least **3 cm in length**. The surgeon should place the specimen on a tongue blade or stiff paper and cover the muscle with Telfa or gauze **moistened** with saline. The specimen must **NOT** be immersed in saline. Muscle clamps should not be used unless the surgeon is experienced with their use. If the muscle contracts before it is placed on the surface, obtain an additional sample so that there is 3 cm total length.

The specimen will be divided in four ways:

- A. snap freezing on embedding medium
- B. snap freezing directly
- C. formalin fixation
- D. electron microscopy (EM) fixation

A. SNAP-FREEZING MUSCLE ON EMBEDDING MEDIUM USING ISOPENTANE IN LIQUID NITROGEN:

Gather equipment needed in gross room: stand, beaker, isopentane, Dewar of liquid nitrogen. Prepare a 1-cm long sample of muscle maintaining the orientation to allow cross sections.

1. Immerse the bottom half of a small plastic beaker containing isopentane into liquid nitrogen. When the isopentane becomes slightly viscous and forms solid white laminate filling the bottom 1/3 of the inside of the beaker (temperature: -160 degrees C) then it is ready for use.
2. Freeze some embedding medium (e.g. OCT) on a chuck (cork, wooden block, or test tube cap) or in a cryomold by dipping it briefly (10 sec) into isopentane. Ideally, a cryomold filled with embedding medium can be prepared ahead of time in a freezer.
3. Place a **small** amount of fresh embedding medium on the frozen embedding medium and carefully touch the end portion of the fresh muscle to the embedding medium. The muscle will stick. **It is important NOT to surround the muscle with embedding medium. It is important to maintain the cross sectional orientation.**
4. Lower the chuck with the attached muscle into the isopentane bath. The usual freezing time is 7-15 seconds, depending on specimen size and composition. Immersion in the freezing solution should not last more than is needed to completely freeze the specimen. Larger fatty specimens usually take longer (15 seconds); smaller dense muscle takes a shorter time (7 seconds). Freezing too long will fracture the tissue block, too short will cause ice crystal formation. A well-frozen specimen should be chalky white.
5. Once the specimen is frozen it should be placed in a small plastic bag and immediately stored in a deep freezer at -70C or placed in dry ice for shipping or storing at -70C.

B. SNAP FREEZE A PIECE OF MUSCLE DIRECTLY:

1. Place a 1-cm length of muscle directly in liquid nitrogen. The tissue may be held with forceps or hemostat.
2. Remove the frozen muscle to a small plastic bag prelabeled with the patient's name or accession number.
3. Place the bag in dry ice until transfer to -70°C freezer or shipping container.

C. FOR ROUTINE STAINS (FORMALIN FIXATION):

Put a piece of muscle on a piece of heavy paper, cardboard or tongue blade, maintaining its longitudinal orientation and fix by immersion in buffered formalin.

D. FOR ELECTRON MICROSCOPY (EM):

For possible electron microscopy, place a small piece of muscle in EM fixative (e.g. Karnovsky's or Trumps). (Stored in the gross room refrigerator)

During regular hours the fresh muscle biopsy can be sent to the Harborview Neurohistology laboratory by placing the specimen in a container (e.g. Petri dish or specimen cup), placing it in a sealable bag and placing the bag in wet ice. Request help from the Histology/Gross room staff to arrange this.

CAP Cancer Protocols and Checklists

Neuromuscular System

Click the link to open .pdf document.		
Brain/Spinal Cord	Checklist	Full Protocol

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Eye & Ocular Adnexa

Section 1 - Eye Specimens

Authors: Jing Zhang, MD PhD & Don Born, MD PhD

Section 2 - CAP Cancer Protocols and Checklists

Including: Retinoblastoma, Uveal Melanoma

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Eye Specimens

Jing Zhang, MD PhD & Don Born, MD PhD

Specimens from the eye including cornea, conjunctiva and globe will be accessioned to Neuropathology and transported to Harborview Medical Center. The gross description, any dissection and embedding will be handled there.

Membrane peel and trabeculectomy, which is hardly done now: These are often quite small and should be described and processed like other very small specimens. One good way to avoid losing these is to add some mercurochrome to the formalin, which colors the specimen, then filter the specimen through a **tea bag**, and finally mark the location of the specimen on the tea bag with a pencil. Order PAS stain.

Conjunctival Biopsy: If called by the clinicians, instruct them to orient the specimen and put it between paper towels before the tissue is dropped into formalin. Cut the specimen perpendicularly and submit the tissue in a **tea bag**. Conjunctival biopsy should be handled like skin biopsy (on edge and H&E X 2). Also, when a bulbous lesion is suspected, one piece of the specimen should be fixed in Michel's fixative for immunofluoresce studies.

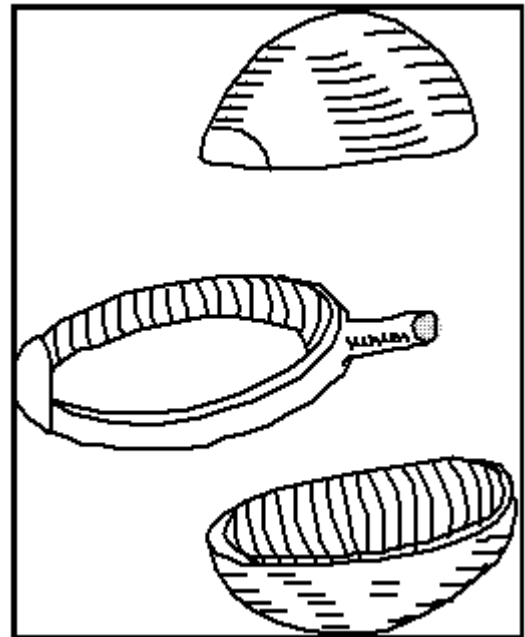
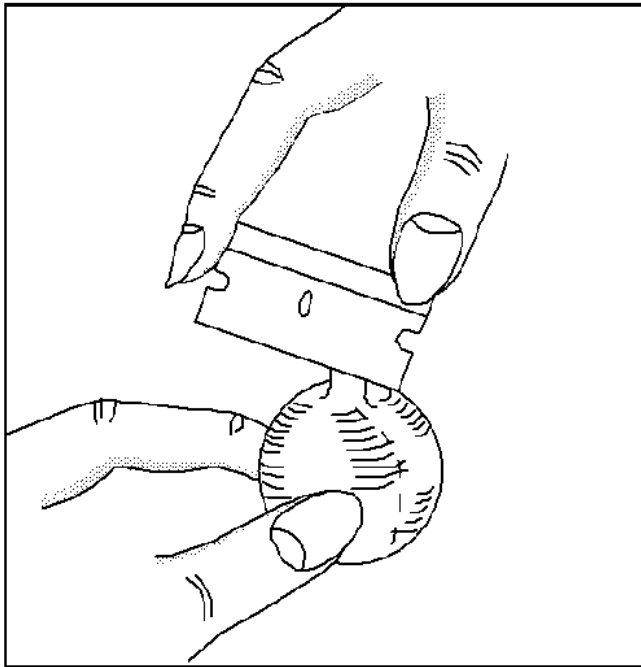
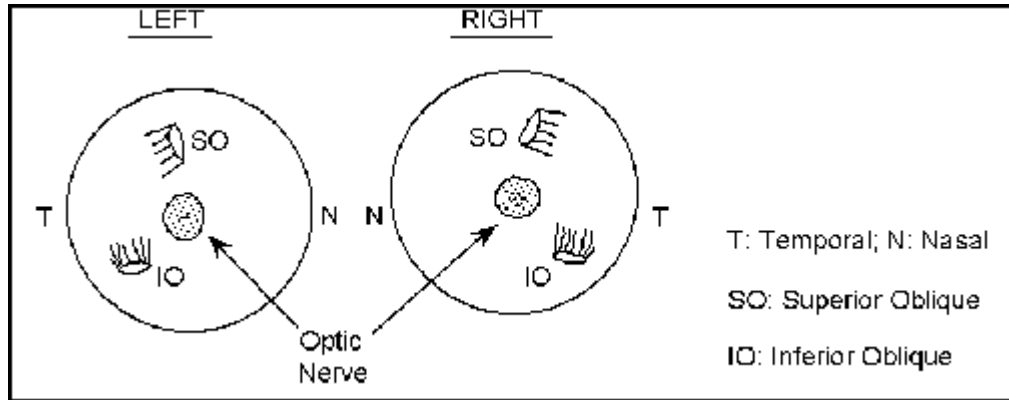
Cornea (penetrating or lamellar keratoplasty): Measure and examine the cornea button under dissecting scope. Bisect the button perpendicularly through any focal lesion with the concave side facing up. Then, bisect one of the two halves again with the smaller piece submitted with the other half cornea in a **tea bag**. Order PAS and Masson stains regularly except in trauma cases. Order iron stain when keratoconus is suspected. If there is a history of suspected microbial keratitis, also order Gram, AFB and GMS stains.

Enucleated Globe: NOTIFY OPHTHALMIC PATHOLOGIST BEFORE PROCESSING

Fix in formalin with volume of 20 times that of the eye, e.g., about 300 cc. for 48-72 hours. Occasionally, a fresh cut may be needed to select tissue for cytogenetics, etc. Wash fixed specimen before cutting. If there is history of foreign body or globe feels unusually hard, x-ray specimen before cutting.

Orient and measure in 3 dimensions (horizontal, vertical and anteroposterior). The laterality of an eye is determined by identifying key anatomic landmarks. They include the long posterior ciliary vessels, which appear as blue lines on the posterior sclera on either side of the optical nerve; the cornea, whose horizontal diameter is usually 1 mm longer than its vertical diameter; and the insertions of the superior and inferior oblique muscles. If the pathologist examines the posterior surface of the eye, assuming the position of the standing at the apex of the orbit, the position of the inferior oblique muscle determines the laterality of the eye: if the muscle (without a tendon) inserts to the right (left) of the optical nerve, the eye is the right (left) eye (see the diagram below). Both inferior and superior oblique muscle (with a tendon) are at temporal or lateral side. Measure length of optic nerve. Measure cornea and describe any corneal lesions. Transilluminate globe (use light source for dissecting scope in darkened room) to identify lesions. This will help determine the plane of section, which is ordinarily in horizontal plane through the macula, but should be adjusted if there is a transillumination defect. It is useful to examine the cut sections with dissecting scope.

Sections: Submit midsagittal section through pupil and adjacent to optic nerve and additional sections as needed to demonstrate extent of tumor. Order 2 H&E and 1 PAS section and 3 unstained, except trauma cases. In addition, order bacterial stain and GMS for suspected endophthalmos. **Important:** for retinoblastoma, submit optic nerve stump, marking surgical margin with India ink.



CAP Cancer Protocols and Checklists

Eye & Ocular Adnexa

Click the link to open .pdf document.		
Retinoblastoma	Checklist	Full Protocol
Uveal Melanoma	Checklist	Full Protocol

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Required Data Elements from CAP Cancer Checklists Mandated for Use by the American College of Surgeons Commission on Cancer Effective January 1, 2004

Updated April 5, 2005

Please read the important information below about the CAP cancer checklists.

[Summary of All Changes in the current revision.](#) (PDF, 91 K)
[What does the American College of Surgeons mandate?](#)
[Does the CAP provide additional information to help me use the cancer checklists?](#)
[How can I comment on the checklists?](#)
[What does the mandate mean?](#)
[How will compliance be determined?](#)
[What if we don't meet the standard?](#)
[What if we're going through the approvals process for the first time?](#)
[How can I know that I am using the most current version of the checklists?](#)
[How can I get copies of the checklists and background documentation?](#)
[Why were the protocols revised?](#)
[Glossary of terms](#)

The College of American Pathologists produces cancer protocols as a resource to pathologists in effectively delivering the information necessary to provide quality patient care. The protocols consist of cancer case summaries (checklists) accompanied by background documentation. The background documentation includes detailed outlines, explanatory notes, and references, and it is presented to you for information only. The American College of Surgeons Commission on Cancer (ACS CoC) has recognized the value of the CAP cancer checklists in caring for cancer patients. Starting January 1, 2004, it mandated that pathologists at CoC-approved cancer programs include only the scientifically validated or regularly used data elements of the checklists in their surgical pathology reports on cancer specimens.

What does the American College of Surgeons mandate?

Beginning January 1, 2004, the American College of Surgeons Commission on Cancer mandated new standards through its approvals program. New ACS CoC standards have been published and are available through the ACS CoC. One new standard requires that pathologists at CoC-approved cancer programs include all scientifically validated or regularly used *data elements* of the checklists in their reports for each site and specimen. **The required data elements are the non-asterisked elements in the checklists. The ACS standard does not require the actual use of the CAP checklist. The ACS mandate also does not require a specific format for pathology reports. Further, the data elements mandated by the ACS CoC are not exclusive of any other data, but are the minimum requirement for inclusion in the pathology report.**

Not all elements of each checklist are scientifically and peer validated or regularly used in patient care; therefore, some elements are not required as part of the ACS mandate. Elements that are not scientifically validated or regularly used in patient care are marked with an asterisk on the checklists. Although the asterisked elements are not yet fully validated or regularly used, they may be clinically important and are, therefore, included in the checklists as suggested elements of the pathology report.

Does the CAP provide additional information to help me use the cancer checklists?

Yes. Each checklist is accompanied by detailed background documentation in support of the checklist elements. The background documentation includes detailed outlines, explanatory notes, and references. It provides highly useful information about the meaning of various data elements. When indicated, the background documentation elucidates how to translate the pathologist's macroscopic and microscopic findings into the checklist data item. The ACS CoC mandate does not require use of the background documentation. It is presented to you for information only. In addition, a special feature of each updated checklist is the Summary of Changes, which highlights changes, if any, to the data elements of the checklist(s) since the previous revision.

Additionally, SNOMED CT encoded CAP cancer checklists provide the CAP cancer checklists encoded on an item for item basis with SNOMED CT in three formats for standardized capture, retrieval and transmission of essential cancer data with a structured report. This subset is used with the SNOMED CT Concepts file to isolate the concepts for the checklists. It can be used for automated upload to a database or file system; can be used for SNOMED-based data entry/storage/retrieval; or to view this portion of SNOMED through subset-enabled software.

[Complete text of the CAP cancer protocols](#) supplied for integration into a vendor's application to supplement the SNOMED encoded synoptic cancer checklists is also available through SNOMED.

How can I comment on the checklists?

Cancer checklist users are invited and encouraged to comment on the checklists. You may provide feedback by clicking the "Comment" button on the checklist index page.

All feedback will be forwarded to the CAP Cancer Committee for its consideration.

What does the mandate mean?

In order to comply with the ACS mandate, cancer programs will be expected to show that 90 percent of pathology reports include all scientifically validated or regularly used elements of the appropriate checklists.

How will compliance be determined?

Through the ACS CoC approvals program, cancer programs are surveyed every three years by a physician surveyor who is specially trained to evaluate compliance with all of the standards that are required for approval. Use of the elements of the CAP cancer checklists is one of the 36 standards evaluated during a survey. The surveyor will randomly sample 25 medical records and review pathology reports in these records. The sample will be based upon the five major cancer sites seen by the cancer program during the previous year.

What if we don't meet the standard?

If fewer than 90 percent of all cancer reports randomly sampled during your CoC survey include all required scientifically validated or regularly used data elements, you may receive one deficiency.

A full three-year approval is granted to a program if all standards are met and no deficiencies are found.

A three-year approval with contingency is granted with one to seven deficiencies.

Please note that a program with one to nine deficiencies is allowed 12 months to document changes for administrative review in order to receive full approval.

If a program fails to meet 8 or more standards, it will receive non-approval. These programs are encouraged to improve their performance and may reapply.

What if we're going through the approvals process for the first time?

If your program is going through the approvals process for the first time and the program is deficient in one standard, deferred status may be granted. Programs granted deferred status have 12 months to document compliance, at which time full approval may be granted. If deficiencies are not resolved within 12 months, the program must reapply for consultation and survey.

How can I know that I am using the most current version of the checklists?

The most up-to-date checklists and background documentation may be [downloaded from the CAP Web site](#) and integrated into your practice. The revision date appears near the top of the title page of current checklists. In addition, a special feature of each updated checklist is the Summary of Changes on page 3. This summary highlights changes, if any, to the data elements of the checklist(s) since the previous revision. A document, [Summary of All Changes in the current revision](#), also can be downloaded from the CAP Web site.

The SNOMED CT Encoded Cancer Protocols are updated and released biannually.

How can I get copies of the checklists and background documentation?

CAP cancer checklists and background documentation are now available without charge and can be [downloaded from the CAP Web site](#). A printed version also is available for purchase (call CAP Customer Service at 1-800-323-4040 option 1#).

The free download authorization does not extend to reproduction or other use of any substantial portion of these protocols for commercial purposes.

For commercial use of the checklists and protocols, [contact SNOMED International](#). Information on obtaining the SNOMED CT encoded cancer checklists and protocols is [available on the SNOMED Web site](#).

Why were the protocols revised?

The CAP's Cancer Committee revised the CAP Cancer Protocols to reflect the new American Joint Committee on Cancer (AJCC) Cancer Staging Manual, sixth edition, and the most recent WHO tumor classification system. As part of this revision, the Cancer Committee has made the protocols more consistent and has streamlined the checklists. The current revision reflects feedback received from users of the protocols.

The protocols will be reviewed and updated documents published on the Web and in hardcopy on an annual basis, as appropriate. New or significantly revised protocols will continue to be published in *Archives of Pathology & Laboratory Medicine*.

The SNOMED CT Encoded cancer protocols are updated and released biannually.

Glossary of Terms

Cancer protocols

The "protocol" is the entire document, including the introductory information, the checklist (or cancer case summary) and the background documentation.

Checklists

The "checklist" is the cancer case summary, or short form. It includes a list of elements pathologists may use when completing a surgical pathology report on a cancer specimen. **Only the nonasterisked data elements of each checklist are required, by the American College of Surgeons Commission on Cancer, to be included in pathology reports.**

Background documentation

The "background documentation" is the supporting information, including detailed outlines, explanatory notes, and references. This material is to be used for information about the meaning of various data elements in the checklists. **Use of the background documentation is not required as part of the ACS CoC mandate.**

SNOMED CT Encoded CAP Cancer Checklists

The College of American Pathologists (CAP) cancer checklists are encoded on an item for item basis with SNOMED CT for standardized capture, retrieval and transmission of essential cancer data with a structured report.

Source:

http://www.cap.org/apps/docs/cancer_protocols/protocols_intro.html

January 2005 CAP Cancer Protocol Revision: Summary of All Changes to the Data Elements of the Checklists Since the 2004 Revision

Adrenal Gland

No changes have been made to the data elements of the checklist(s) since the January 2004 protocol revision.

Ampulla of Vater

The following changes have been made to the data elements of the checklist(s) since the January 2004 protocol revision.

Ampullectomy Checklist

Microscopic

Tumor Size: An optional data element was added to record two additional dimensions in addition to the greatest dimension, as shown below

Tumor Size
Greatest dimension: ____ cm
*Additional dimensions: ____ x ____ cm
____ Cannot be determined (see Comment)

Anus

No changes have been made to the data elements of the checklist(s) since the January 2004 protocol revision.

Bone Marrow

No changes have been made to the data elements of the checklist(s) since the January 2004 protocol revision.

Brain

No changes have been made to the data elements of the checklist(s) since the January 2004 protocol revision.

Breast

No changes have been made to the data elements of the checklist(s) since the January 2004 protocol revision.

Colon and Rectum

The following changes have been made to the data elements of the checklist(s) since the January 2004 protocol revision.

Polypectomy Checklist

Macroscopic

Distance of Invasive Carcinoma from Anal Verge and Distance of Adenoma from Anal Verge: these optional reporting elements have been added, as shown below

***Distance of Invasive Carcinoma from Anal Verge (per clinical report)**

*Specify: ____ cm

* ____ Distance from anal verge unknown

***Distance of Adenoma from Anal Verge (per clinical report)**

*Specify: ____ cm

* ____ Distance from anal verge unknown

Endometrium

No changes have been made to the data elements of the checklist(s) since the January 2004 protocol revision.

Esophagus

No changes have been made to the data elements of the checklist(s) since the January 2004 protocol revision.

Extrahepatic Bile Ducts

No changes have been made to the data elements of the checklist(s) since the January 2004 protocol revision.

Fallopian Tube

No changes have been made to the data elements of the checklist(s) since the January 2004 protocol revision.

Gallbladder

No changes have been made to the data elements of the checklist(s) since the January 2004 protocol revision.

Heart

No changes have been made to the data elements of the checklist(s) since the January 2004 protocol revision.

Kidney

No changes have been made to the data elements of the checklist(s) since the January 2004 protocol revision.

Liver

No changes have been made to the data elements of the checklist(s) since the January 2004 protocol revision.

Lung

No changes have been made to the data elements of the checklist(s) since the January 2004 protocol revision.

Lymphoma: Gastrointestinal

The following changes have been made to the data elements of the checklist(s) since the January 2004 protocol revision.

Resection Checklist**Microscopic**

Phenotyping: "Tumor, Immunophenotyping" was changed to "Phenotyping," as shown below

Phenotyping

___ Performed, see separate report ___ Performed Specify methods and results:

___ Not performed _____

Lymphoma: Hodgkin

No changes have been made to the data elements of the checklist(s) since the January 2004 protocol revision.

Lymphoma: Non-Hodgkin

No changes have been made to the data elements of the checklist(s) since the January 2004 protocol revision.

Neuroblastoma

This is a new protocol; expected release date of 2005.

Ovary

No changes have been made to the data elements of the checklist(s) since the January 2004 protocol revision.

Pancreas (Endocrine)

The following changes have been made to the data elements of the checklist(s) since the January 2004 protocol revision.

Protocol in General

Tumors with mixed endocrine and acinar cell differentiation are no longer included in this protocol (see Exocrine Pancreas protocol).

Excisional Biopsy (Enucleation), Resection Checklist**Macroscopic**

Specimen Type: Excisional biopsy (enucleation) was added, as shown below

Specimen Type

- ☐ Excisional biopsy (enucleation)
- ☐ Pancreaticoduodenectomy (Whipple resection), partial pancreatectomy
- ☐ Pancreaticoduodenectomy (Whipple resection), total pancreatectomy
- ☐ Pylorus sparing pancreaticoduodenectomy, partial pancreatectomy
- ☐ Pylorus sparing pancreaticoduodenectomy, total pancreatectomy
- ☐ Partial resection, pancreatic body
- ☐ Partial resection, pancreatic tail
- ☐ Other (specify): _____
- ☐ Not specified

Pancreas (Exocrine)

The following changes have been made to the data elements of the checklist(s) since the January 2004 protocol revision.

Resection Checklist**Microscopic**

Regional Lymph Nodes (pN): the subclassification of pN1 into pN1a and pN1b have been changed from required to not required, as shown below

Regional Lymph Nodes (pN)

___pNX: Cannot be assessed

___pN0: No regional lymph node metastasis

___pN1: Regional lymph node metastasis

* ___ N1a: Metastasis in single regional lymph node

* ___ N1b: Metastasis in multiple regional lymph nodes

Specify: Number examined ___

Number involved: ___

Peritoneum

No changes have been made to the data elements of the checklist(s) since the January 2004 protocol revision.

PNET / Ewing Sarcoma

This is a new protocol for 2005.

Prostate

No changes have been made to the data elements of the checklist(s) since the January 2004 protocol revision.

Retinoblastoma

No changes have been made to the data elements of the checklist(s) since the January 2004 protocol revision.

Rhabdomyosarcoma

No changes have been made to the data elements of the checklist(s) since the January 2004 protocol revision.

Skin: Carcinoma

No changes have been made to the data elements of the checklist(s) since the January 2004 protocol revision.

Skin: Melanoma

No changes have been made to the data elements of the checklist(s) since the January 2004 protocol revision.

Small Intestine

No changes have been made to the data elements of the checklist(s) since the January 2004 protocol revision.

Stomach

No changes have been made to the data elements of the checklist(s) since the January 2004 protocol revision.

Testis

No changes have been made to the data elements of the checklist(s) since the January 2004 protocol revision.

Thoracic Mesothelium

The following changes have been made to the data elements of the checklist(s) since the January 2004 protocol revision.

Pleura / Pericardium Resection Checklist

Macroscopic

Tumor Configuration and Size: the "Cannot be determined" data element was expanded, as shown below

*Tumor Configuration and Size (check all that apply)

* ☐ Localized

*Greatest dimension: cm

*Additional dimensions: x cm

* ☐ Diffuse

*Maximum thickness: cm

* ☐ Tumor configuration cannot be determined (see Comment)

* ☐ Tumor size cannot be determined (see Comment)

Thymoma and Thymic Carcinoma

No changes have been made to the data elements of the checklist(s) since the January 2004 protocol.

Thyroid Gland

No changes have been made to the data elements of the checklist(s) since the January 2004 protocol revision.

Trophoblast

No changes have been made to the data elements of the checklist(s) since the January 2004 protocol revision.

Upper Aerodigestive Tract (Including Salivary Glands)

The following changes have been made to the data elements of the checklist(s) since the January 2004 protocol revision.

Upper Aerodigestive Tract and Minor Salivary Glands: Incisional and Excisional Biopsy, Resection Checklist

Microscopic

Histologic Type: Carcinomas of the Upper Aerodigestive Tract:

Adenocarcinoma, Non-salivary Gland Type, was modified to include high, intermediate, and low grade adenocarcinoma NOS, as shown below

Histologic Type

Carcinomas of the Upper Aerodigestive Tract

Adenocarcinoma, Non-salivary Gland Type

☐ Papillary adenocarcinoma

☐ Intestinal-type adenocarcinoma

☐ Adenocarcinoma not otherwise specified (NOS), low grade

☐ Adenocarcinoma NOS, intermediate grade

☐ Adenocarcinoma NOS, high grade

Histologic Type: Carcinomas of Minor Salivary Glands:

Adenocarcinoma NOS was modified to include high, intermediate, and low grade, as shown below

Histologic Type**Carcinomas of Minor Salivary Glands**

- ☐ Acinic cell carcinoma
- ☐ Adenoid cystic carcinoma
- ☐ Adenocarcinoma not otherwise specified (NOS), low grade
- ☐ Adenocarcinoma NOS, intermediate grade
- ☐ Adenocarcinoma NOS, high grade, etc

Major Salivary Glands: Resection Checklist**Macroscopic**

Specimen Type: "Tumor Site" was relabeled "Specimen Type," as shown below

Specimen Type

- ☐ Resection, submandibular gland
- ☐ Resection, sublingual gland
- ☐ Superficial parotidectomy
- ☐ Total parotidectomy
- ☐ Other (specify): _____
- ☐ Not specified

Microscopic

Histologic Type: Adenocarcinoma NOS was modified to include high, intermediate, and low grade, as shown below

Histologic Type

- ☐ Acinic cell carcinoma
- ☐ Adenoid cystic carcinoma
- ☐ Adenocarcinoma not otherwise specified (NOS), low grade
- ☐ Adenocarcinoma NOS, intermediate grade
- ☐ Adenocarcinoma NOS, high grade, etc

Urinary Bladder, Ureter, and Renal Pelvis

No changes have been made to the data elements of the checklist(s) since the January 2004 protocol revision.

Uterine Cervix

No changes have been made to the data elements of the checklist(s) since the January 2004 protocol revision.

Uveal Melanoma

No changes have been made to the data elements of the checklist(s) since the January 2004 protocol revision.

Vagina

No changes have been made to the data elements of the checklist(s) since the January 2004 protocol revision.

Vulva

No changes have been made to the data elements of the checklist(s) since the January 2004 protocol revision.

Wilms Tumor

The following changes have been made to the data elements of the checklist(s) since the January 2004 protocol revision.

Kidney: Resection for Wilms Tumor Checklist

Macroscopic

Tumor Characteristics: The option, "Cannot be determined," was added under dimensions, as shown below

Tumor Characteristics (check all that apply)

Number of tumor nodules: ____

For each nodule:

Greatest dimension: ____ cm

*Additional dimensions: ____x____ cm

____ Cannot be determined (see Comment)

Location(s) (specify): _____

____ Cannot be determined (see Comment)

Source:

http://www.cap.org/apps/docs/cancer_protocols/protocols_index.html

