General & Systemic Histopathology

Pathology C601 & C602
Laboratory Manual
Dr Mark Braun

Medical Sciences Program

General and Systemic Histopathology
Lab Manual for c601 and c602
by Dr. Mark Braun

Indiana University
Medical Sciences Program

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Laboratory Manual
Pathology c601/c602

This manual is intended as a companion to the student slide set. Each picture is of a slide from that set and the pertinent features have been highlighted. Many of these slides are also now available for review by means of the virtual microscope. This manual, the accompanying CD and website are not a substitute for the microscope, either virtual or optical, rather they are designed to help the learner identify the important and diagnostic features of the various pathologic conditions. Please don't make the faulty assumption that all that's needed is to study these photographs. Slide lists, organized both numerically and by system, are at the end of the photo section of this manual.

The accompanying CD and web site provide all the pictures in living color as well as on-line quizzes to test your knowledge. The smart person will always see to the self-help quizzes. Some of the questions are likely to turn up later. The web site address is:

http://www.indiana.edu/~c602

This manual, its accompanying CD and web site would never have come into being were it not for the efforts of those who work in the *Teaching and Learning Technology Laboratory* here at Indiana University. The author especially wants to acknowledge Cordah Robinson and Kathryn Propst. Both worked beyond all expectation on the manuscript and web site. Not only were their editorial skills tested to the limit, but their delightful sense of humor and "can do" attitude saved the day on many occasion. The author also wishes to thank Sue Childress for her thorough review of this text and her many helpful suggestions.

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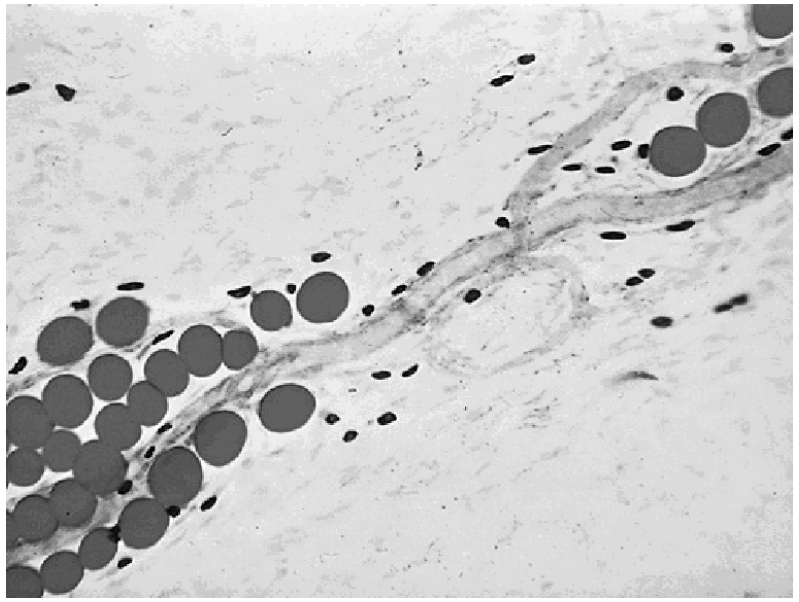
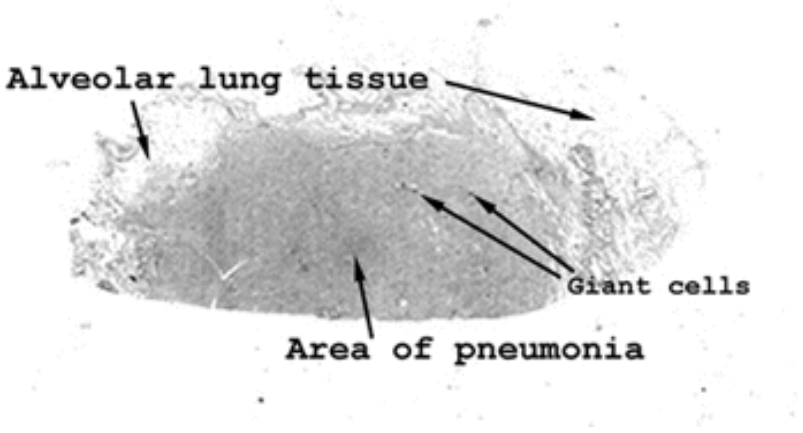
General and Systemic Histopathology
C601 and C602

Section 1 *Inflammation and Repair*

In this section you will learn to recognize specific types of inflammatory cells and infiltrates in a histologic setting. I am sure you will gain a quick appreciation for how different the histology will be in the diseased state. Cells and tissue architecture that you may feel quite familiar with will have a substantially different appearance. After this exercise you should be familiar with appearance and components of an acute and chronic inflammatory infiltrate, as well as the major actors in the repair process. You should also know the difference between an exudate and transudate. Although the slides for study are listed in numerical order, I recommend studying them in the following order: 27, 90, 48 and 19 first, then go to 9 and 139, then the chronic inflammatory conditions 1, 76 and 77, and finish with the repair cases 7, 43 and 59. Good luck!

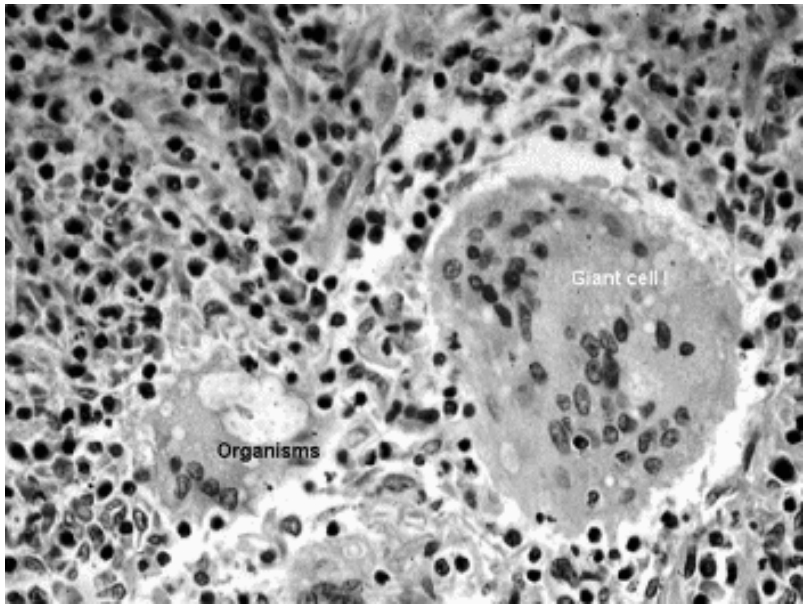


Slide 1: Cryptococcal Pneumonia, a higher power.



This is a picture of the tissue as it appears on your slide. See if you can orient it as it appears here and then locate the alveolar lung tissue with central area of inflammatory infiltrate. You might even be able to spot some of the giant cells without any magnification. When you put the slide on the stage of your scope, start with the lowest power first, review the entire slide and then go progressively to the higher levels of magnification.

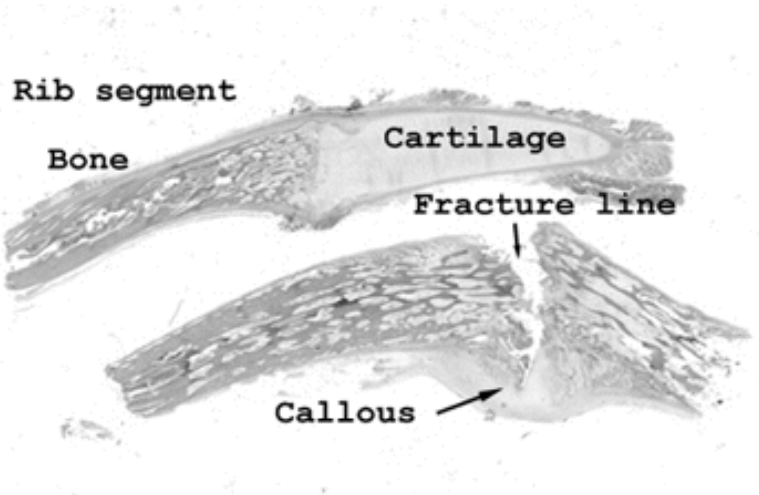
Your observations



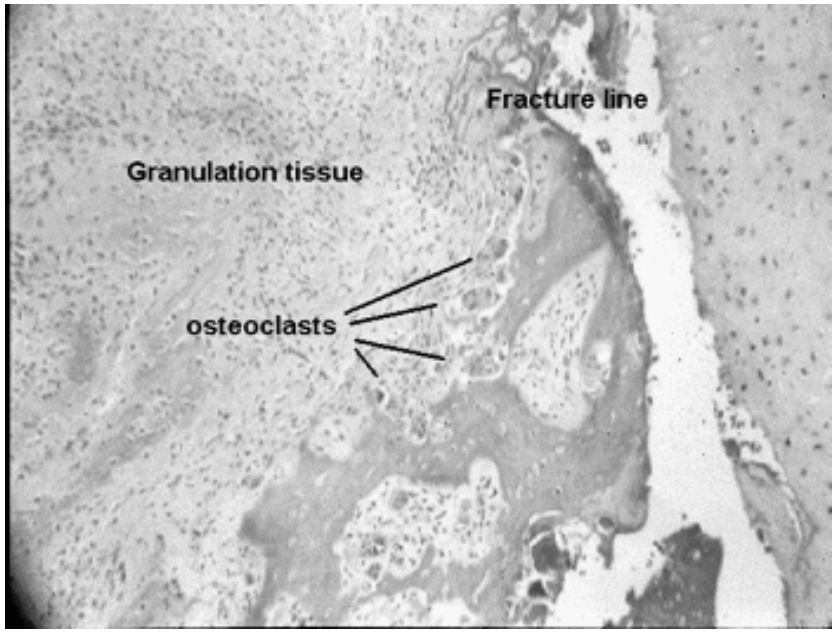
In this picture you can see the term "giant cell" is aptly applied. The cryptococcal organisms are quite evident in one of the smaller giant cells. As you may recall, the organisms possesses a large capsule so they tend to stand out in the cytoplasm of the giant cells. The giant cells are unique participants in our response to this type of injury. They are commonly seen in association with agents the body cannot easily rid itself of. We will see them again in the inflammatory response to tuberculosis and foreign material that has been injected or left behind in the body. Can you think of situations in which foreign material might find its way into the body (I mean external matter, not an infectious agent)?

Slide 7: Healing fracture of bone.

Your observations

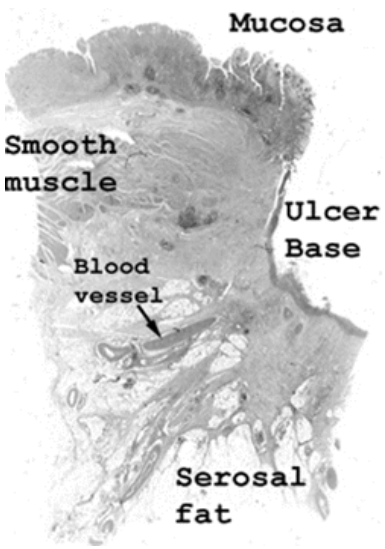


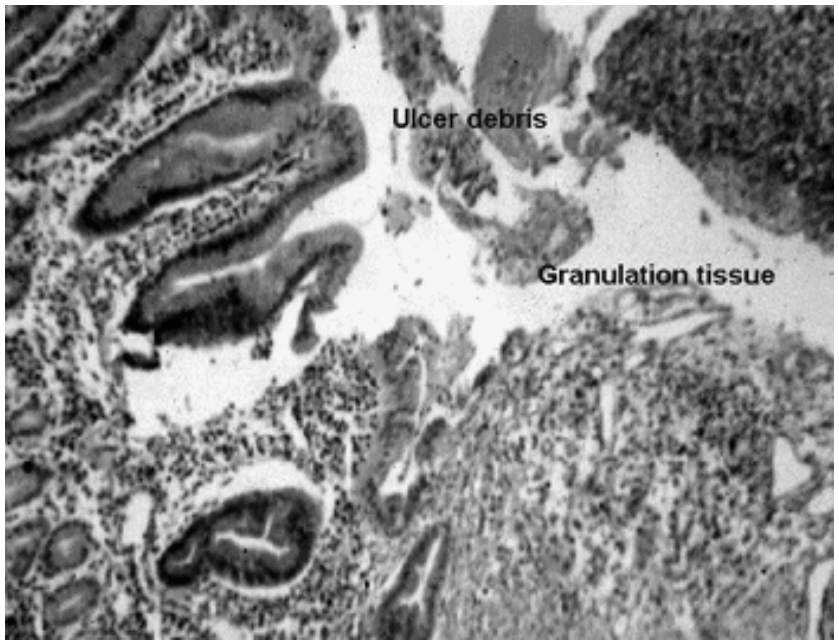
This slide obviously has two sections of tissue. Both are of a rib and the lower portion shows a partially healed fracture line. You can see the developing callous on one side and there is abundant granulation tissue in the fracture line itself. We split the fracture line open at the time the specimen was embedded so as to highlight where to look for the healing process. In life, the fracture was closed and the edges were knit together with the newly formed granulation tissue.



This healing "fracture" is a approximately two weeks old, and shows early changes of the healing process. Note the remodeling taking place by the osteocclasts and the rather marked degree of fibrosis (scarring) that is taking place as the new bone is being formed. In your slide, you should be able to
see many active fibroblasts and angioblasts as part of the initial healing "team." See if you can find the area just by looking at your slide.

Slide 9: Stomach with gastric ulcer.





This picture actually represents about half of the tissue on your slide. Just imagine it's got a mirror image right half and you'll have it. The photomicrograph to the left comes from the edge where the ulcer meets the mucosa. Note the bright pink layer of fibrin and digested protein material that lines the ulcer base. The granulation tissue begins just beneath this. See how the ulcer has eroded completely through the muscle and is about to perforate through the serosal fat. What do think is the significance of the inflitrate seen just to the left of the ulcer base?

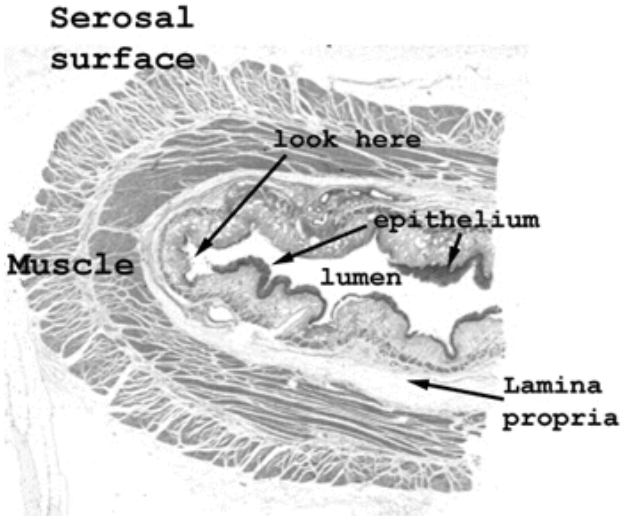
Your slide includes only about half the ulcer. Before going to the microscope, hold the slide up to the light or look at it on a white background. You should be able to easily spot the area of the ulcer. Try to get yourself oriented before diving in with the scope. Observe the "granulation tissue" in the ulcer base and be sure you can identify angioblasts and the numerous reactive fibroblasts. There is considerable digested debris on the surface of the ulcer, don't confuse this for the reparative elements of granulation tissue. The digested junk contains epithelial cells, inflammatory elements, bacteria and who knows what all.

What's the bacterial agent of such renown in this disease?

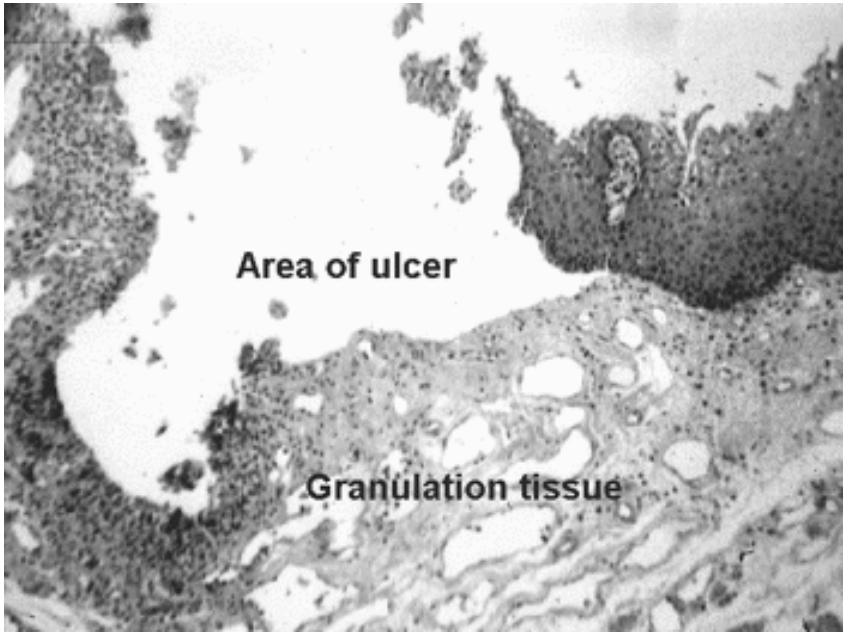
Your observations

Slide 19: Acute Erosive Esophagitis

Your observations



Your slide shows almost a complete cross section of the esophagus. Note there are several areas of mucosal ulceration and some relatively large, thin walled vessels are present in the lamina propria.

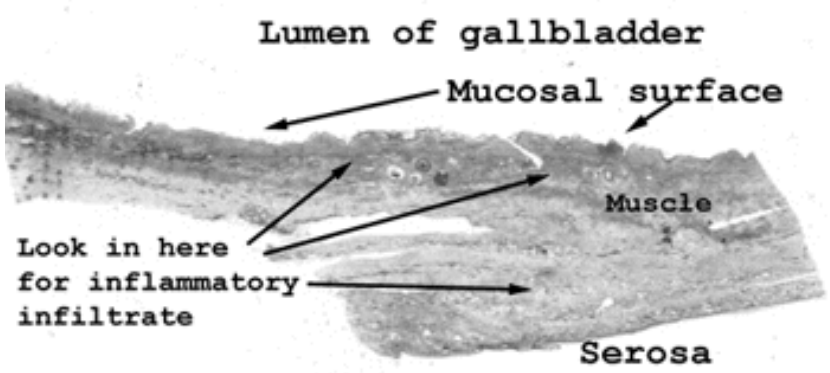


If you simply look at the slide on a white background, you can see the area of erosion quite nicely. Note the areas of healing and repair at the margins of the ulcer. Some acute inflammatory cells are seen in the base of the lesion, and many very dilated vessels are present in this area as well. These large superficial vessels are not part of the healing process, and represent part of another pathologic process in this person.

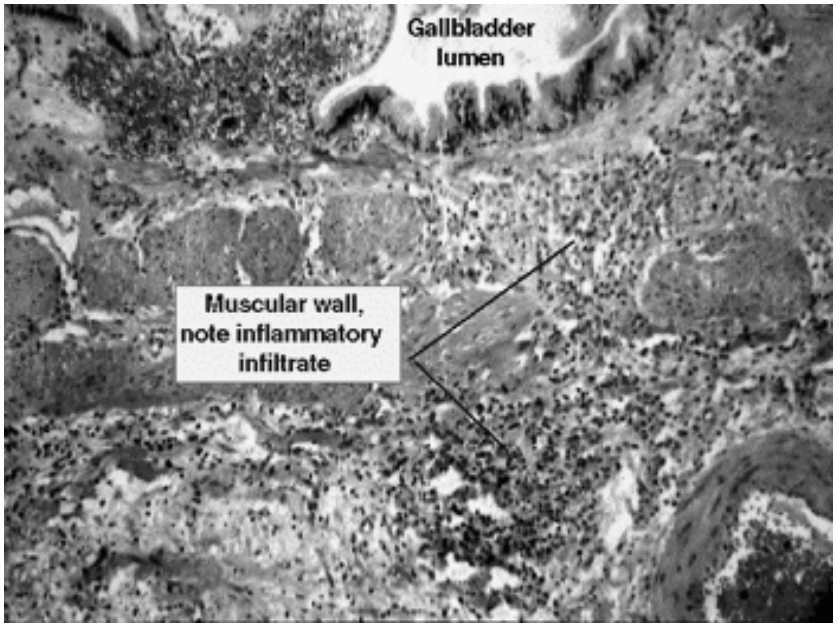
What condition could lead to these dilated vessels? Where would you expect to find others?

Slide 27: Gallbladder with acute and chronic inflammation .

Your observations

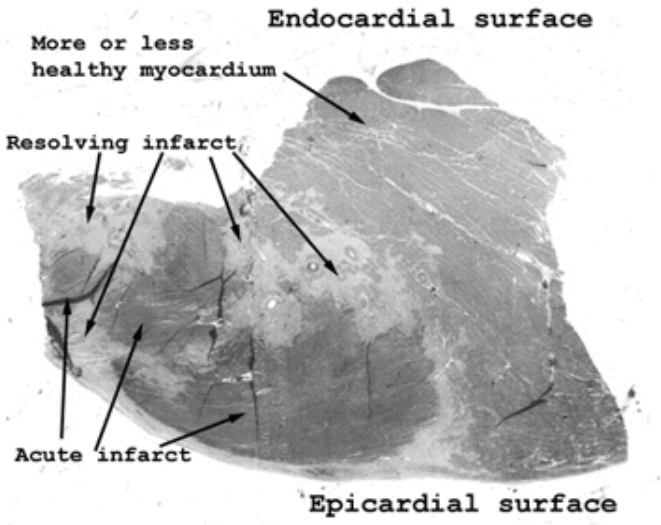


This section represents only a small slice out of a dilated, inflamed (and no doubt painful) gallbladder. Undoubtedly there were stones present as well, but we don't have any direct microscopic evidence for them. Find the mucosa and then work your way through the wall to the serosa. Pay attention to the inflammatory cells and where you see them. What about the lamina propria?



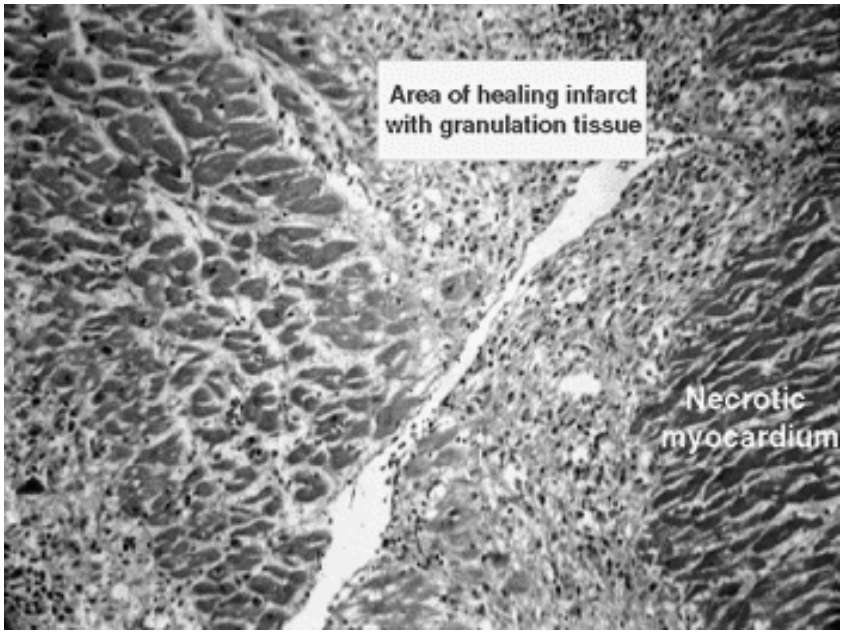
Find the lumen and try to have yourself oriented before looking for the infiltrate. You will see a mixed inflammatory infiltrate consisting of both "acute" and "chronic" inflammatory cells, again lymphocytes are to be expected in the submucosa of a structure associated with the gastrointestinal system. You will see a large amount of granulation tissue on the serosal surface.

Slide 43: Heart with Myocardial Infarction.



There's a lot to be seen in this piece of tissue. We have more or less normal heart tissue right beneath the endocardium. There are several myocardial infarctions of various ages and demonstrating various stages of development. In this picture, the areas identified as "resolving infarct" consist mostly of granulation tissue and represent an infarction of about two to three weeks duration. The bright pink areas represent a second and much more recent infarction. After you've read the section on myocardial infarctions, see if you can establish the duration of this second one. What do you think was the most likely cause of death?

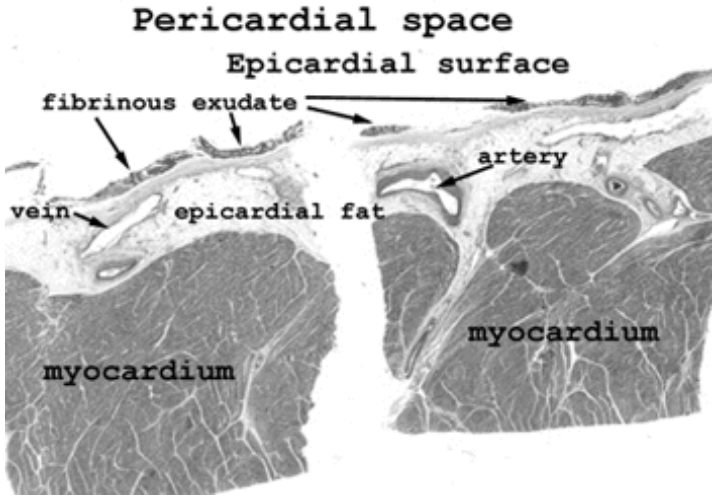
Your observations



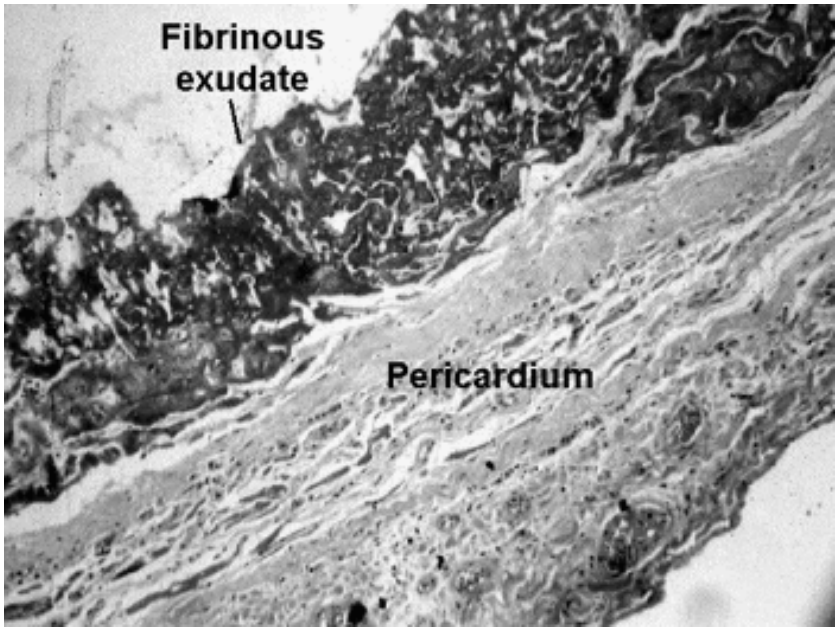
By this time it should be obvious that a lot can be learned from a slide without using the microscope. See if you can find the area of infarction before putting the slide on the stage of your microscope. Hold it to the light or put it on a white background. This area of infarction is about two weeks old, and shows substantial removal of the dead muscle with early replacement with granulation and fibro-connective tissue. Some inflammatory cells remain. This person died with an arrhythmia.

Slide 48: Fibrinous pericarditis.

Your observations



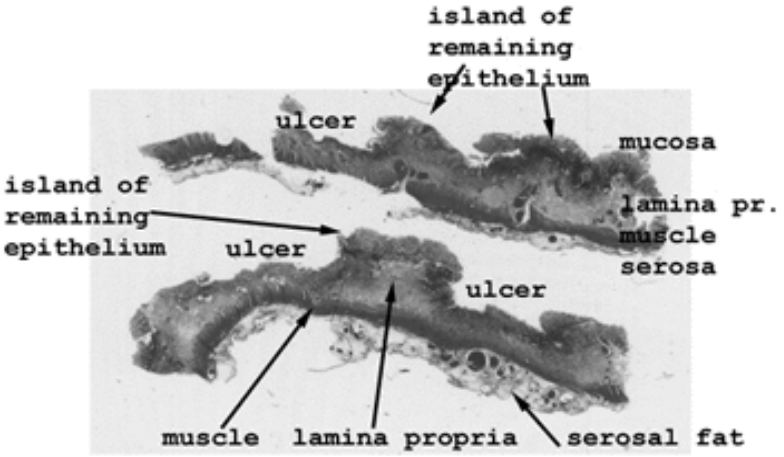
In this case, we're looking for a thin band of homogeneous, pink staining, proteinaceous material on the epicardial surface of the heart. This represents an exudate composed largely of protein material. You will see very few inflammatory cells.



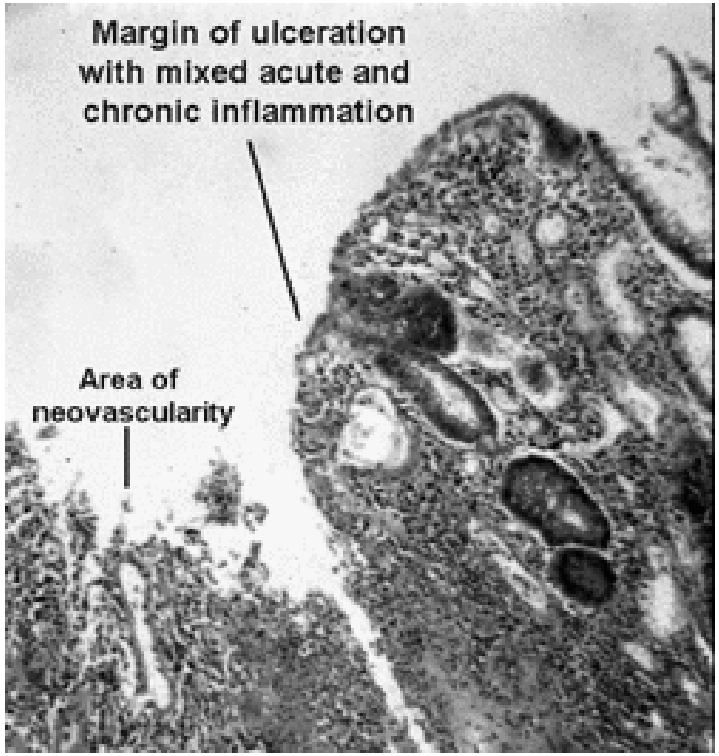
Before putting the slide on the microscope stage, look at the tissue to find the epicardial surface. This is where you will find the exudate. This exudate is almost totally devoid of inflammatory cells, and consists almost totally of protein (fibrin plus other trash). It looks the way I think "tofu" would look if sectioned and stained. This exudate is a product of renal failure, is completely sterile. It occurs secondary to the crystallization of nitrogenous wastes on the epicardial and pericardial surfaces. Renal failure is consequence of many forms of long term kidney disease.

Slide 59: Colon with acute ulcerative colitis

Your observations



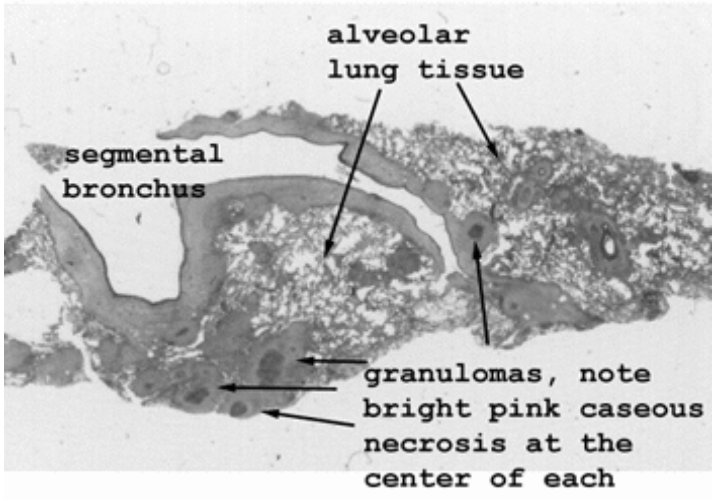
This can be a challenging slide. There are only islands of remaining mucosa, separated by large expanses of ulceration. Look in the base of the ulcers and just to the edge of the residual mucosa for the best examples of granulation tissue.



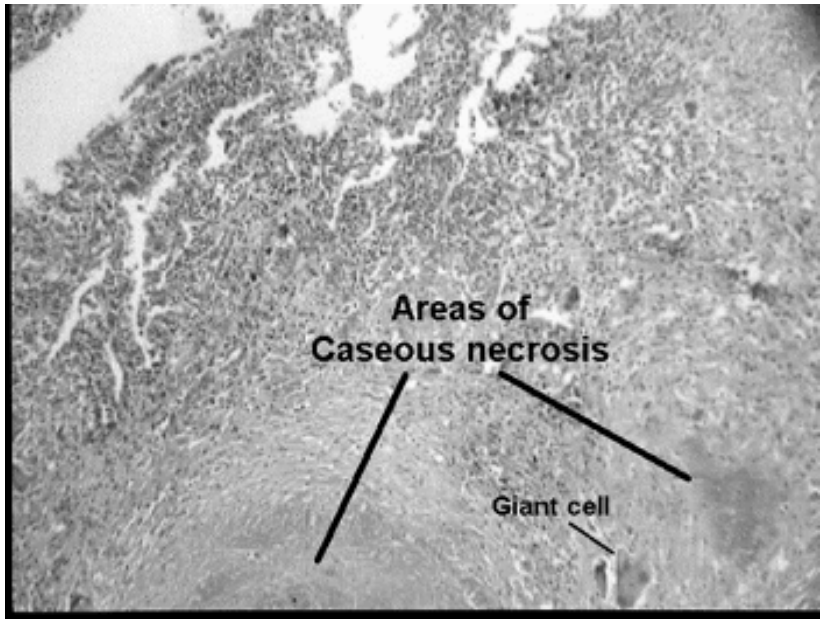
The picture is from the edge of an ulcer, and shows focal absence of the mucosa. There is a mixed acute and chronic inflammatory infiltrate in the base of the ulcer with lots of granulation tissue. You will see many angioblasts and reactive fibroblasts in these areas of healing. Crypt abscesses are seen in the base of the crypts. This feature may not be very apparent as this case is relatively advanced and these earlier changes are simply overwhelmed by the degree of inflammation.

Slide 76: Lung with tuberculosis

Your observations



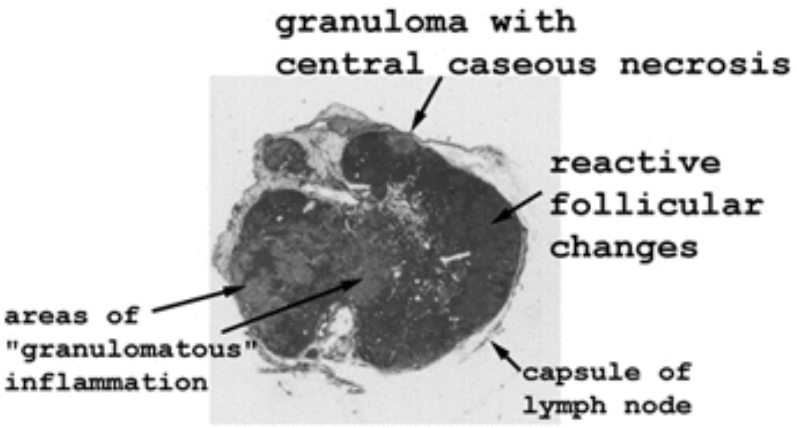
Look carefully at the lung tissue for the little pink areas of caseous necrosis. These are the areas of tubercular infection. They don't show a well developed granuloma architecture, but you'll see the evolving features and should have no trouble finding the giant cells.



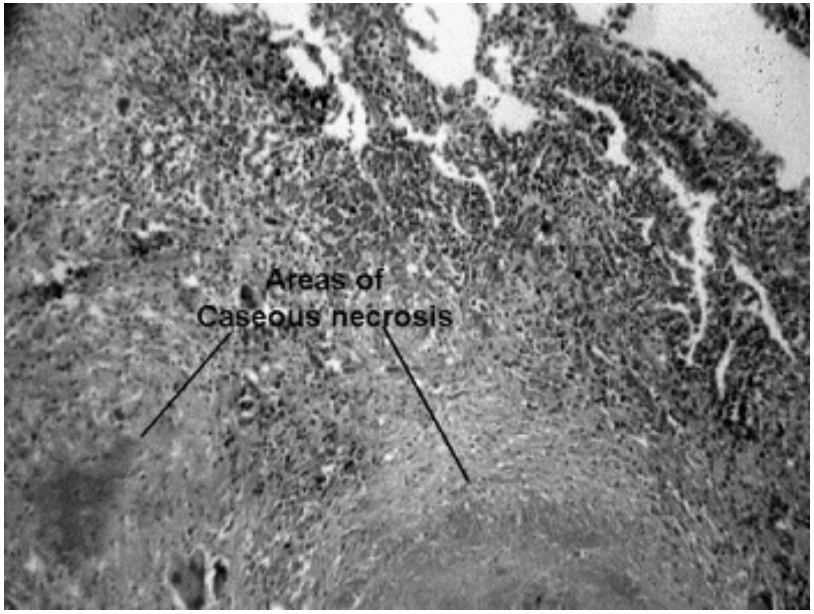
This section of lung is largely replaced with a single granuloma. Note the structure of the granuloma and the fact that it has a "caseous" center. There are numerous giant cells and the fibrous margin of the granuloma is only partially formed at this time. The caseous center of the granuloma is very characteristic of TB. The granuloma itself, and the giant cells, represent a general reaction to an agent the body cannot eliminate or destroy.

Slide 77: Lymph node with tuberculosis

Your observations



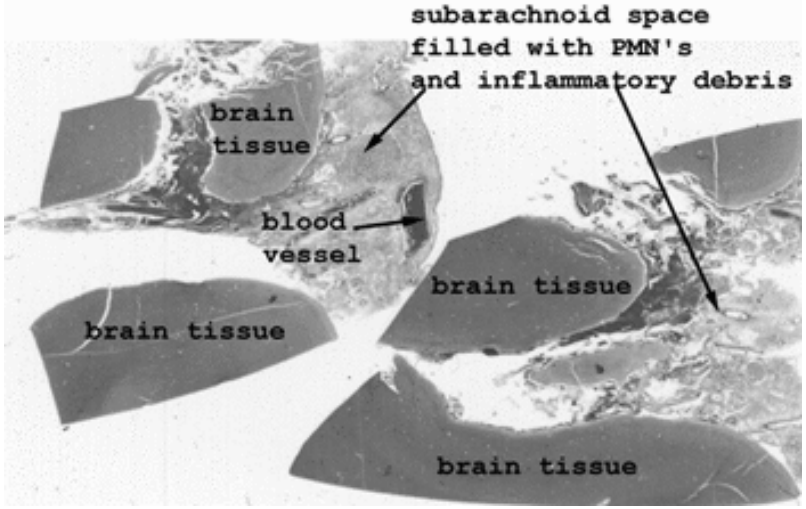
Although this slide is a bit faded, you should be able find the areas of granulomatous inflammation. In some areas there are well developed granulomas with giant cells.



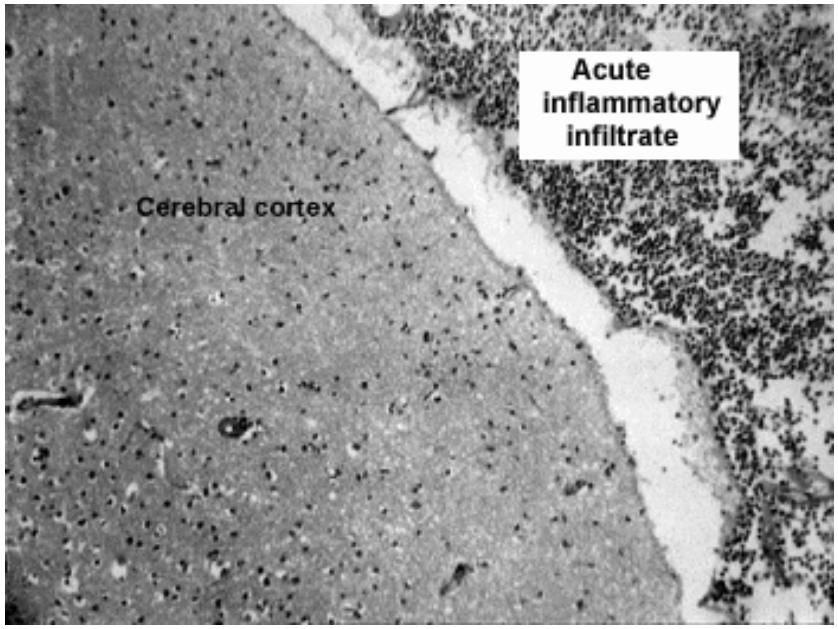
This is a pulmonary hilar lymph node showing a granuloma and many giant cells. It is from the person that also gave you slide #76, and demonstrates the body's reaction to TB. As with slide #76, the overall pattern of the granuloma is the same.

Slide 90: Acute meningitis

Your observations

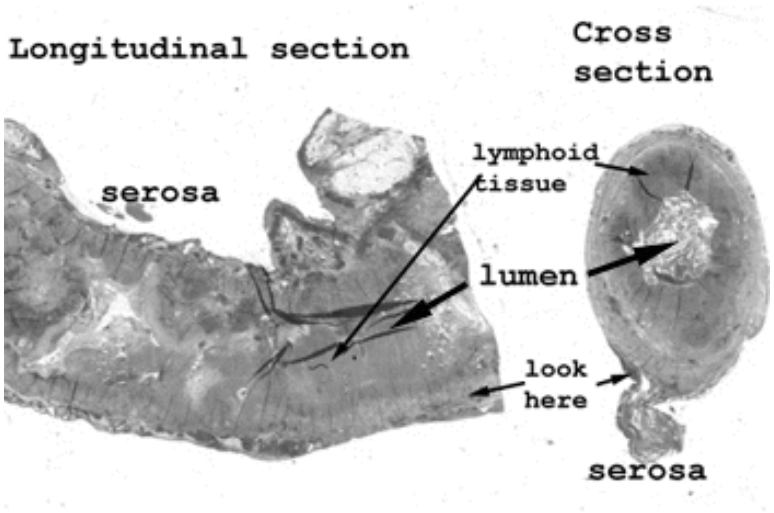


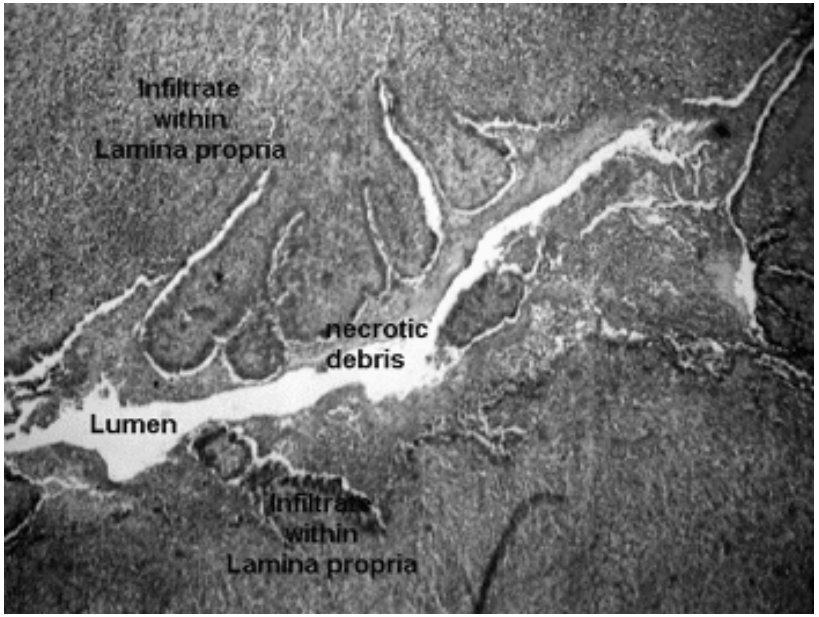
Here you see the unbelievably expanded subarachnoid space containing numerous polymorphonuclear leukocytes. What do you suspect the exudate looked like grossly?



This slide shows a profound acute inflammatory infiltrate associated with Hemophilus influenza meningitis. The organism most likely gained entrance into the subarachnoid space by way of the blood stream. The child with this condition died shortly after being admitted to the hospital, despite vigorous antibiotic therapy. Unfortunately, the child was not brought in until he was virtually moribund. You should have no trouble finding the polymorphonuclear leukocytes in this slide.

Slide 139: Acute Appendicitis





Here you have two sections of the appendix. The one on the left is a longitudinal section in which the lumen is not well defined. It contains lots of necrotic debris. The section on the right is a little easier to understand as a hollow organ. Still the lumen is partially obliterated by necrotic debris and inflammatory material.

Start reviewing this slide in the lumen and work your way methodically to the serosal surface. Pay attention to all the elements and make notes on what you see. Compare your notes to what you expect in the normal or healthy situation.

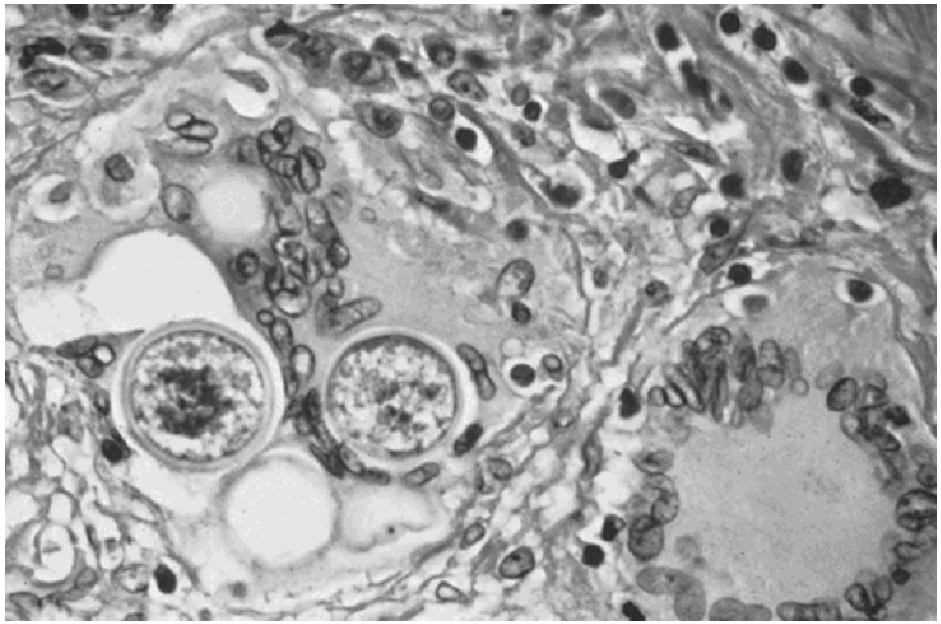
In this slide, the mucosa of the appendix is largely missing and there is a profound acute inflammatory infiltrate in the lamina propria. There is also a lot of necrotic debris in the lumen of the organ. This is a difficult slide because the acute inflammatory infiltrate is intermixed with the normally occurring lymphoid tissue of the appendix. Remember that in the healthy state you would find many lymphoid aggregates in the lamina propria of the appendix, and throughout the length of the bowel for that matter. You may also see some newly forming granulation tissue on the serosal surface. As far as that goes, your best shot at seeing the constituents of the acute infiltrate will be in the serosal surface itself. In some of the slides there is marked lymphoid hyperplasia in the lamina propria (a finding you might expect), so it is probably best to steer away from lumen and the centrally located portions of this tissue for right now.

Your observations

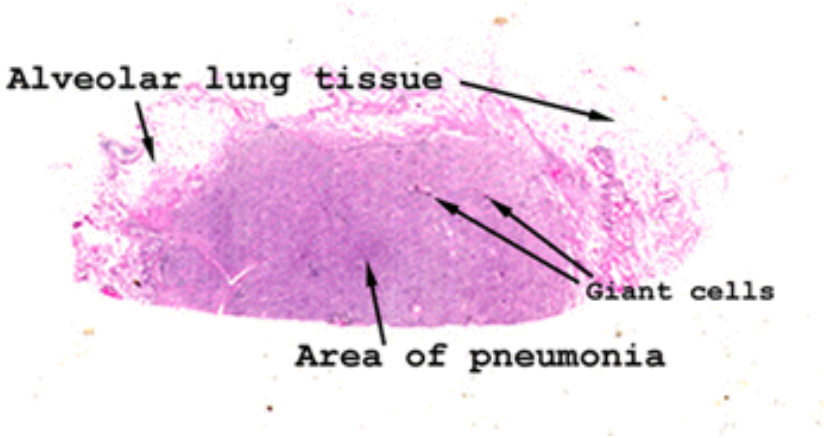
General and Systemic Histopathology
C601 and C602

Section 2 *Infectious Diseases*

In this section we will be looking at some of the same slides we studied in the inflammation and repair unit, but from a different point of view. When finished, you should be able to identify the general inflammatory patterns associated with bacterial, fungal, tubercular and viral infections. Although there are just a few slides to be reviewed, the basic patterns can be applied to many situations. Also upon completion of this unit, you should understand the basic mechanisms of injury of infectious organisms and be able to identify their common inflammatory patterns such as: acute and chronic inflammatory exudates, abscesses, granulomas and necrotizing processes. As slide 131 will show, finding the culprit may require some diligence.

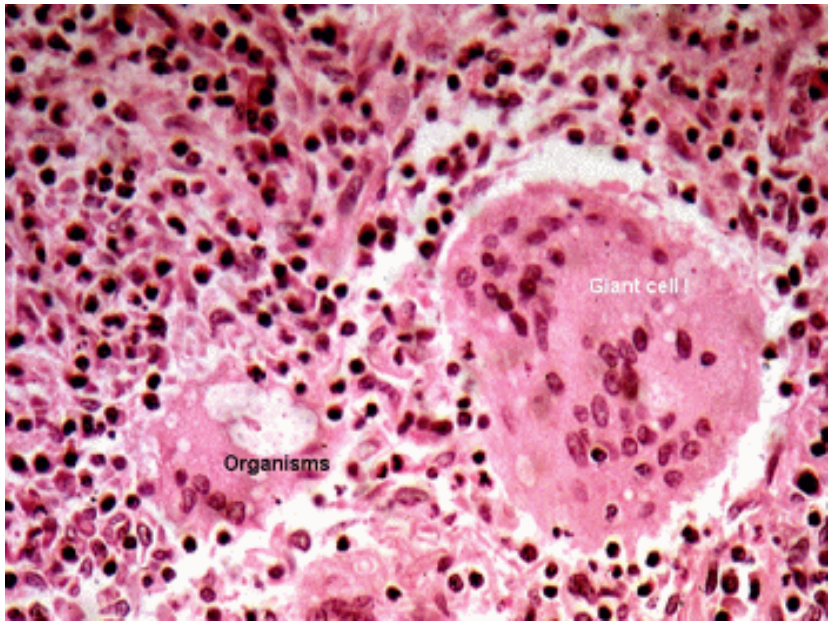


Slide 1: Cryptococcal Pneumonia



Your observations

This is a picture of the tissue as it appears on your slide. See if you can orient it as it appears here and then locate the alveolar lung tissue with central area of inflammatory infiltrate. You might even be able to spot some of the giant cells without any magnification. When you put the slide on the stage of your scope, start with the lowest power first, review the entire slide and then go progressively to the higher levels of magnification.



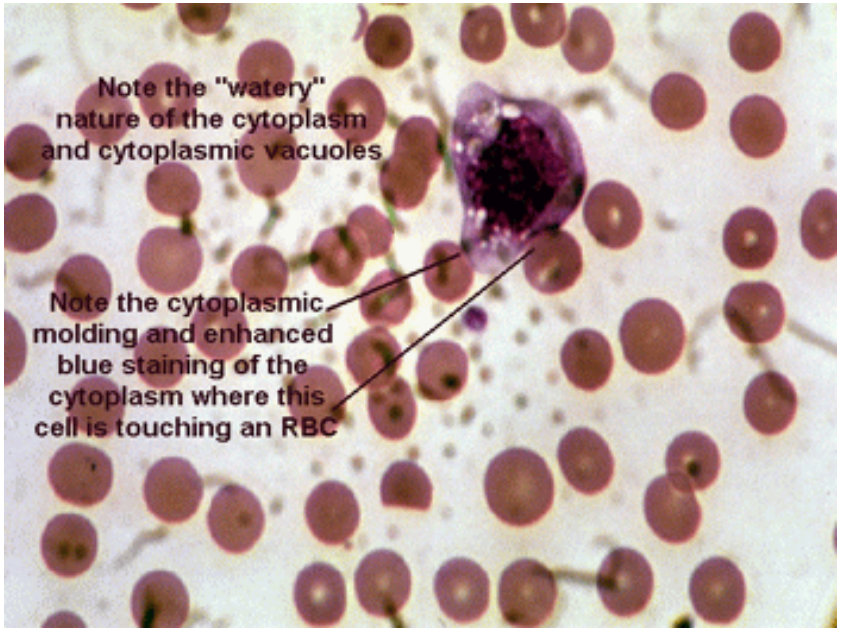
The cryptococcal organisms are quite evident in one of the smaller giant cells. As you may recall, the organisms possess a large capsule so they tend to stand out in the cytoplasm of the giant cells. The giant cells are unique participants in our response to injury. They are commonly seen in association with injurious agents the body cannot easily rid itself of. We will see them again in the inflammatory response to tuberculosis and foreign material that has been injected or left behind in the body.

Hematology case 13: Infectious mononucleosis

Your observations

Looking at blood smears can be a little tricky. Be sure you are at the furthest edge where the blood is the thinnest. You want to be where the RBC's are just touching each other.

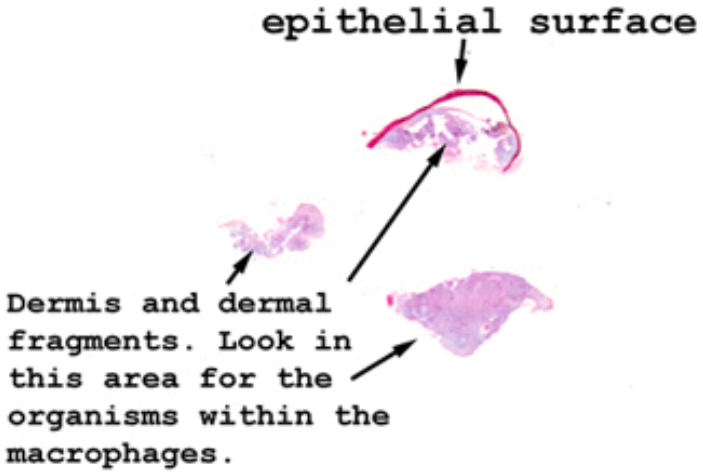
This is an online and blood smear found in your slide collection



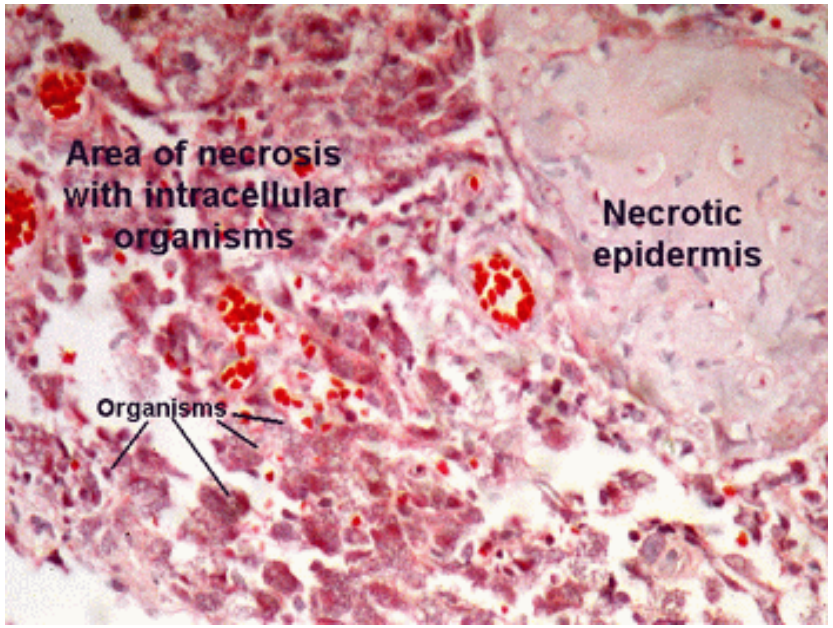
The blood smears don't come off so well in this digitized format, sorry. You will see many lymphocytes of the type depicted in this picture. Note the "watery" pale blue cytoplasm of the cells and the enhanced blue staining of the membrane where the cells touch an adjacent RBC. Some of the lymphocytes have cytoplasmic vacuoles and most show stimulated or reactive appearing nuclei. Unfortunately, we have referred to these cells in the past as "atypical," which now has a more sinister connotation. These are B lymphocytes that are infected with the EB virus. What is the initial infected cell? What can happen to the spleen?

Slide 17: Skin with leishmaniasis

Your observations

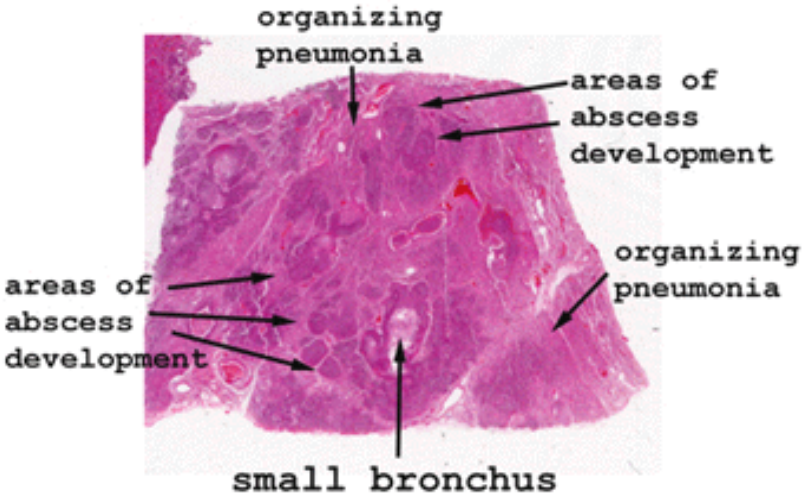


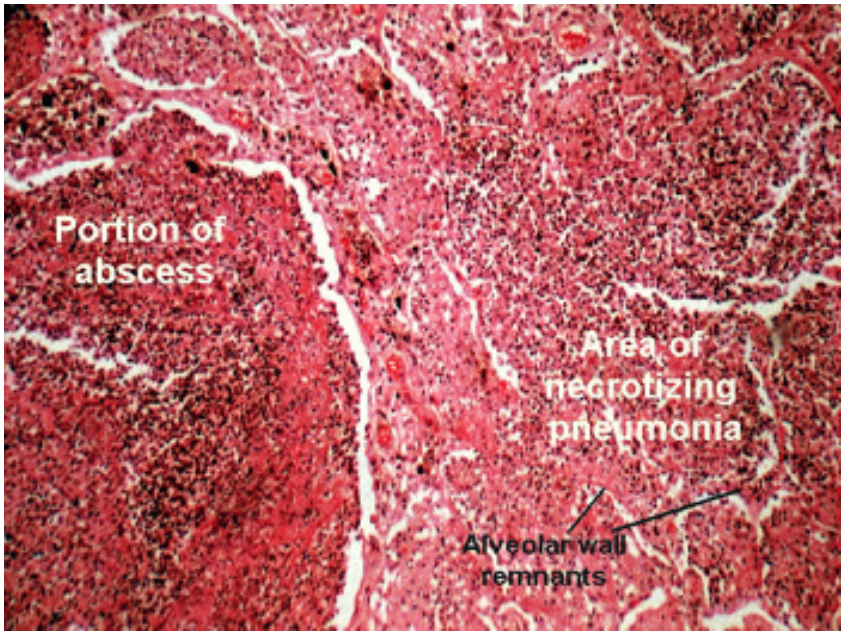
This specimen consists of little fragments of skin and it's difficult to get oriented. You want to be looking in the dermis for histiocytes containing the organisms. There is a lot of necrosis along with the inflammatory infiltrate.



This slide is not H&E stained. We used a stain to highlight the organisms. In some slides there is an ulcer with granulation tissue in the base. Look in the dermis and you will see an infiltrate composed largely of mononuclear cells. The organisms are in the monocytes, and appear as small dots with a cleared area or "halo" around them. They are quite small. Some may appear in the tissue, but I think this reflects rupture of the cells, possibly even as a tissue processing artifact. This slide is to further your education, and I'll tell you right now I don't have a sample of this in my quiz slide collection.

Slide 58: Lung with abscess





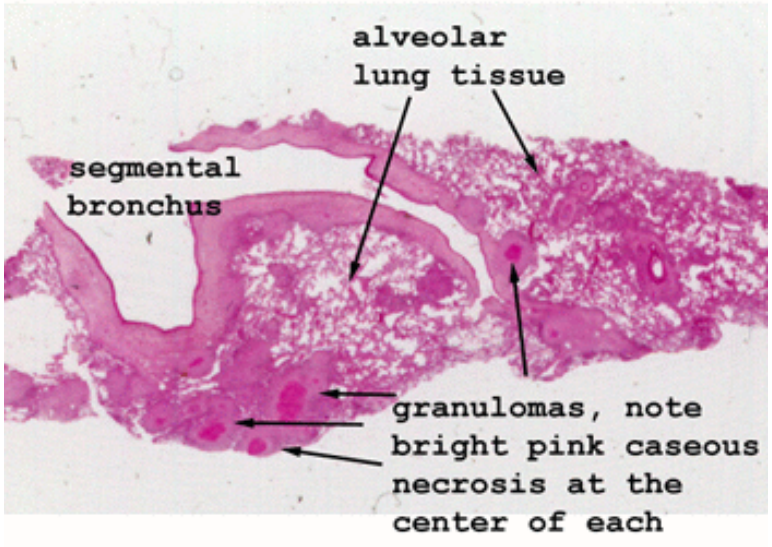
Your observations

There is such consolidation in this section of lung, that it is hardly recognizable for what it is. Just looking at the piece of tissue on the slide, you'll see the diffuse infiltrate as well as the darker areas that represent the complete breakdown of the pulmonary tissue. Start by looking at the edge of the tissue to see if you can find any "normal" lung to help you get oriented.

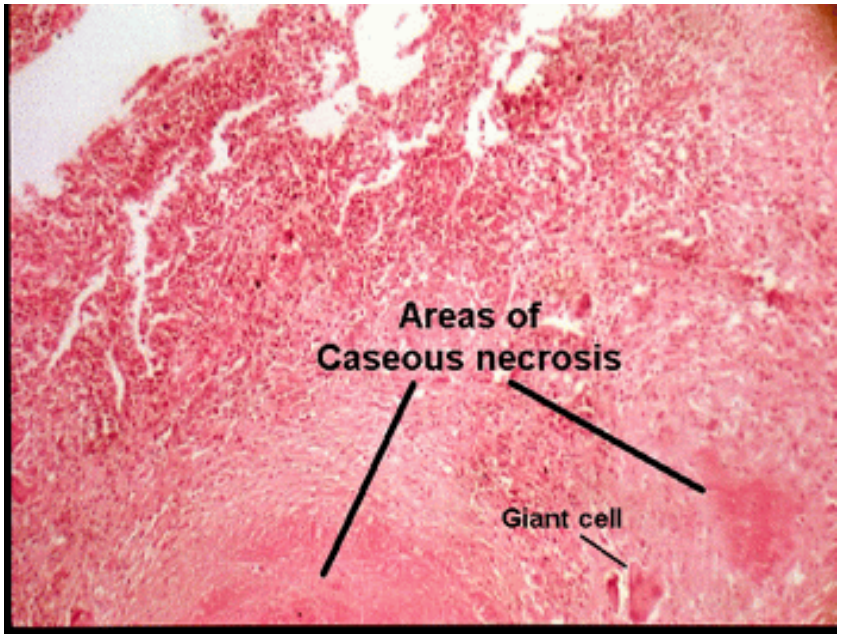
This condition could be due to any number of bacterial organisms, or even a mixture of bugs, but it happens to be staphylococcus. The general alveolar outlines will be hard to find in the areas of necrosis, so go to the edge of the tissue to get your bearings. You will need to be pretty familiar with normal lung architecture to see anything in the background. Much of the lung parenchyma has been destroyed by the digestive enzymes of the bugs. You will see many acute inflammatory cells along with the amorphous digested debris. Clearly, once the lung tissue has been destroyed and the abscess formed, that lung tissue is gone for good.

Slide 76: Lung with tuberculosis

Your observations



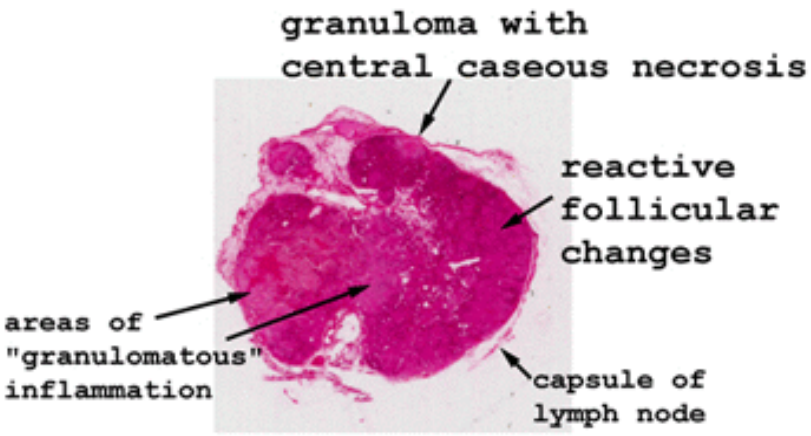
Look carefully at the lung tissue for the little pink areas of caseous necrosis. These are the areas of tubercular infection. They don't show a well developed granuloma architecture, but you'll see the evolving features and should have no trouble finding the giant cells.



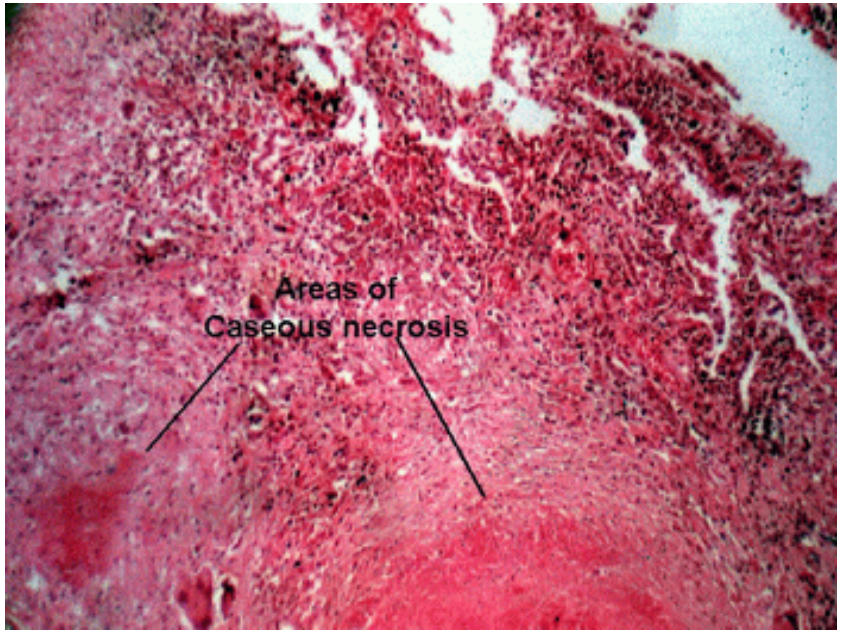
This section of lung is largely replaced with a single granuloma. Note the structure of the granuloma and the fact that it has a "caseous" center. There are numerous giant cells and the fibrous margin of the granuloma is only partially formed at this time. The caseous center of the granuloma is very characteristic of TB. The granuloma itself, and the giant cells, represent a general reaction to an agent the body cannot eliminate or destroy.

Slide 77: Lymph node with tuberculosis

Your observations



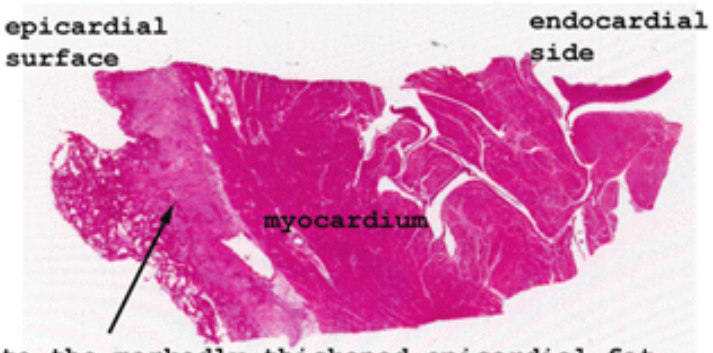
Although this slide is a bit faded, you should be able find the areas of granulomatous inflammation. In some areas there are well developed granulomas with giant cells.



This is a pulmonary hilar lymph node showing a granuloma and many giant cells. It is from the person that also gave you slide #76, and demonstrates the body's reaction to TB. As with slide #76, the overall pattern of the granuloma is the same.

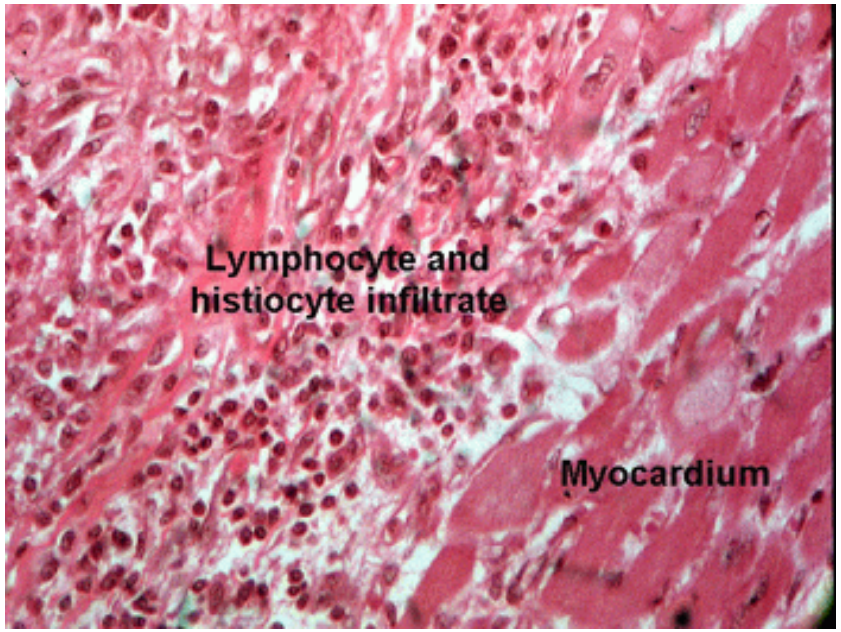
Slide 78: Tuberculous pericarditis

Your observations



Note the markedly thickened epicardial fat. Look here for a lymphocyte and plasma cell infiltrate. There are no well formed granulomas

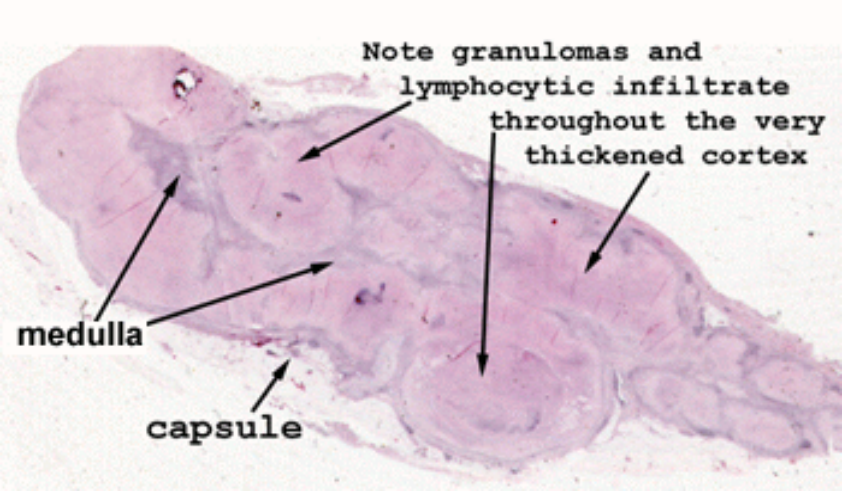
Here you will see an unbelievable thickened pericardium with a marked chronic inflammatory infiltrate. The exudate is partially "organized," but no well defined granulomas are present. We know this was tuberculosis because of the history and positive autopsy cultures.



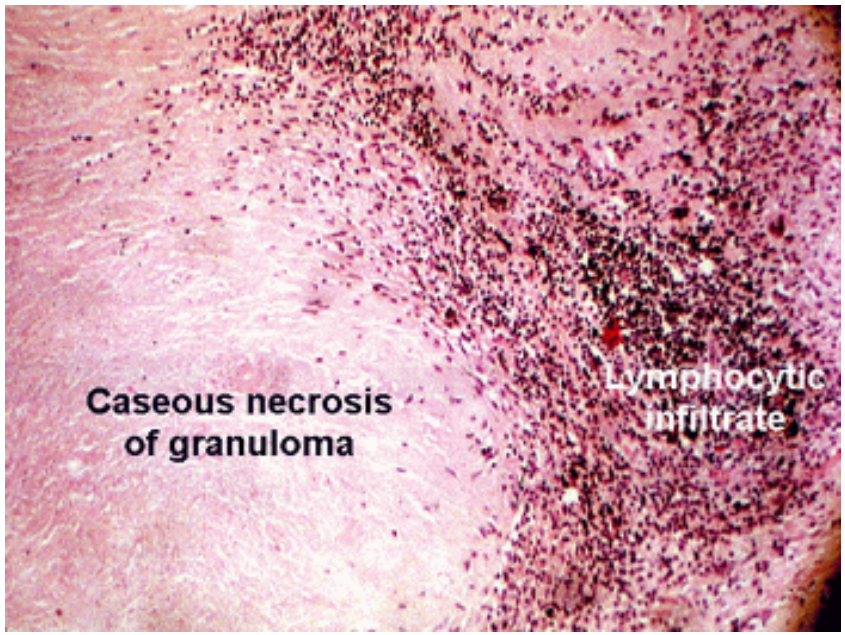
This slide does not show well developed granulomas, rather a marked chronic inflammatory infiltrate with a large amount of granulation tissue. By the way, be sure you know the difference between "granuloma" and "granulation tissue," even if the two seem to blend together here. In this slide there are many plasma cells along with the angioblasts and fibroblasts in, and on, the surface of the epicardium. Histologically it's not really possible to make a diagnosis of TB from what you have. We know it because of the patient's history and a successful culture. I am not trying to fool you or give you something you can't diagnose, rather I am showing you how it can look.

Slide 97: Adrenal tuberculosis

Your observations



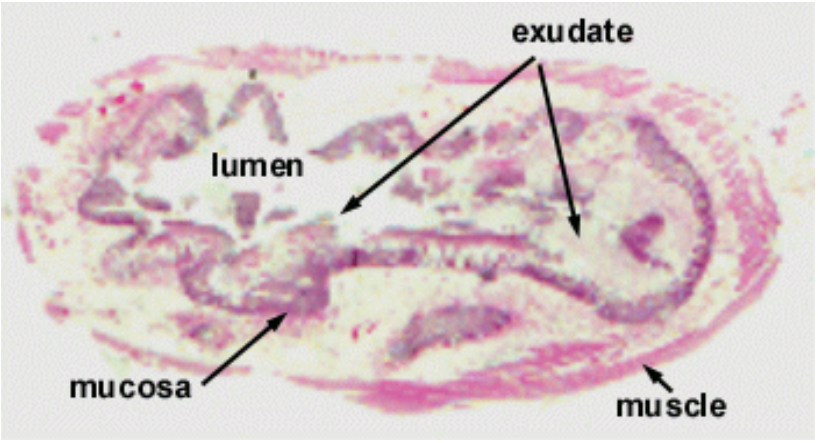
Just by looking at the tissue on the slide, you can see the marked alteration in the normal appearance of this adrenal gland. When disseminated, TB often goes to the adrenals. Even without the microscope you can see the extensive areas of caseous necrosis throughout the cortex.



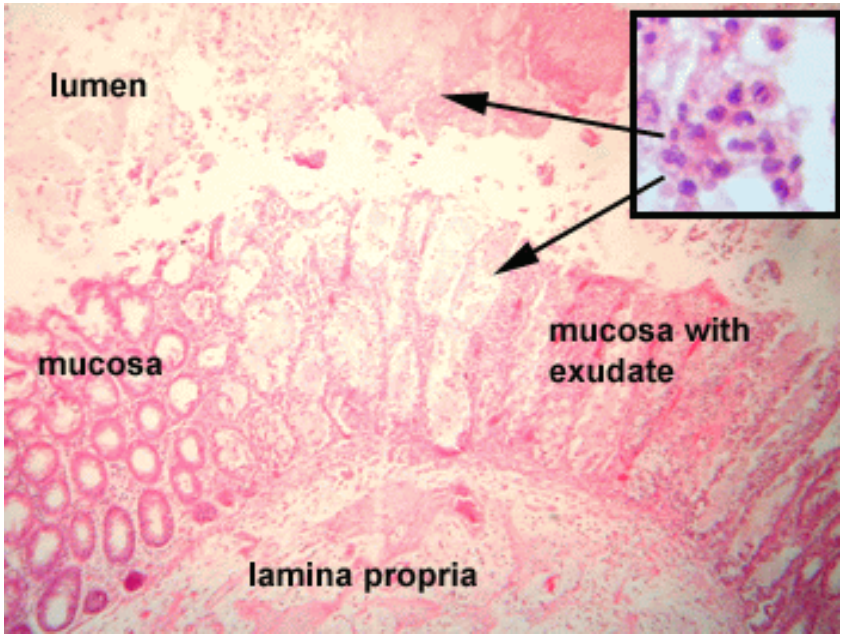
This is a pretty washed out slide, do your best, but don't waste a lot of time. As you will see, there is practically no adrenal gland left. We would be hard put to even tell the organ had it not been for its location at the time of autopsy. Observe the granuloma with caseous necrosis at its center. There are few giant cells, but the principal remaining inflammatory pattern is of non-specific chronic inflammation. You will see lymphocytes and plasma cells comprising the majority of the inflammatory pattern.

Slide 131: Colon with pseudomembranous colitis

Your observations



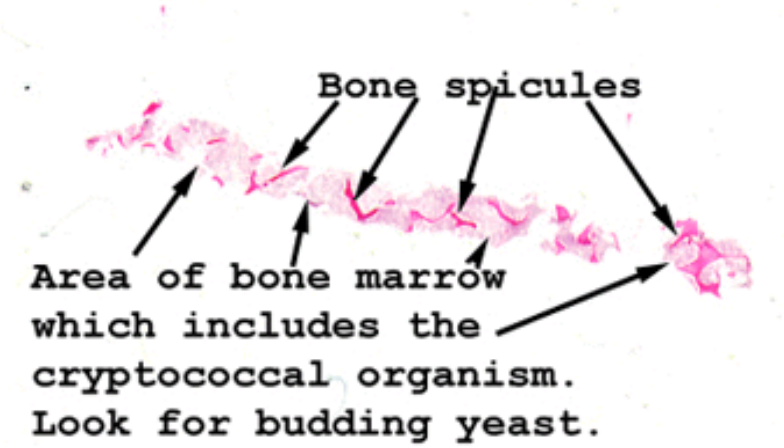
This specimen is a complete cross section of colon and the action is taking place on the mucosal surface and the mucus seen in the lumen (the detached junk). In this case, the history of the patient is key to making the diagnosis. What history do we mean?



As you may know, this condition is caused by antibiotic usage. The causative organism is a clostridial organism that can sporulate, and return after the antibiotic has disappeared. The bug is actually on the surface of the bowel, and elicits a marked acute inflammatory response. Here you will see an acute inflammatory exudate in some of the crypts and on the surface of the mucosa. You won't be able to see the organisms in all likelihood.

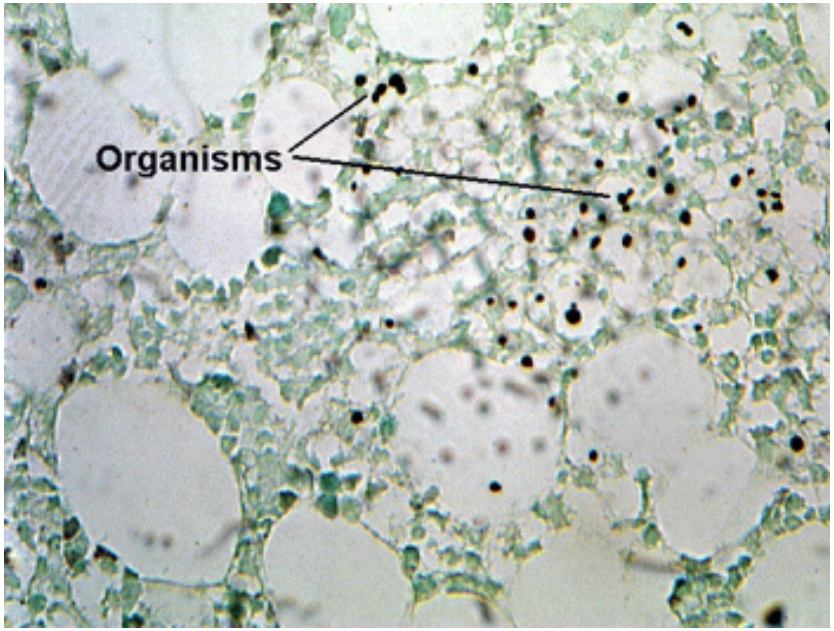
The insert shows the PMNs in the mucus.

Slide 166: Bone marrow with cryptococcal infection



Your observations

This is a small core biopsy of bone which shows only minimal replacement of the bone marrow space with an inflammatory infiltrate. It takes the special stain to show the organisms. Obviously, the history was very important in knowing what to do make the diagnosis in this case.



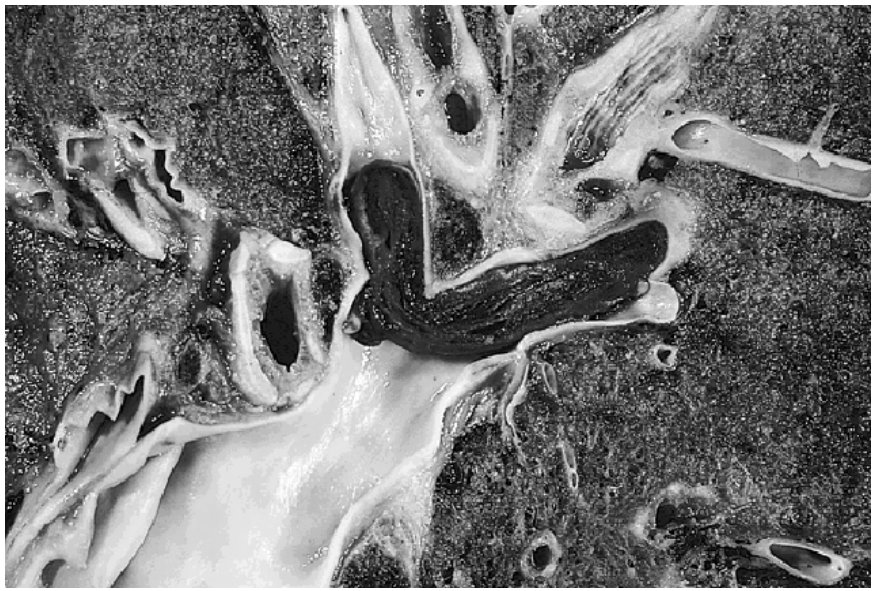
This is one of two slides of the same tissue. The H&E stained slide (#165) does not show the organisms. You will see a fairly "bland" infiltrate diffusely throughout the marrow composed of monocytes. Additionally, there is an overall depression of the number of myeloid precursors present. These two factors, coupled with the history are significant elements in leading the pathologist to the next move, which will lead to the diagnosis

The definitive findings are seen here (slide 166), which is stained using a silver salt procedure. Here the organisms can be identified as budding yeasts.

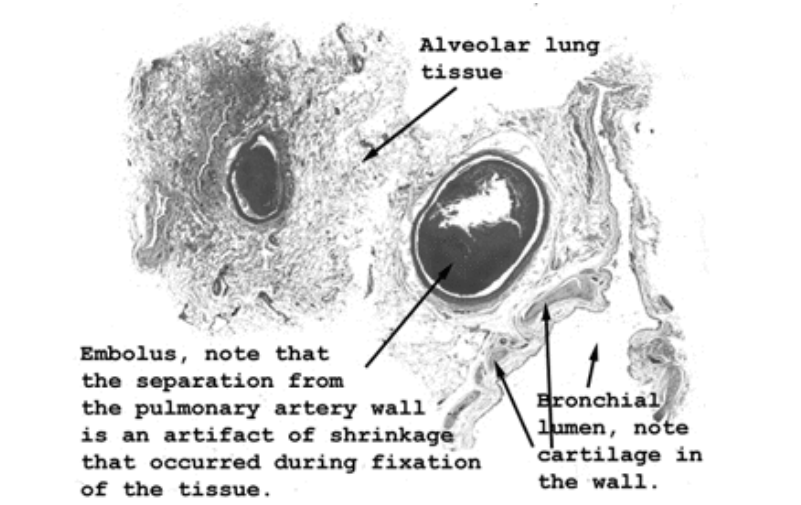
General and Systemic Histopathology
C601 and C602

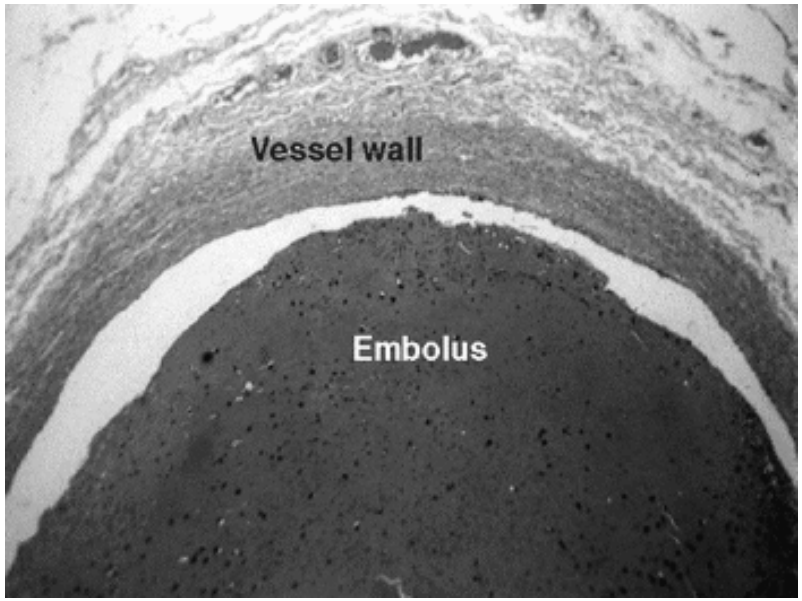
Section 3 *Hemodynamic Disorders*

This unit will focus on aspects of "compartmentalization" of body water, states of vascular congestion and hemostasis. We will be discussing pulmonary and other organ consequences of congestive heart failure, and in this context you will need to understand the difference between transudate and an exudate. If these ideas are unclear, better review them in your lecture notes.



Slide 14: Lung with pulmonary embolus



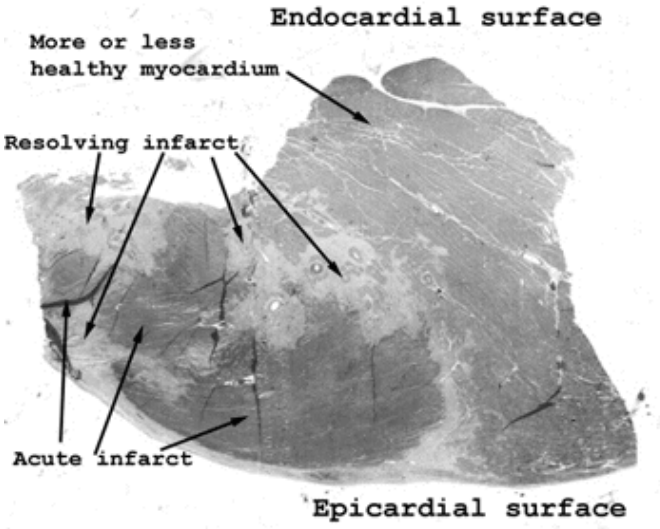


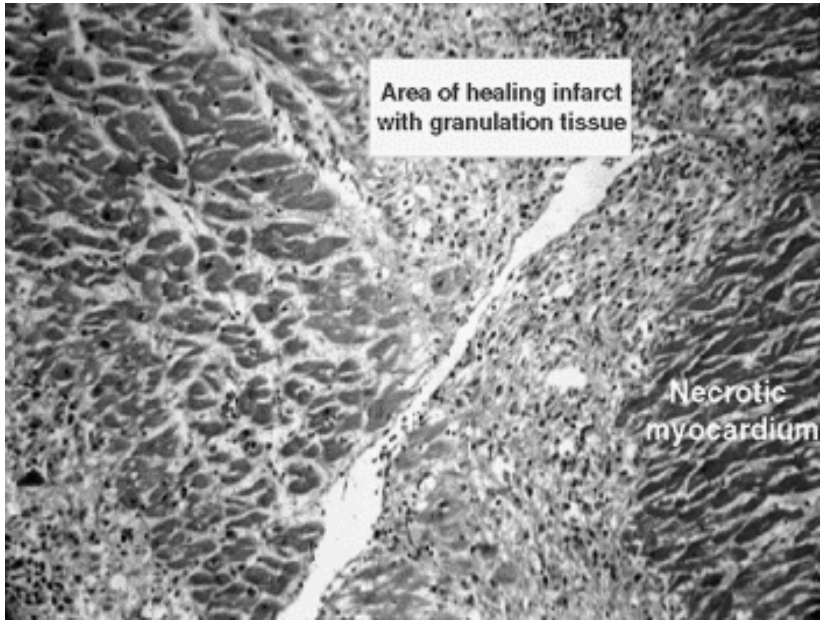
The picture pretty much says it all. You should have no trouble finding the clots in the pulmonary vasculature.

This slide shows a pulmonary embolus lodged in a major pulmonary artery. An embolus is a blood clot that formed somewhere else, broke free, traveled through the vascular system and lodged in the pulmonary vasculature. Do you know the difference between a thrombus and embolus? Many things can become an "embolus," the term is not specific: bullets, bone chips, amniotic fluid, even air. This slide shows a fairly typical artifact of formalin fixed tissue. At the time of death, the blood clot filled the vessel, the area of "clearing" between the vessel wall and the clot that we see now represents shrinkage during processing of the tissue.

Your observations

Slide 43: Myocardial infarction





By this time it should be obvious that a lot can be learned from a slide without using the microscope. See if you can find the area of infarction before putting the slide on the stage of your microscope. Hold it to the light or put it on a white background.

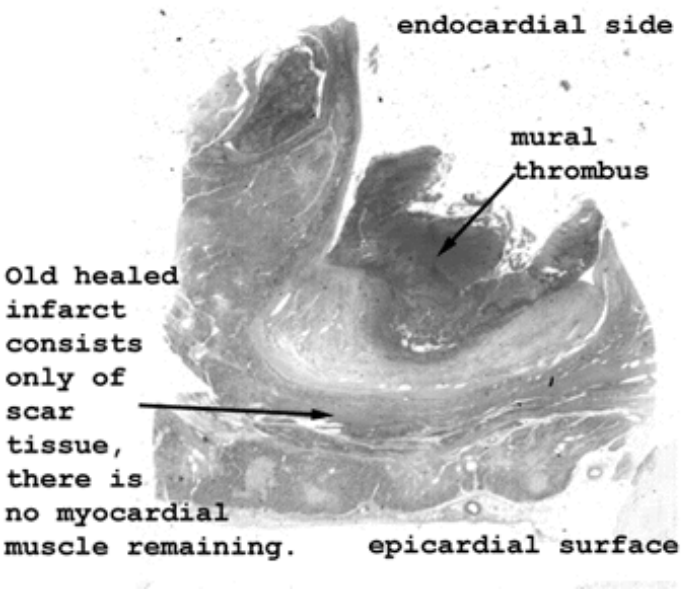
Here the stages of a myocardial infarction are pretty evident. This slide shows several events separated by about three weeks. The paler gray or blue areas represent areas of granulation tissue from an infarct of about two weeks duration and the brighter pink areas are from the more recent event.

This area of infarction is about two weeks old, and shows substantial removal of the dead muscle with early replacement with granulation and fibro-connective tissue. Some inflammatory cells remain. This person died with an arrhythmia.

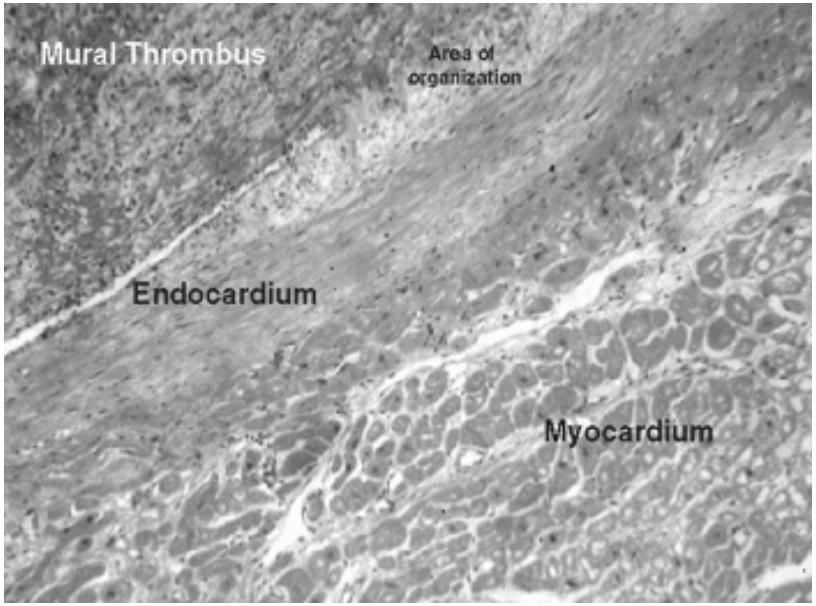
Your observations

Slide 44: Myocardial infarction with mural thrombus

Your observations



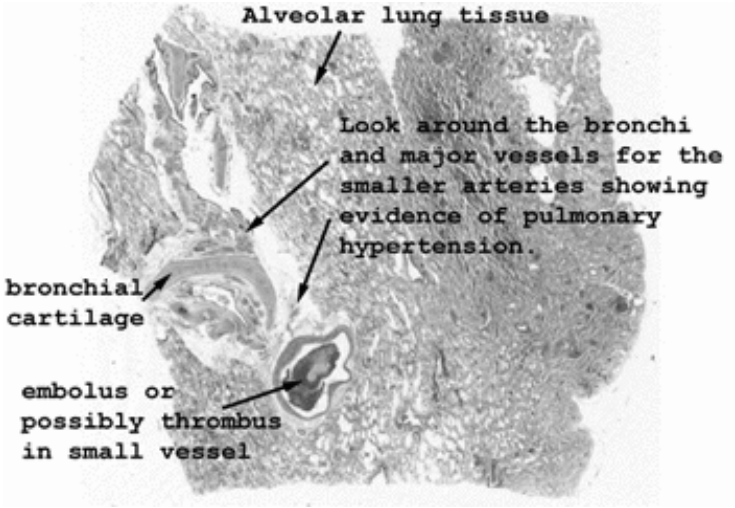
What remains of the heart muscle in this case is just a little band of connective tissue. No, you won't find much in the way of myocardium. Note the mural thrombus on the endocardial surface. What do you think happens if part of this should break free?



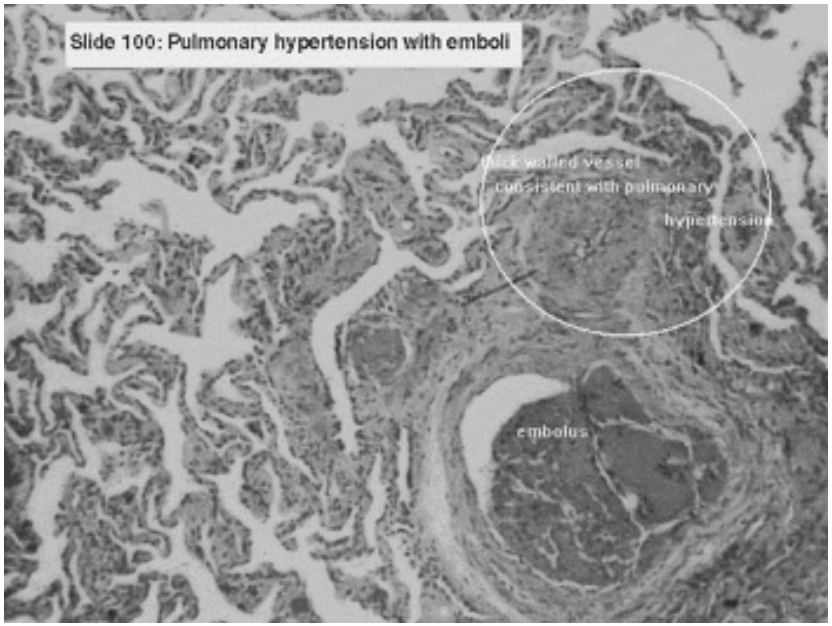
As you know by now, always try to spot the area of disease on the slide before going to the microscope. This slide demonstrates a common problem with myocardial infarcts; the formation of "mural thrombus." That is the formation of a blood clot on the endothelium of the heart in the region of the infarct. This may happen rapidly, and probably occurs because of the release of platelet activating agents at the site of the infarct.

Slide 100: Pulmonary hypertension and embolus

Your observations



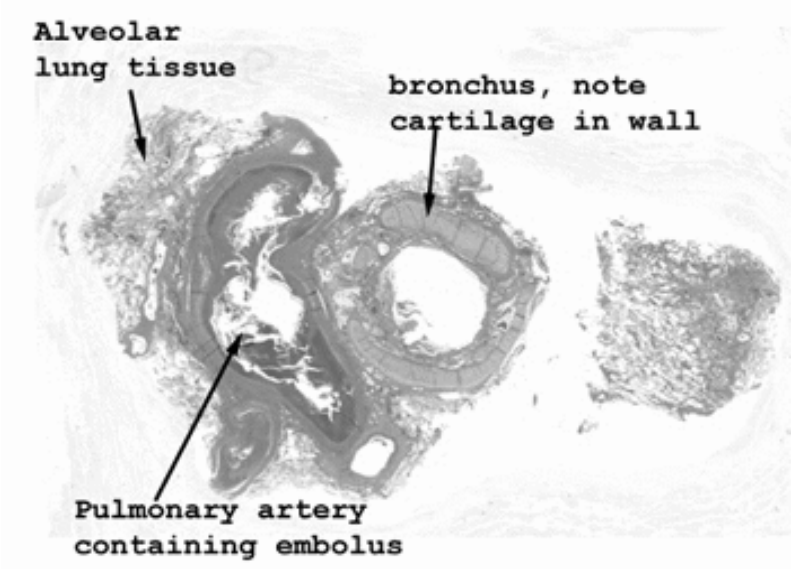
The changes are subtle in this tissue. Look at the smaller muscular arteries for the hyperplastic changes. It might be wise to review normal lung to get an idea of what these vessels should look like before tackling this slide.



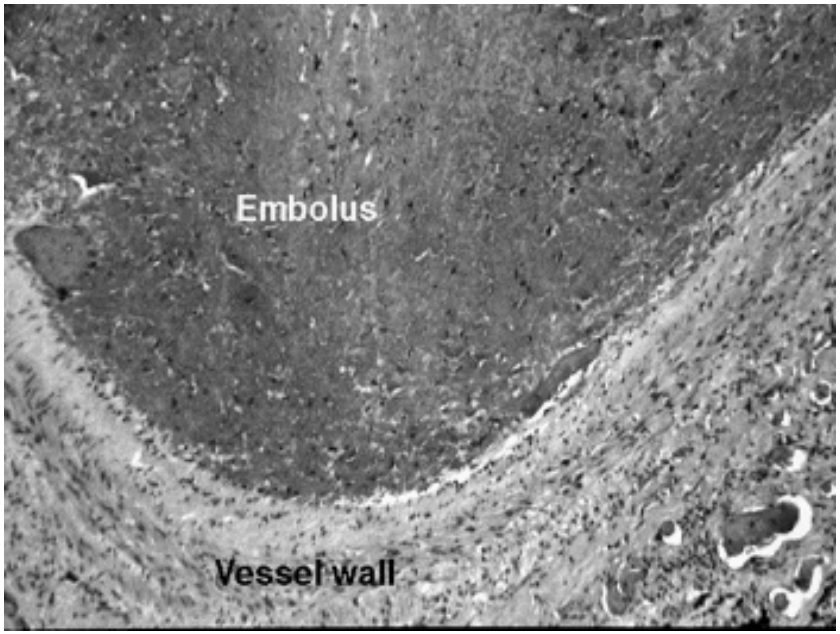
There are actually two things of interest in this slide. First, notice the thickened muscular walls of the smaller arteries and arterioles; changes of pulmonary hypertension. The pulmonary vessels are undergoing hyperplasia to "adapt" to higher than normal pulmonary vascular pressures. This feature contributes to the resistance in the pulmonary vascular bed, and will lead to right sided heart failure. What are some causes of increased pulmonary vascular pressure? Also, note the pulmonary emboli. Could these be thrombi? What is the difference?

Slide 108: Lung with pulmonary embolus

Your observations

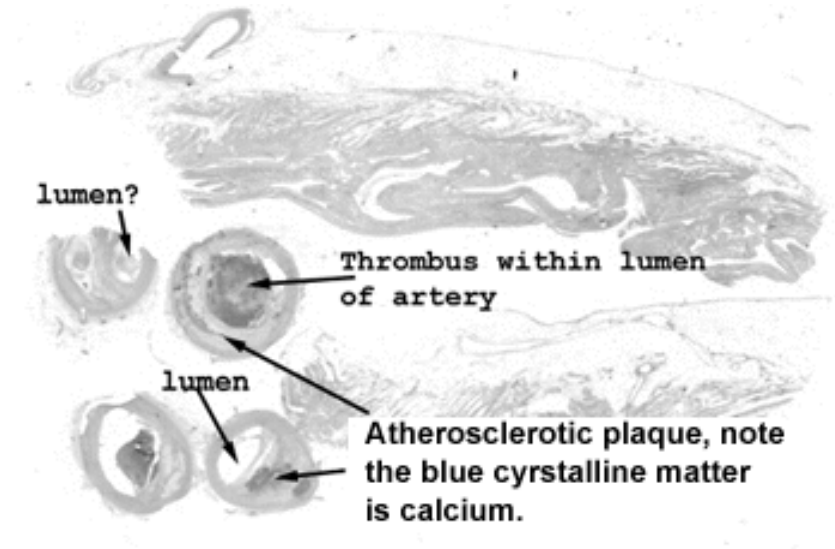


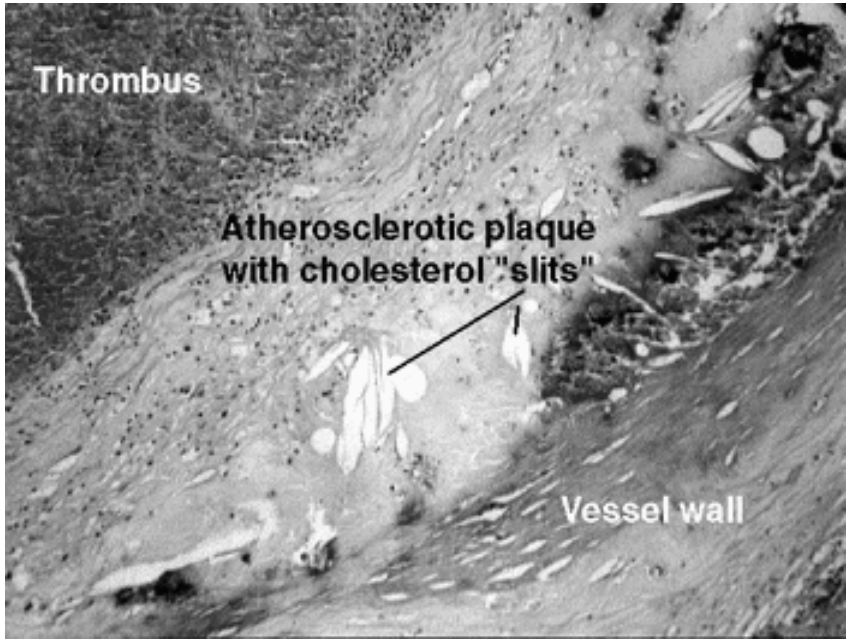
There are several pieces of tissue on the slide. The one with the pulmonary embolus should be obvious. The hole in the middle of the clot is an artifact of sectioning. It was in fact solid but partially chipped out when it was sectioned.



There is nothing real fancy in this slide. It is a pulmonary embolus. Be sure you know the difference between a thrombus and an embolus, as well as the sorts of things that can potentially embolize. For that matter, be sure you know the factors that contribute to the formation of a thrombus. Remember there are the differences in formation on the venous and arterial sides of the circulation. Here's an interesting problem I almost always ask about on the written exams: paradoxical embolization. Know what it is?

Slide 110: Artery with atherosclerosis and thrombosis





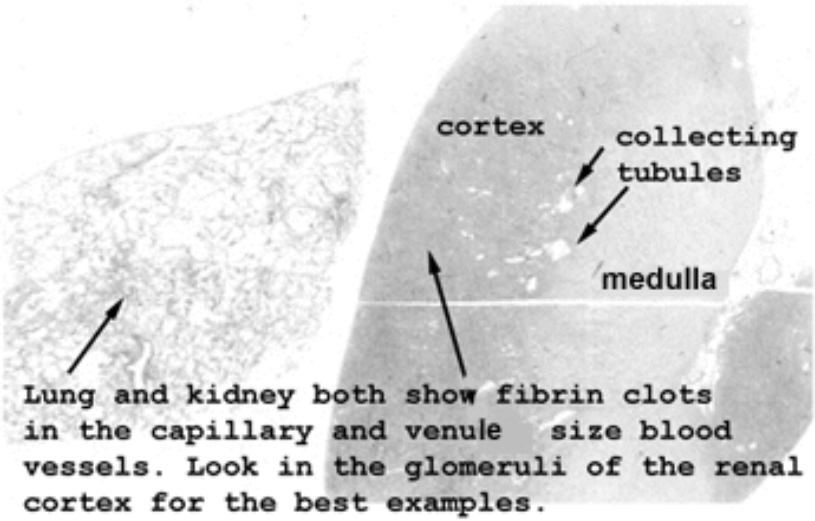
Spotting the vessels with the atherosclerosis, narrowed lumens and thrombi should not be to much of a challenge. Look at how compromised the lumen is even in the absence of the thrombus. What you see here are multiple serial sections of the same coronary artery.

Although this condition will be dealt with in detail in various sections of this course, here's a chance for you to study the basic morphology of the plaque for its own sake. This slide is of an elastic artery with a classical atherosclerotic plaque with secondary thrombosis. The plaque is in the sub-intima and is a fairly complex structure. Observe the cholesterol "slits." The cholesterol was "washed out" during the processing of the tissue, leaving behind the little spaces where the deposits had been. As far as problems associated with this disease, a plaque can weaken the wall of an artery, potentially causing a rupture of the vessel; it can cause thrombosis (as it did here) and thereby complete occlusion of the lumen; and it can continue to "grow." What do you think happened to the patient that gave us this slide?

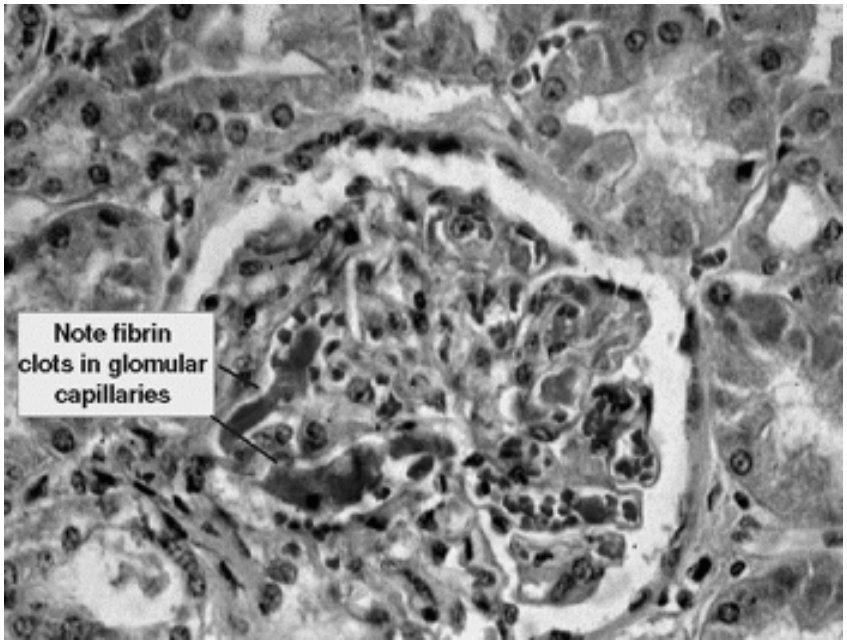
Your observations

Slide 135: Kidney with DIC

Your observations



The best bet here is to look in the small vessels of the cortex, especially the glomeruli for the diagnostic changes. You're looking for thrombi composed only of protein. If you see what looks like thrombi with lots of RBC's in them, it's not what we're
looking for.

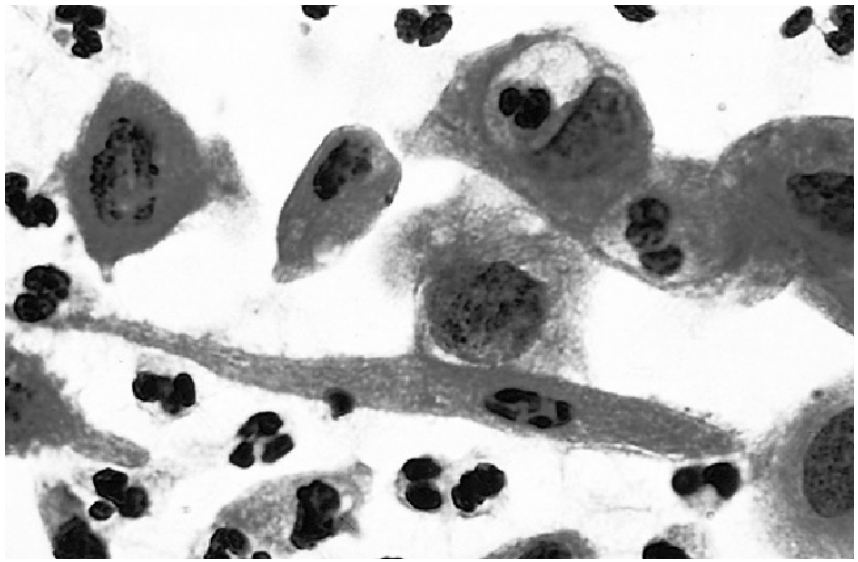


With disseminated intravascular coagulation (DIC), the person experiences "run away" intravascular blood clotting. This condition never just happens out of the proverbial blue. It is always a complication of something else that can trigger the clotting system, such as the leakage of amniotic fluid into the circulatory system in the course of some obstetrical disaster. As you might expect, there will be small thrombi in vessels throughout the body. This becomes an ischemic disease on the cellular level. People bleed with this condition because of the breakdown of the small vessels and consumption of the clotting agents. Causes are gram negative sepsis, massive trauma, OB disasters, etc.

General and Systemic Histopathology C601 and C602

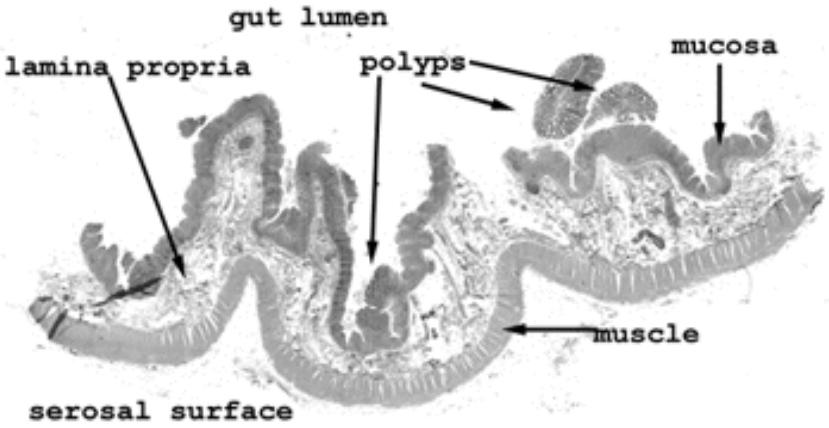
Section 4 *Neoplastic Disease*

In this laboratory, we are looking at the differences between cells that exhibit normal cell growth and those that have unregulated or altered growth. It's not the purpose to study the individual malignancies, rather the process and general histologic appearance. The term "neoplasia" does not necessarily imply malignancy. It simply means "new growth." It applies to both benign and malignant processes. When you have finished this laboratory, you should know what is meant by the terms: metaplasia, dysplasia and malignancy. In dealing with cytological aspects of malignant cells, we talk about the nuclear/cytoplasmic ratio as well as nuclear hyperchromasia and angulation of the nuclear margins, nuclear molding as well as the mitotic count. These are terms you will need to be familiar with. On the histologic level, you will encounter terms such as: gland within gland. Be sure you can define terms such as carcinoma, sarcoma and adenocarcinoma.

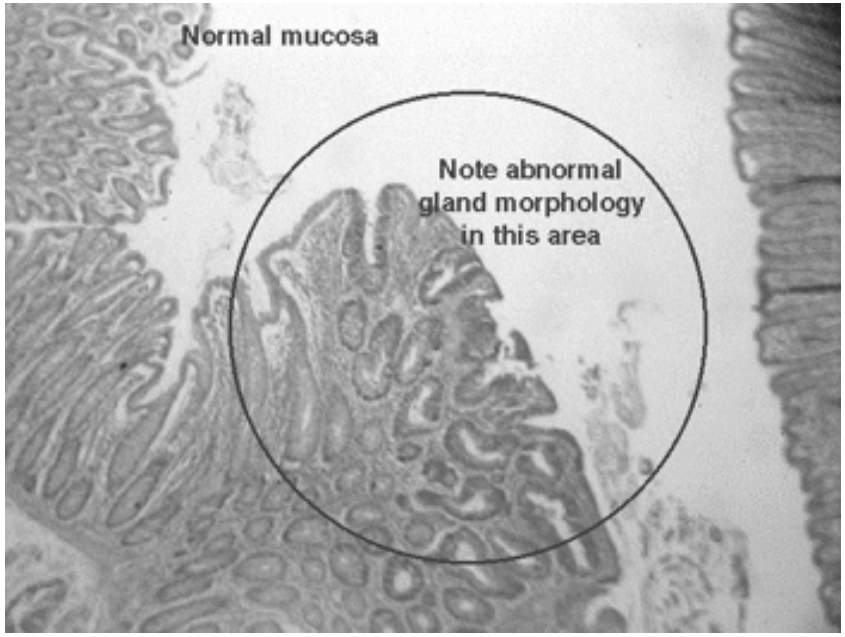


Slide 21: Familial polyposis of the colon.

Your Observations



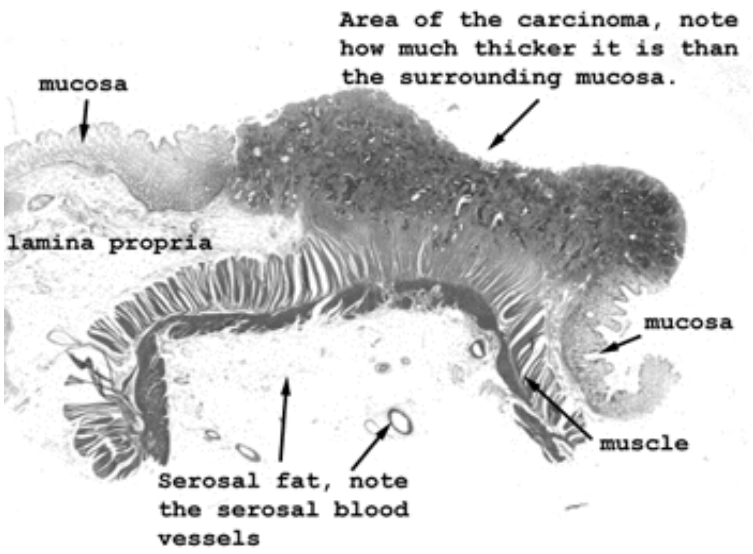
The changes are subtle here. You really must look at the tissue on the slide before going to the microscope. You will see little areas of thickening of the mucosa and that's about it. In some areas there may even be a polypoid formation but the earliest changes are not easy to see.



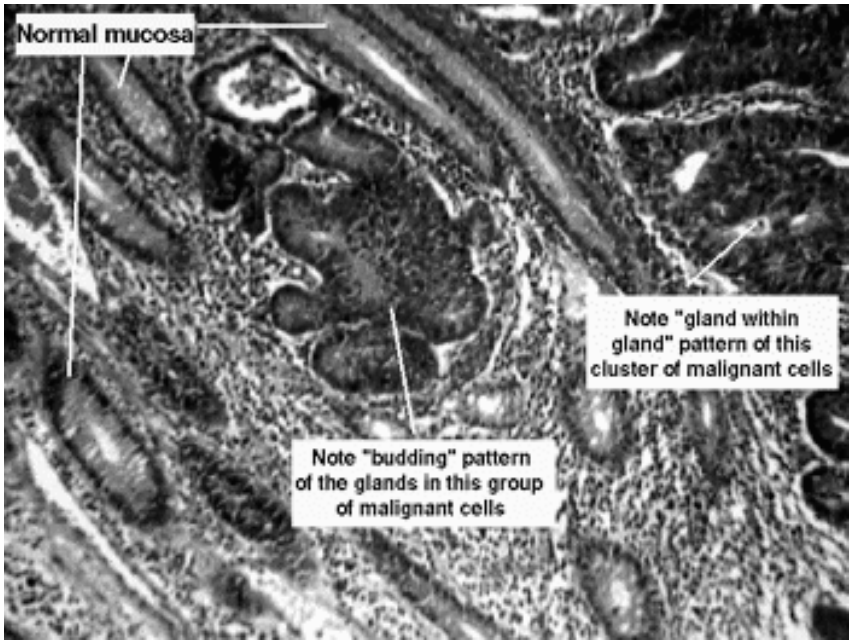
This slide shows the subtle changes in the bowel mucosa that can lead to big troubles later. You will need to be on low power to initially identify the mucosal areas of abnormality. Once you go to higher power, note the "branching" margins of the glands of the polyps and the "piling up" of the epithelium. You should have no trouble finding mitotic figures even though these lesions are benign. This congenital condition often leads to cancer of the colon later in life. Cancers of glandular origin are called adenocarcinomas, and frequently have histologic patterns similar to the organ in which they arose. To reemphasize the point, however, what we are looking at here is benign.

Slide 32: Adenocarcinoma of rectum

Your Observations



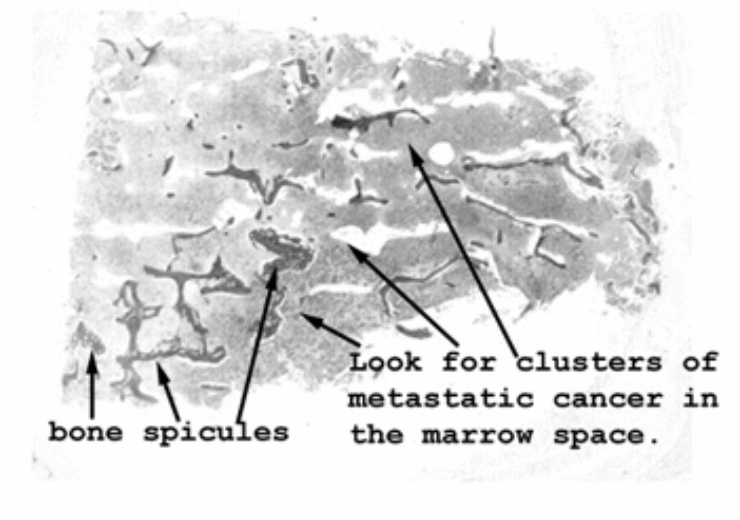
Here the region of the tumor is pretty obvious. Look to see how it is spreading at the lateral and deep margins. If we assume no node or distant metastasis what would the Dukes classification of this lesion be? What of the TMN classification?



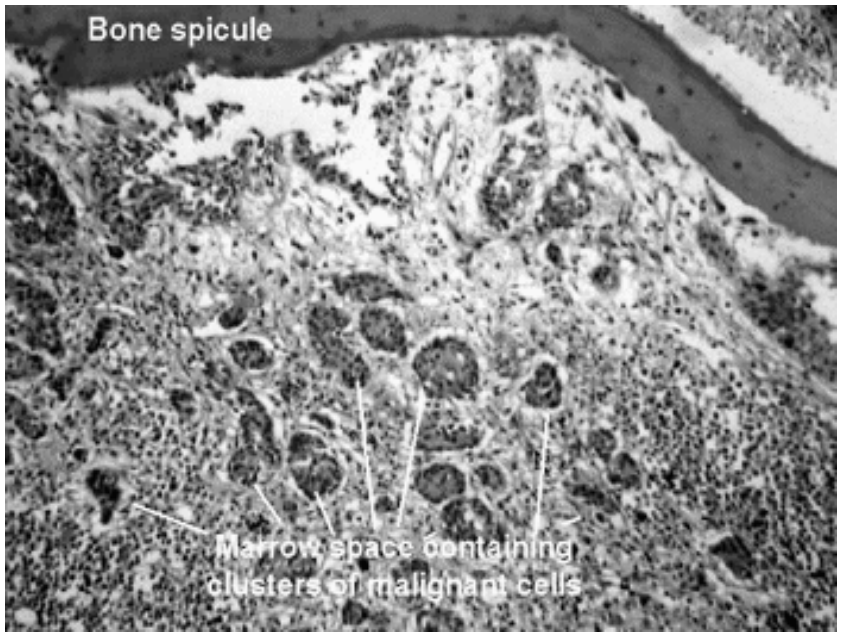
This is a fairly high power view of the cancer with normal tissue at the edges. On low power, you should be able to readily spot the different types of mucosa. In the area of the cancer, observe the "branching and arborizing" gland margins as well as the "gland within gland" pattern of the malignant cells. See what we mean by "nuclear atypia" of the epithelial cells. They are hyperchromatic with irregular nuclear staining and "angulated" nuclear margins. Mitoses are every place. Note the spread into the lamina propria of the malignant cells. Can you think of conditions that are associated with an increased incidence of this condition?

Slide 23: Metastatic transitional cell carcinoma

Your Observations



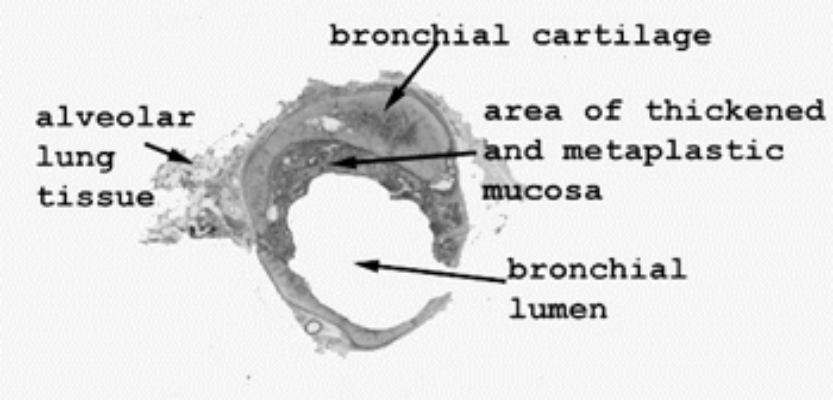
Note how "meaty" the bone marrow space is. Much of the hematopoietic space has been replaced by scar tissue and tumor.



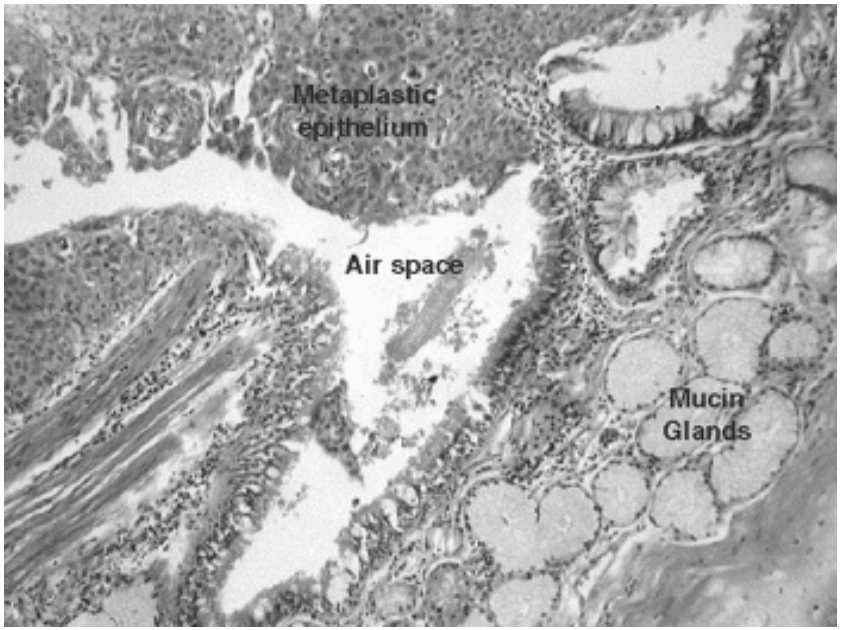
This slide shows metastatic "transitional cell carcinoma" in the bone marrow. What are the sources of "transitional cell carcinoma?" First, try to get oriented by finding some bone spicules and hematopoietic tissue. The malignant cells occur in clusters and closely resemble malignant squamous cells. Although these cells don't look too wild, they are not in the right place. Observe the "desmoplasia" (i.e. fibrosis) associated with the groups of tumor cells.

Slide 64: Squamous metaplasia of bronchial mucosa

Your Observations

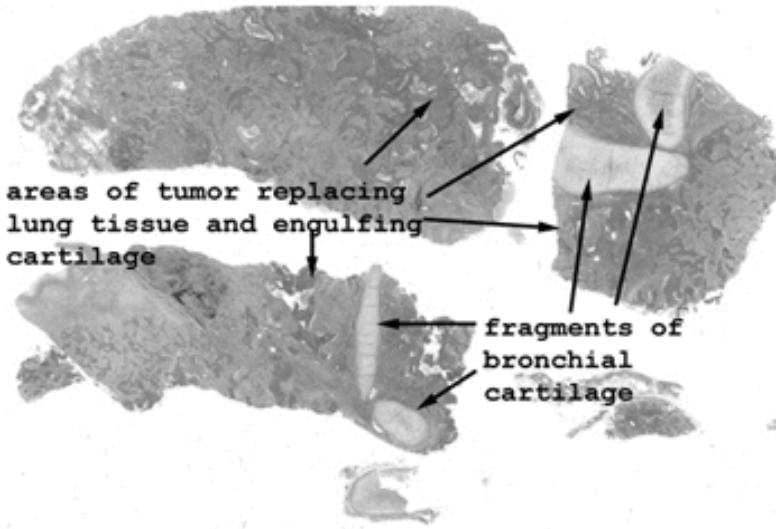


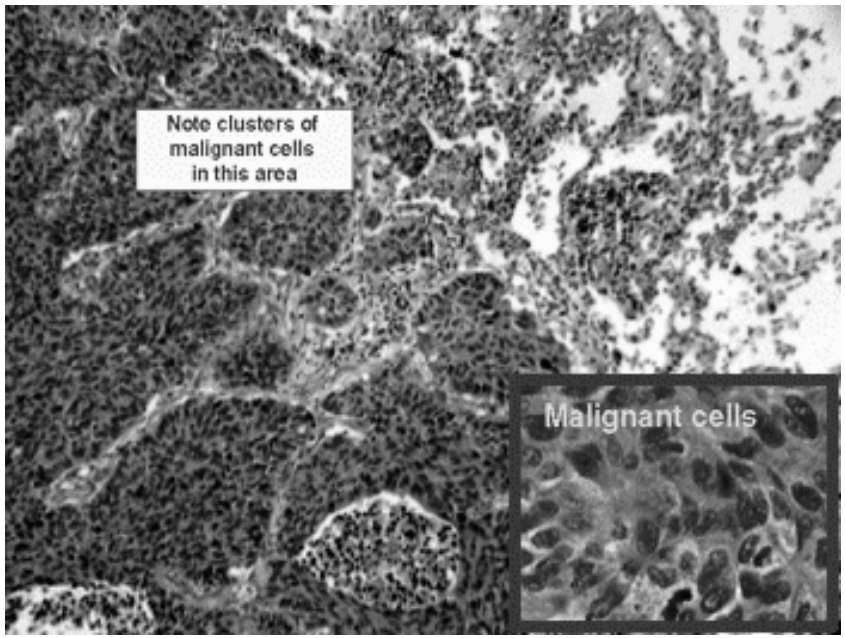
The process of metaplasia is found intermixed with the typical ciliated columnar epithelium. This is a reactive or adaptive process and not a true malignancy. What is the definition of metaplasia?



This picture is of bronchial mucosa, showing the reactive replacement of one type of epithelium for another. It is technically not a neoplastic process, although continued injury of the sort that lead to the metaplasia, can lead to dysplasia and possibly cancer. Here we see respiratory epithelium being replaced by squamous. Smoking was the injury that led to this alteration. Observe the inflammatory reaction beneath the mucosa.

Slide 101: Squamous cell carcinoma of lung





Very little alveolar lung is to be found on this slide. The tumor has pretty much replaced everything in the region of the sample. Note how the tumor surrounds and encases the fragments of bronchial cartilage.

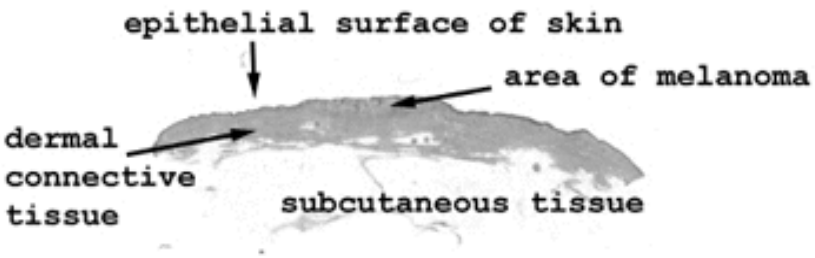
This slide shows a typical squamous cell carcinoma of the lung. Mitotic figures will be common and some "tripolar" mitoses might be present. You should be able to spot the "intercellular bridges" (as opposed to the Madison County type) that characterize squamous cell malignancies. You will see great variation in size of cells and nuclei, but the basics of malignant nuclear features are all here: nuclear/cytoplasmic ratio, angulated nuclear margins and nuclear hyperchromasia. The type of epithelium that gave rise to this malignancy is not normally found in the lung, where do you think it came from?

The insert shows a higher power view of the squamous cell malignancy. The nuclear atypia and mitotic figures are pretty evident.

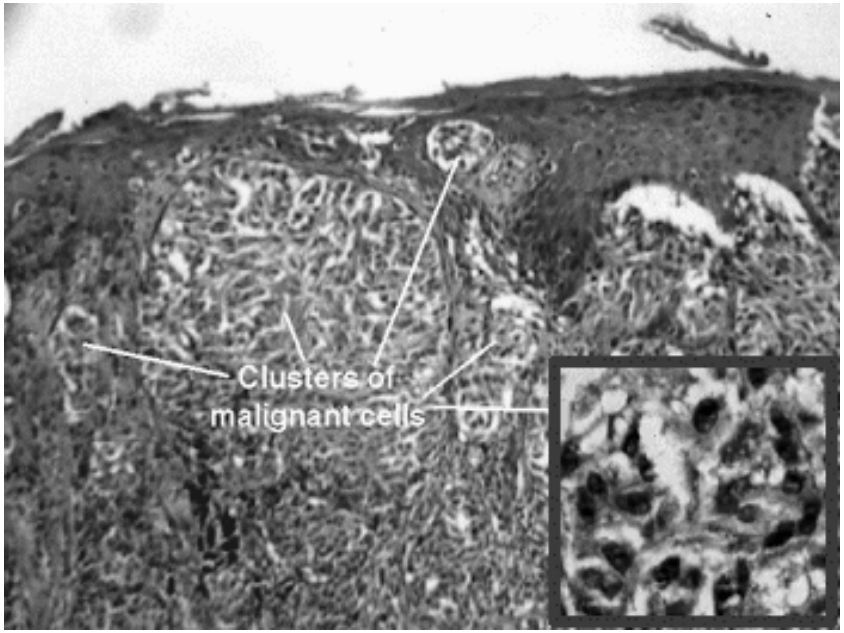
Your Observations

Slide 116: Skin with malignant melanoma

Your Observations



Although this is just a little shave biopsy of skin, you can easily see the central area of thickening where the melanoma is.

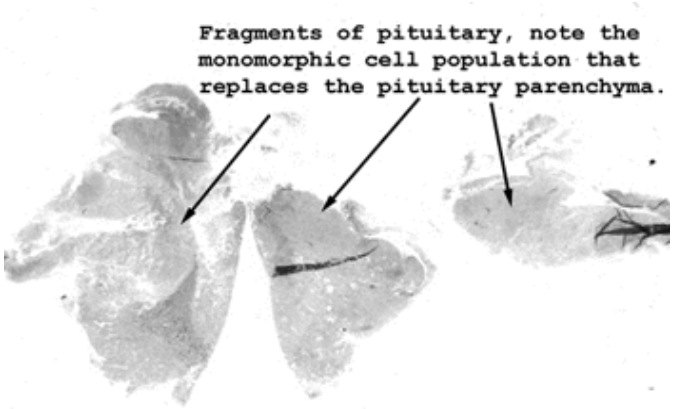


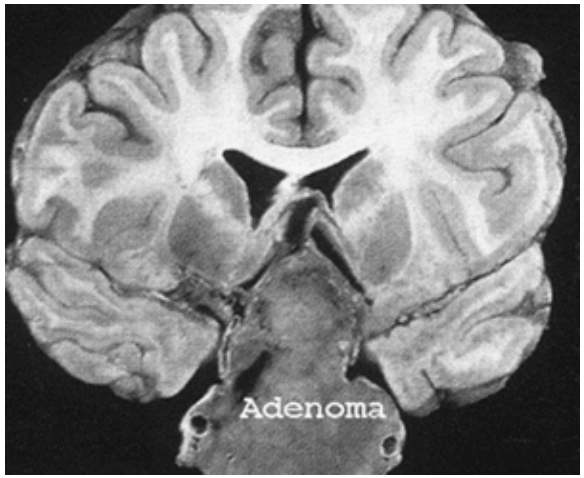
The skin in this slide shows clusters of malignant melanocytes in the dermis. Observe the lack of "cohesion" of the cells. Nuclear features of malignancy should be obvious, and many cells will show abundant pigment. There is no "maturation from surface to base" in this lesion, an important consideration in distinguishing this from its benign counterpart, a "nevus." Depth of penetration is a critical part of "staging" this lesion.

A higher power view of one of the clusters of malignant melanocytes is seen in the insert. Here you can see the lack of cohesion of the cells and the rather marked degree of nuclear atypia.

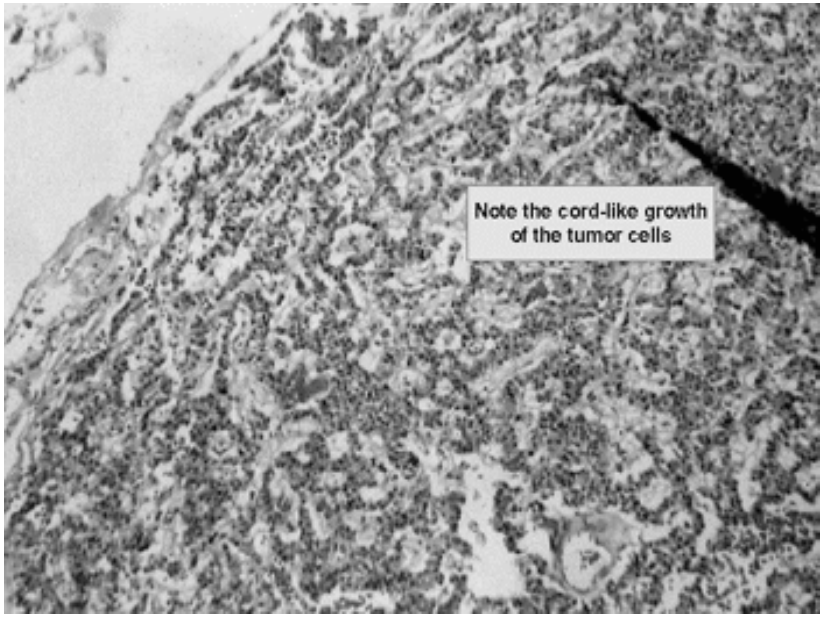
Slide 149: Pituitary adenoma

Your Observations





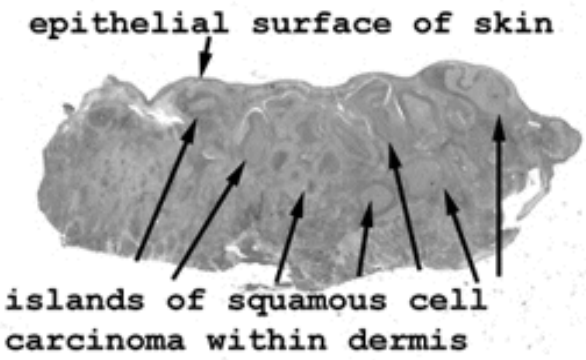
This gross photo of the brain with the adenoma was initially published in Laboratory Medicine, volume 29, number 10, 612. It had been submitted as one of the photographs in the 1998 Art and Science of Medicine Photography contest. It was taken and submitted by Dr. James M. Gulizia of Brigham and Women's Hospital, Boston.



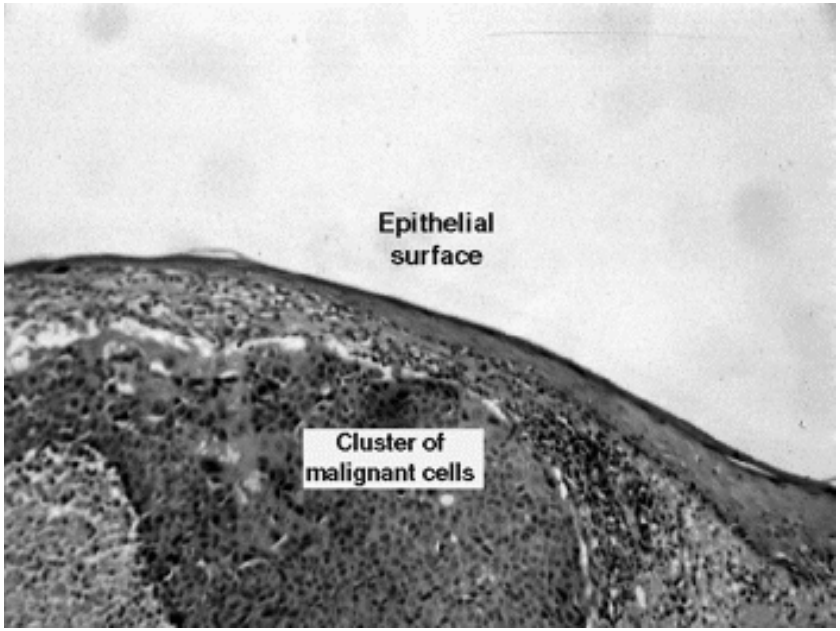
This picture is of a "benign" pituitary adenoma. Although biologically benign, it is sure in the wrong place and can be lethal just because of its location. You will see clusters and cords of the tumor cells, and it may be tricky to distinguish the tumor from the surrounding normal pituitary. Does the term "tumor" apply here? You should see no mitoses.

Slide 157: Skin with recurrent squamous cell carcinoma

Your Observations

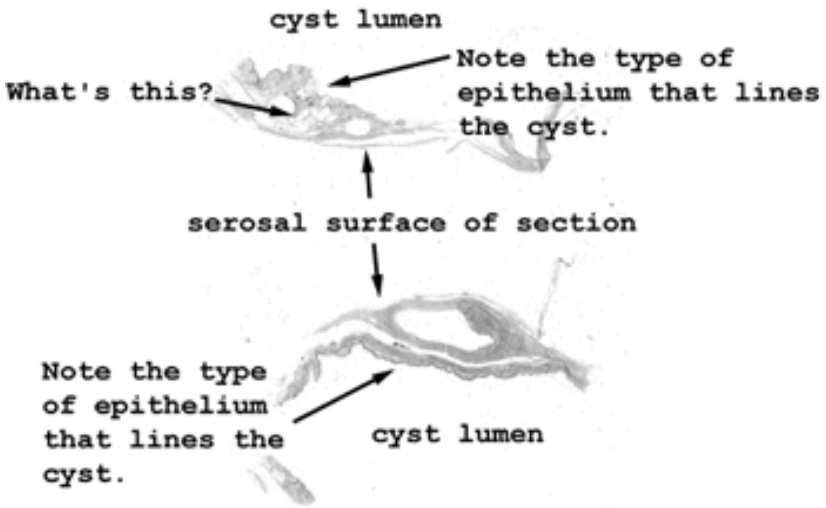


Here you see the groups of malignant cells within the dermis but seemingly having no connection to the epidermis. What's the explanation?



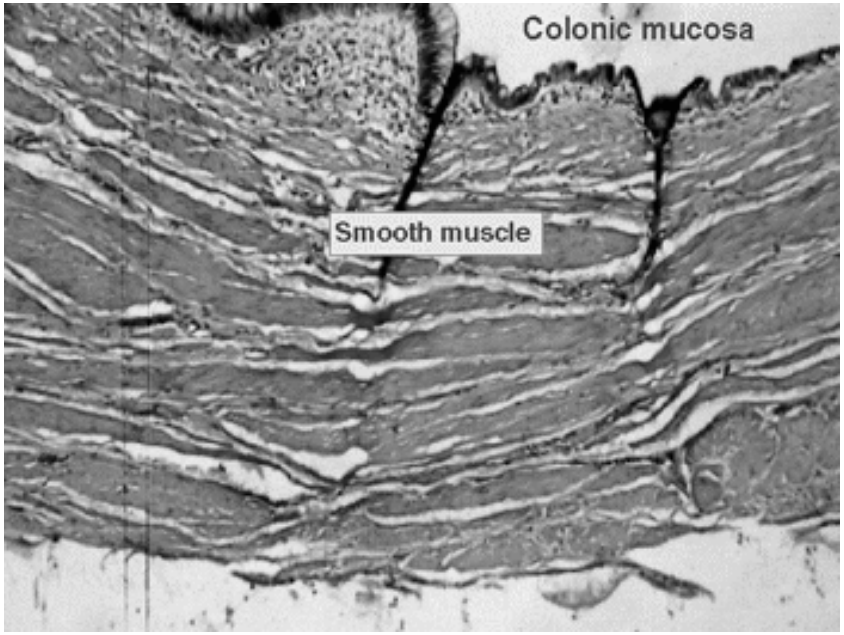
The picture of this slide could be in focus a little better, but it's what we have. Note the epithelium does not show changes of nuclear atypia nor cancer. The squamous cancer is in the dermis, and represents a recurrence from a previously removed malignancy. On your slide, you should be able to see the hallmark nuclear features of cancer i.e. angulated nuclear margins, hyperchromasia and reduced nuclear to cytoplasmic ratio. Look for "intracellular" bridges between the malignant cells.

Slide 159: Teratoma of ovary



This tissue just looks like little nondescript strips of tissue, but if you look far enough you may actually find a bit of ovarian tissue to help you get oriented. But, on the other hand, maybe there's not any on your slide. If that's the case, you'll just have to believe me that ovary is the origin. What you will see are a great number of different tissue types lining the cyst and within the cyst wall. I realize it may be a bit bewildering, but these are fairly common benign tumors.

Your Observations

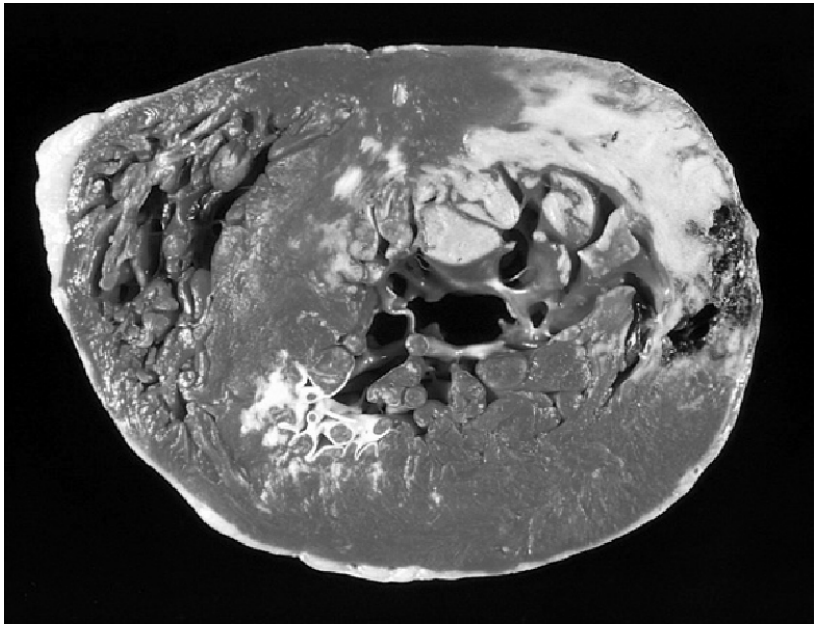


This is a rather peculiar, yet common and almost always benign tumor of the ovary. It often has several "germ lines" present, giving a hodge-podge appearance of "mature" tissue types. This picture is from an area with pretty representative benign colonic mucosa and bowel wall. You will likely find other tissue types in your slide. Be sure you cruise your slide and are able to identify the ovarian tissue from which this lesion arose.

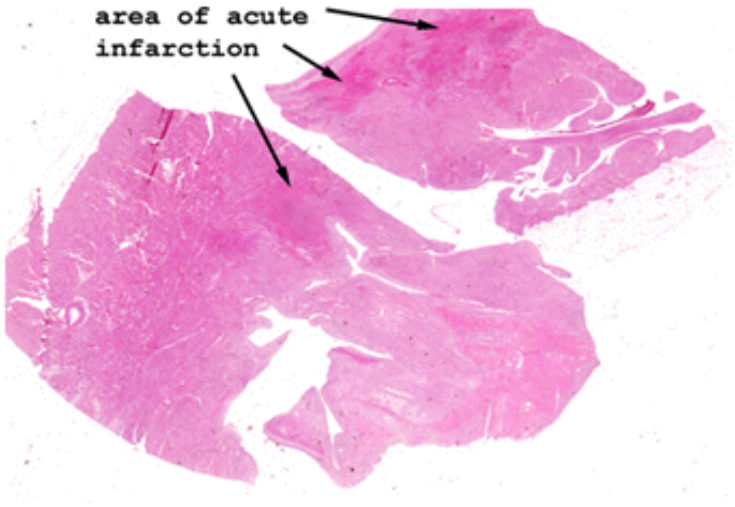
General and Systemic Histopathology C601 and C602

Section 5 *Cardiovascular Disease*

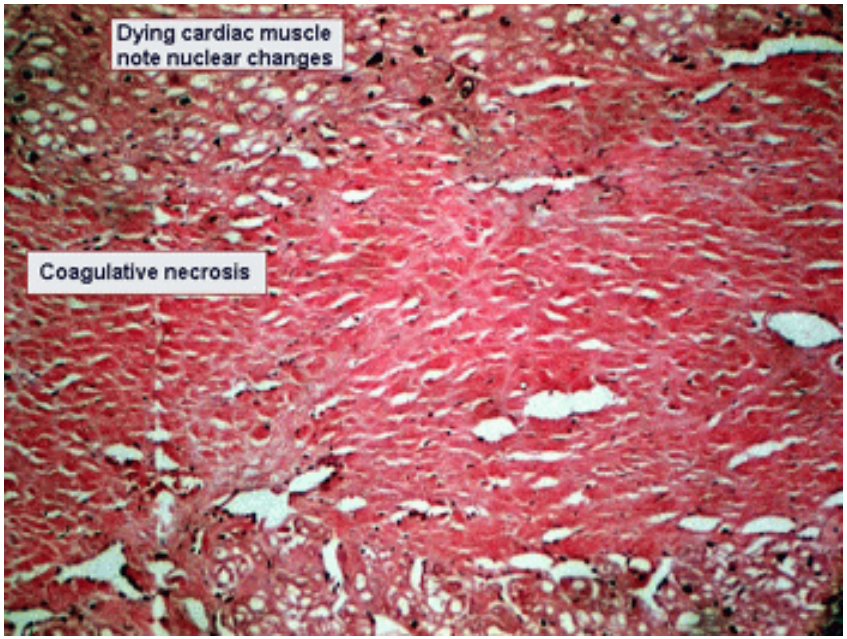
Although the cardiovascular unit will focus on the disorders we frequently encounter in the western world, we are not going to leave out less common conditions. Clearly, you will need to be familiar with all aspects of atherosclerosis and its sequelae, but as you will see there's a lot more to vascular disease than just compromise of the vessel lumen. You will need to understand inflammatory conditions of the vessels as well neoplastic disease involving the vascular system. Freely floating matter, such as blood clots, fragments of bone marrow or atherosclerotic material, amniotic fluid and even air also constitute important pathological processes of the vascular system. And as we will learn, the vascular system is even the target organ for some microbial agents.



Slide 6: Myocardial infarction, low power view



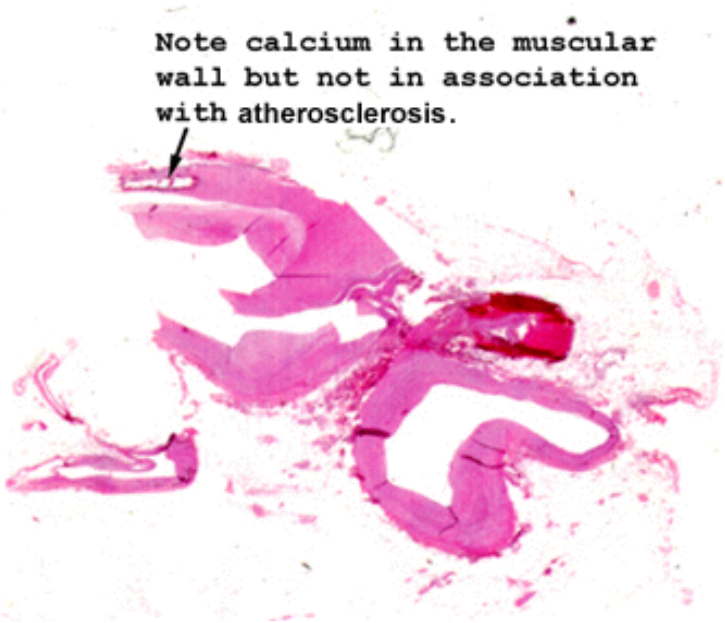
In this slide, look for the areas of bright pink. They will represent the areas of acute infarction. Can you place an age on this lesion?



Here the infarct shows areas of scar formation, but still you can see the typical coagulative necrosis that typifies anoxic injury. The cells develop a glassy eosinophilic appearance, eventually lose their nuclei, lyse and are removed by scavenger cells such as monocytes. You should know the basic stages of the development of a myocardial infarction, and what you would expect to see grossly and microscopically at day 1, 3, 5, 7 and 10, assuming the patient lives that long. You must also know what are the causes of "sudden" death with a myocardial infarction. For example, between day five and seven, the area of the infarct is the weakest and could rupture. What to you suppose happens when the heart ruptures? No, surprisingly, the patient does not bleed to death.

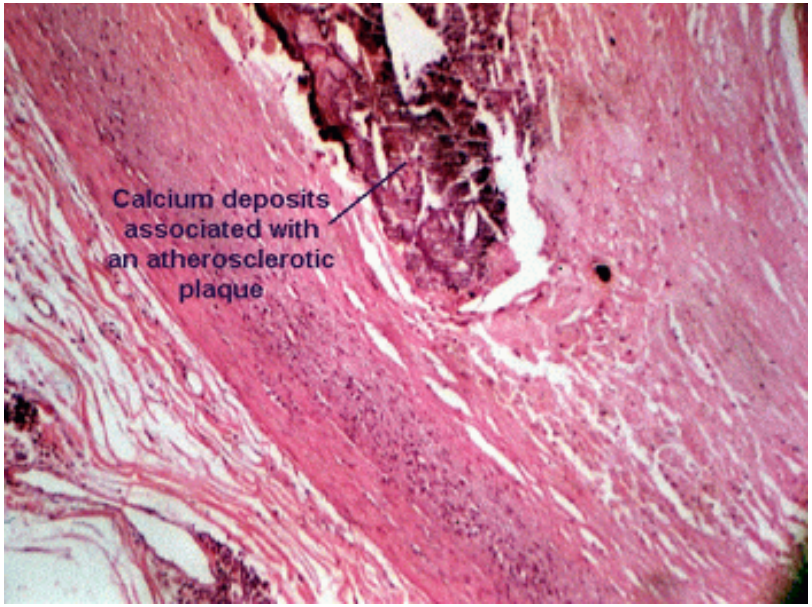
Your observations

Slide 2: Monckeberg's medial calcific sclerosis



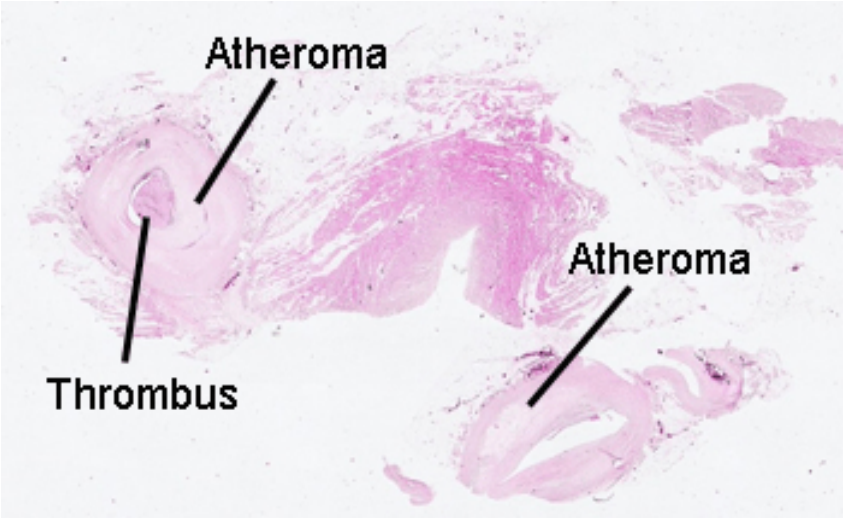
Ok, the changes aren't real striking in this slide, but see if you can find the calcium anyway. If there were extensive changes such as this throughout a person's medium sized arteries, what change would you expect that to have on the feeling of one's pulse?

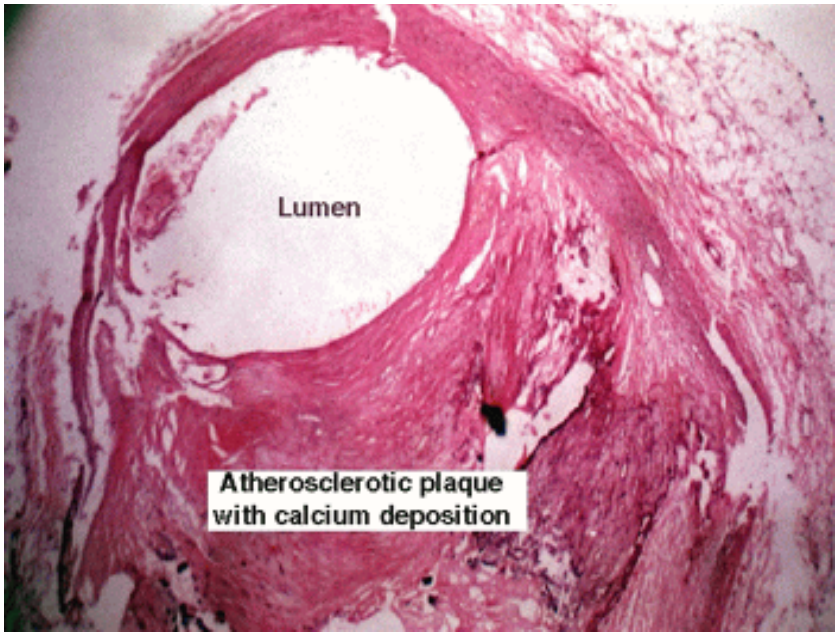
Your observations



This slide actually has Monckeberg's and atherosclerosis together. In the case of Monckeberg's sclerosis, the calcium deposits occur in the media and are not associated with cholesterol deposits. It is a condition of the elderly and only infrequently leads to clinical problems. It is not associated with high serum cholesterol, but is sometimes seen as an incidental finding along with other vascular conditions, such as atherosclerosis. This brings up the question of what is meant by the term "hardening of the arteries?"

Slide 3: Coronary artery with atherosclerosis





These pictures pretty much says it all. Look how markedly narrowed the lumen is in some of these serial sections. You can easily see the calcium deposits in some of the plaques. Obviously it wouldn't take much to fully occlude the lumen in several of these sections.

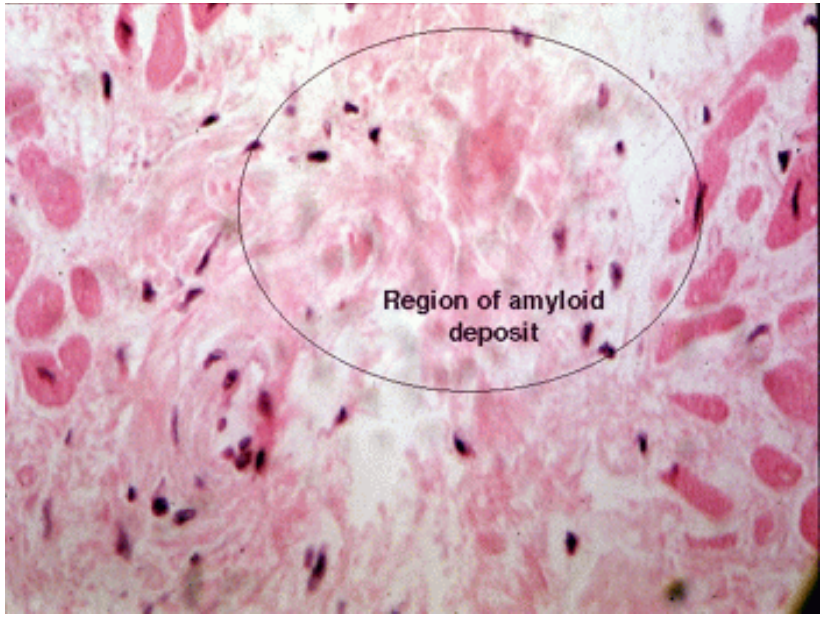
This picture is of only a small portion of the vessel wall. Note the calcium in the atherosclerotic plaque (blue crystals), and the "cholesterol slits." The plaque has a complex structure and starts out as an intimal lesion. Other conditions can have calcium deposits in the walls of vessels, but the deposits of an atheroma occur in the subendothelium. If thrombus should form on the surface of the plaque, the vessel will become completely occluded. Sometimes the material of the plaque can "embolize" i.e. break free and head down stream, causing small vessel arterial occlusion at a location distant from the plaque itself.

Your observations

Slide 8: Heart with amyloid deposition

Your observations

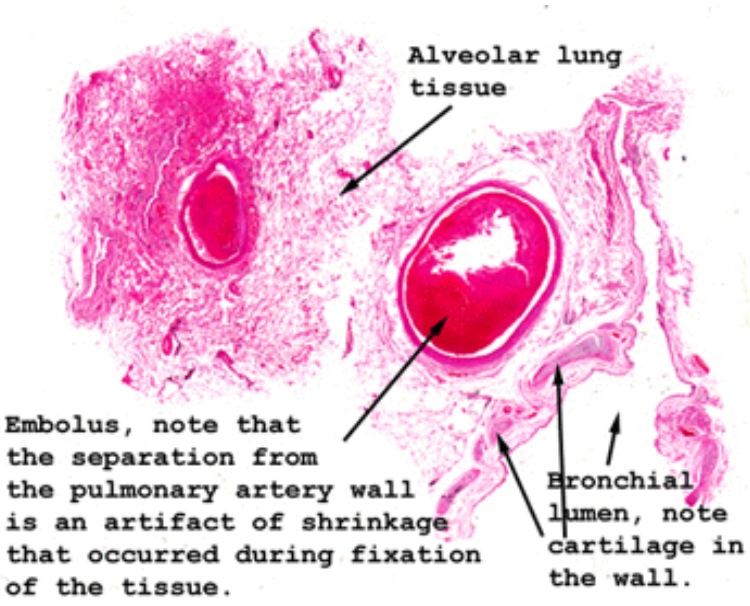
Sorry, there is no low power scan for this slide.



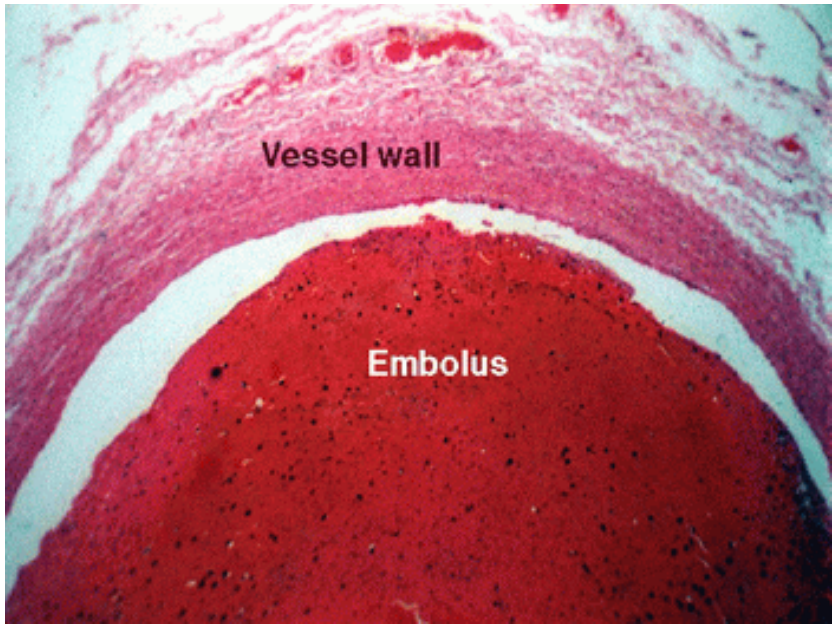
It is difficult to recognize the amyloid protein in this slide. It appears as an amorphous staining pink or orange fibrillary material in between the myocytes that make up the heart muscle. It may be easier to spot in the walls of the smaller arteries that feed the myocardium. It shows up best with a "congo red" stain. How do you think the addition of lots of non compliant protein in between the muscle fibers would alter the action of the heart?

Slide 14: Lung with pulmonary embolus

Your observations

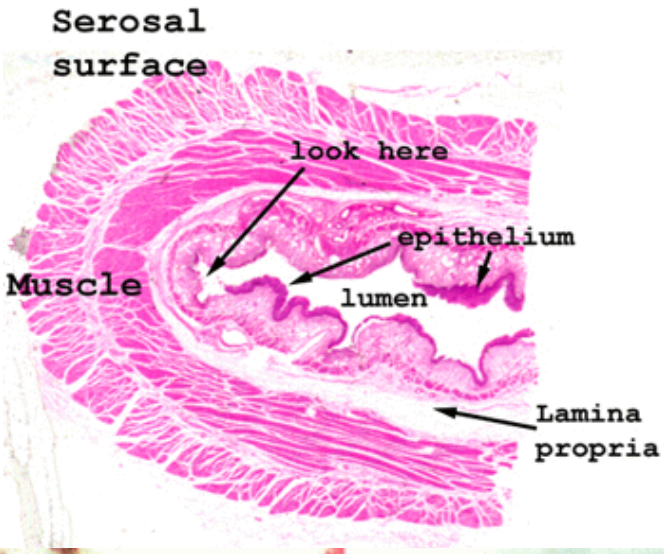


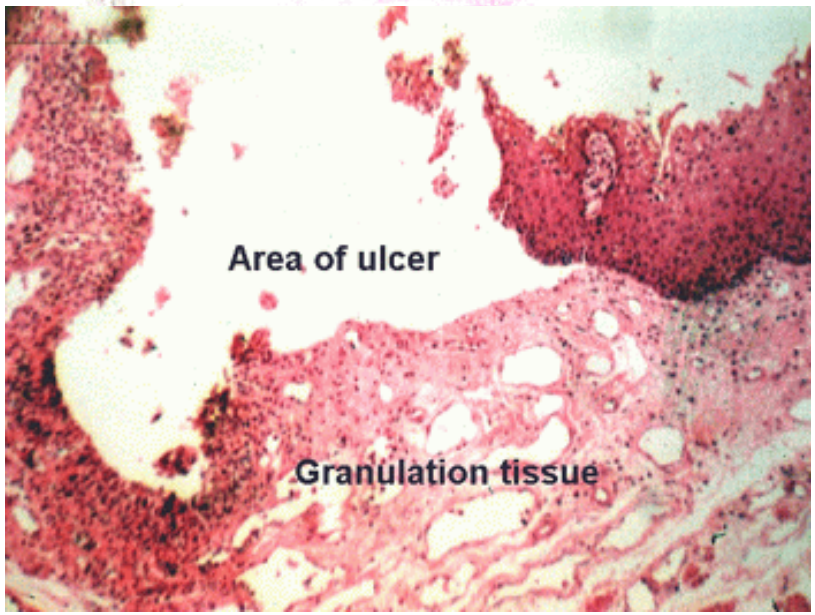
The picture pretty much says it all. You should have no trouble finding the clots in the pulmonary vasculature.



This slide shows a pulmonary embolus lodged in a major pulmonary artery. An embolus is a blood clot that formed somewhere else, broke free, traveled through the vascular system and lodged in the pulmonary vasculature. Do you know the difference between a thrombus and embolus? Many things can become an "embolus," the term is not specific: bullets, bone chips, amniotic fluid even air. This slide shows a fairly typical artifact of formalin fixed tissue. At the time of death the blood clot filled the vessel, the area of "clearing" between the vessel wall and the clot that we see now represents shrinkage during processing of the tissue.

Slide 19: Acute Erosive Esophagitis





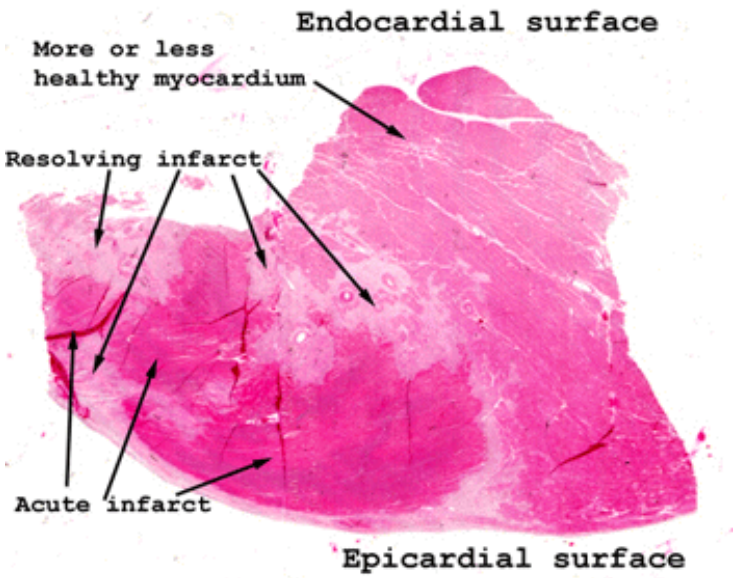
Your slide shows almost a complete cross section of the esophagus. Note there are several areas of mucosal ulceration and some relatively large, thin walled vessels are present in the lamina propria.

Your observations

If you simply look at the slide on a white background, you can see the area of erosion quite nicely. Note the areas of healing and repair at the margins of the ulcer. Some acute inflammatory cells are seen in the base of the lesion, and many very dilated vessels are present in this area as well. These large superficial vessels are not part of the healing process, and represent part of another pathologic process in this person. What condition could lead to these dilated vessels? Where would you expect to find others?

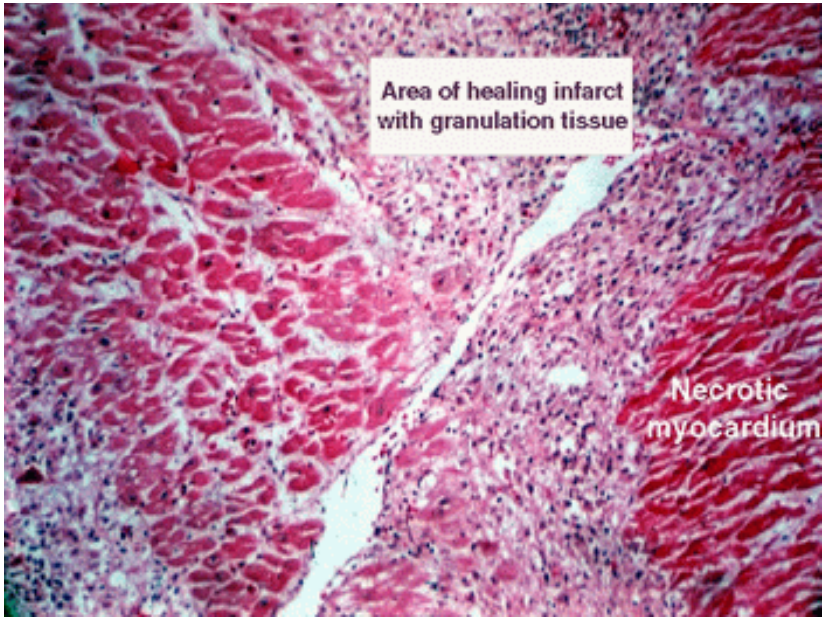
Slide 43: Heart with Myocardial

Infarction



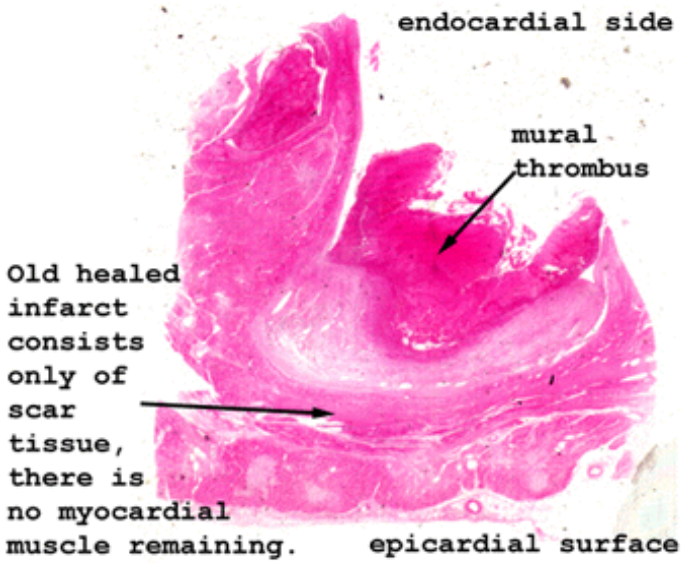
There's a lot to be seen in this piece of tissue. We have more or less normal heart tissue right beneath the endocardium. There are several myocardial infarctions of various ages and demonstrating various stages of development. In this picture, the areas identified as "resolving infarct" consist mostly of granulation tissue and represent an infarction of about two to three weeks duration. The bright pink areas represent a second and much more recent infarction. After you've read the section on myocardial infarctions, see if you can establish the duration of this second one. What do you think was the most likely cause of death?

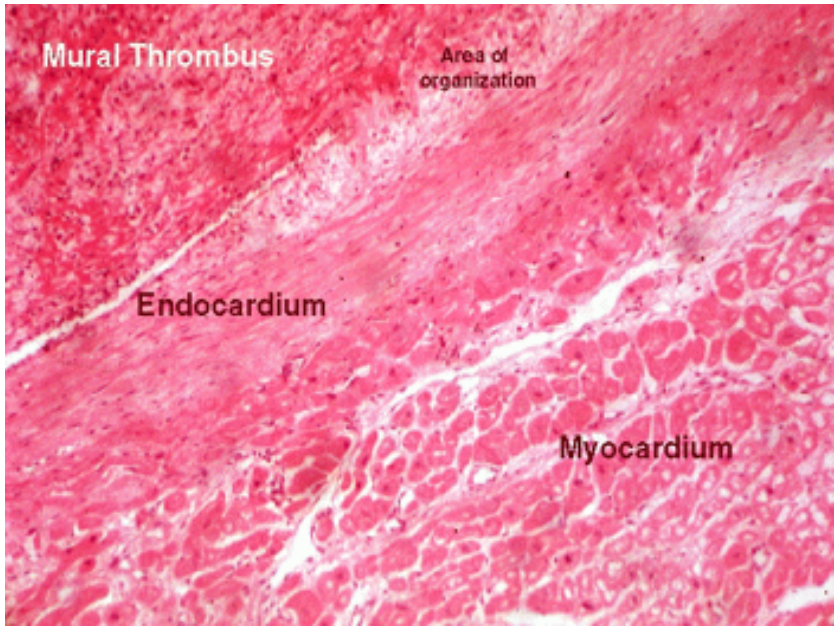
Your observations



By this time it should be obvious that a lot can be learned from a slide without using the microscope. See if you can find the area of infarction before putting the slide on the stage of your microscope. Hold it to the light or put it on a white background. This area of infarction is about two weeks old, and shows substantial removal of the dead muscle with early replacement with granulation and fibro-connective tissue. Some inflammatory cells remain. This person died with an arrhythmia.

Slide 44: Myocardial infarction with mural thrombus



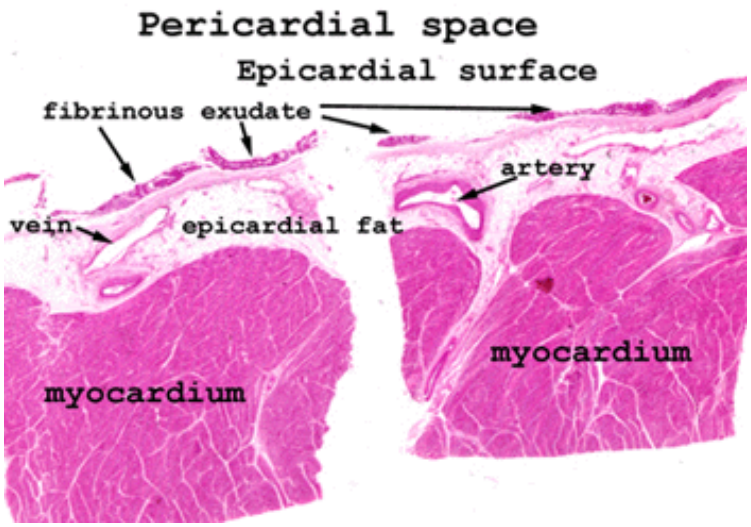


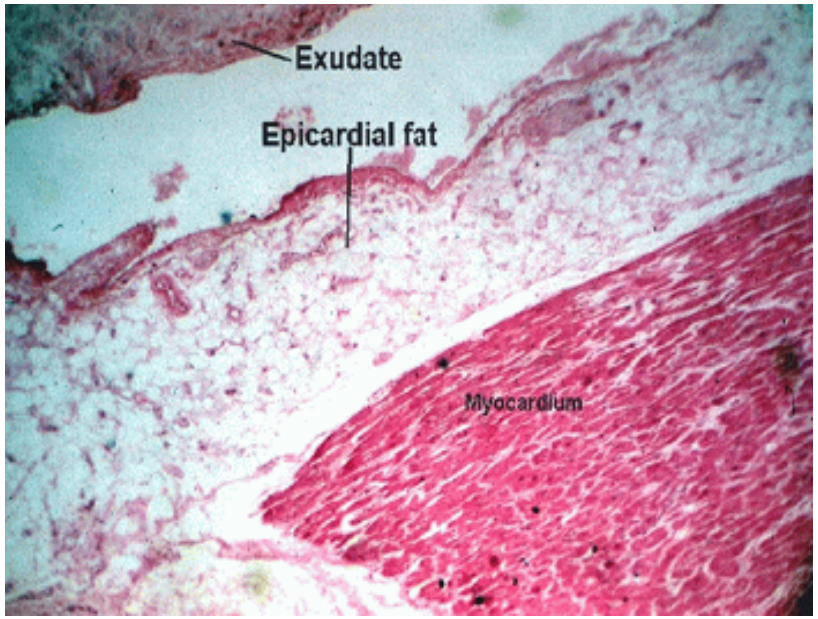
What remains of the heart muscle in this case is just a little band of connective tissue. No, you won't find much in the way of myocardium. Note the mural thrombus on the endocardial surface. What do you think happens if part of this should break free?

As you know by now, always try to spot the area of disease on the slide before going to the microscope. This slide demonstrates a common problem with myocardial infarcts; the formation of "mural thrombus." That is the formation of a blood clot on the endothelium of the heart in the region of the infarct. This may happen rapidly, and probably occurs because of the release of platelet activating agents at the site of the infarct.

Your observations

Slide 48: Fibrinous pericarditis





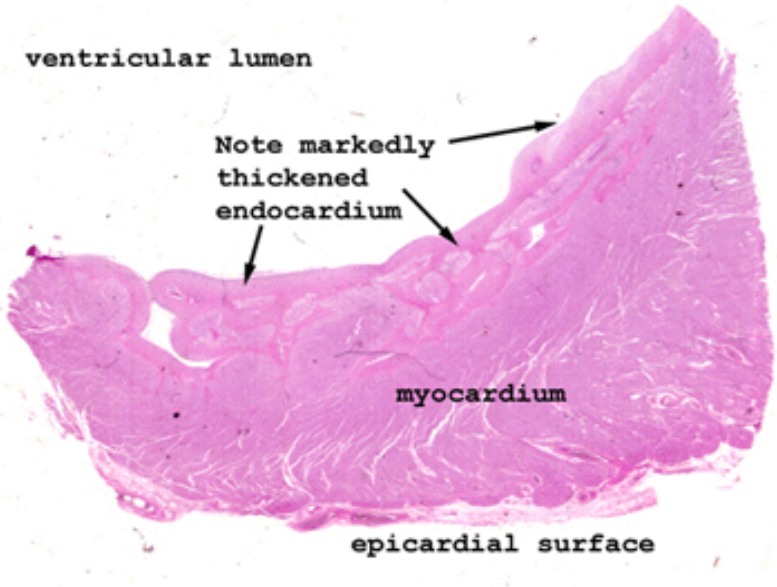
In this case, we're looking for a thin band of homogeneous, pink staining, proteinaceous material on the epicardial surface of the heart. This represents an exudate composed largely of protein material. You will see very few inflammatory cells.

This exudate is almost totally devoid of inflammatory cells, and consists almost totally of protein (fibrin plus other trash). It looks the way I think "tofu" would look if sectioned and stained. This "exudate" is a product of renal failure, is completely sterile, and occurs secondary to the crystallization of nitrogenous wastes on the epicardial and pericardial surfaces. This is a consequence of many forms of long term kidney disease that eventuate in renal failure.

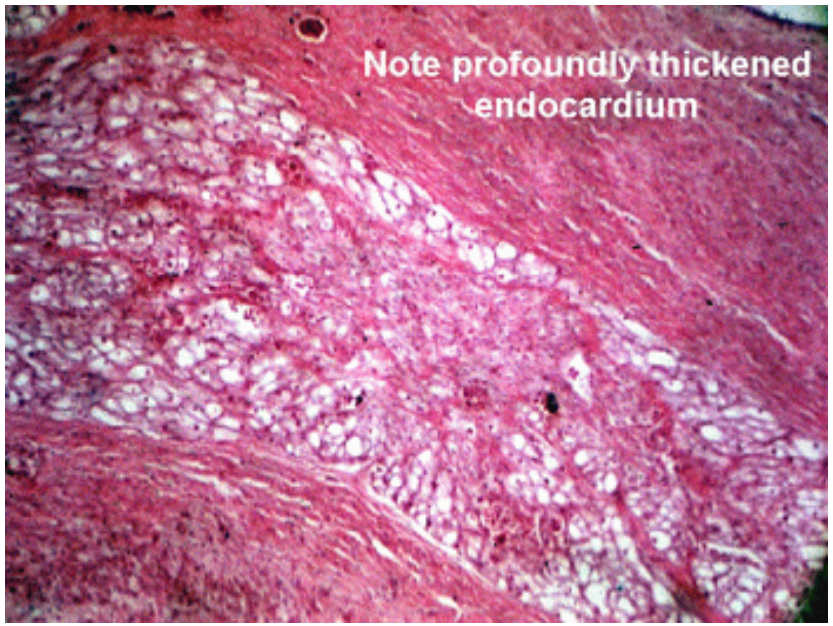
Your observations

Slide 50: Heart with endocardial fibroelastosis

Your observations

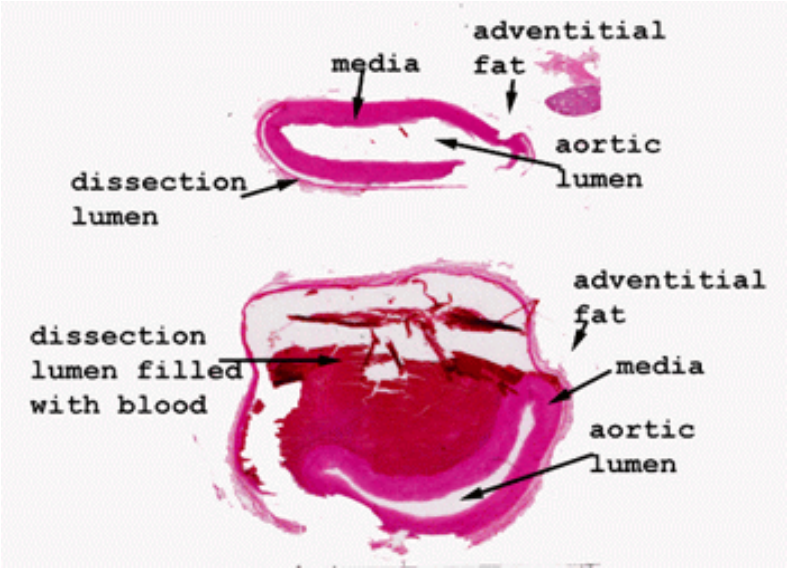


Even without the aid of a stain highlighting collagen or elastic tissue, you can see how markedly thickened the endocardium has become. This process will obviously lead to a significant restriction in the dilation and filling of the ventricles.



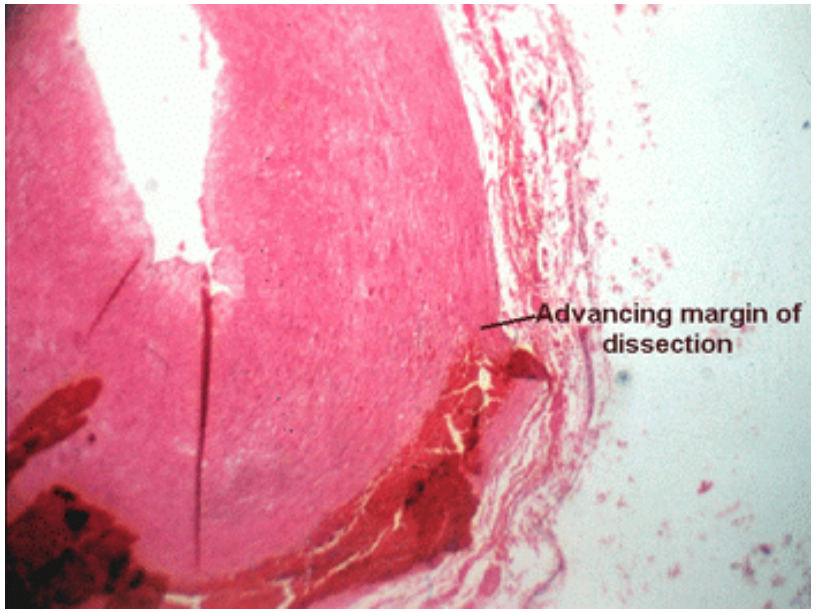
This is an H&E of an uncommon disease; endocardial fibroelastosis. See how markedly thickened the endocardium is and note the extension of fibrous tissue into the superficial myocardium. Slide #119 shows this with a stain that highlights the collagen. This alteration greatly restricts the ability of the heart to fill and pump effectively.

Slide 53: Dissecting aortic aneurysm



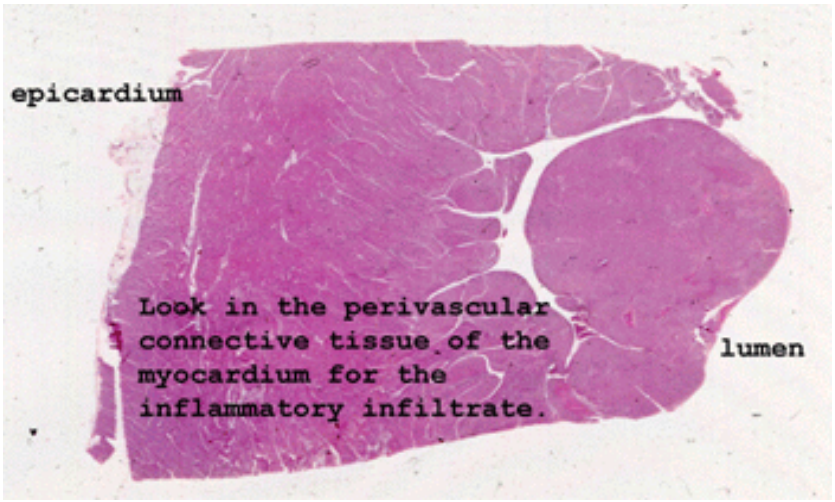
It may be a little hard to imagine what's happening here, but if you study this scan of the tissue and try to sketch, it may become clear. Somewhere in the wall of the aorta, a tear in the intima developed (no, you can see the tear in this picture), allowing the blood to "dissect" into and separate the muscle layers of the aortic wall. Here we see what appears to be a "double barreled" lumen, but in fact only one "true" aortic lumen is present. The other blood filled space is the compartment created by the tearing and separation of the aortic wall by means of the blood pressure pushing the blood into the wall through the intimal defect.

Your observations



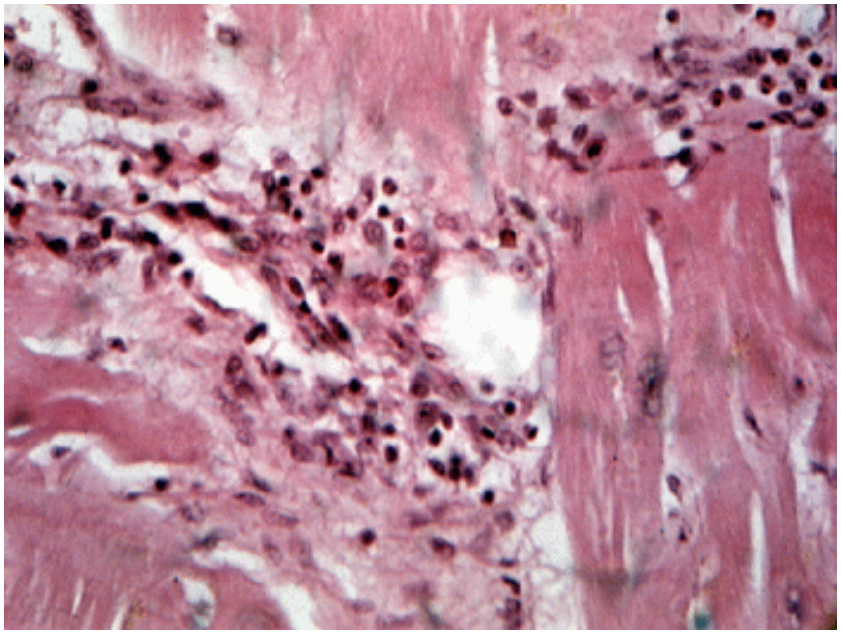
Again, look at this slide on a white background first. You should easily be able to see the advancing edge of the dissecting aneurysm. This condition may complicate an atherosclerotic aneurysm, but may also be seen in the absence of atherosclerosis. It sometimes happens in people with hypertension. Typically it is very painful as the leading edge of the dissection tears the muscle of the aorta. The dissection may stop, "blow" through the wall into the surrounding fat or pericardial space, or even open another "rent" in the intima and reenter the lumen of the aorta.

Slide 54: Heart with myocarditis



Not a lot here grossly to tell you what's going on. Be sure to look carefully at all parts of the tissue, but the inflammatory infiltrate is easiest to see in the perivascular connective tissue of the myocardium.

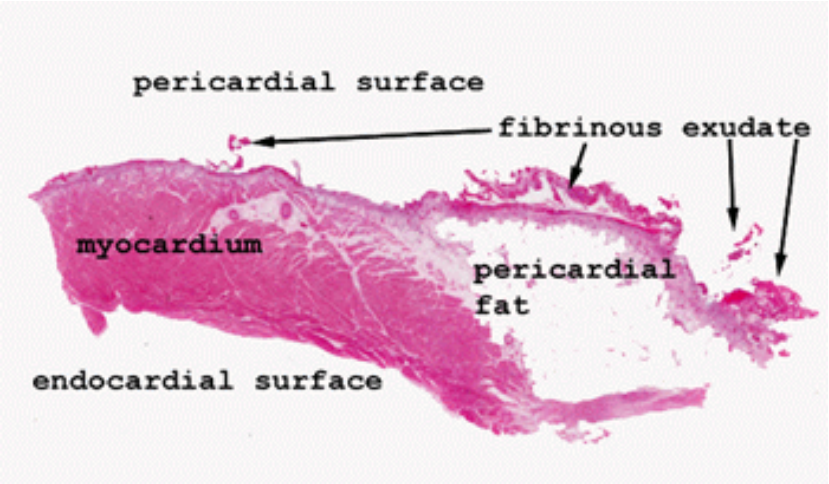
Your observations



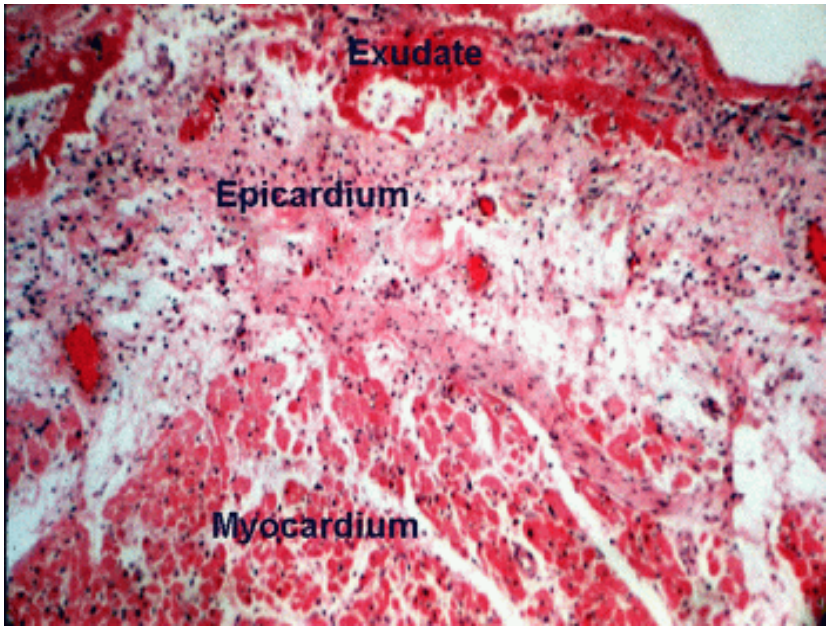
Look around the smaller vessels of the myocardium for the inflammation in this slide. You should see an infiltrate composed predominately of chronic inflammatory cells. This condition was most likely of viral origin. I noticed in the walls of some of the vessels a pink fibrillary material like amyloid, but doubt that is what it is.

Slide 55: Heart with uremic pericarditis

Your observations

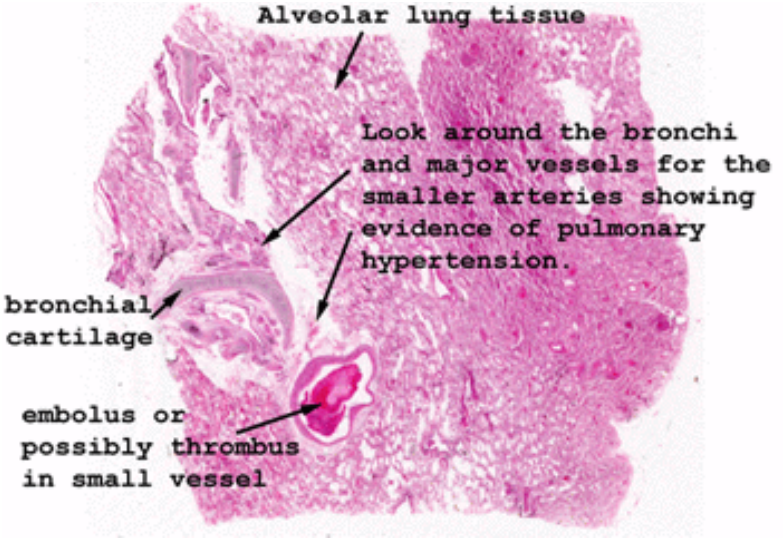


Again, getting yourself oriented on the slide will save lots of time. You're looking for the exudate and inflammatory reaction on the epicardial surface. You will see some "organization" of the exudate. That is to say ingrowth of granulation tissue. But there is still very little in the way of an acute inflammatory reaction.



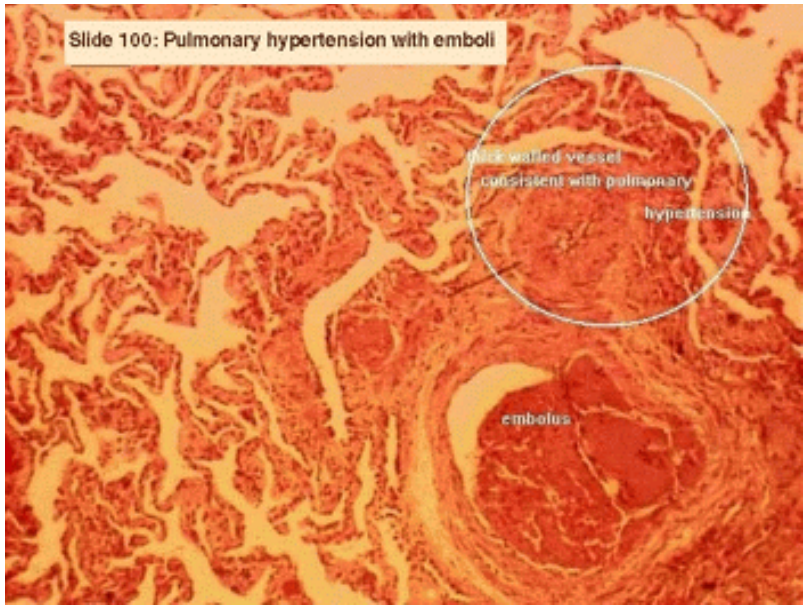
This slide shows one of the common problems of renal failure: sterile inflammation of mesothelial surfaces. Evidently the uremic products crystallize on these surfaces and elicit an inflammatory reaction. Pleura, abdominal cavity lining, pericardium and even esophagus are sites of this type of injury. Note the granulation tissue (not granulomas, there is a big difference), in the epicardial fat. The exudate is largely proteinaceous.

Slide 100: Lung with pulmonary hypertension and embolus



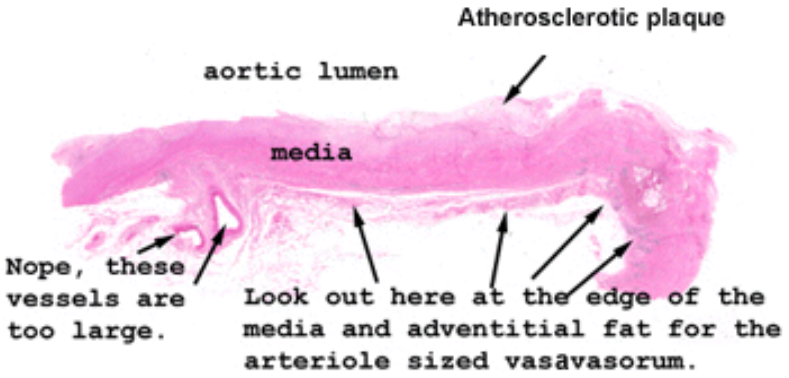
The changes are subtle in this tissue. Look at the smaller muscular arteries for the hyperplastic changes. It might be wise to review normal lung to get an idea of what these vessels should look like before tackling this slide.

Your observations



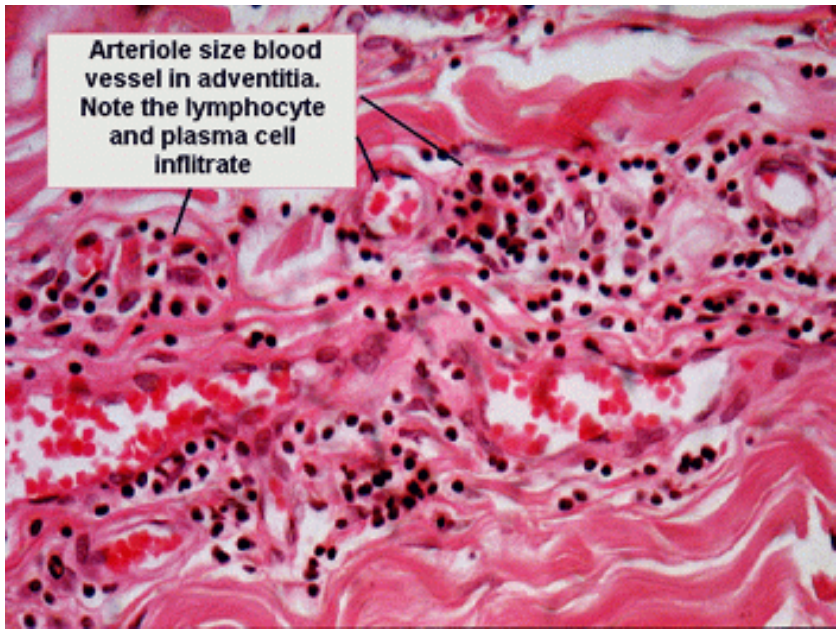
There are actually two things of interest in this slide. First, notice the thickened muscular walls of the smaller arteries and arterioles; changes of pulmonary hypertension. The pulmonary vessels are undergoing hyperplasia to "adapt" to higher than normal pulmonary vascular pressures. This feature contributes to the resistance in the pulmonary vascular bed, and will lead to right-sided heart failure. What are some causes of increased pulmonary vascular pressure? Also, note the pulmonary emboli. Could these be thrombi? What is the difference?

Slide 106: Syphilitic aortitis



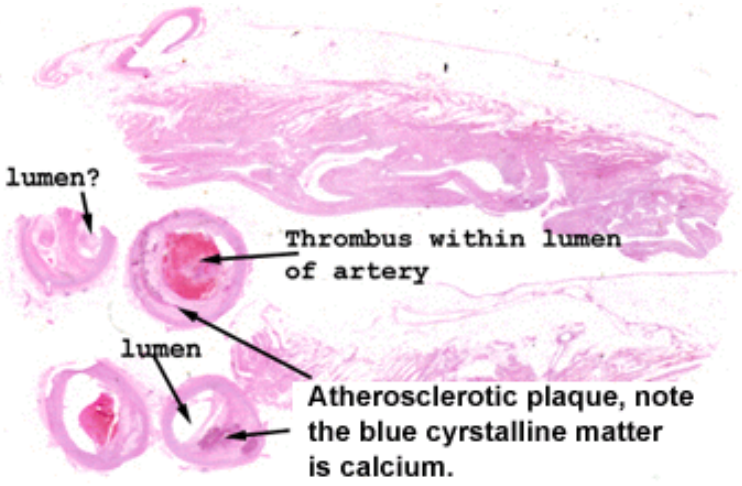
You have to use your imagination a bit here. The tissue you have is just a little strip out of a large aneurysm of the thoracic aorta. There is no way a complete section would fit on your slide. So, the first thing to do is to get yourself oriented as to where the lumen of the aorta is and where the adventitial surface is. The atherosclerosis here is an incidental finding and not necessarily part of the reaction to the treponemal bugs. After all, this person is entitled to more than one disease.

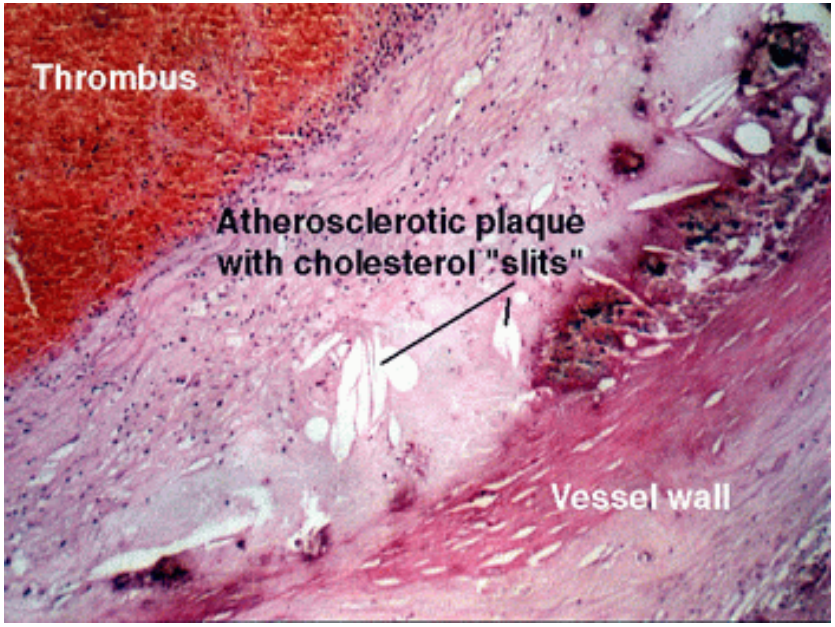
Your observations



The inflammatory changes in the wall of the aorta are subtle and observed only in the outer layers of the muscular wall and the adventitia. The organism causes an obliterative "end arteritis," and what you see is the chronic inflammatory infiltrate surrounding the vasa vasorum. It is these smaller vessel that become the "target organ" of the treponemal bug. The H&E stain does not stain the organisms. It would take a special silver stain to highlight the typical corkscrew pattern of this pathogen. Even with this stain, they would be hard to find, as so few organisms are present.

Slide 110: Elastic artery with atherosclerosis



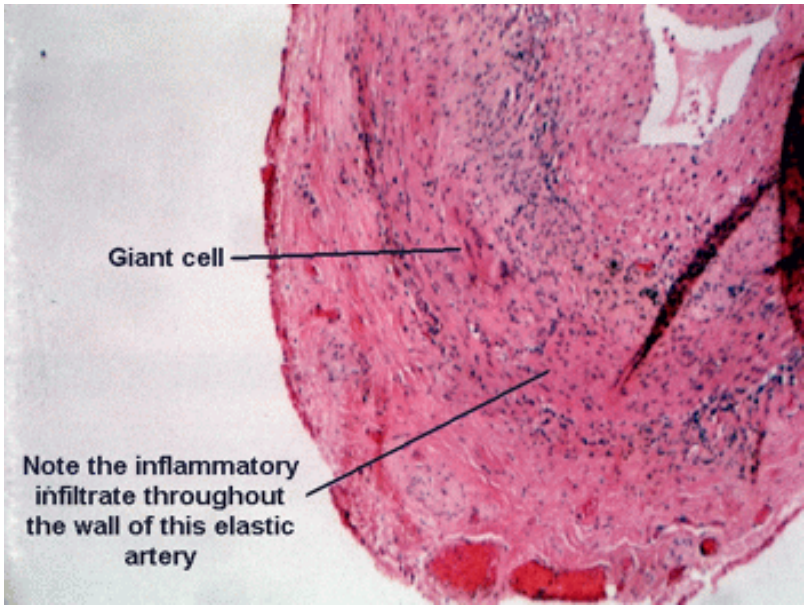


As with so many of these conditions, just looking at the tissue on the slide tells us the story. You can see how profoundly narrowed the vascular lumen is from the atherosclerosis. Add to that the complete occlusion due to the thrombus and there's not much left to say.

Here is a condition you want to know well. Although this condition will be dealt with in detail in various sections of this course, here's a chance for you to study the basic morphology of the plaque for its own sake. This slide is of an elastic artery with a classical atherosclerotic plaque with secondary thrombosis. The plaque is in the sub-intima and is a fairly complex structure. Observe the cholesterol "slits." The cholesterol was "washed out" during the processing of the tissue, leaving behind the little spaces where the deposits had been. As far as problems associated with this disease, a plaque can weaken the wall of an artery, potentially causing a rupture of the vessel; it can cause thrombosis (as it did here) and thereby complete occlusion of the lumen; and it can continue to "grow." What do you think happened to the patient that gave us this slide?

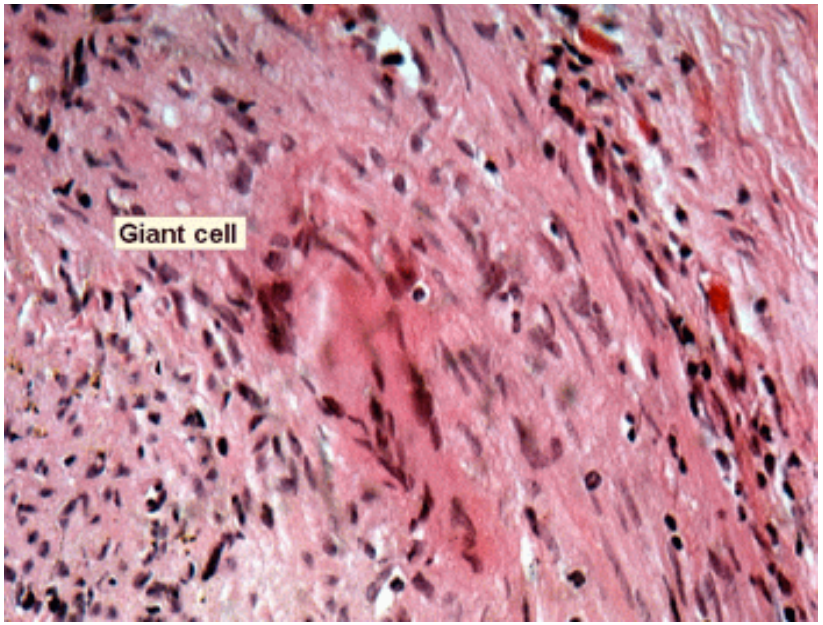
Your observations

Slide 147: Giant cell arteritis



In this low power view of the vessel wall, you can see the marked inflammatory infiltrate and even recognize some of the giant cells. Note the narrowing of the lumen secondary to the inflammation of the vessel. What is the focus of attention of these inflammatory cells?

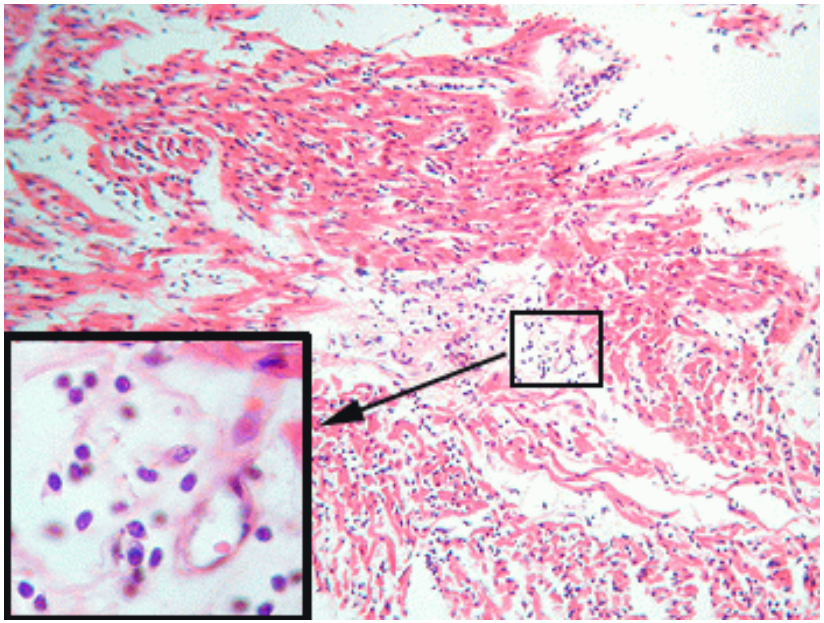
Your observations



One of the many giant cells making up this infiltrate. Note how intense this chronic inflammatory infiltrate is.

Slide 208: Acute viral myocarditis

Your observations

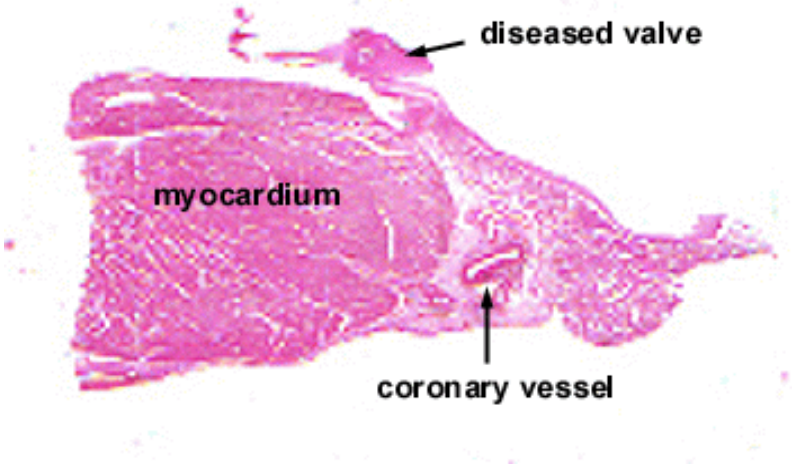


The inflammatory infiltrate is seen diffusely throughout the muscle. As you would guess, it's mostly lypmphocytes. Look in the perivascular connective tissue first. You'll see plenty. Move into the myocardium once you know what you're looking at. It's a good idea to break out the normal heart slide first to convince yourself there should be no inflammatory cells at all where we see these.

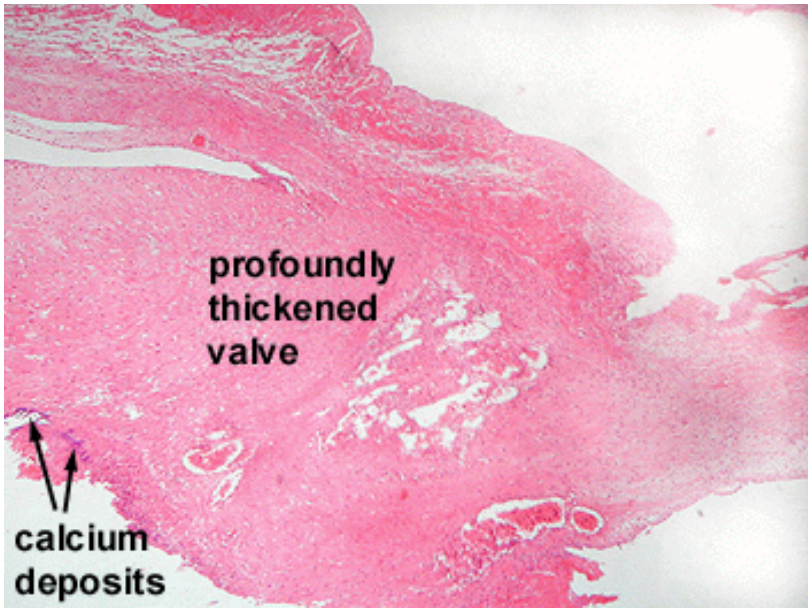
There are likely to be a few PMNs scattered around. These guys are here to clean up the dead and dying cells, and not as part of the actual infiltrate fighting the virus.

Slide 209: mitral valvulitis

Your observations

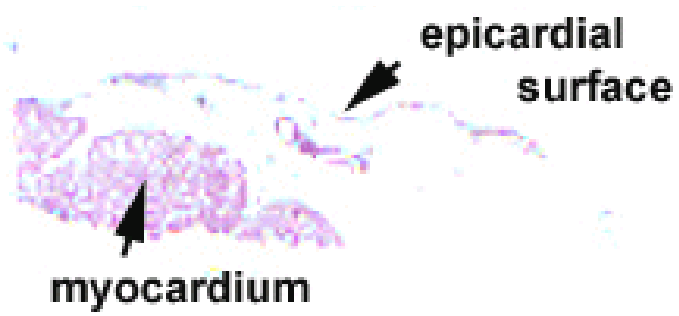


It's pretty easy to see the thickened and damaged mitral valve. Note the extensive fibrosis.



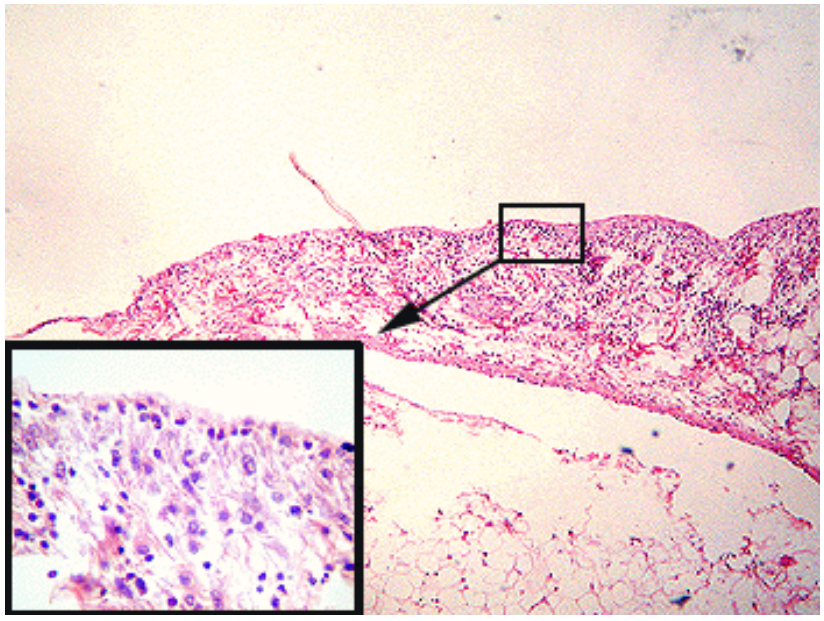
Again, it may be helpful to look at the normal condition to appreciate the marked fibrosis of this valve. There are even what appear to be calcium deposits. Bacterial colonies on the valve margin can look like this as well, but in that case one would expect substantial acute inflammatory reaction. This we don't see.

Slide 210: infectious pericarditis



This is a narrow strip of heart, including myocardium and epicardial fat. You want to look along the edge of the epicardium for the inflammatory cells. Again, looking at the normal condition will help you appreciate how much inflammation is really here.

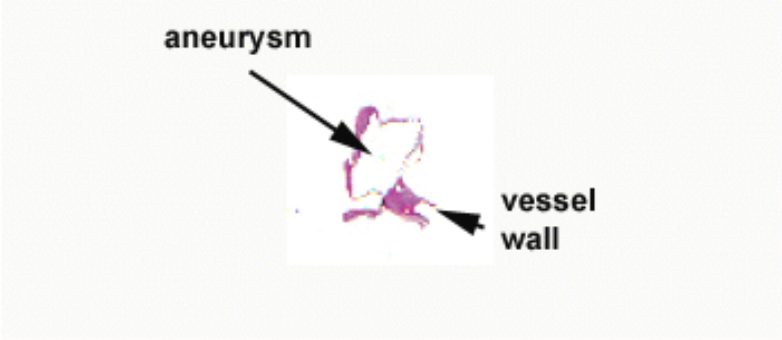
Your observations



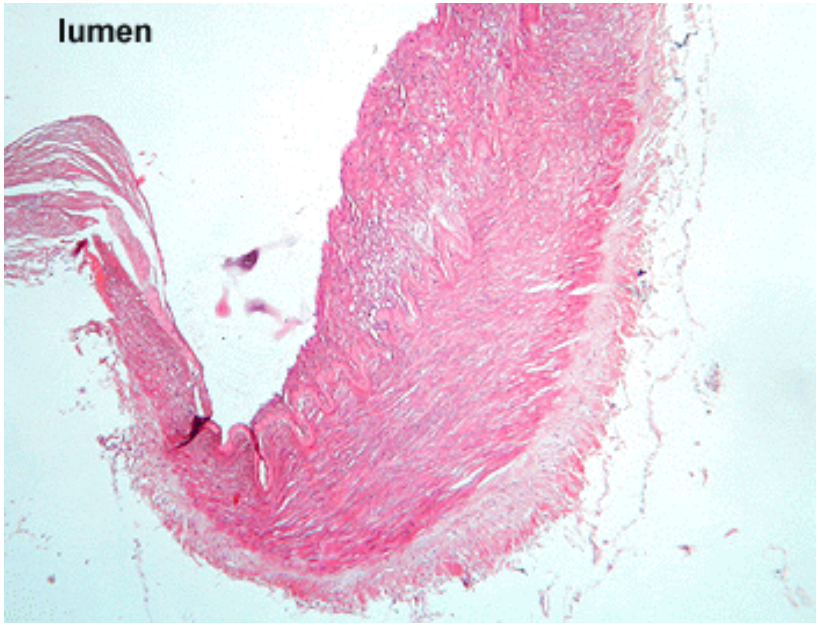
Some of the cells here are part of granulation tissue. What cell do you identify as the principal inflammatory cell? What does say about the infectious agent if lymphocytes represent the majority of the inflammatory reaction? PMNs?

Slide 213: berry aneurysm

Your observations



It's called a berry aneurysm because it looks like a little berry. It's not named for Thadeus J. Berry. Very thin walled, you can imagine what will happen when this thing ruptures.

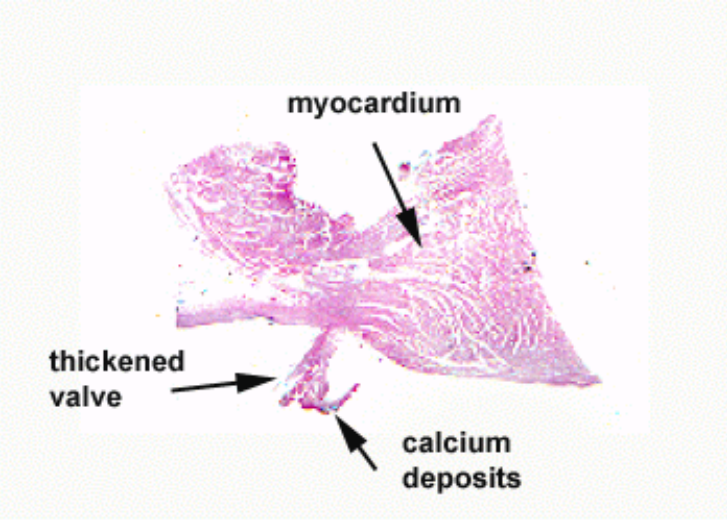


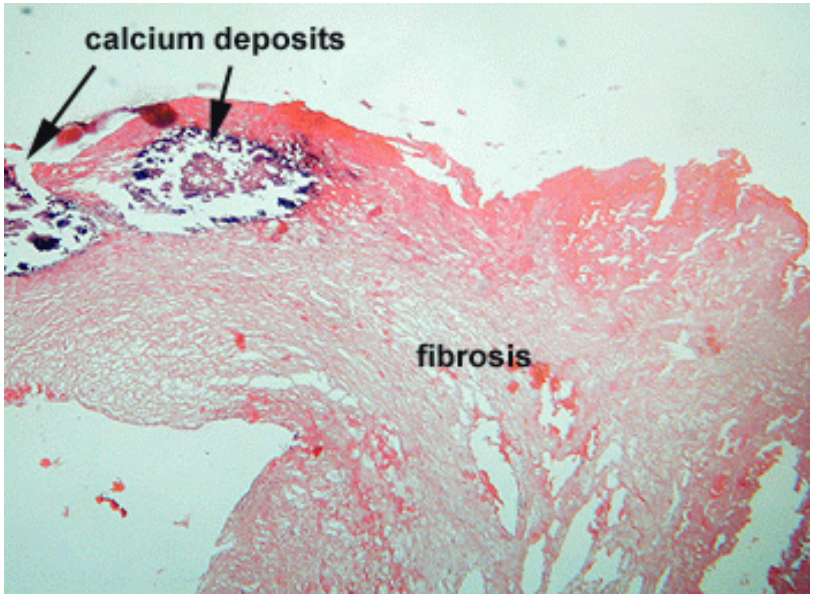
It's easy to see the aneurysm expanding off the edge of this elastic artery. Where in the vascular system do you anticipate seeing such a aneurysm? What would be the outcome of a ruptured berry aneurysm?

Slide 214: rheumatic valvulitis

This slide is a good bit like 209. Even in this low power, you can see the profound thickening of the mitral valve

Your observations

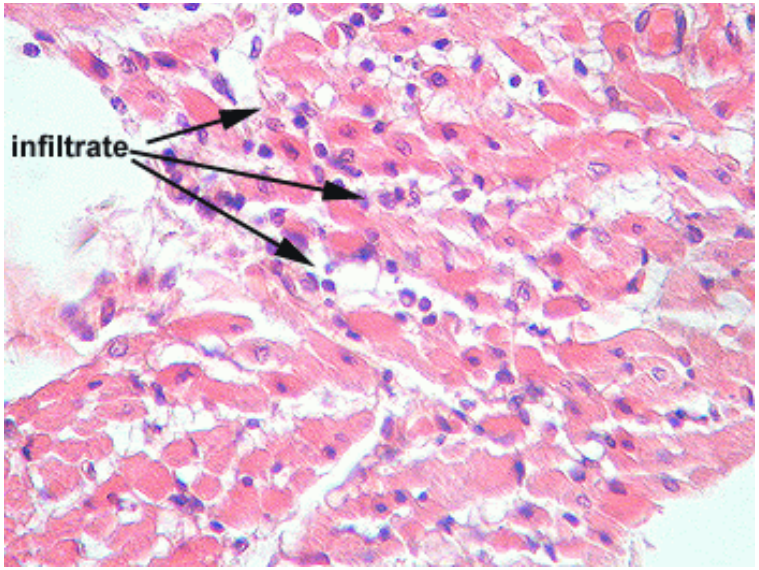




Lots of fibrosis and focal calcification. Do you think this valve was moving very freely? What's the mechanism of injury with rheumatic heart disease? Why do we use the word "rheumatic" at all?

Slide 215: diphtheria myocarditis

Your observations

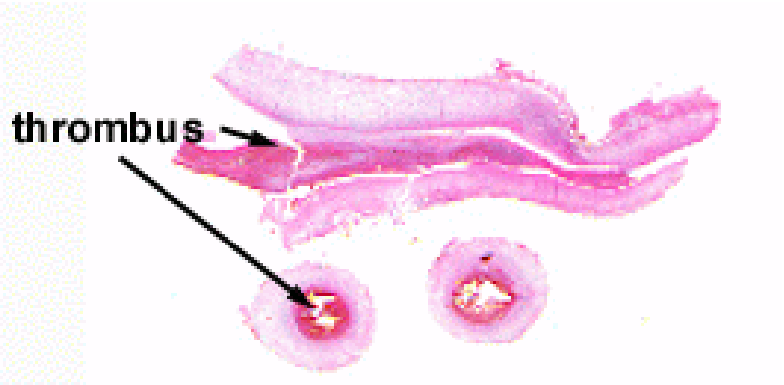


True, this condition is largely, but not entirely, of historical value today. The fact that almost no child dies of this disease today is a result of childhood immunizations. Diphtheria is the “D” in DPTT. Even so, not every kid is immunized, even here in Camelot, so sporadic cases are seen.

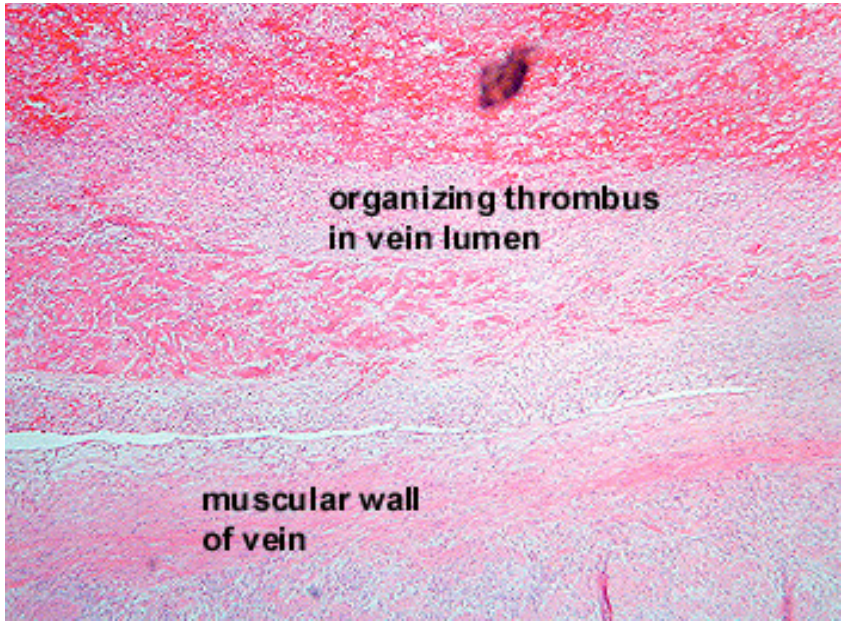
You will see an inflammatory infiltrate in the interstitium as well as some myocardial cell necrosis. Recall that the bacteria is in the throat and upper airway and the toxin is actually part of a lysogenic phage. The tremendous degree of necrosis and copious exudate in the airways often leads to asphyxial death. The pain from the airway inflammation is said to be excruciating.

Slide 217: vein with thrombus

Your observations



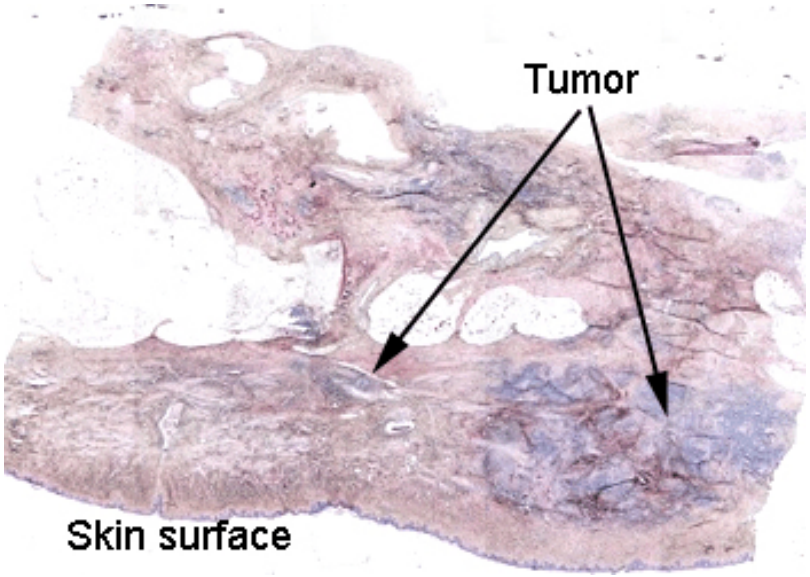
This slide consists of one longitudinal and two cross sections of the thrombosed vein. The thrombus is partially organized and you will see it attached to and being incorporated into the vein wall in several areas.



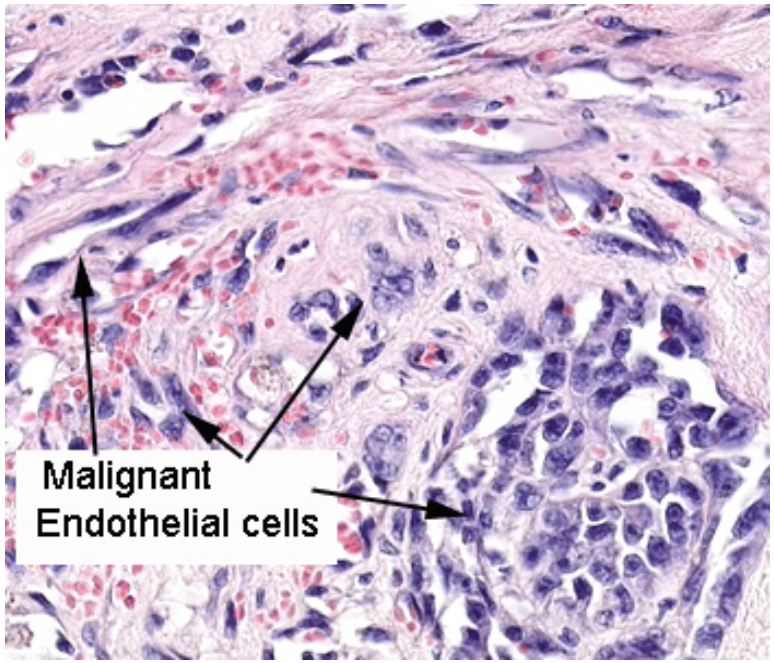
Here we see the ingrowth of granulation tissue, hence the term “organization.” In the lower right hand portion of this image you can see the attachment to the vein wall.

Slide 224, Angiosarcoma of Breast

Your observations



This is an unfortunate example of second malignancy arising as a consequence of the treatment of the first one. This is an angiosarcoma that arose in the area of the previous cancer surgery, which was followed by irradiation.



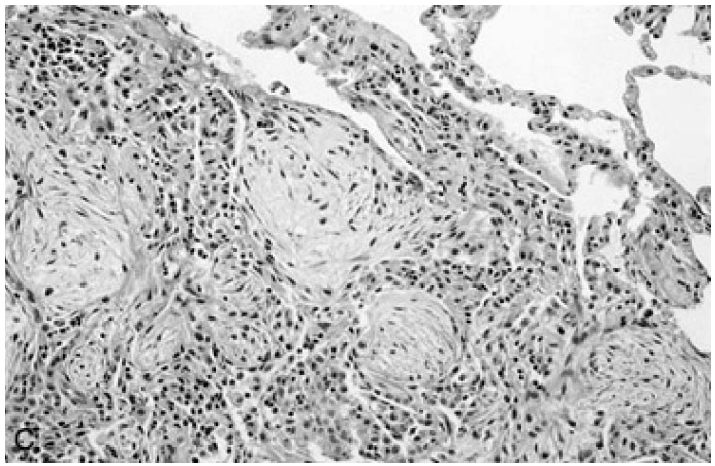
Throughout this region you will see malignant endothelial cells, some aggregated into vascular structures. RBCs are within the vascular slits, and elsewhere they have been leaked into the surrounding tissue space.

General and Systemic Histopathology
C601 and C602

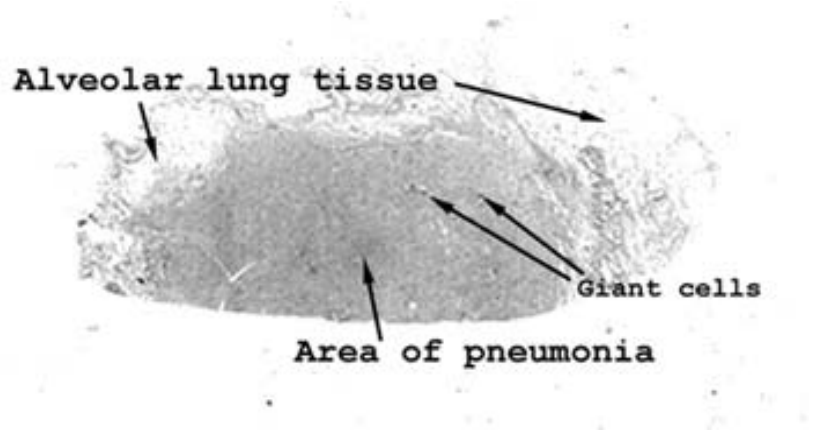
Section 6 *Pulmonary Disease*

The lung is subject to injury in a number of ways including what may be termed "innocent bystander" conditions. In this laboratory, we will be looking at the full gamut of diseases, ranging from hyaline membrane disease of the newborn to metastatic carcinoma in the elderly. As will become evident, conditions that alter the membrane's oxygen exchange membrane's capacity to function will have almost immediate consequences. In this regard, you will want to understand the mechanism of pulmonary involvement in congestive heart failure, pulmonary embolization (think of the various things that can embolize) and primary inflammatory conditions of the lung.

Contrary to the public posturing of the tobacco industry, smoking leads to increased incidences of practically every pulmonary disorder. One the most common smoking related pulmonary diseases is emphysema, a condition in which pulmonary tissue is lost for good. To understand the process of emphysema you will need to know the difference between obstructive and restrictive conditions affecting of the lung. Practically everyone knows of the association of smoking and lung cancer, but what histologic type of cancer is most common among smokers? These and other fascinating issues will be addressed in the pages that follow. Read on.

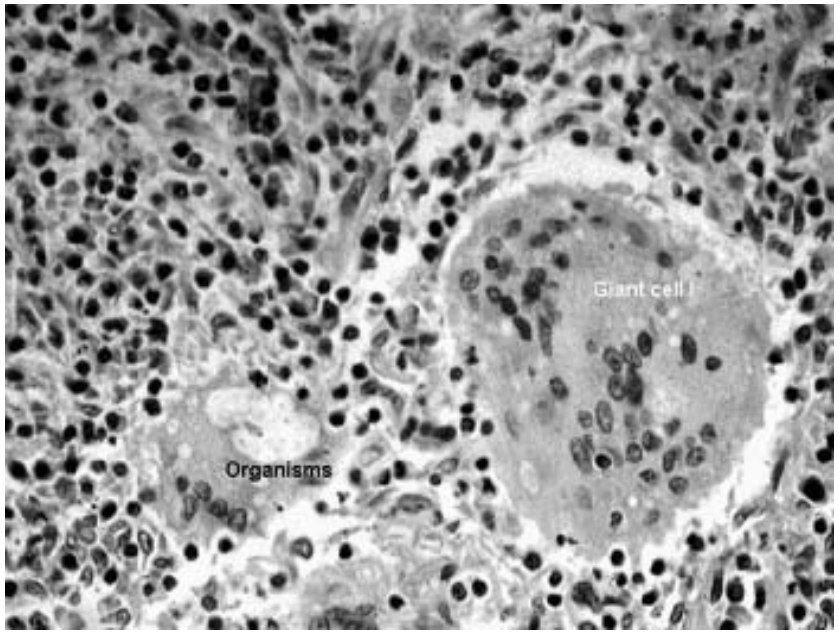


Slide 1: Cryptococcal Pneumonia, higher power view



This is a picture of the tissue as it appears on your slide. See if you can orient it as it appears here and then locate the alveolar lung tissue with central area of inflammatory infiltrate. You might even be able to spot some of the giant cells without any magnification. When you put the slide on the stage of your scope, start with the lowest power first, review the entire slide and then go progressively to the higher levels of magnification.

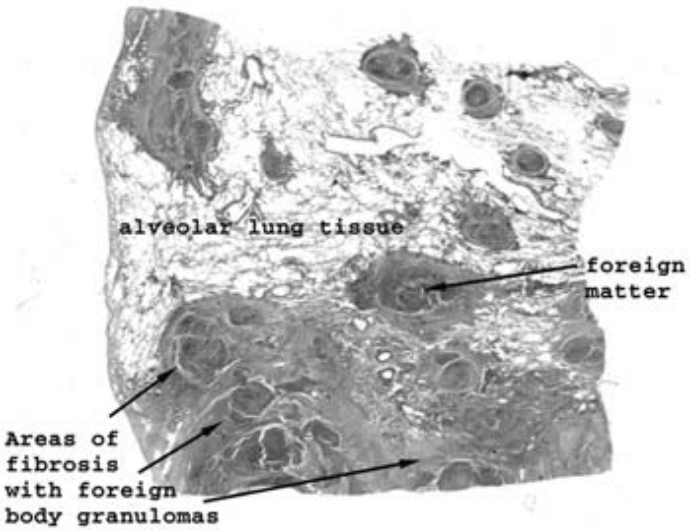
Your observations



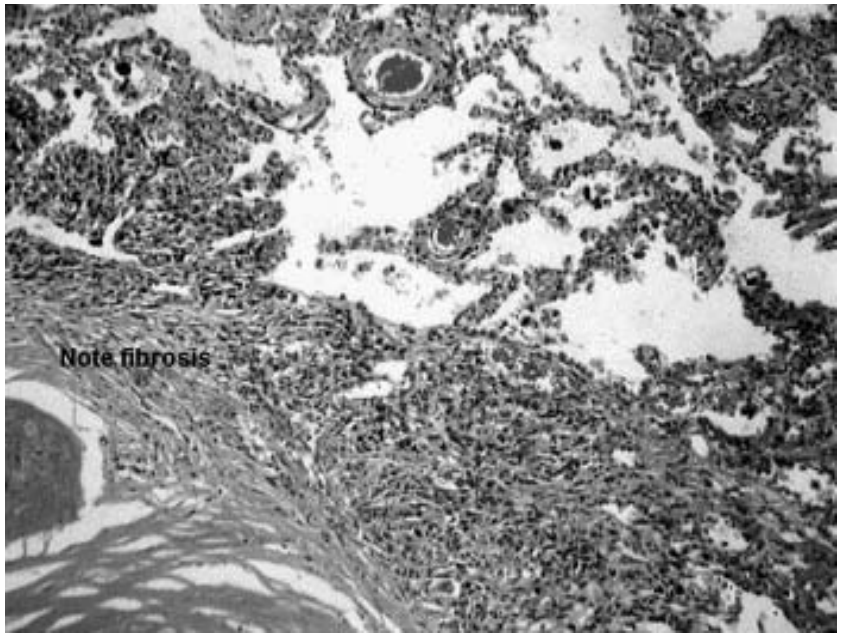
The cryptococcal organisms are quite evident in one of the smaller giant cells. As you may recall, the organisms possess a large capsule so they tend to stand out in the cytoplasm of the giant cells. The giant cells are unique participants in our response to injury. They are commonly seen in association with injurious agents the body cannot easily rid itself of. We will see them again in the inflammatory response to tuberculosis and foreign material that has been injected or left behind in the body. Can you think of situations in which foreign material might find its way into the body (I mean external matter, not an infectious agent)?

Your observations

Slide 36: Lung with pneumoconiosis



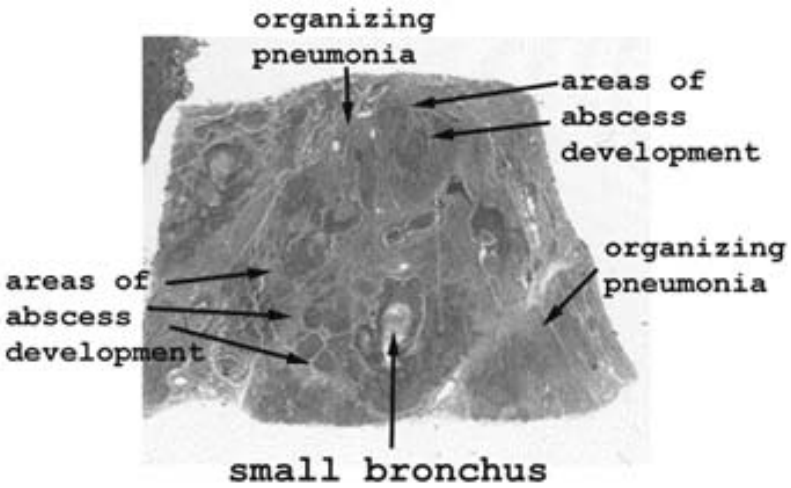
Here the areas of fibrosis are quite evident. First take a look at the uninvovled lung to get your berrings. Then move into the areas of fibrosis and granuloma formation. What about all the pigmented material?



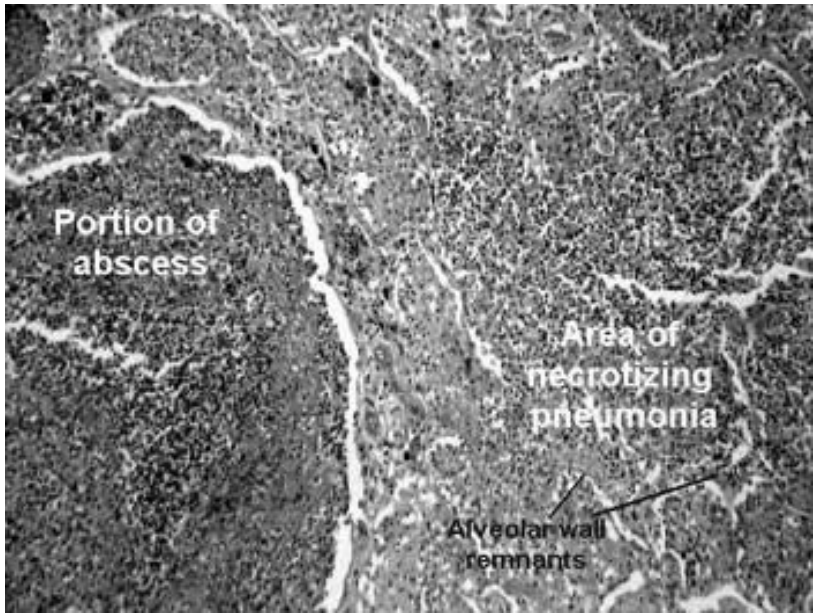
Here the real story is the profound degree of fibrosis in the interstitial tissue of the lung. There are even a few granulomas present. This condition is a result of the particulate matter inhaled, and may be seen in stone workers, coal workers and anyone exposed to lots of fine air borne particulate matter. The scarring really predisposes the person to tuberculosis and other pulmonary infections. Will this lead to a restrictive or obstructive pulmonary picture clinically?

Slide 58: Lung with abscess

Your observations



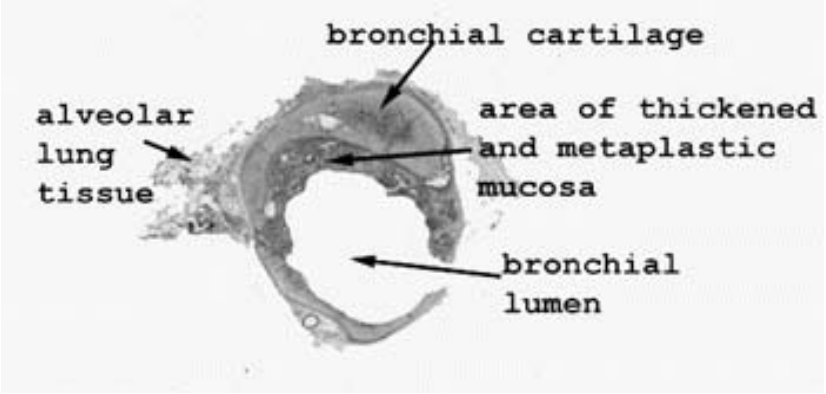
There is such consolidation in this section of lung, that it is hardly recognizable for what it is. Just looking at the piece of tissue on the slide, the diffuse infiltrate is easily seen. The darker areas represent the complete breakdown of the pulmonary tissue. Start by looking at the edge of the tissue to see if you can find any "normal" lung to help you get oriented.



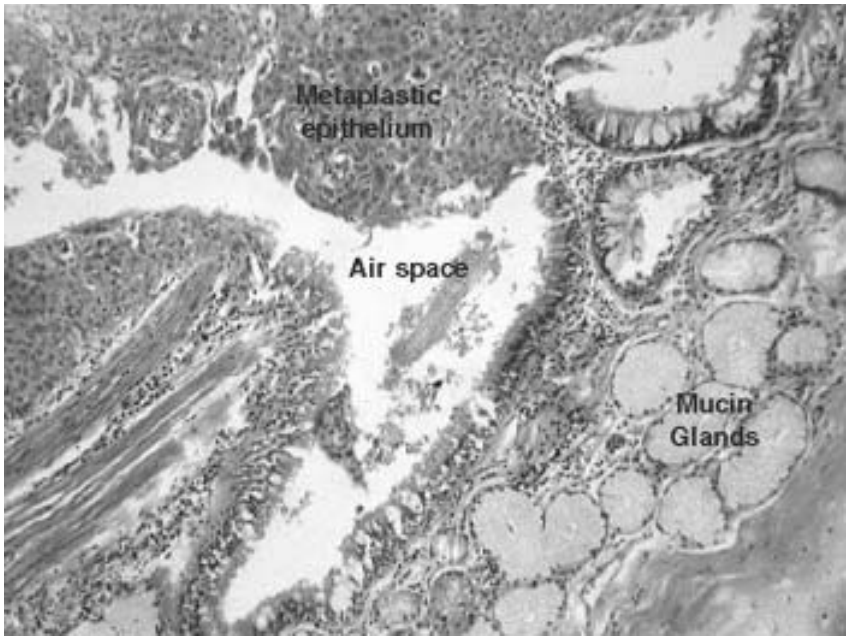
This condition could be due to any number of bacterial organisms, or even a mixture of bugs, but it happens to be staphylococcus. The general alveolar outlines will be hard to find in the areas of necrosis. It will help to go to the edge of the tissue to get your bearings before going to the area of the lesion. You will need to be pretty familiar with normal lung architecture to see anything in the background. Much of the lung parenchyma has been destroyed by the digestive enzymes of the bugs. You will see many acute inflammatory cells along with the amorphous digested debris. Clearly, once the lung tissue has been destroyed and the abscess formed, that lung tissue is gone for good.

Slide 64: Lung with squamous metaplasia of bronchial mucosa

Your observations



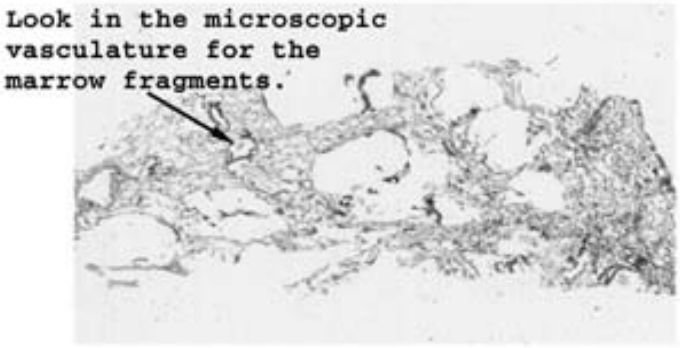
The process of metaplasia is found intermixed with the typical ciliated columnar epithelium. This is a reactive or adaptive process and not a true malignancy. What is the definition of metaplasia?



This picture is of bronchial mucosa, showing the reactive replacement of one type of epithelium for another. It is technically not a neoplastic process, although continued injury of the sort that lead to the metaplasia, can lead to dysplasia and possibly cancer. Here we see respiratory epithelium being replaced by squamous. Smoking was the injury that led to this alteration. Observe the inflammatory reaction beneath the mucosa.

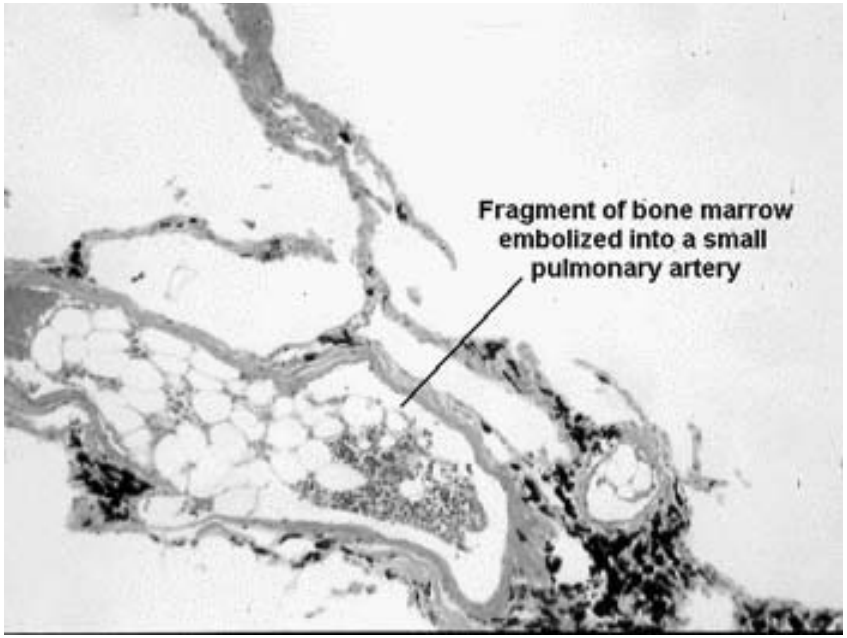
Slide 68: Lung with bone

marrow embolus



This stuff is hard to find, but once you see it you'll know what we're talking about. These are microscopic sized fragments of bone marrow, so don't expect to see them with the unaided eye. What's more, be prepared to look at a number of areas to find this alteration.

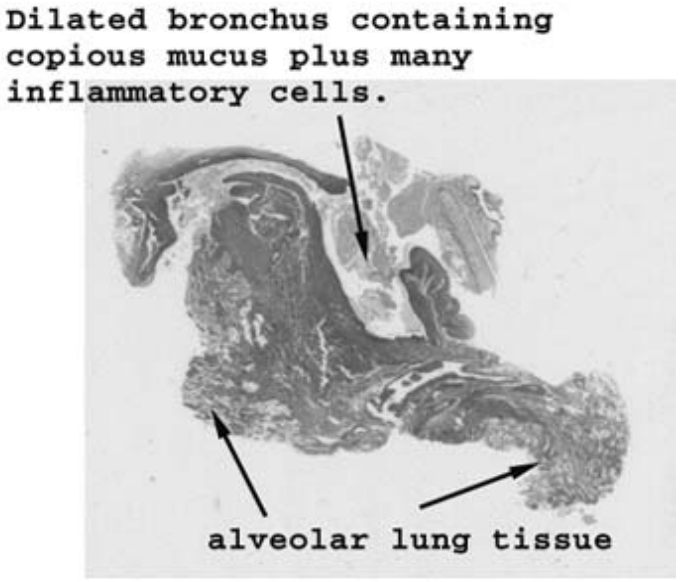
Your observations



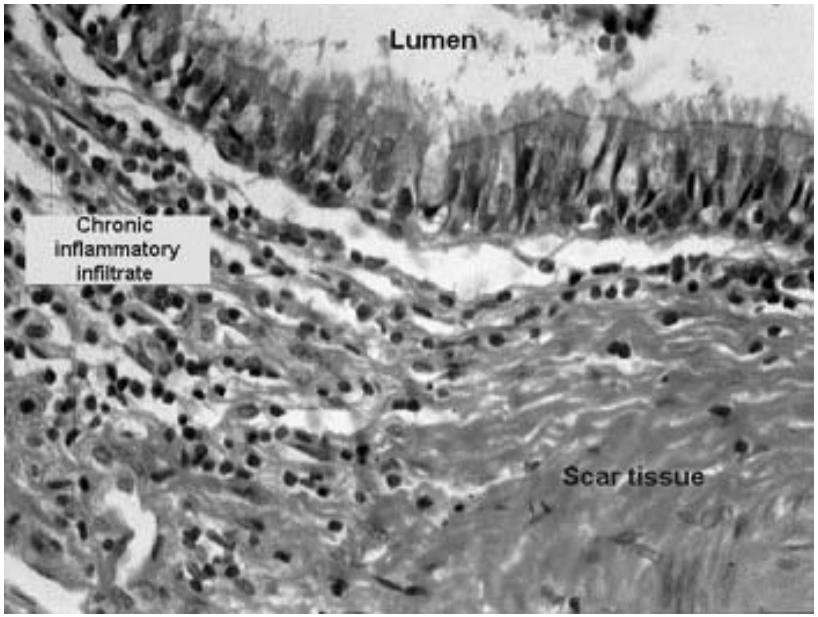
Look in the smaller blood vessels of this section of lung. You will see small fragments of fat and hematopoietic tissue. These are little, intact, fragments of bone marrow that were dislodged because this patient sustained major long bone fractures in an auto accident. Some of the bone marrow gained entrance into the circulatory system, and then became lodged in the lung vasculature. This person died shortly after the event. Can you imagine other conditions that could cause this?

Slide 70: Lung with bronchiectasis

Your observations



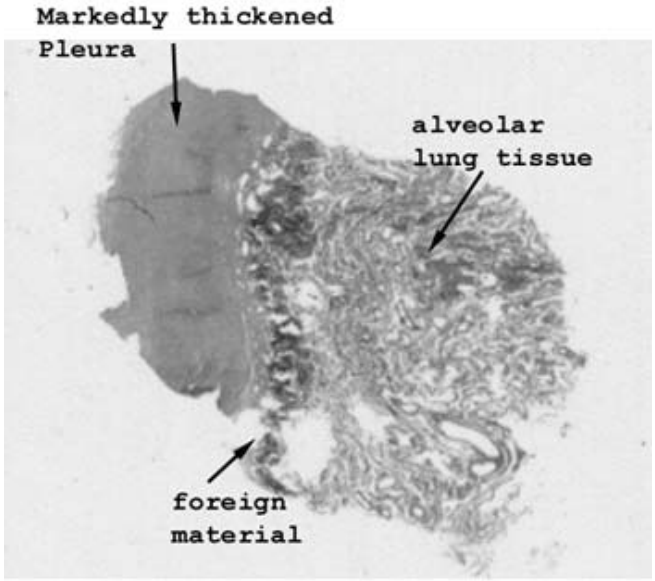
Things to look for in this slide include the amount of fibrosis and inflammation in the wall of the bronchus as well as the mucus in the bronchial lumen. What about the number of goblet cells in the mucosa.



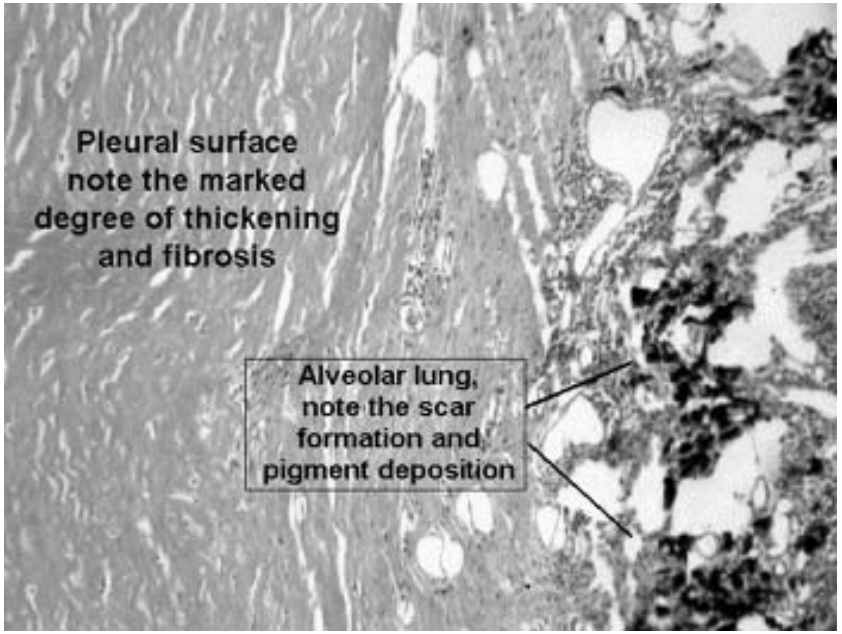
This condition is hard to show on a microscopic slide. In bronchiectasis, the bronchi become dilated and often fill with mucus, bugs and inflammatory debris. People with this condition cough and bring up lots of sputum, and generally have a heck of a time with infections. Sometimes the infections can spread via the blood stream to other organs. Look in the wall of the bronchus in this section and see the degree of inflammation. It is hard to get the perspective of a markedly dilated bronchus though.

Slide 72: Lung with healed pleuritis

Your observations



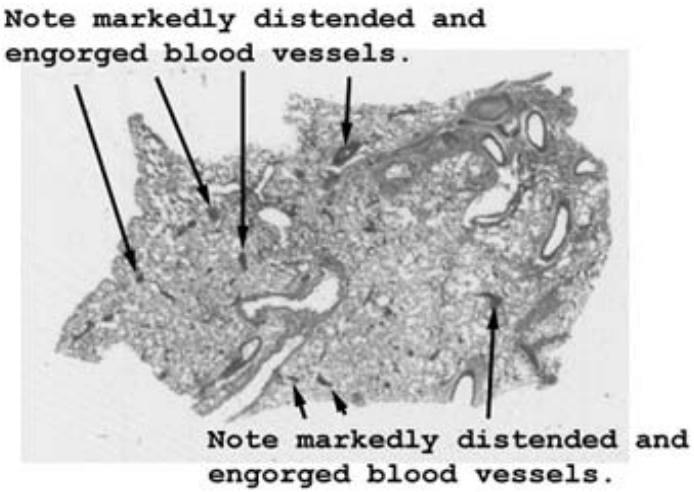
The thickening of the pleura is quite striking here. What do you make of the pigmented material in this section?



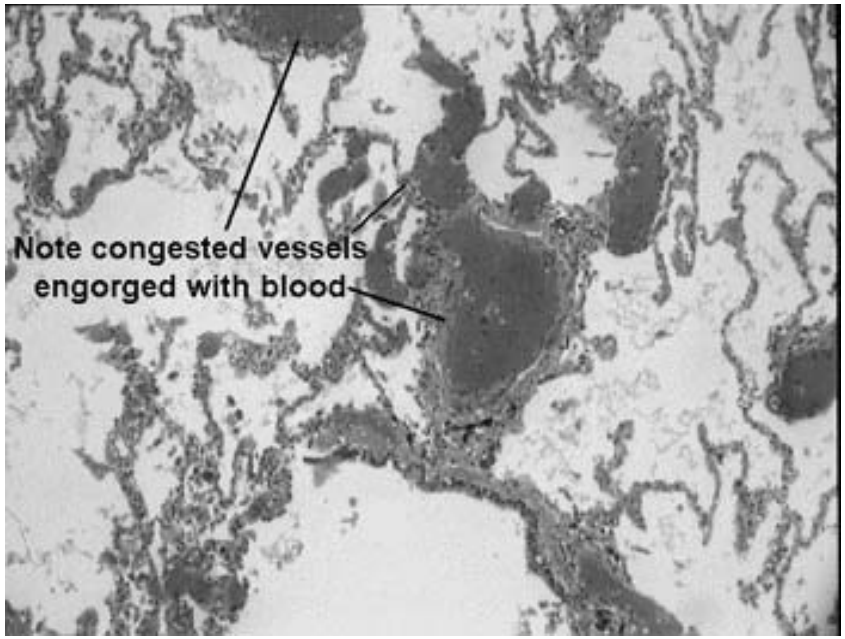
This slide shows a profoundly thickened and scarred pleural surface. This is the end stage of a pleuritis and is likely years old. The original pleuritis probably was the result of a bacterial pneumonia. Observe the highly collagenized scar tissue with a relative paucity of inflammatory infiltrate. This scarred pleura very likely produced an impairment in chest wall expansion and thereby probably had an effect on pulmonary function. Also note the lung tissue adjacent to the scarred pleura. The air sacks are enlarged and there is some interstitial fibrosis as well. These are representative changes of emphysema.

Slide 74: Lung with passive congestion

Your observations

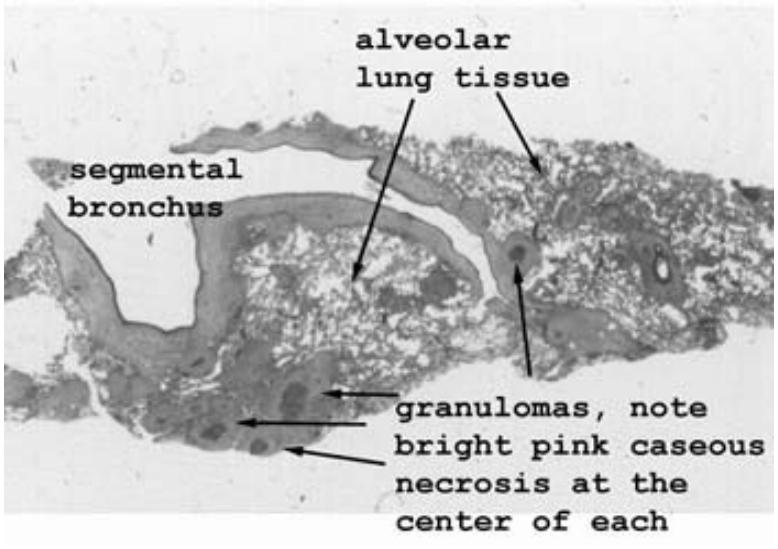


The congested vessels literally leap out of the tissue on this slide. Look not only at the vessels, but also the frothy material that has collected within the alveolar spaces. What's going on here?



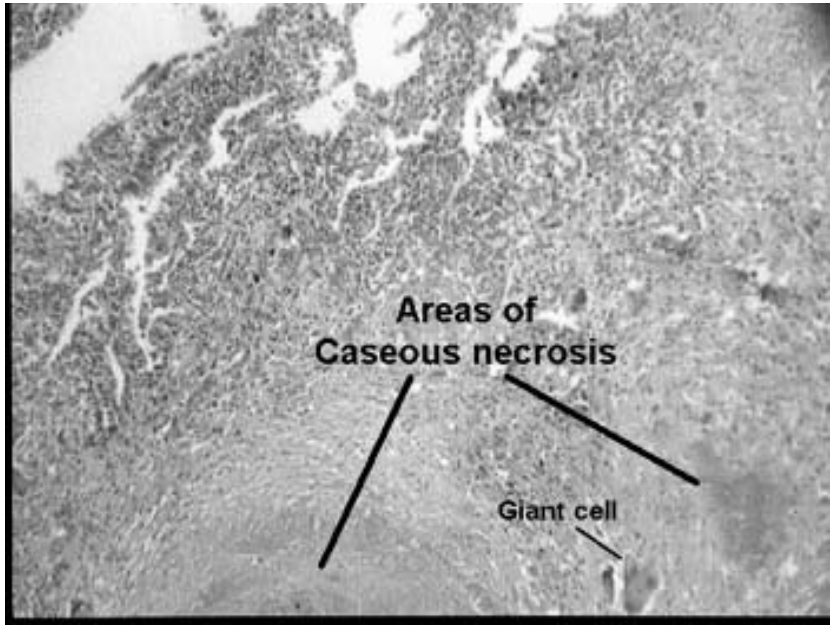
The changes here are a little subtle. The blood vessels are distended and "over filled" with blood. They have became dilated, in this case, because of the back up of blood in the pulmonary circulation due to an abruptly failing left ventricle. This person had a myocardial infarction, and experienced sudden failure of the pump. You may see evidence of pulmonary edema in the alveolar air spaces. The edema fluid will appear as a faint pink stained material in the background of the air spaces. It represents the extravasation of fluid through the vessel wall as a result of the increased lumenal pressure.

Slide 76: Lung with tuberculosis



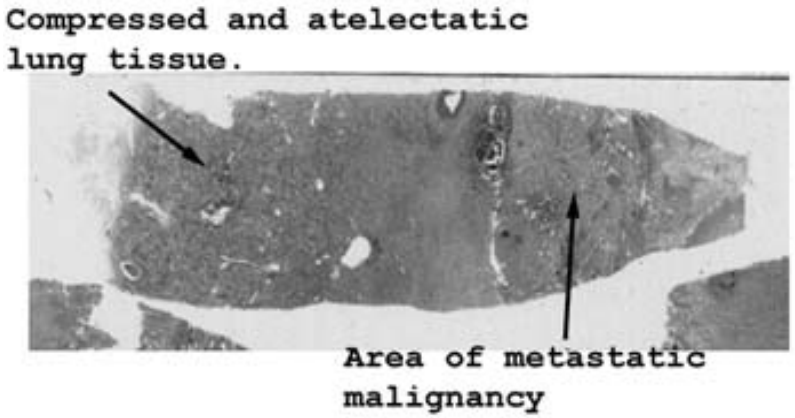
Look carefully at the lung tissue for the little pink areas of caseous necrosis. These are the areas of tubercular infection. They don't show a well developed granuloma architecture, but you'll see the evolving features and should have no trouble finding the giant cells.

Your observations



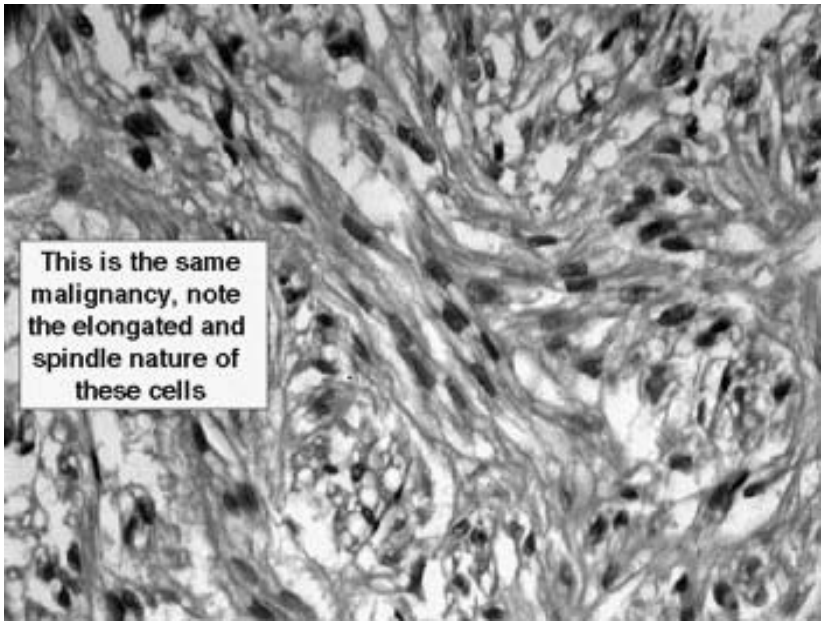
This section of lung is largely replaced with a single granuloma. Note the structure of the granuloma and the fact that it has a "caseous" center. There are numerous giant cells and the fibrous margin of the granuloma is only partially formed at this time. The caseous center of the granuloma is very characteristic of TB. The granuloma itself, and the giant cells, represent a general reaction to an agent the body cannot eliminate or destroy.

Slide 80: Lung with metastatic renal cell carcinoma, spindle cell pattern



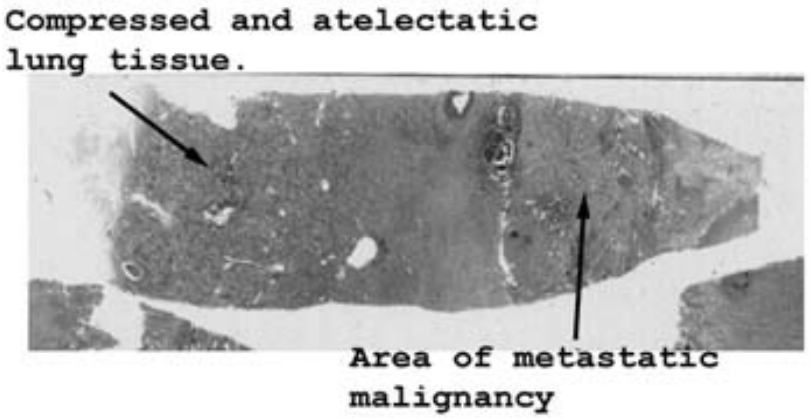
The appearance of this malignancy is a little atypical. Generally the metastases pretty faithfully reproduce the histologic pattern of the primary lesion. Renal cell is probably the one tumor that most consistently breaks this rule. Here we see two patterns in the same metastatic focus; a spindle pattern and the more typical clear cell pattern.

Your observations



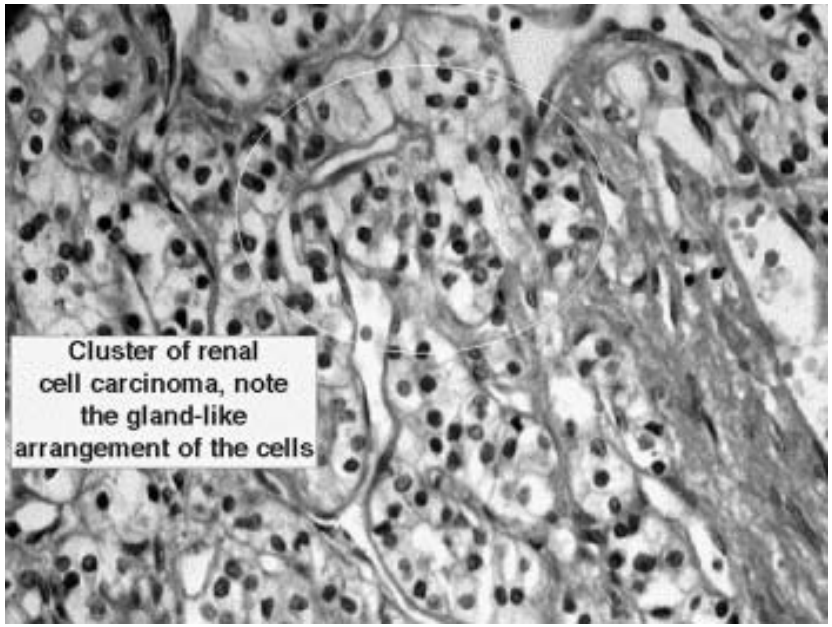
This slide shows the "spindle cell" variant of this malignancy. It is actually not the typical appearance, but the next slide does show the more characteristic so-called clear cell pattern. This slide shows lung tissue essentially replaced with metastatic renal cell carcinoma. Notice how in this area the malignant cells have an elongate or spindle appearance. Some cancers, especially renal cell carcinoma, can show a multifaceted histologic pattern. It would be very difficult to make an accurate diagnosis as to the origin of this tumor if this were the only piece of tissue given the pathologist.

Slide 80: Lung with metastatic renal cell carcinoma, clear cell pattern



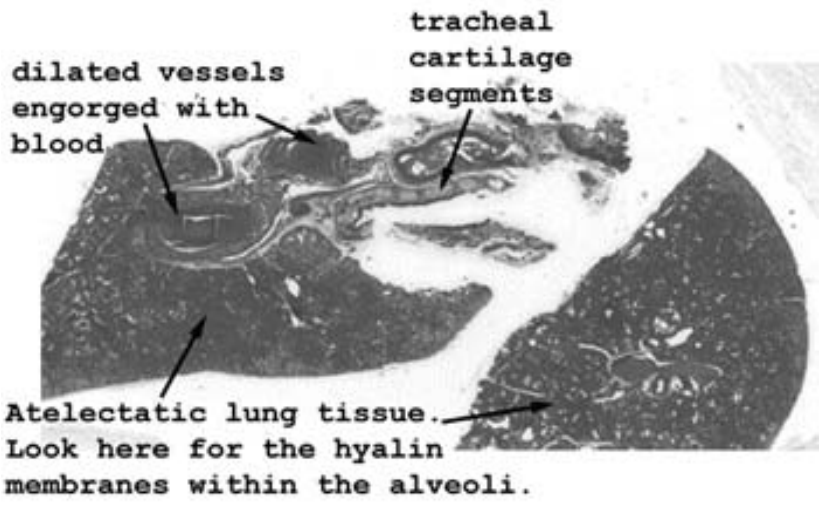
The appearance of this malignancy is a little atypical. Generally the metastases pretty faithfully reproduce the histologic pattern of the primary lesion. Renal cell is probably the one tumor that most consistently breaks this rule. Here we see two patterns in the same metastatic focus; a spindle pattern and the more typical clear cell pattern.

Your observations



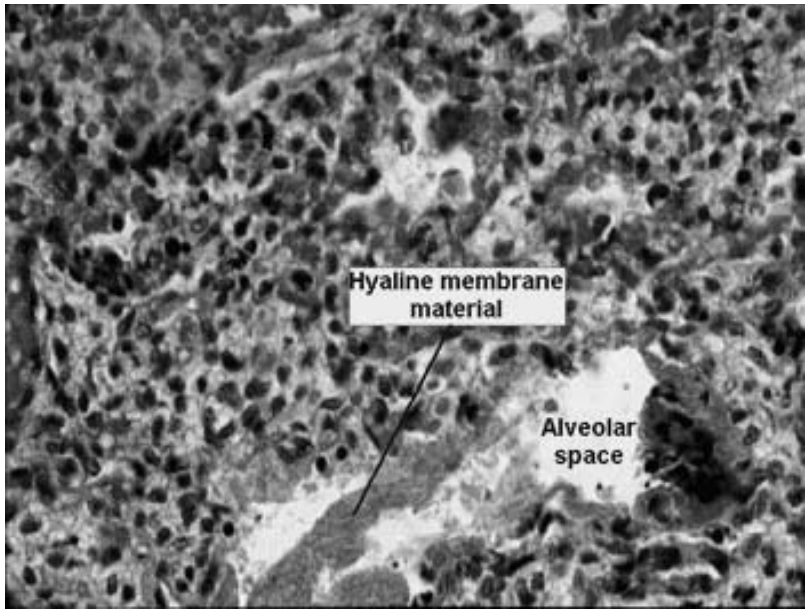
This slide shows lung tissue that is essentially replaced with metastatic renal cell carcinoma. You will see clusters of cells with very clear, washed out appearing, cytoplasm. The cells appear in clusters that mimic the configuration of a renal tubule. The cells are clear because the lipid they once contained was "washed out" by the xylene during the processing of the tissue in preparation for sectioning.

Slide 89: Infant lung with hyaline membrane disease



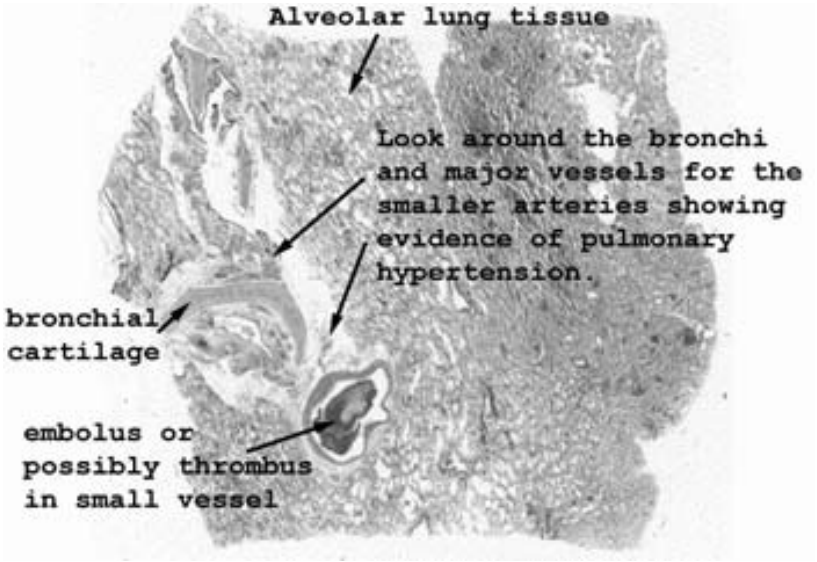
The lung tissue here is quite "meaty," and may not even appear as lung to you. Fetal lung looks much like this, although in this case there is extensive atelectasis along with the accumulation of the alveolar proteinaceous material. See how many aspects of pulmonary histology you can identify in this slide.

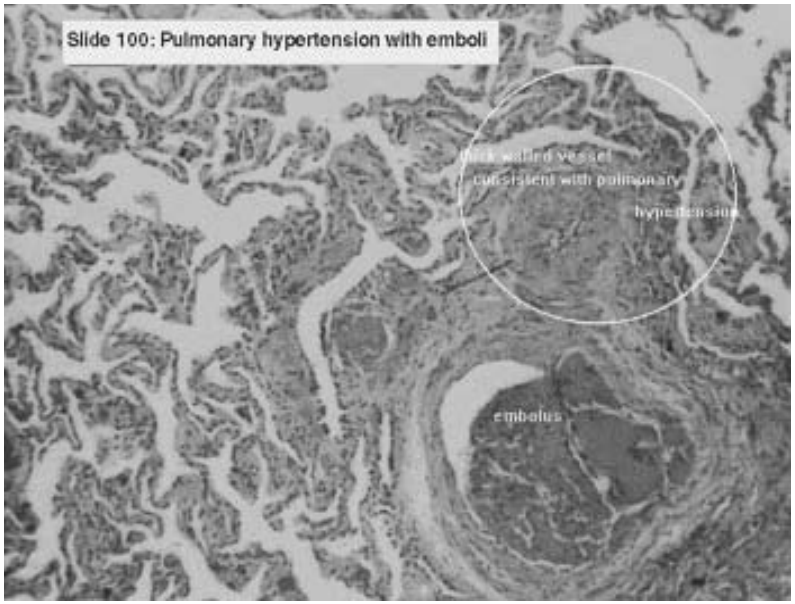
Your observations



Infant lung looks considerably different from adult tissue. Note how much more cellular and thick walled the alveoli are. The vessels are quite congested. The "hyaline membranes" are deposits of pink staining proteinaceous material in the alveolar spaces. They are not continuous, but appear as half moon shaped deposits. They are hard to see at first, but once you have picked them up, they will start to appear all over the slide. What caused this condition? Do adults have something similar?

Slide 100: Lung with pulmonary hypertension and embolus



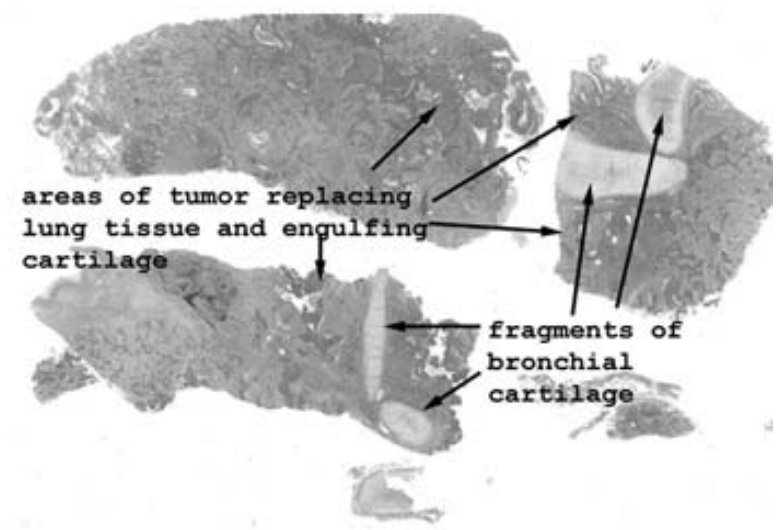


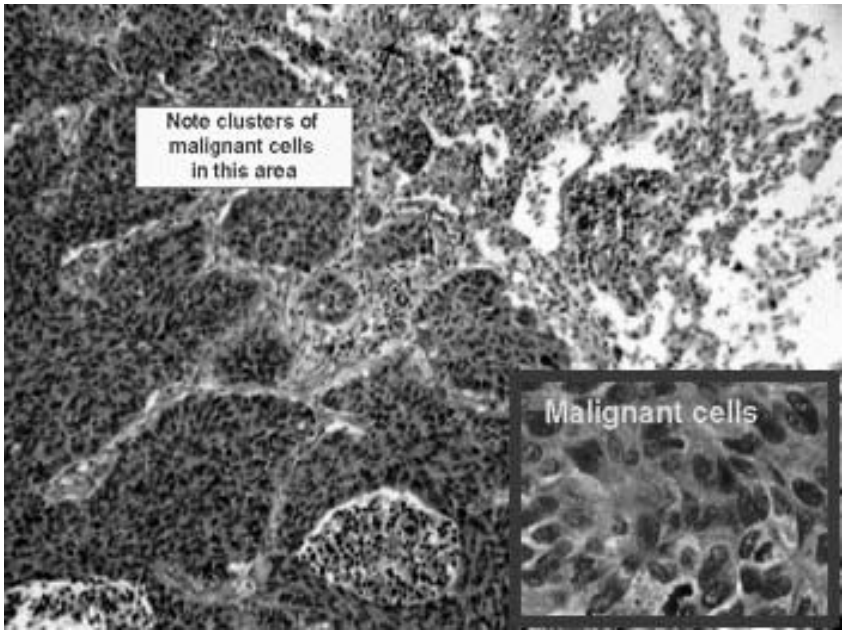
The changes are subtle in this tissue. Look at the smaller muscular arteries for the hyperplastic changes. It might be wise to review normal lung to get an idea of what these vessels should look like before tackling this slide.

There are actually two things of interest in this slide. First, notice the thickened muscular walls of the smaller arteries and arterioles; changes of pulmonary hypertension. The pulmonary vessels are undergoing hyperplasia to "adapt" to higher than normal pulmonary vascular pressures. This feature contributes to the resistance in the pulmonary vascular bed, and will lead to right-sided heart failure. What are some causes of increased pulmonary vascular pressure? Also, note the pulmonary emboli. Could these be thrombi? What is the difference?

Your observations

Slide 101: Squamous cell carcinoma of lung





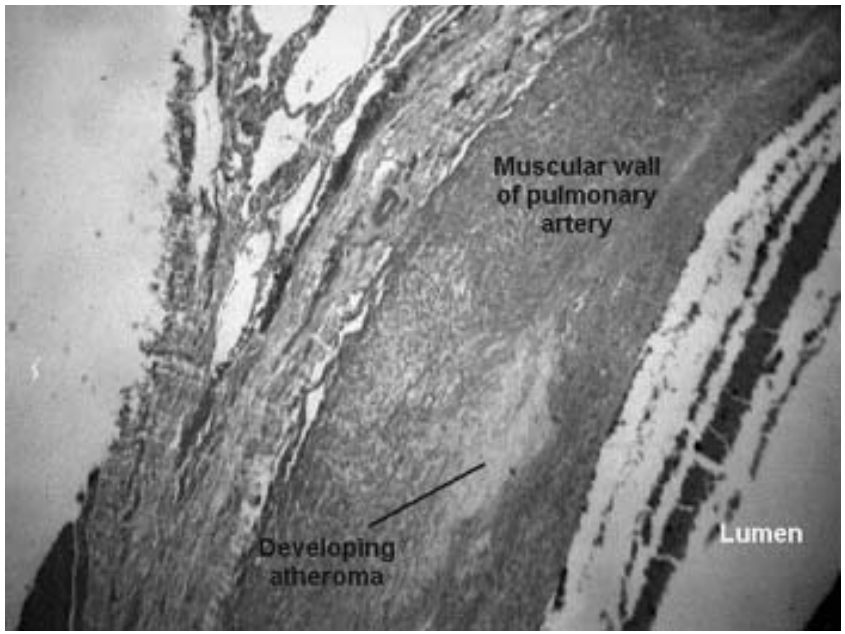
Very little alveolar lung is to be found on this slide. The tumor has pretty much replaced everything in the region of the sample. Note how the tumor surrounds and encases the fragments of bronchial cartilage.

This slide shows a typical squamous cell carcinoma of the lung. Mitotic figures will be common and some "tripolar" mitoses might be present. You should be able to spot the "intercellular bridges" (as opposed to the Madison County type) that characterize squamous cell malignancies. You will see great variation in size of cells and nuclei, but the basics of malignant nuclear features are all here: nuclear/cytoplasmic ratio, angulated nuclear margins and nuclear hyperchromasia. The type of epithelium that gave rise to this malignancy is not normally found in the lung, where do you think it came from?

The insert shows a higher power view of the squamous cell malignancy. The nuclear atypia and mitotic figures are pretty evident.

Your observations

Slide 107: Pulmonary artery with atherosclerosis

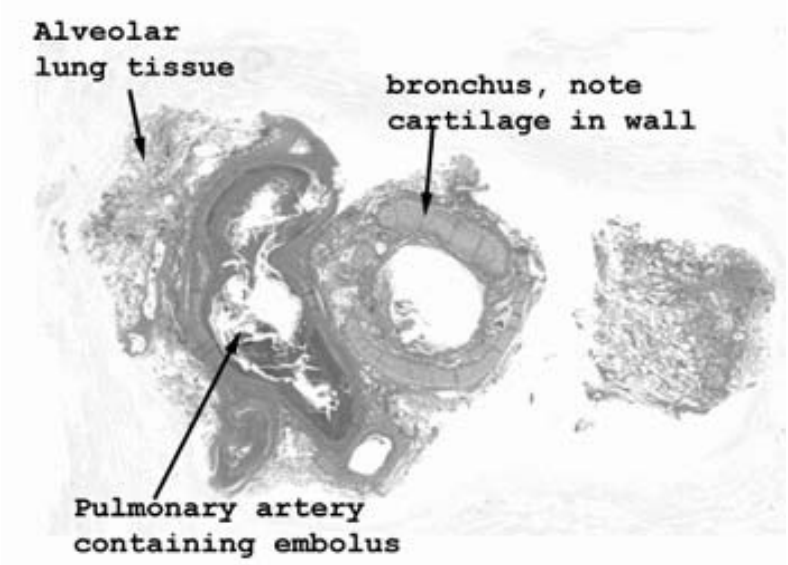


This is an uncommon slide as you might guess. Atherosclerosis is not often seen in the pulmonary circulation because the lung arterial system is such a low pressure circuit. The features of atherosclerosis are just as you would see in the systemic arterial circulation. Mitral stenosis and left to right shunts will lead to this condition.

Your observations

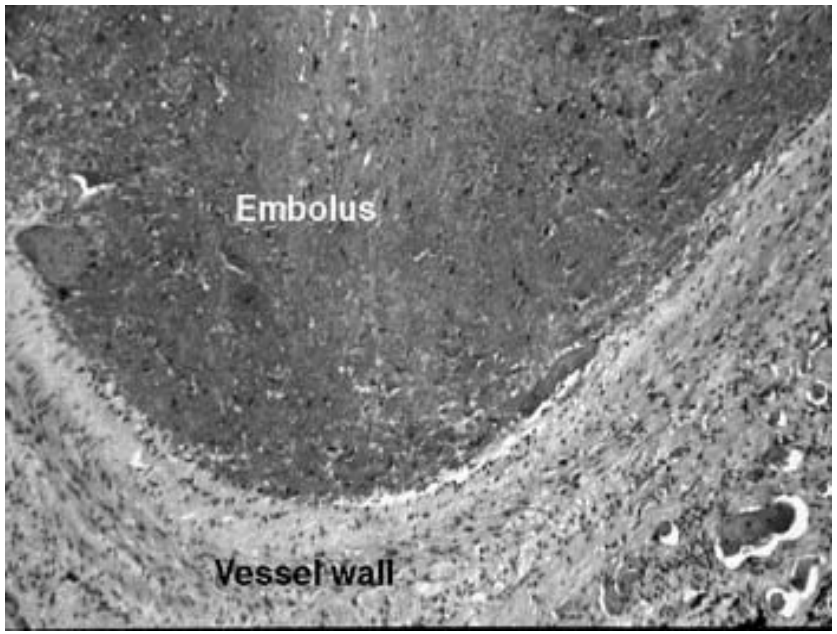
Sorry, no low power of this one.

Slide 108: Lung with pulmonary embolus



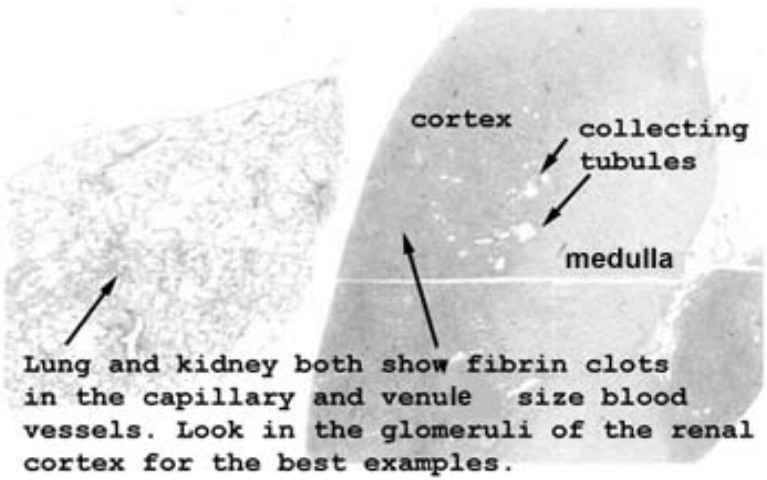
There are several pieces of tissue on the slide. The one with the pulmonary embolus should be obvious. The hole in the middle of the clot is an artifact of sectioning. It was in fact solid but partially chipped out when it was sectioned.

Your observations



There is nothing real fancy in this slide. It is a pulmonary embolus. Be sure you know the difference between a thrombus and an embolus, as well as the sorts of things that can potentially embolize. For that matter, be sure you know the factors that contribute to the formation of a thrombus. Remember there are differences in formation on the venous and arterial sides of the circulation. Here's an interesting problem I almost always ask about on the written exams: paradoxical embolization. Know what it is?

Slide 135: Lung with features of DIC



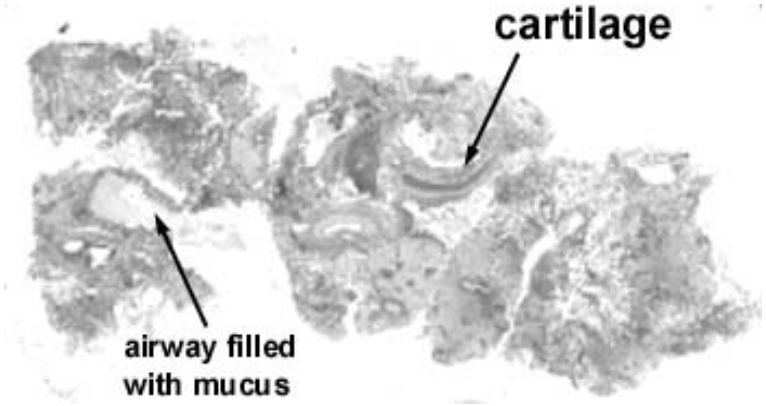
There are two pieces of tissue on this slide, for right now, focus on the section of lung. The best bet is to look in the capillary sized vessels for the diagnostic changes. You're looking for thrombi composed only of protein. If you see what looks like thrombi with lots of RBC's in them, it's not what we're looking for.

Your observations

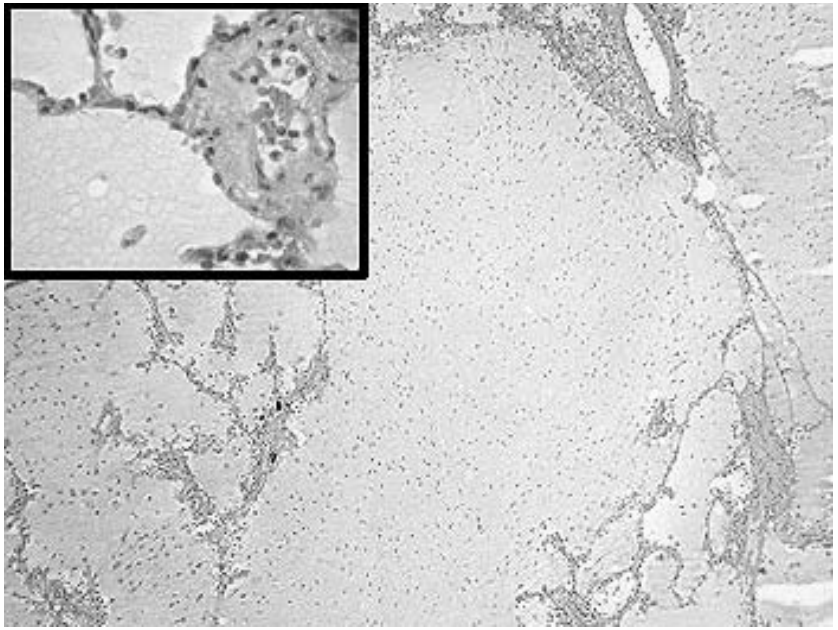
There are two pieces of tissue on this slide, and obviously this is the lung. The pathological features are the same for both the kidney and lung. With disseminated intravascular coagulation (DIC), the person experiences "run away" intravascular coagulation. As you might expect, there will be small thrombi in vessels throughout the body. This becomes an ischemic disease on the cellular level. People bleed with this condition because of the breakdown of the small vessels and the consumption of the clotting agents. Causes are gram negative sepsis, massive trauma and obstetrical disasters, just to name a few. This condition never just arises out of the blue, it is always a complication of something else.

Slide 201: emphysema and bronchial obstruction

Your observations

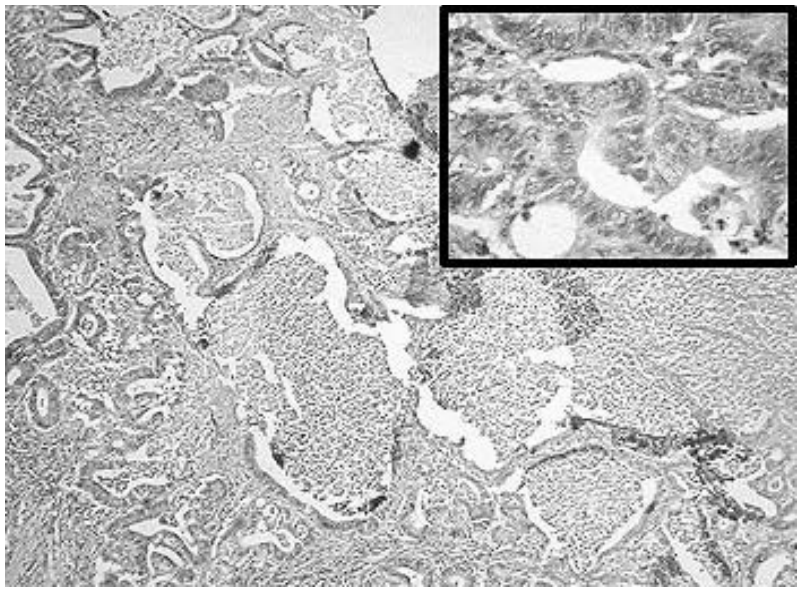


Even at low power, you'll be able to see the enlarged alveolar air sacs and mucus plugging of the airways.



Here we see tremendous enlarged alveolar spaces, filled with pink staining edema fluid. Many of the alveolar lining cells have died and shed into the fluid filling these air spaces. The cells peppered around in the edema are not inflammatory cells. You will, however, see some chronic inflammation in the interstitial tissue and around the vessels and airways.

Slide 202: metastatic cancer from the colon



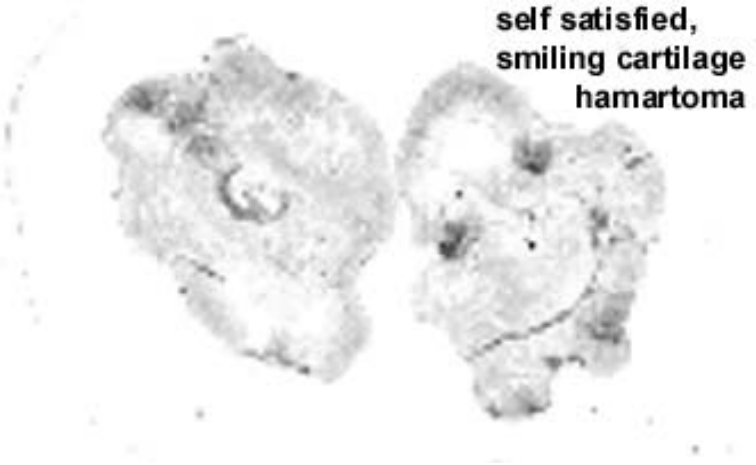
Even though the tumor is pretty obvious, look at all the tissue anyway. It's a good practice to have. This is just one of many metastatic nodules this patient had.

Although we did know the primary in this case, colon cancer would have been high on the list had we not. There is the classic "gland-within-gland" pattern, and then the fact that there are multiple nodules in both lungs didn't hurt. You'll see extensive areas of necrosis and inflammation. The inflammation is in part a response to the necrotic tumor, but areas of pneumonia are also present. The tumor nodules would obviously lead to small airway compression as they expanded. This secondary form of airway obstruction will give rise to pneumonia up-stream (behind) of the point of obstruction, irrespective of the nature of the obstructing process.

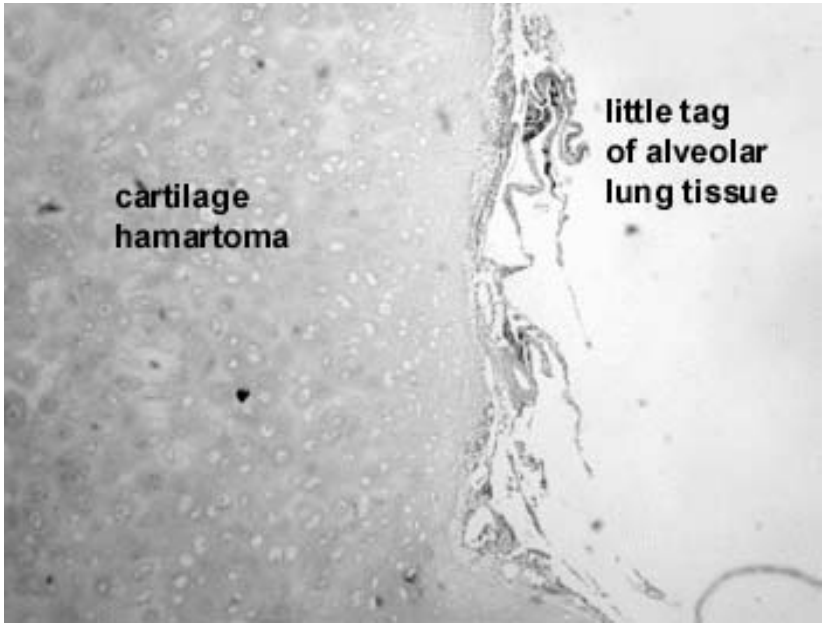
Your observations

Slide 203: cartilaginous hamartoma

Your observations

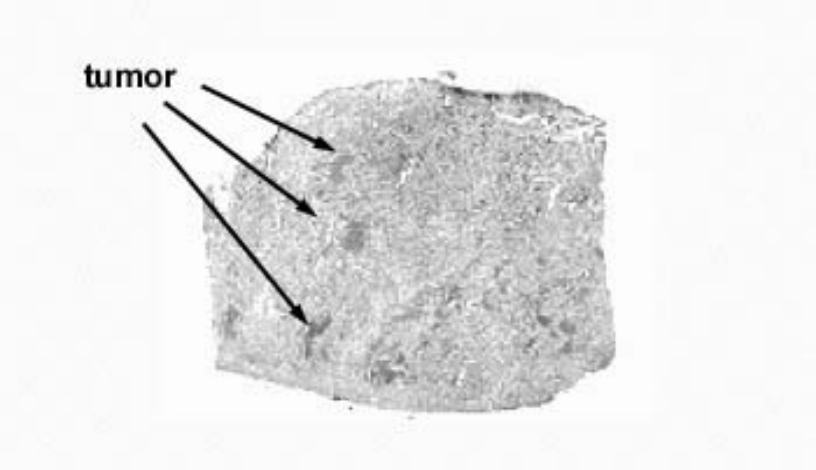


This is a little benign “rest” of cartilage tissue, probably dating from the development of the lung. It’s stable with no intention of metastasizing. The problem is that it appears as a mass on lung X-Ray, and needs to be evaluated, because the X-Ray can’t tell you its real nature. It could, after all, be a malignancy. You don’t know until you’ve biopsied it or removed it entirely.



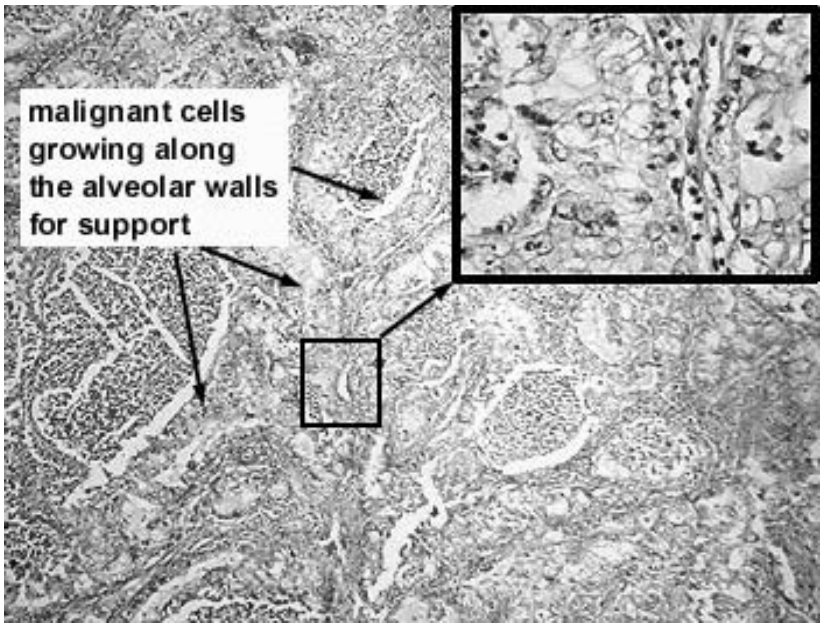
Not all that inspiring. Benign cartilage in the lung. You may have to scoot around the perimeter of the nodule to see any lung tissue; it’s sparse.

Slide 211: alveolar cell adenocarcinoma



In truth, the tumor is pretty much spread throughout this piece of lung. Here you can see concentrated areas.

Your observations



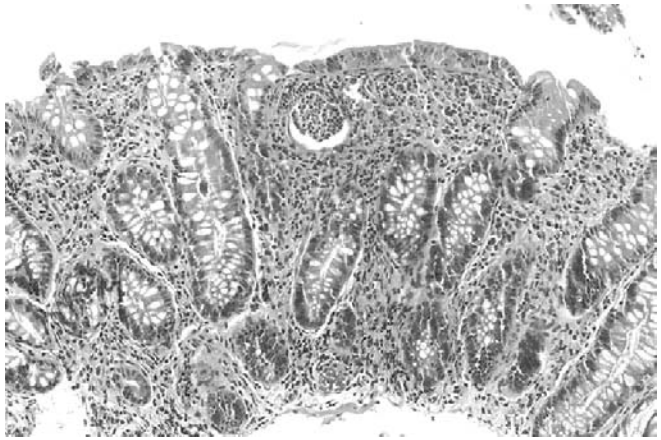
Remember, this is a primary form of lung cancer. It grows using existing structures and alveolar walls as a frame work for support. You will see extensive inflammation as a consequence of the tumor cell death.

General and Systemic Histopathology
C601 and C602

Section 7 *Gastrointestinal Disease*

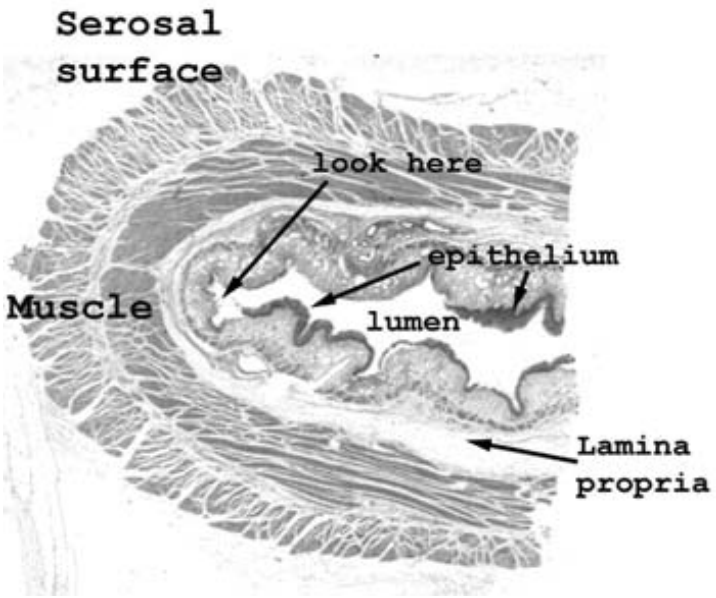
The clinical manifestations of gastrointestinal diseases are not always as straight forward as one might think. Although abdominal pain and diarrhea are generally pretty good indications of bowel disorders, lethargy and easy fatigue may not immediately come to mind. In this unit we will look at a number of conditions that may have some rather peculiar and unexpected presentations. Use the following examples as a starting point to refine and expand your knowledge. In the past it has been very helpful for students to review their observations in small groups and quiz one another on the histology and clinical presentations of these conditions. Here are a few things to concentrate on.

Among the common and important conditions we will study are ulcer disease, enteric infections, neoplastic disease, vascular disorders, even primary endocrine abnormalities of the bowel. A very important category of pathology are the diseases grouped under the heading of "inflammatory bowel disease." Here are two curious abnormalities that can be quite devastating and even fatal, ulcerative colitis and Crohn’s disease. Even today the etiology for both is not fully understood.

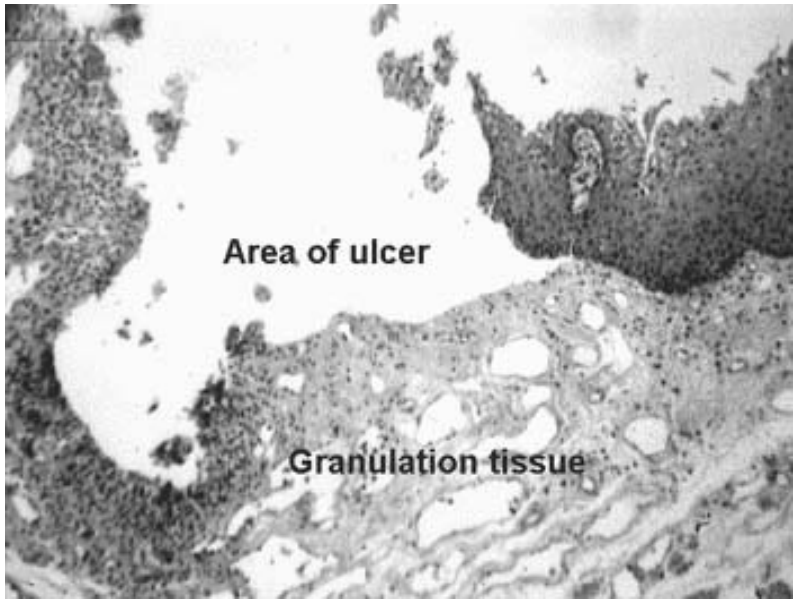


Slide 19: Acute Erosive Esophagitis

Your observations

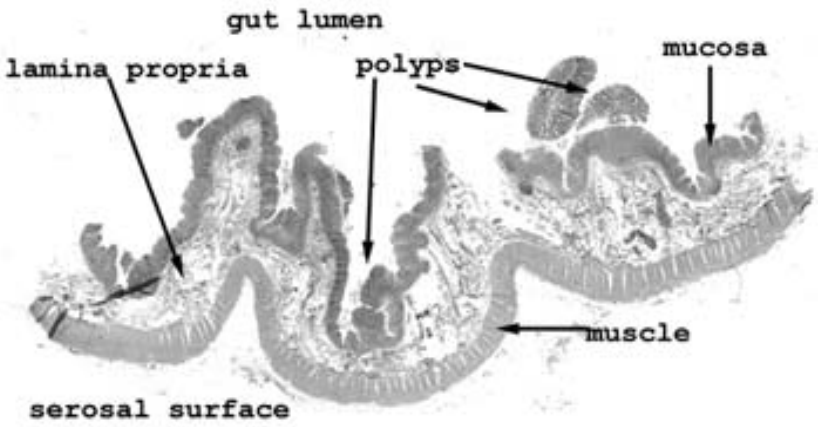


Your slide shows almost a complete cross section of the esophagus. Note there are several areas of mucosal ulceration and some relatively large, thin walled vessels are present in the lamina propria.



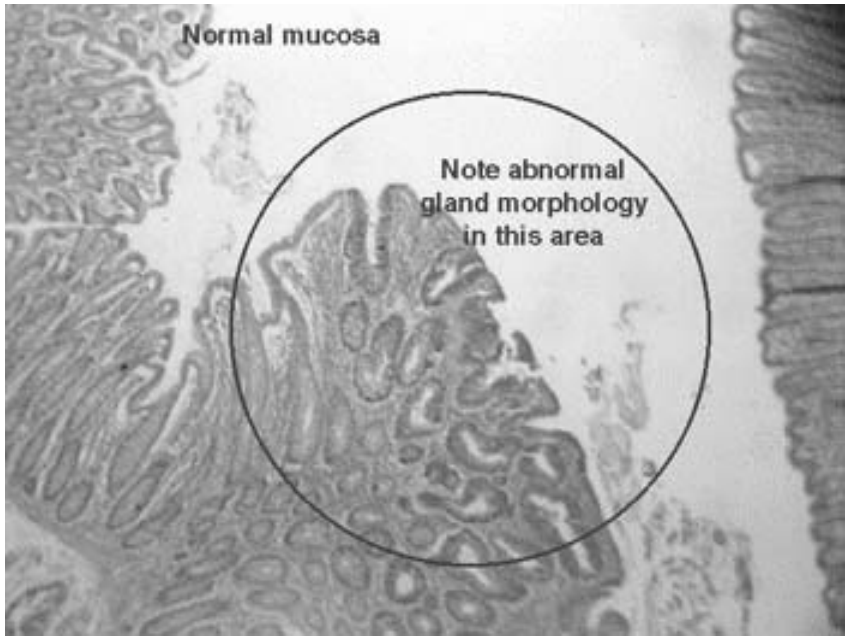
If you simply look at the slide on a white background, you can see the area of erosion quite nicely. Note the areas of healing and repair at the margins of the ulcer. Some acute inflammatory cells are seen in the base of the lesion, and many very dilated vessels are present in this area as well. These large superficial vessels are not part of the healing process, and represent part of another pathologic process in this person. What condition could lead to these dilated vessels? Where would you expect to find others?

Slide 21: Familial polyposis of the colon



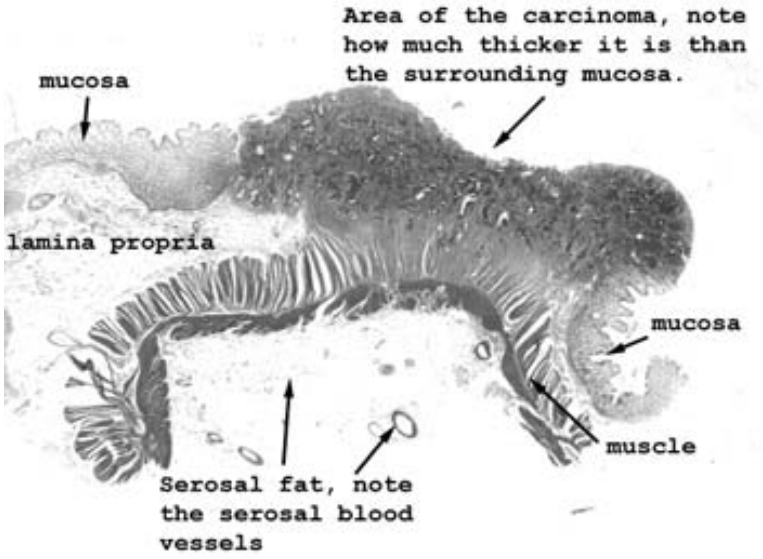
The changes are subtle here. You really must look at the tissue on the slide before going to the microscope. You will see little areas of thickening of the mucosa and that's about it. In some areas there may even be a polypoid formation but the earliest changes are not easy to see.

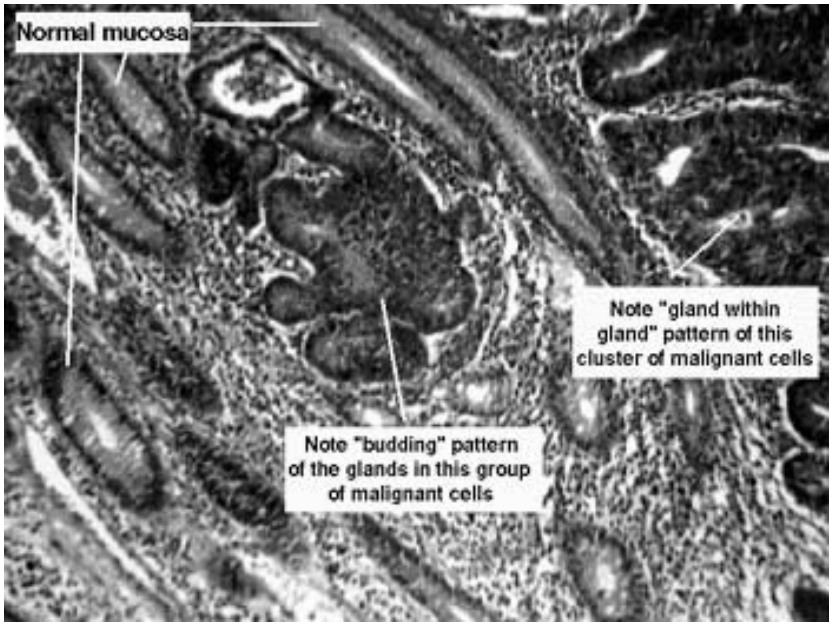
Your observations



This slide shows the subtle changes in the bowel mucosa that can lead to big troubles later. You will need to be on low power to initially identify the mucosal areas of abnormality. Once you go to higher power, note the "branching" margins of the glands of the polyps and the "piling up" of the epithelium. You should have no trouble finding mitotic figures even though these lesions are benign. This congenital condition often leads to cancer of the colon later in life. Cancers of glandular origin are called adenocarcinomas, and frequently have histologic pattern similar to the organ in which they arose. To reemphasize the point, however, what we are looking at here is benign.

Slide 32: Adenocarcinoma of rectum



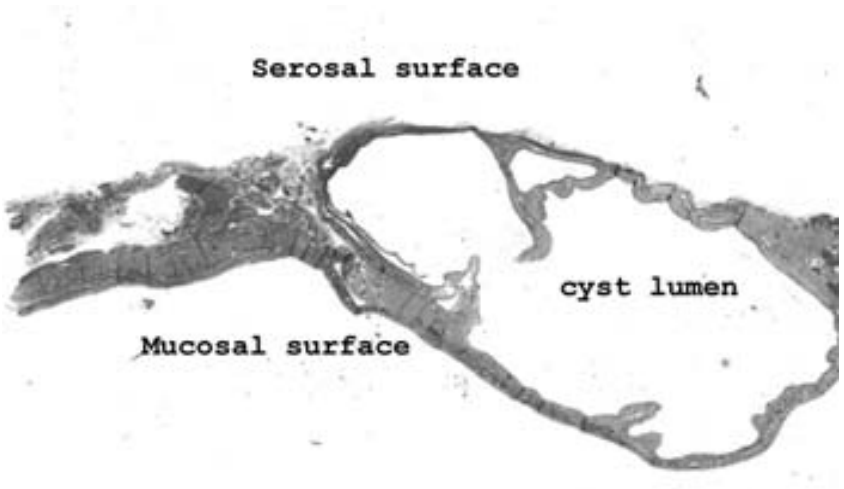


Here the region of the tumor is pretty obvious. Look to see how it is spreading at the lateral and deep margins. If we assume no node or distant metastasis what would the Dukes classification of this lesion be? What of the TMN classification?

This is a fairly high power view of the cancer with normal tissue at the edges. On low power, you should be able to readily spot the different types of mucosa. In the area of the cancer, observe the "branching and arborizing" gland margins as well as the "gland within gland" pattern of the malignant cells. See what we mean by "nuclear atypia" of the epithelial cells. They are hyperchromatic with irregular nuclear staining and "angulated" nuclear margins. Mitoses are every place. Note the spread into the lamina propria of the malignant cells. Can you think of conditions that are associated with an increased incidence of this condition?

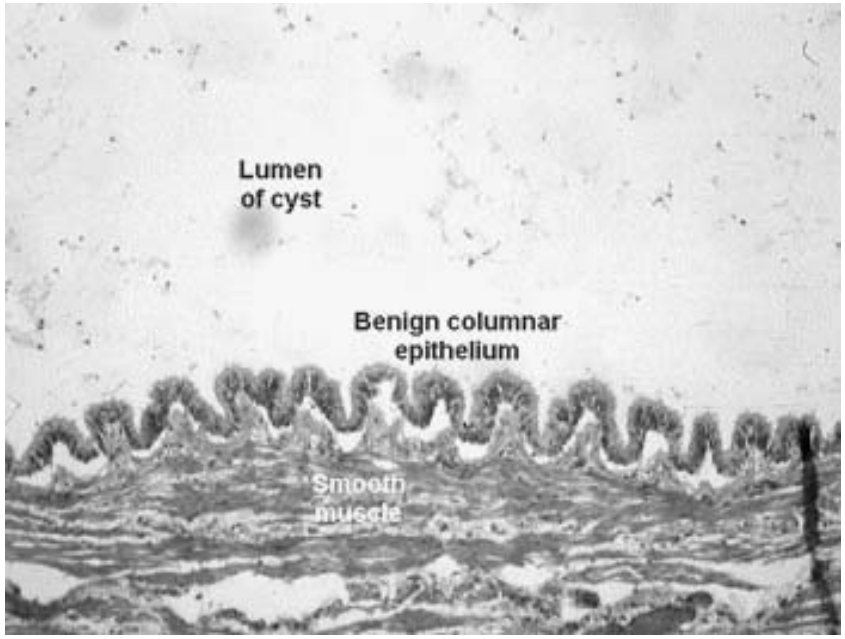
Your observations

Slide 39: Esophagus with mucus cyst



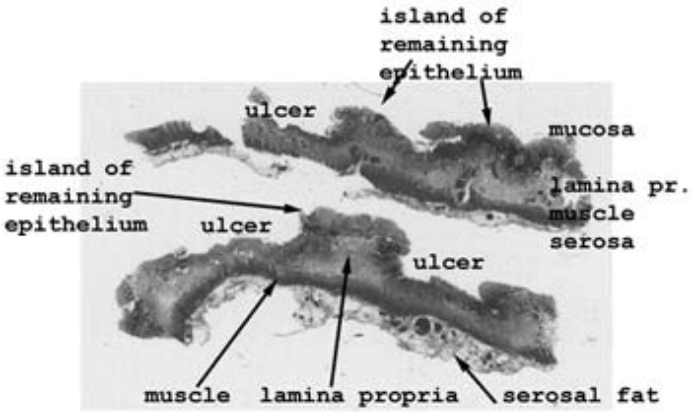
This slide shows a benign mucinous cyst in the wall of the esophagus. First get yourself oriented as to where the mucosal and the serosal surfaces are. Then take note of the cyst lining.

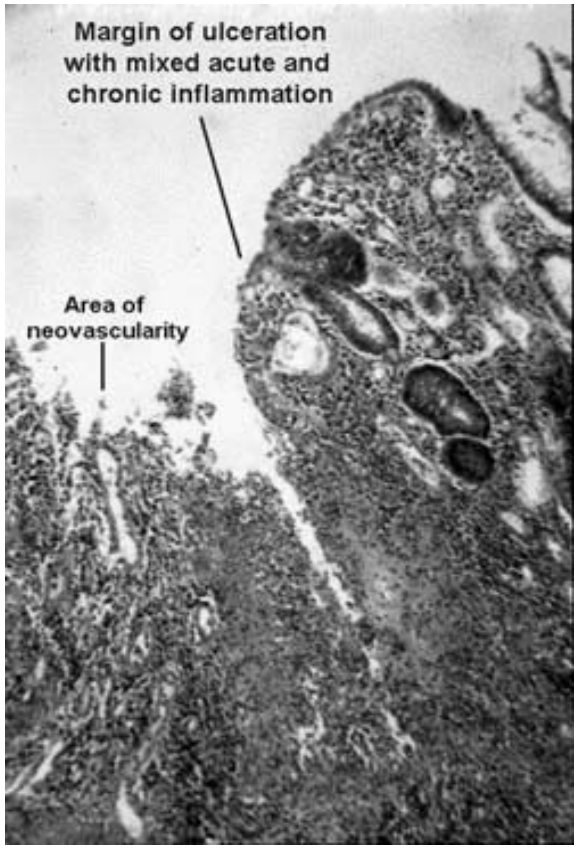
Your observations



The picture in this case shows only the cyst lining and a portion of the muscular wall of the esophagus. Note that the lining of the cyst is columnar and mucous secreting epithelium. That's about it for this slide.

Slide 59: Colon with acute ulcerative colitis



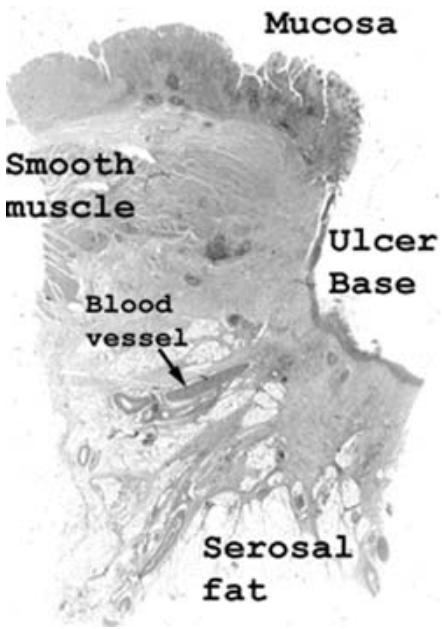


This can be a challenging slide. There are only islands of remaining mucosa, separated by large expanses of ulceration. Look in the base of the ulcers and just to the edge of the residual mucosa for the best examples of granulation tissue.

The picture is from the edge of an ulcer, and shows focal absence of the mucosa. There is a mixed acute and chronic inflammatory infiltrate in the base of the ulcer with lots of granulation tissue. You will see many angioblasts and reactive fibroblasts in these areas of healing. Crypt abscesses are seen in the base of the crypts. This feature may not be very apparent as this case is relatively advanced and these earlier changes are simply overwhelmed by the degree of inflammation.

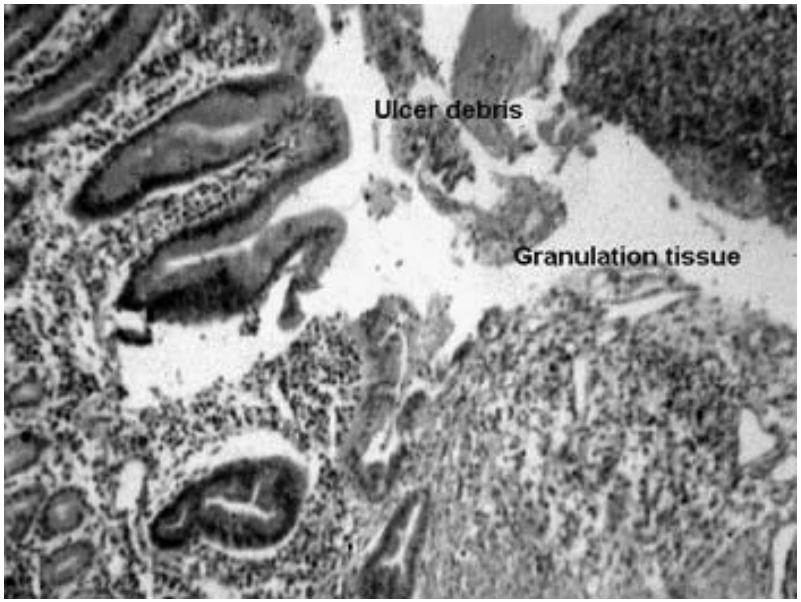
Your observations

Slide 9: Stomach with gastric ulcer



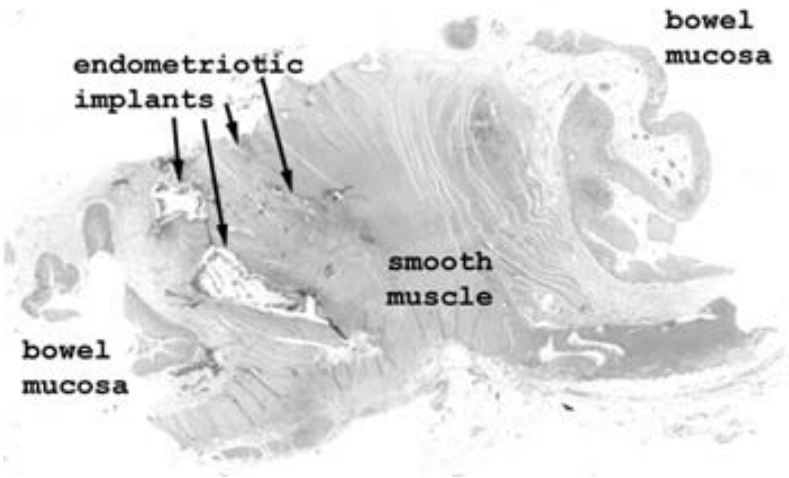
This piece of tissue may not look exactly like the one on your slide, but it's close enough. The photomicrograph below comes from the edge where the ulcer meets the mucosa. Note the bright pink layer of fibrin and digested protein material that lines the ulcer base. The granulation tissue begins just beneath this. See how the ulcer has eroded completely through the muscle and is about to perforate through the serosal fat. What do think is the significance of the large blood vessels seen just to the left of the ulcer base?

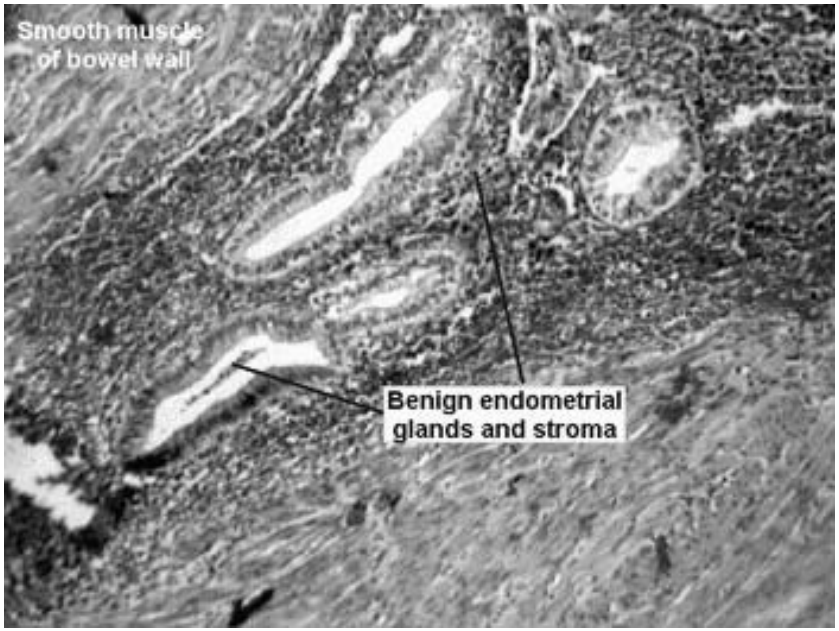
Your observations



Before going to the microscope, hold the slide up to the light or look at it on a white background. You should be able to easily spot the area of the ulcer. Try to get yourself oriented before diving in with the scope. Observe the "granulation tissue" in the ulcer base and be sure you can identify angioblasts and the numerous reactive fibroblasts. There is considerable digested debris on the surface of the ulcer, don't confuse this for the reparative elements of granulation tissue. The digested junk contains epithelial cells, inflammatory elements, bacteria and who knows what all. What's the bacterial agent of such renown in this disease?

Slide 104: Colon with endometriosis



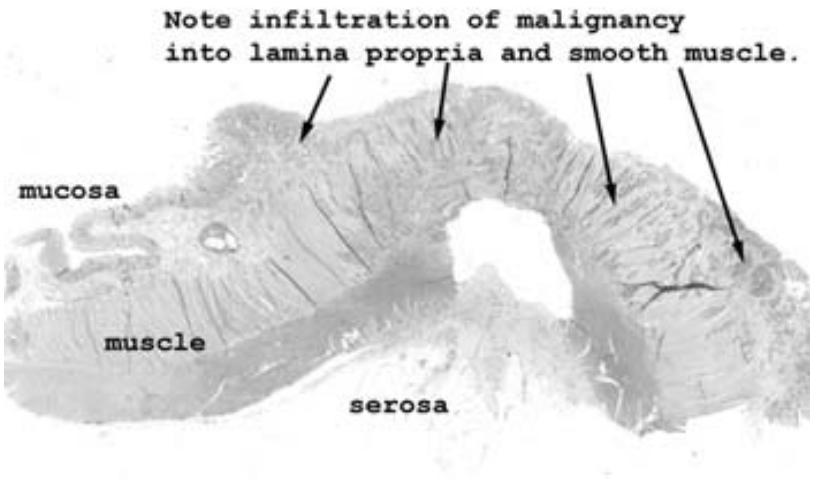


This is a fascinating condition. Little bits of benign endometrium, both glands and stroma, become "seeded" within the peritoneal cavity (and even skin around the umbilicus). These implants grow and respond to the monthly hormonal cycles and can be quite symptomatic. (Would you consider this a metastasis of a benign condition?)

In your slide you will see the implants within the muscle of the wall. Don't be fooled, these foci are benign. If this person were pregnant, or treated with progesterone, these implants would look very different, and could, under this hormonally stimulated condition, be mistakenly called malignant. However, they are still benign. There may be some pigment containing macrophages around the implants. These are iron containing cells, reflecting old areas of hemorrhage, consistent with the monthly cycle these implants go through, just like the rest of the endometrium.

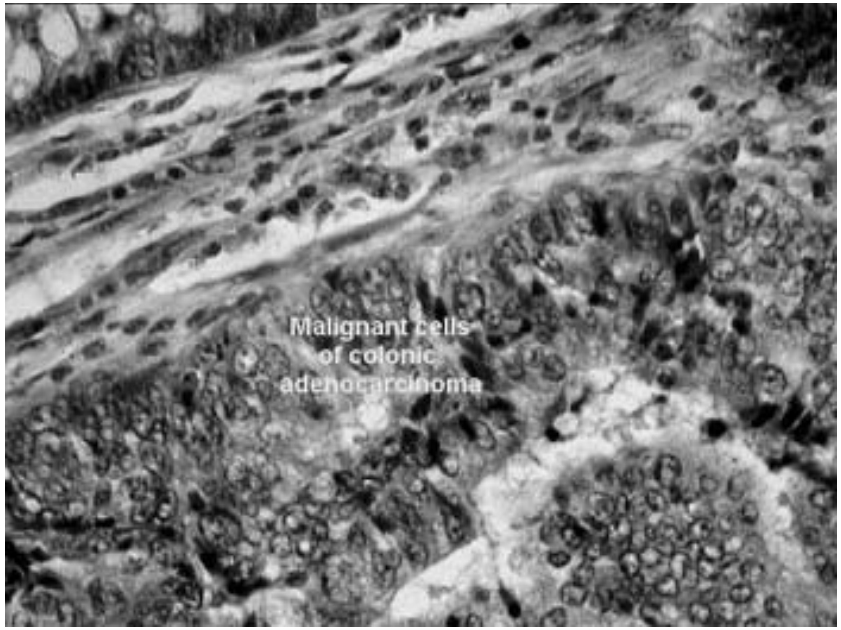
Your observations

Slide 105: Adenocarcinoma of colon



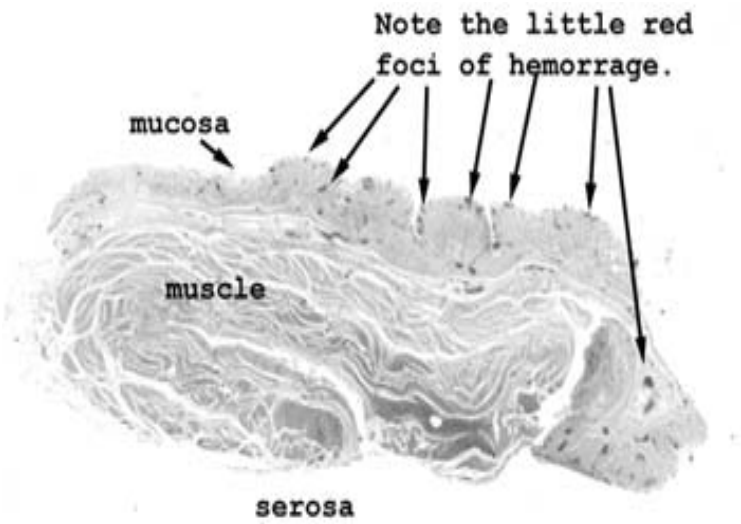
Again, the picture pretty well tells the story here. The malignancy has arisen from the colonic mucosa and spread into the muscular wall. The large clear space in the middle of this tissue is actually an artifact of the sectioning and is not some change brought on by the tumor.

Your observations



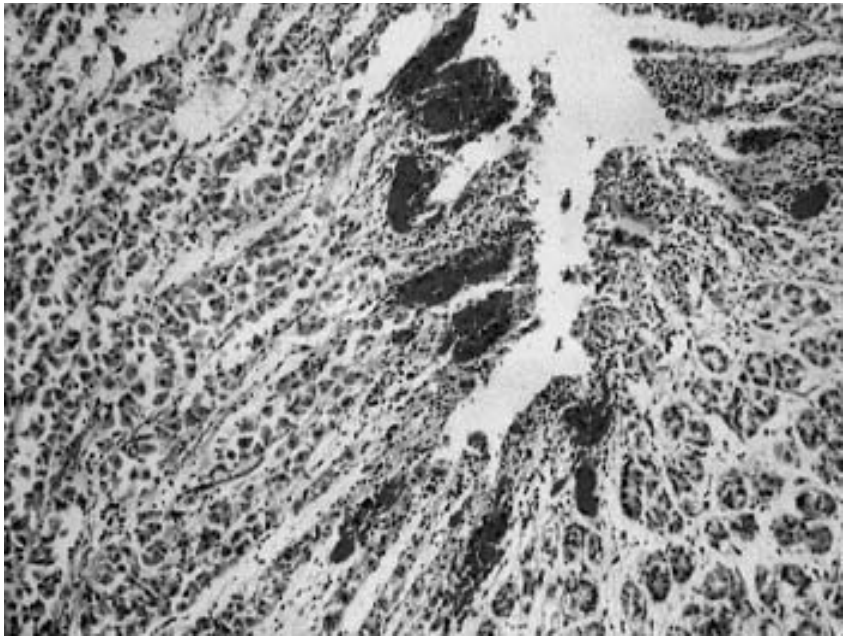
Look at the slide on a white background will help you see the area of malignancy. Microscopically, look at a region where you can see both malignant and benign elements in the same field. The difference in gland and cellular morphology will be much more evident. The malignant glands show "gland within gland" pattern as well as disorganized arborization and branching. The usual cellular features of malignancy are here in abundance: nuclear-cytoplasmic ratio, hyperchromasia, angulated nuclear margins etc.

Slide 128: Stomach with hemorrhagic gastritis



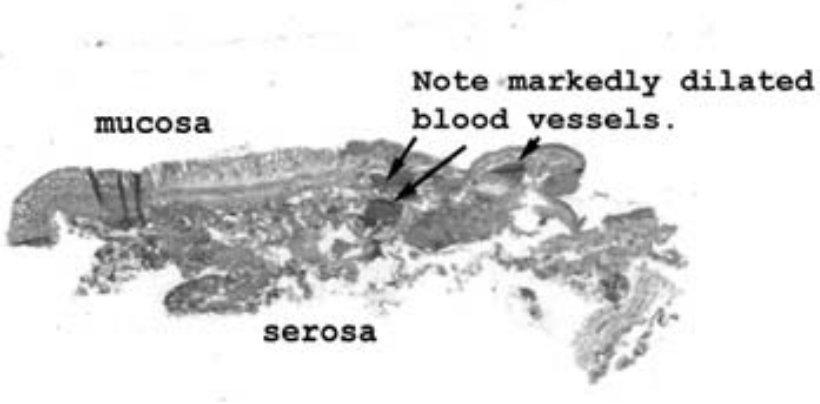
This condition may not look like much right here, but it can be very serious. When you look at the slide on a white background, you will easily spot the little areas of mucosal hemorrhage. Just image how many there must have been over the entire mucosa of this stomach. Yes, there can be significant acute blood loss from these little fellows.

Your observations



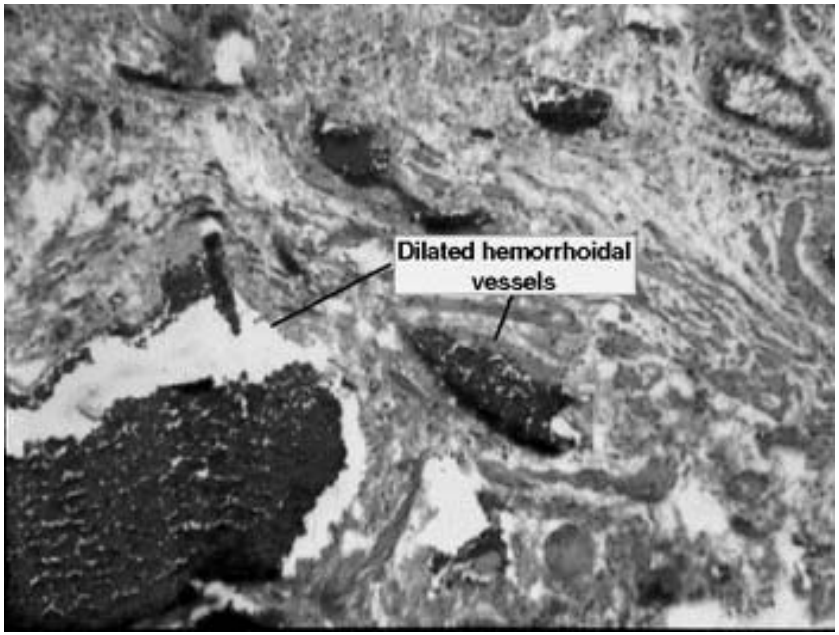
The tissue is not all that well preserved, but that is the way things are in this condition. Note the inflammation in the lamina propria and the areas of hemorrhage in the tips of the mucosal folds. This condition is seen in binge drinking alcoholics, and is also a complication of severe trauma leading to profound physiological stress. It may lead to gastric mucosal erosions, sometimes referred to as "acute or stress ulcers."

Slide 129: Rectal hemorrhoids



This is obviously a strip from the wall of the rectum. If you look at it on a white background, you should be able to easily spot the dilated hemorrhoidal veins.

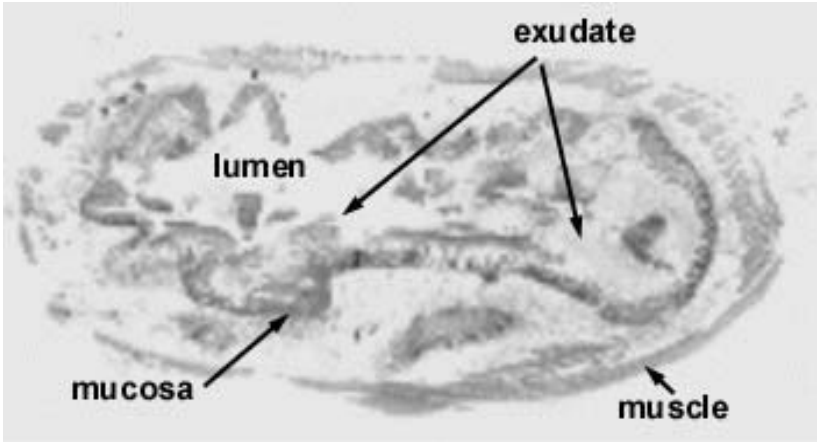
Your observations



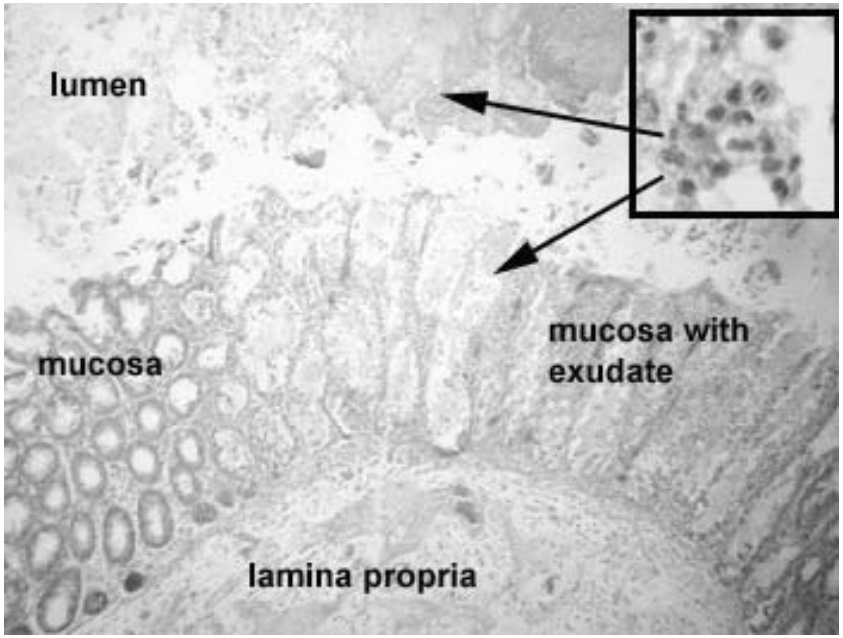
Note the dilated and thin walled vessels in the sub-mucosa. Some are thrombosed, and some may have an inflammatory infiltrate in the wall or the surrounding tissue. What causes this condition? Where else would you expect to find them?

Slide 131: Colon with pseudomembranous colitis

Your observations



This specimen is a complete cross section of colon and the action is taking place on the mucosal surface and the mucus seen in the lumen (the detached junk). In this case, the history of the patient is key to making the diagnosis. What history do we mean?

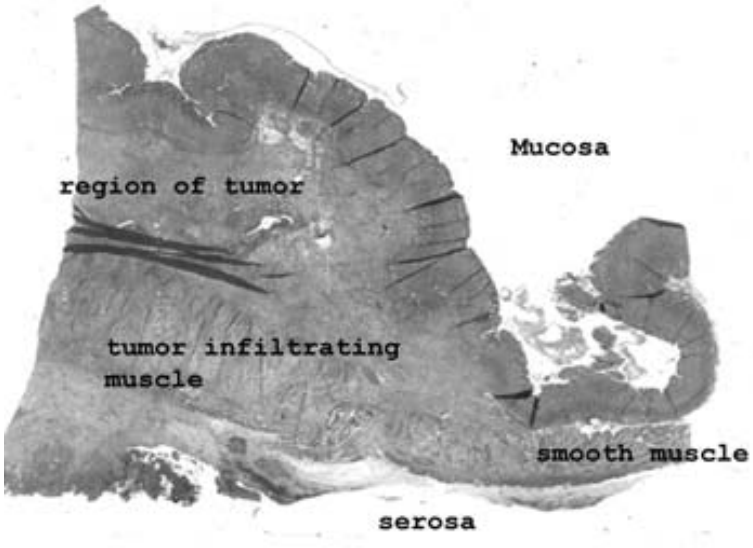


As you may know, this condition is caused by antibiotic usage. The causative organism is a clostridial organism that can sporulate, and return after the antibiotic has disappeared. The bug is actually on the surface of the bowel, and elicits a marked acute inflammatory response. Here you will see an acute inflammatory exudate in some of the crypts and on the surface of the mucosa. You won't be able to see the organisms in all likelihood.

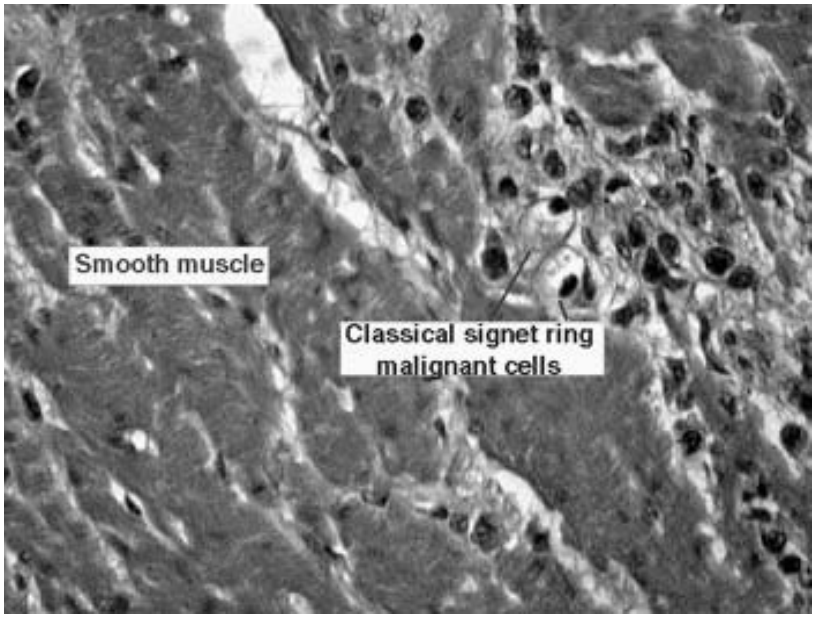
The insert shows the PMNs in the mucus.

Slide 138: Stomach with signet ring cell carcinoma

Your observations

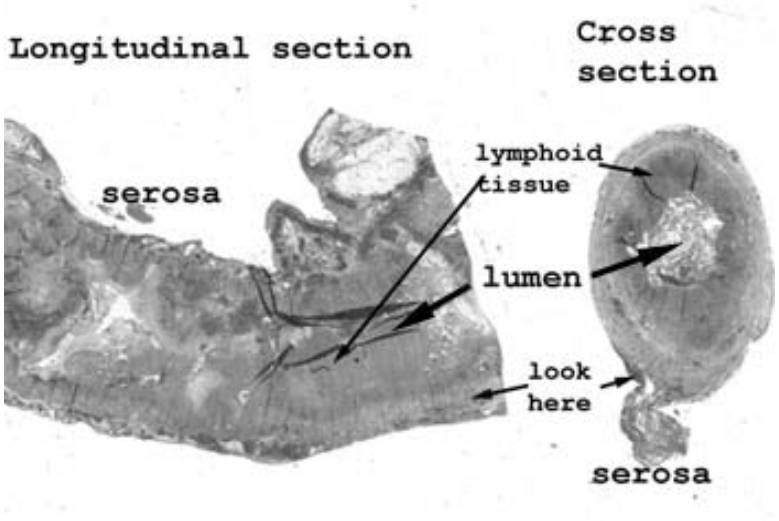


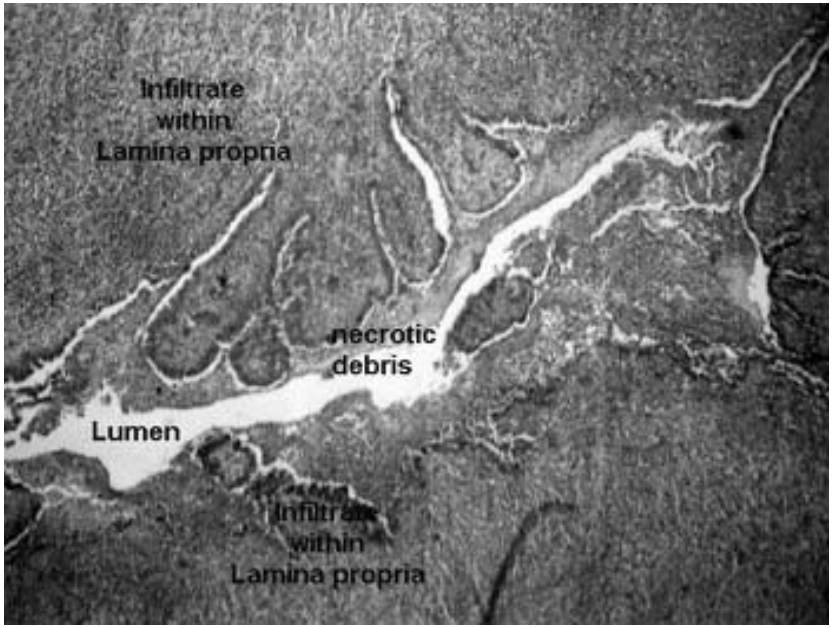
In this picture of the tissue, you can see how greatly expanded the lamina propria and muscular layers are. The type of cancer represented here is rather peculiar. There may not be any evidence on the mucosal surface, yet there will be extensive infiltration of the wall. The cells do not, as a rule, organize themselves into gland-like structures, rather the diagnosis of adenocarcinoma is made by seeing the large intracellular mucin vacuole in each cell.



The changes here are subtle. The tumor is not on the mucosal surface, but down in the muscle and lamina propria. It may look like an inflammatory infiltrate spread around between the bundles of muscle cells. Look for the hallmark features of malignancy in the cytology of the cells. Only a few really diagnostic signet ring cells will be present. These cells will have a large vacuole off-setting the nucleus, thereby giving the "signet" ring appearance.

Slide 139: Acute Appendicitis





Here you have two sections of the appendix. The one on the left is a longitudinal section in which the lumen is not well defined. It contains lots of necrotic debris. The section on the right is a little easier to understand as a hollow organ. Still the lumen is partially obliterated by necrotic debris and inflammatory material.

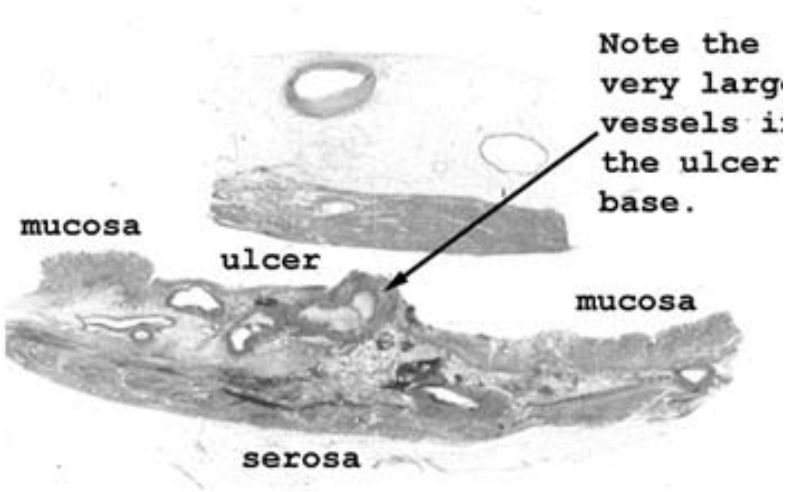
Start reviewing this slide in the lumen and work methodically through to the serosal surface. Pay attention to all the elements and make notes on what you see. Compare your notes to what you expect in the normal or healthy situation.

In this slide, the mucosa of the appendix is largely missing and there is a profound acute inflammatory infiltrate in the lamina propria. There is also a lot of necrotic debris in the lumen of the organ. This is a difficult slide because the acute inflammatory infiltrate is intermixed with the normally occurring lymphoid tissue of the appendix. Remember that in the healthy state you would find many lymphoid aggregates in the lamina propria of the appendix, and throughout the length of the bowel for that matter. You may also see some newly forming granulation tissue on the serosal surface. As far as that goes, your best shot at seeing the constituents of the acute infiltrate will be in the serosal surface itself. In some of the slides there is marked lymphoid hyperplasia in the lamina propria (a finding you might expect), so it is probably best to steer away from the lumen and the centrally located portions of this tissue for right now.

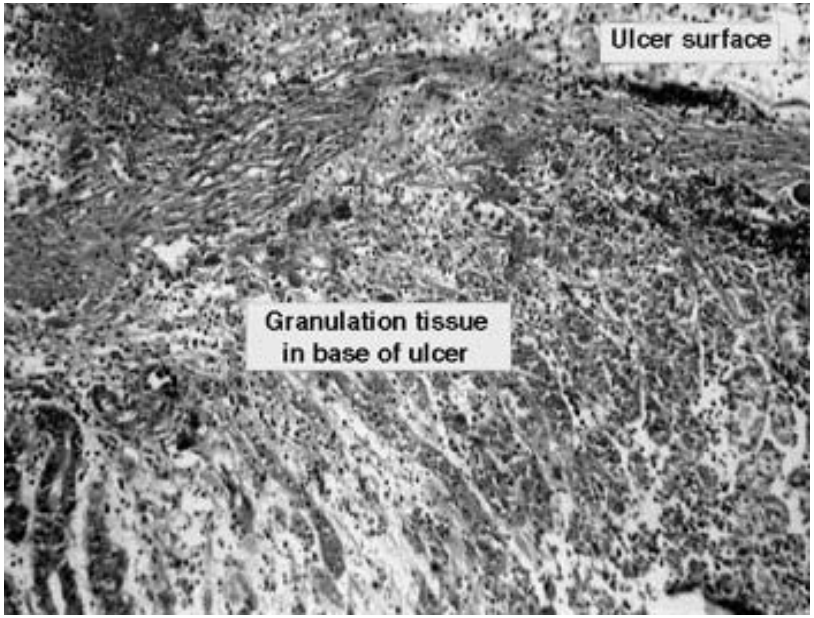
Your observations

Slide 141: Gastric ulcer

Your observations



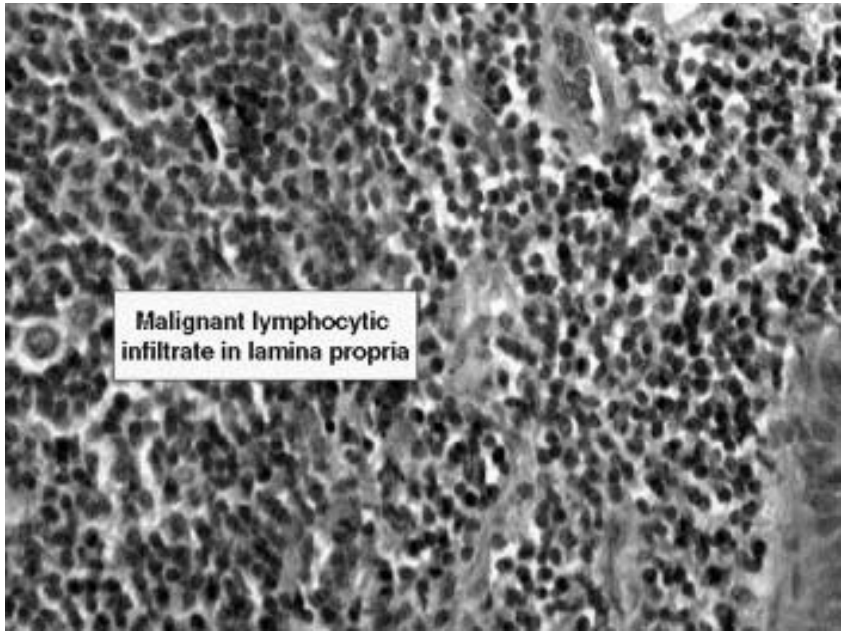
In this picture the ulcer is pretty evident. Note the large vessel in the base of the ulcer. What do think was the cause of death for this guy?



This slide is similar to your slide 9. Here you see the granulation tissue in the base of the ulcer. You should see an acute inflammatory infiltrate. In some of the student sections, it is possible the major vessel is seen to actually open into the stomach lumen.

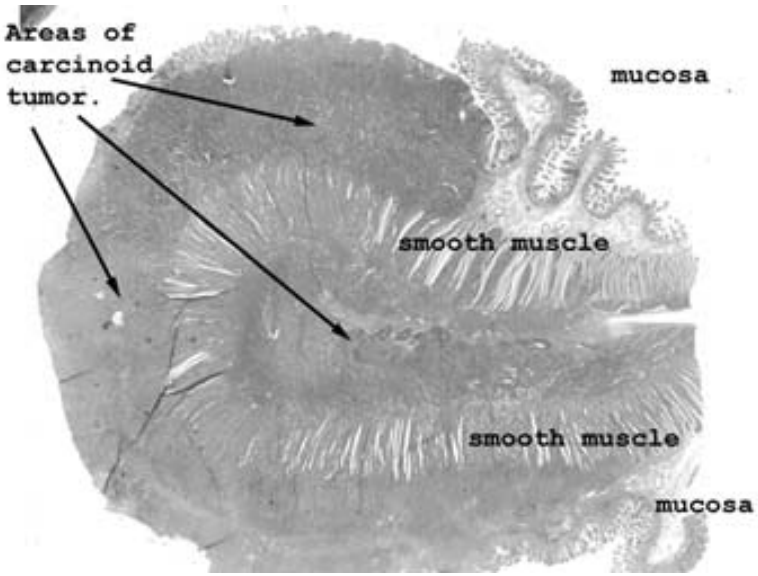
Slide 142: Malignant lymphoma of small bowel ***Your observations***

Sorry, no low power of this slide.

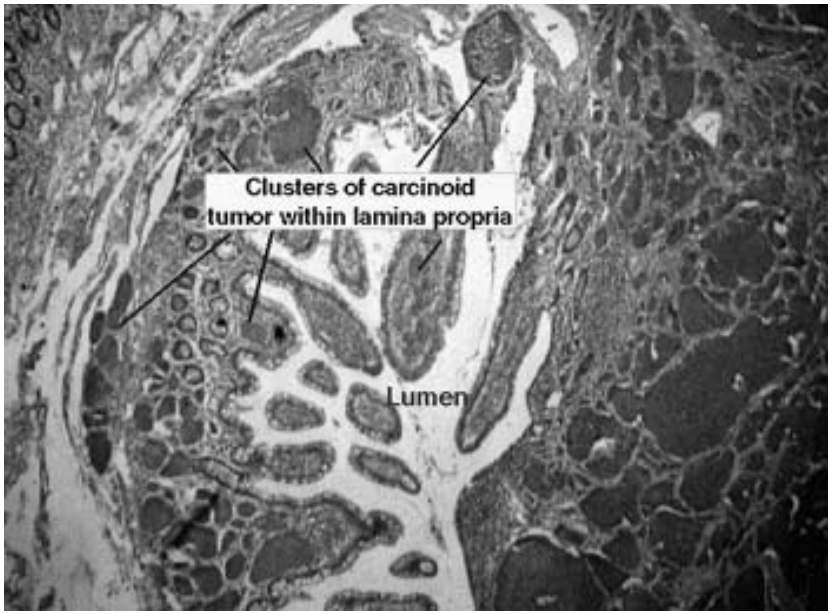


Grossly the tissue of a malignant lymphoma looks like raw fish. Think about that next time you are chowing down on a plate of sushi. Microscopically, this slide just looks like the tissue has been run over by lymphocytes. There will not likely be any follicular arrangement you can see in the lymphocytic infiltrate, and the terms diffuse and follicular are applied to lymphomas observed only in lymph nodes themselves. See if you can find the classical nuclear features of malignancy, they should be easy to discern.

Slide 143: Carcinoid tumor of small bowel



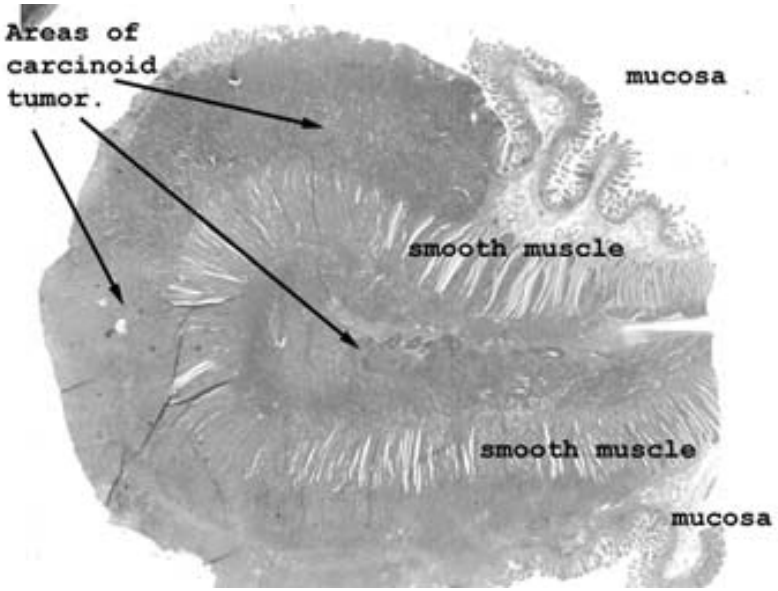
The section of bowel is actually bent or doubled back on itself, effectively creating a "kink." This is a real common configuration of the gross specimen with this condition because of the marked degree of fibrosis that comes with this lesion. Sometimes the local fibrotic reaction around the tumor will actually lead to bowel obstruction just from the compression. Anyway, here you can see the tremendous degree of infiltration of the lamina propria, muscle and even serosal surface by this tumor.



Note the clusters of regular and monotonous looking small ("fried egg like") cells that make up this tumor. There may be marked fibrosis at the site of the lesion. This scarring develops as a result of the hormonal products elaborated by this tumor, serotonin, bradykinin and so forth. Be sure you know what is meant by the term "carcinoid syndrome" and the special circumstances in which it will appear. And no it's not just because there's a carcinoid tumor in the ileum. What urinary test is helpful in diagnosing this condition?

Your observations

Slide 143: Carcinoid tumor of small bowel



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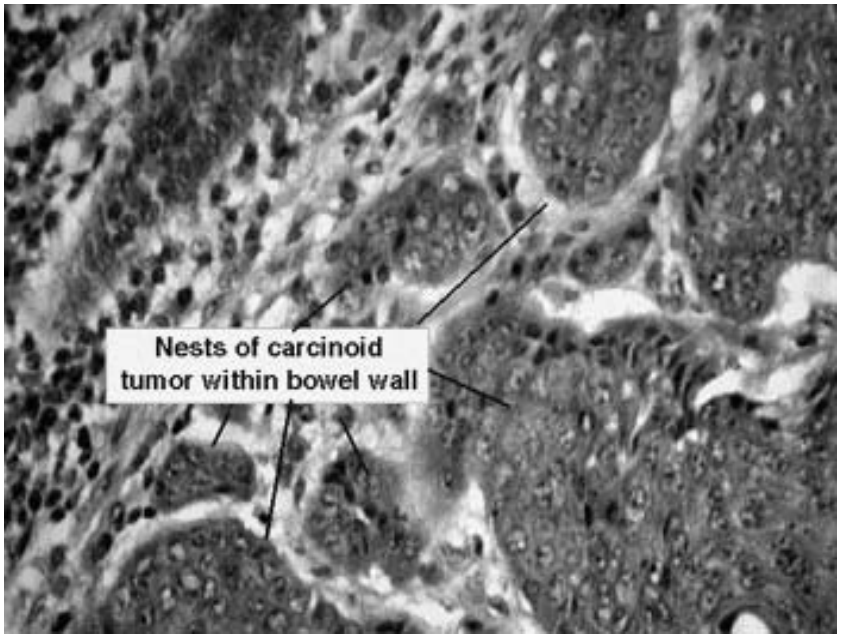
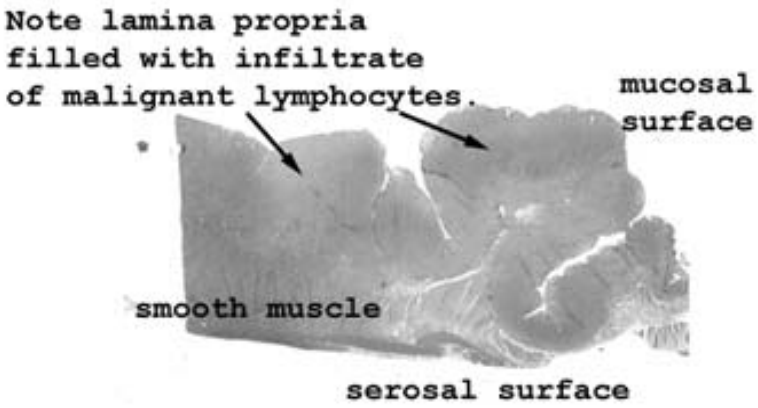
Your observations

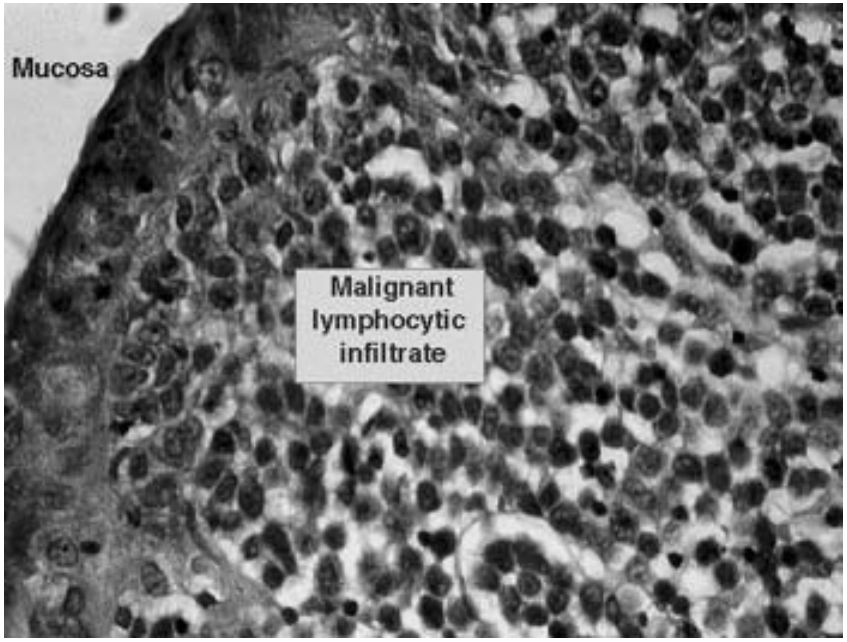


Note the clusters of regular and monotonous looking small ("fried egg like") cells that make up this tumor. There may be marked fibrosis at the site of the lesion. This scarring develops as a result of the hormonal products elaborated by this tumor, serotonin, bradykinin and so forth. Be sure you know what is meant by the term "carcinoid syndrome" and the special circumstances in which it will appear. And no it's not just because there's a carcinoid tumor in the ileum. What urinary test is helpful in diagnosing this condition?

Slide 167: Intestinal lymphoma



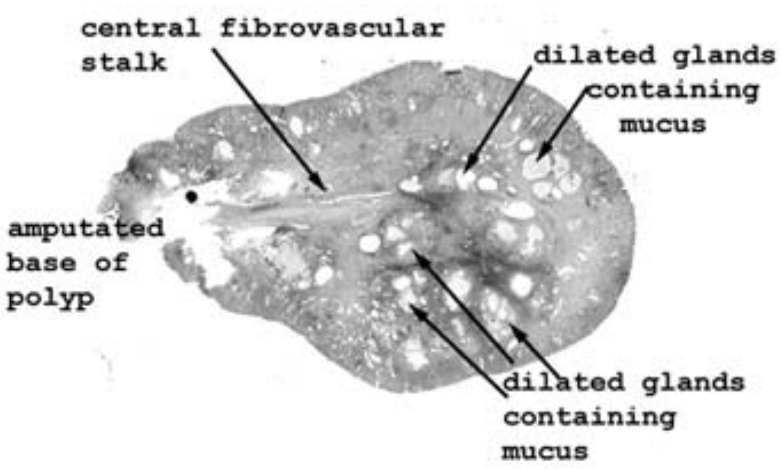
Again, look how obvious the lesion appears in this picture. You can easily see the lymphoid infiltrate and muscular wall. It may be that your slide doesn't include any "normal" bowel. If that's the case, I'm sorry, look at one of the two ends of the section and I think you'll see something approximating normality.



This is the second such example of this type of tumor in your set. The features are essentially the same as in slide 142. See which is the better example in your set and spend time with that one. You will see the malignant lymphoid infiltrate in the submucosa and possibly extending through the muscular wall. Note the monomorphic nature of the malignant lymphocytes. The distinction of nodular and diffuse does not apply here; these terms only have reference in lymph nodes themselves.

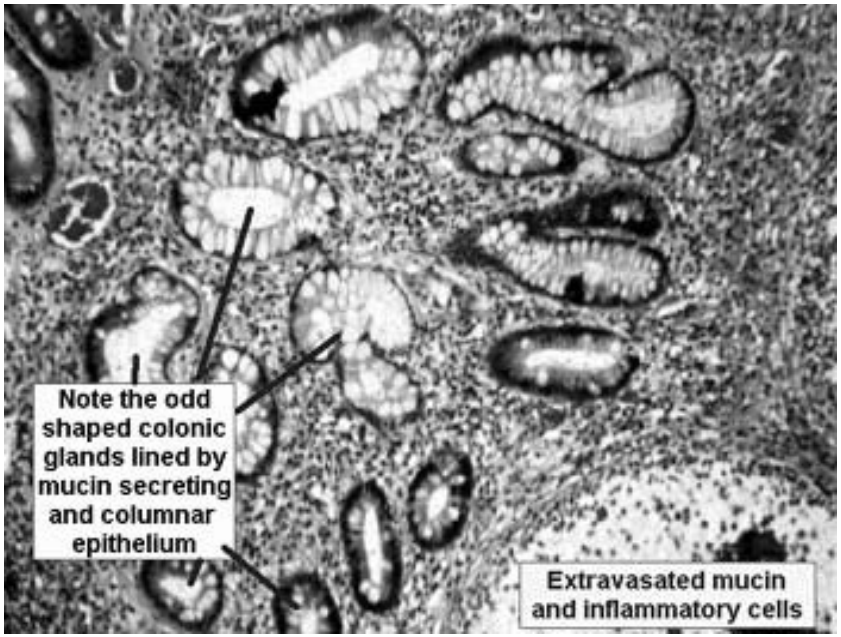
Your observations

Slide 183: Inflammatory polyp of colon



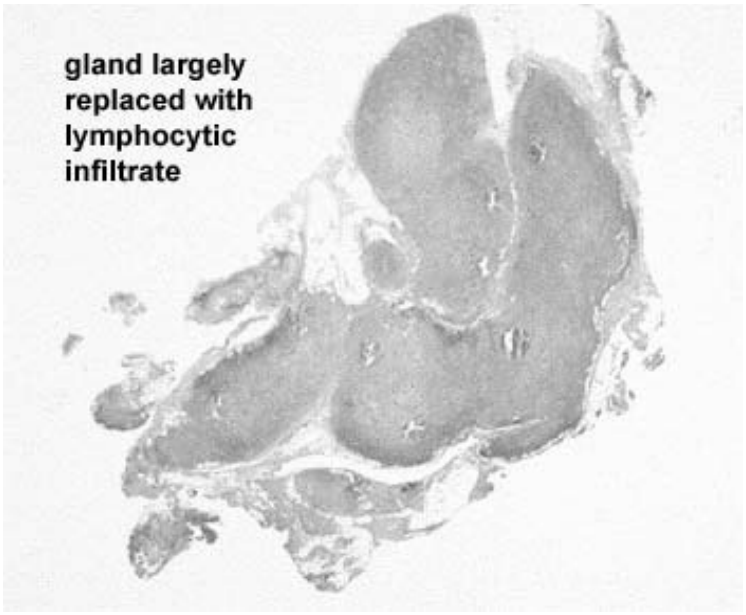
Hey, this chunk of tissue really looks like a polyp doesn't it. Here you can easily see the central fibrovascular stalk and where the polyp was amputated at its base. Note the many dilated colonic glands containing mucin. That's one of the hallmark features of this lesion.

Your observations



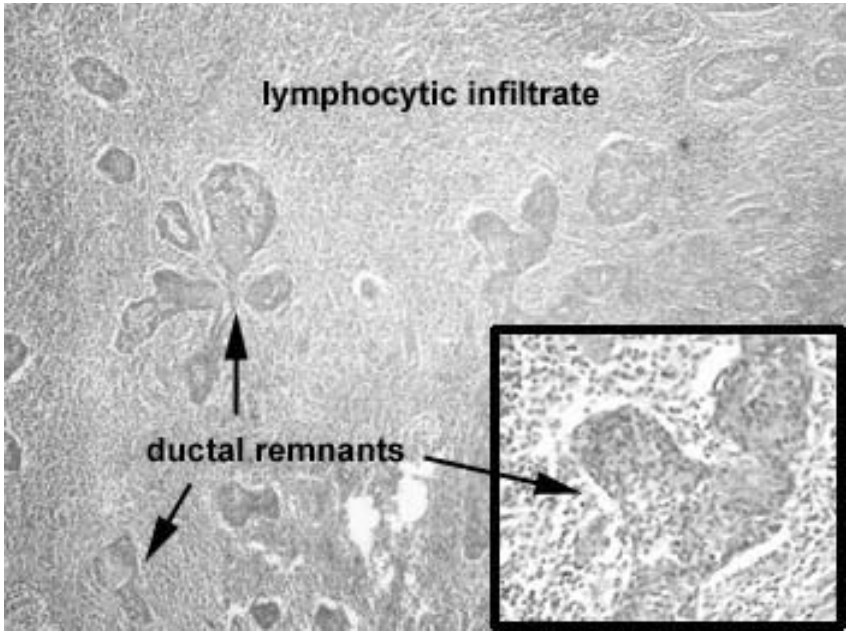
This polyp is purely inflammatory in nature, and has no malignant potential. It is seen in the elderly and children, and is probably related to stool consistency. You will see some dilated and possibly ruptured colonic glands with extravasation of the mucin into the surrounding lamina propria. There will be many acute inflammatory cells as well.

Slide 199: parotid with Sjogren's syndrome



In this case it's going to be difficult to convince yourself this was ever a salivary gland. The gland has been almost totally replaced with a lymphoid infiltrate. You will see many islands of what will appear to be glandular tissue, but it's really the remnants of the parotid duct work.

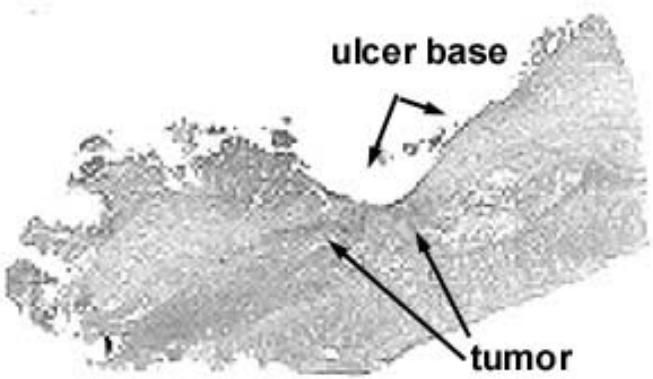
Your observations



This gland is completely overrun by reactive, medium sized lymphocytes. The strands and clusters of pink, squamousy looking cells are actually what's left of the parotid ducts.

What kind of ocular finding might be present in this person?

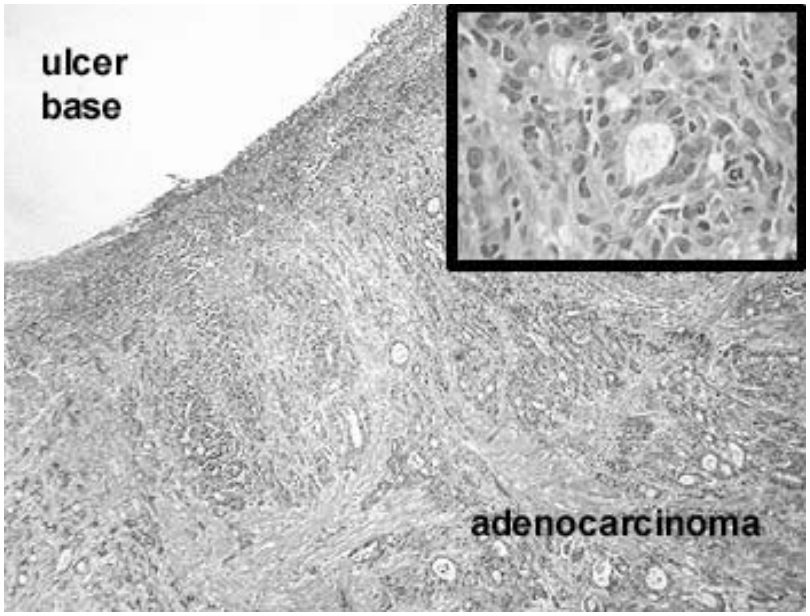
Slide 207: gastric ulcer with cancer



The base of the ulcer is easy to spot in this section. You will see all the expected inflammatory details of a gastric ulcer, but in this case there is an infiltrative adenocarcinoma extending into the muscle. This is an example of a malignancy of the stomach that ulcerated. Because there was a malignancy in the mucosa, the mucosa was compromised, allowing the digestive forces to create the ulcer.

Ulcers that become malignant are exceedingly rare, and some believe it never happens at all.

Your observations

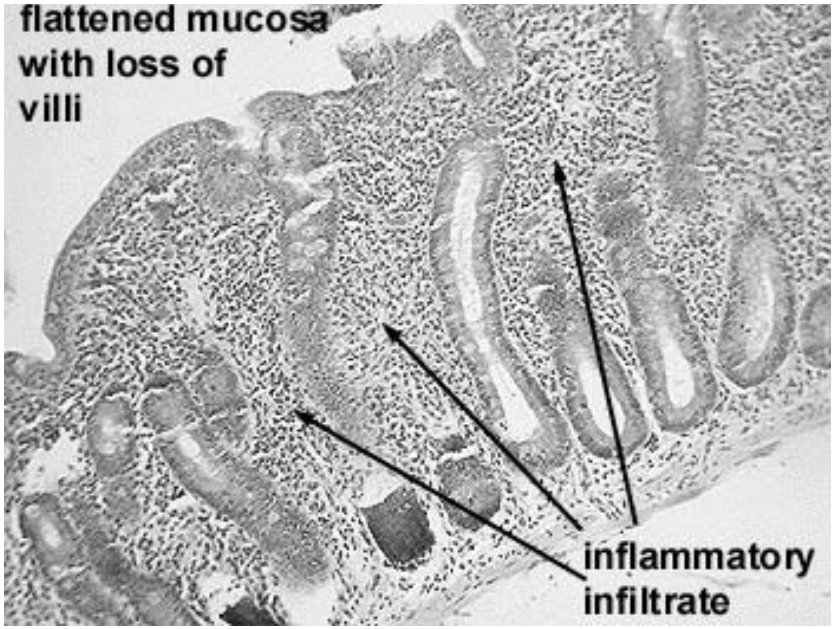


Here we see the typical gland-within-gland pattern that is so distinctive of adenocarcinomas. There is extensive growth of the neoplasm into the muscular wall of the stomach.

Slide 212: small intestine with sprue

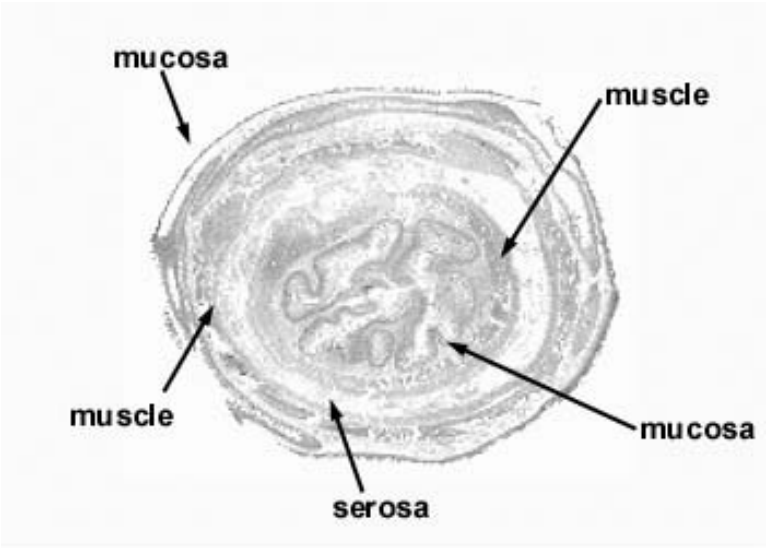
Your observations

No question about it, if you blink, you'll miss this little guy. This is a little endoscopic biopsy from someone who was being worked up for malabsorption.



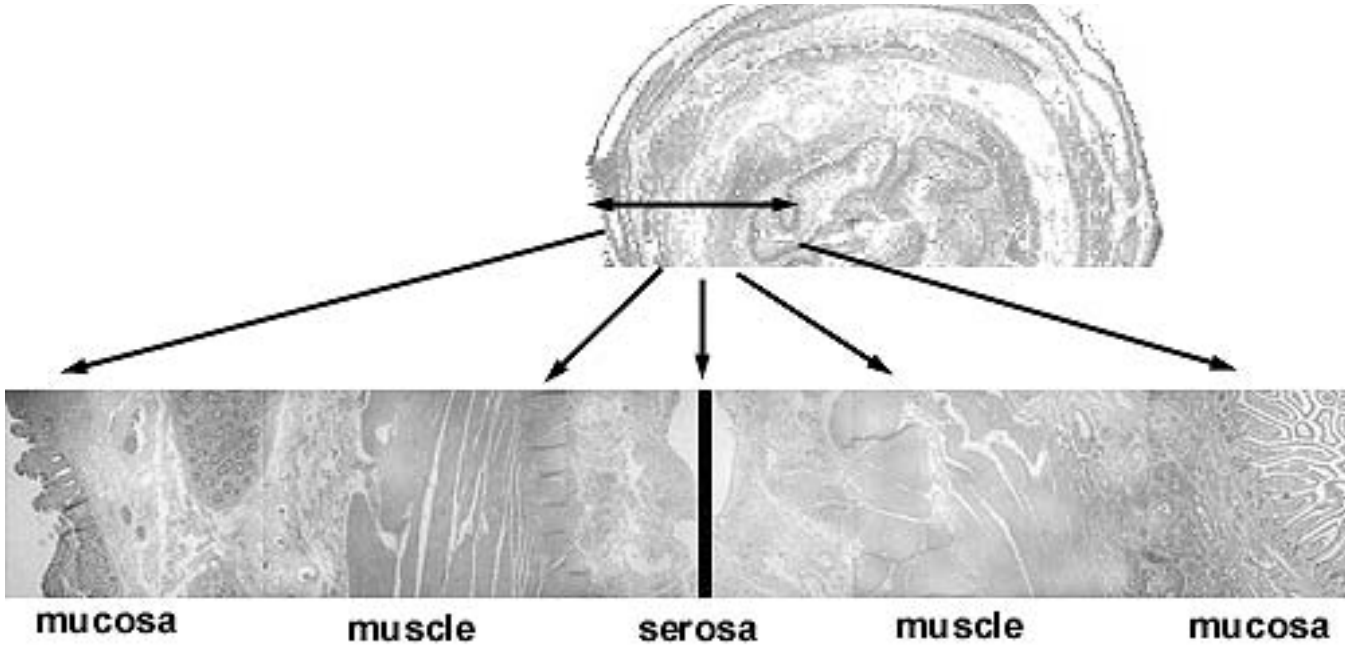
The mucosal atrophy in this section is pretty profound. You will see no villial folds, and overall the mucosa is just a shadow of what it should be. There is considerable inflammation in the lamina propria, and not lymphoid aggregates as you would expect. Instead, it's throughout, and is part of the destructive process. See how many eosinophils you can find. Remember, this is a condition of gluten sensitivity, but once the bowel gets to this stage, there is sparingly little absorption going on. The bacteria of the gut love it though.

Slide 216: small bowel, intussusception



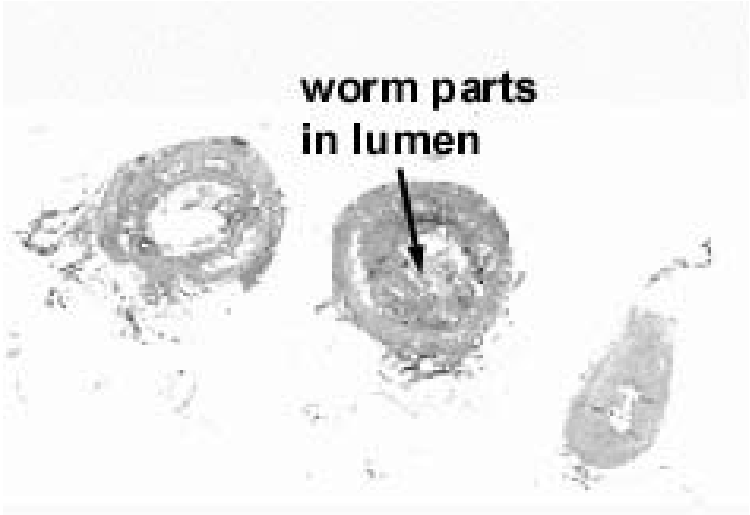
This is a section of bowel that has been sleeved inside of another portion of bowel. The peristaltic action has picked up one piece of bowel and pulled inside the portion just downstream. Kind of like getting coat sleeves turned inside out several times over. It's very painful and if not reduced, will lead to vascular compromise and infarction of the segment of bowel tucked inside.

Your observations



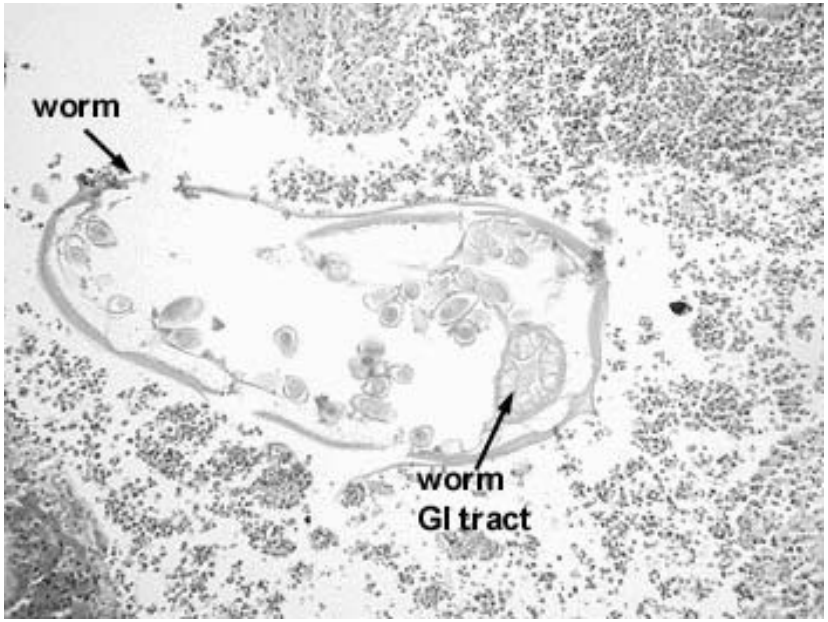
Slide 222: appendix with pin worms

Your observations



This is a section from Bloomington Hospital, not some third world country. We've got worms here too.

Look in the stool in the lumen of the appendix and you'll see the worm (perhaps more than one) in section.



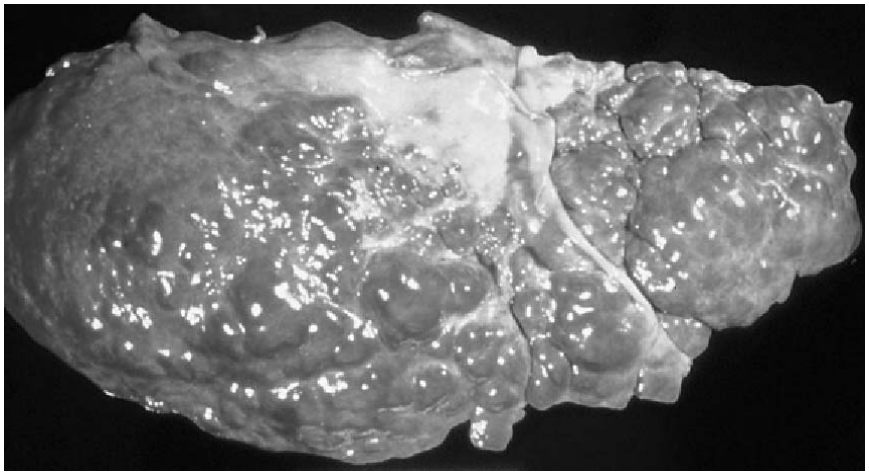
Sure, these can cause obstruction of the lumen, thereby producing an acute appendicitis. Most times they're incidental (to say nothing of surprising) findings.

General and Systemic Histopathology
C601 and C602

Section 8 *Liver and Gallbladder*

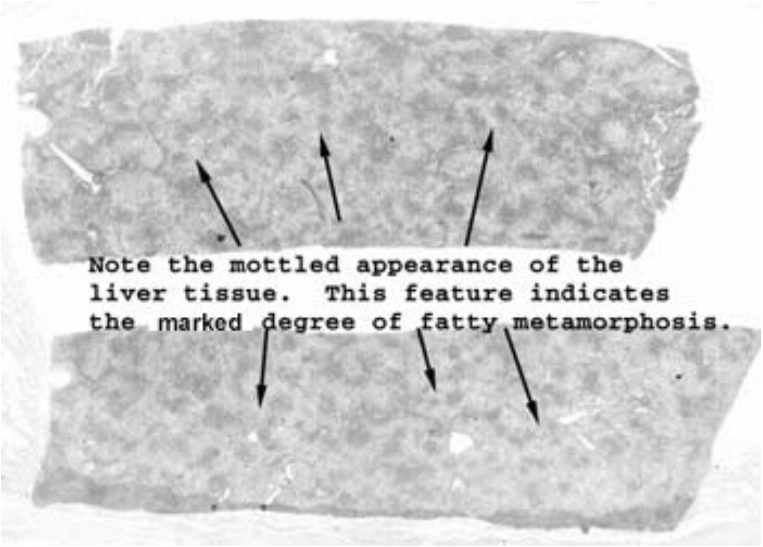
As we will see in this unit, the liver is subject to many types of injury. Additionally, many systemic diseases have a liver component and sometimes it's hard to know what might have started a particular problem. We will be studying examples of infectious, vascular, nutritional, obstructive, neoplastic and iatrogenic injury of the liver. It's going to be very important to know the micro architecture of the liver.

The liver is an organ that has a remarkable capacity for regeneration, assuming the underlying reticular (lobular) framework is intact Unfortunately, in the case of chronic and ongoing injury, complicated by loss of the basic reticular architecture, the drive to repair substantially misses the mark. In this connection, we are going to look at a number of examples and causes of cirrhosis and it's complications. Additionally, the study of hepatitis is going to be very important, but don't make the mistake of thinking that all cases of hepatitis are viral in nature, or for that matter, have a microbiological etiology. Many medications cause liver cell injury that can lead to overt hepatitis. And, as I am sure everyone knows, ethanol has rather marked liver toxic properties. One of the leading causes of acute hepatitis is acute alcohol injury. We will see others as well.

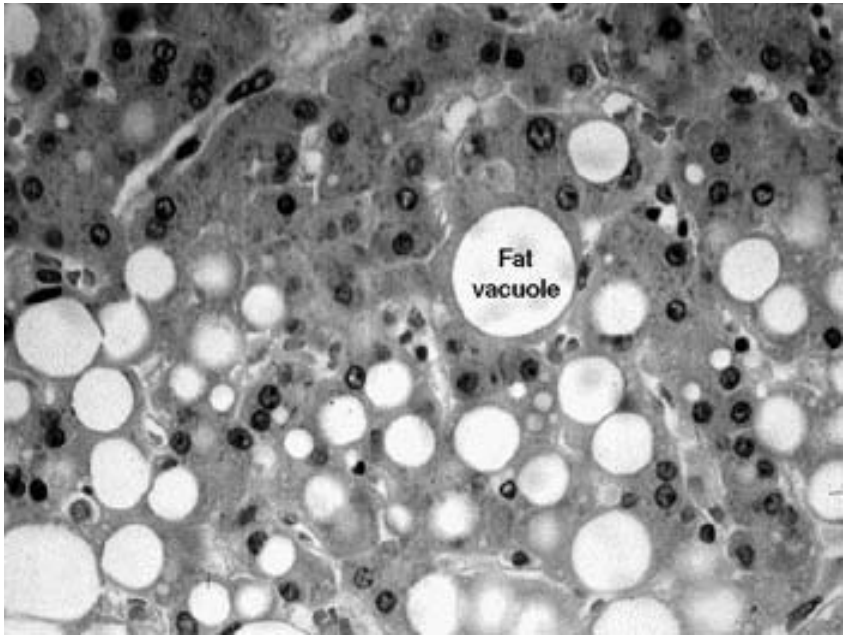


Slide 4: Liver with fatty metamorphosis

Your observations

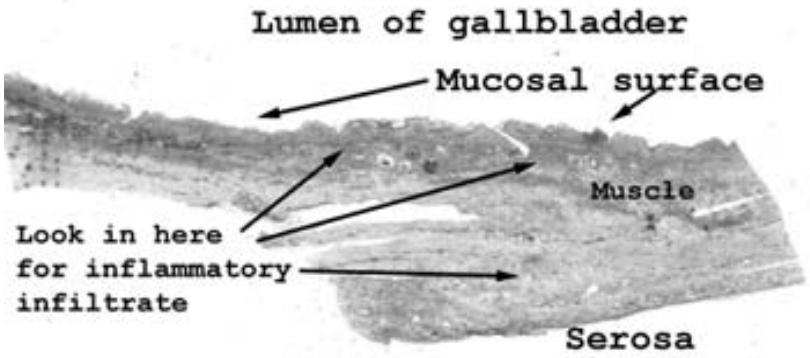


The mottled staining pattern of the tissue is quite evident in this slide. This tells us there is a lot of something that doesn't actually belong here. Basically something of a non-water soluble nature.



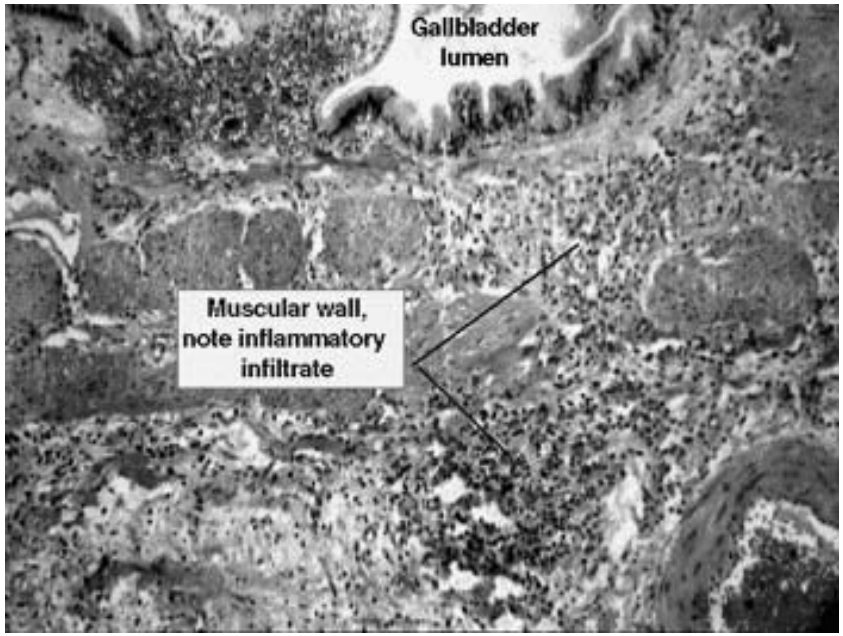
This condition goes by several names. By some authors it is called fatty metamorphosis and by others fatty change. The former is the most widely used. It is a rather nonspecific alteration, but one we see commonly in biopsies of the liver. The fat vacuoles are within the hepatocytes. There is no "invasion" of the liver with lipocytes. In this slide there is little inflammation and the architecture of the liver is well preserved. The tissue is most likely from a diabetic patient, although the changes are common in alcoholics, those with various nutritional deficiencies and many other metabolic problems.

Slide 27: Gallbladder with acute and chronic inflammation



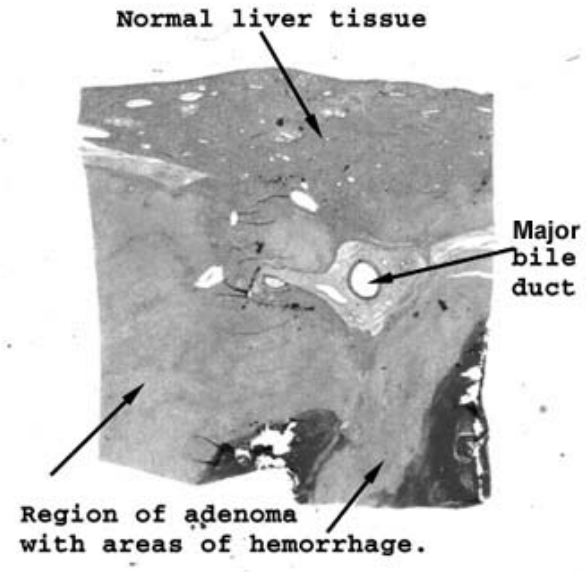
This section represents only a small slice out of a dilated, inflamed (and no doubt painful) gallbladder. Undoubtedly there were stones present as well, but we don't have any direct microscopic evidence for them. Find the mucosa and then work your way through the wall to the serosa. Pay attention to the inflammatory cells and where you see them. What about the lamina propria?

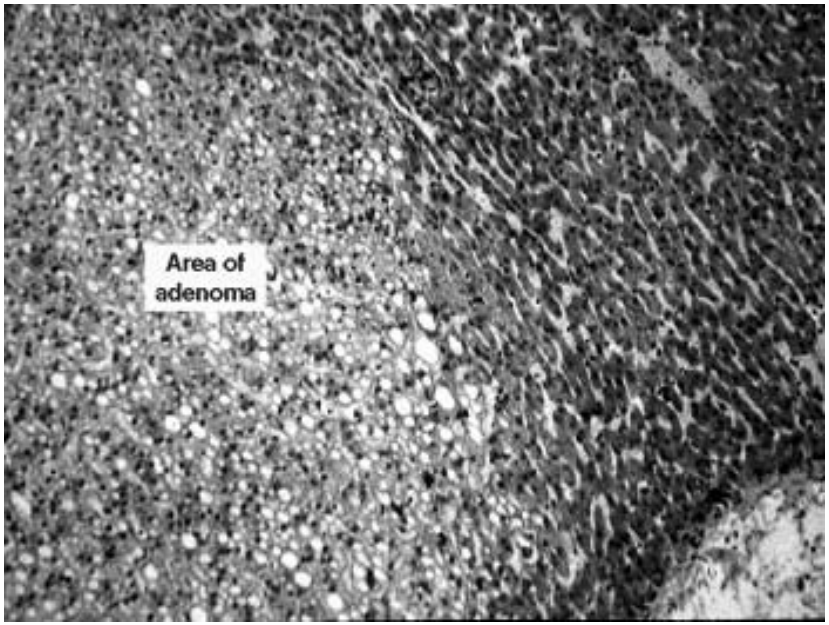
Your observations



Find the lumen and try to have yourself oriented before looking for the infiltrate. You will see a mixed inflammatory infiltrate consisting of both "acute" and "chronic" inflammatory cells, again lymphocytes are to be expected in the submucosa of a structure associated with the gastrointestinal system. You will see a large amount of granulation tissue on the serosal surface.

Slide 29: Liver with hepatic adenoma



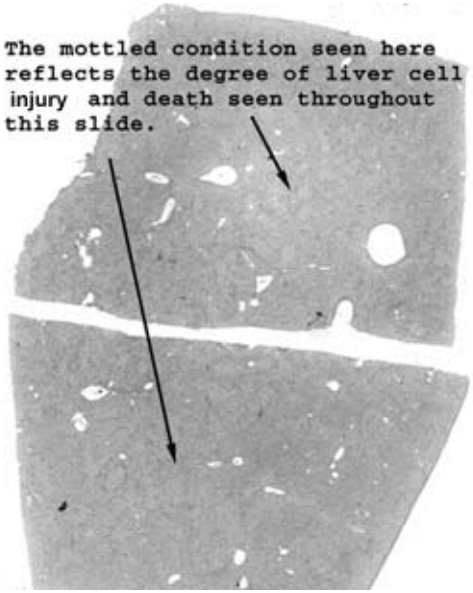


It's a little tricky to see the area of the adenoma if all you do is slap the slide on the stage of your scope. See if you can match the
areas of the tissue as depicted to the left and then look with your microscope right at the margin of the tumor. With situations like this, it's really important to see both cell types in one field.

Be sure to look at this one on a white background and use low power on your scope. The area of the adenoma will be very evident if you follow these simple rules. The cells that make up this benign tumor do not show much of a lobular arrangement. There are no triads. The individual cells have a "foamier" cytoplasm and somewhat more vesiculated nucleus. I don't think you will find any mitosis. These can become symptomatic by bleeding, and can even cause death by this mechanism. What is associated with these? Hint: think common exogenous hormones women may take.

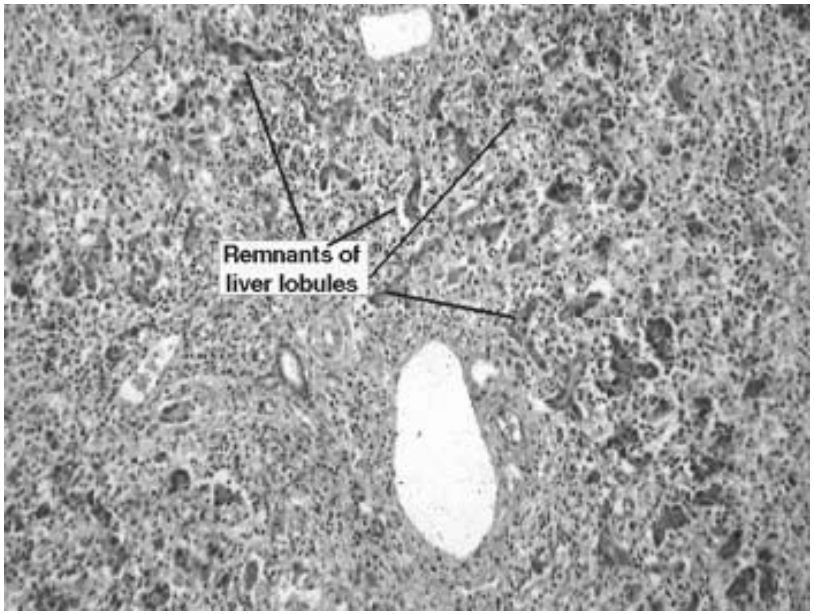
Your observations

Slide 40: Liver with acute yellow atrophy



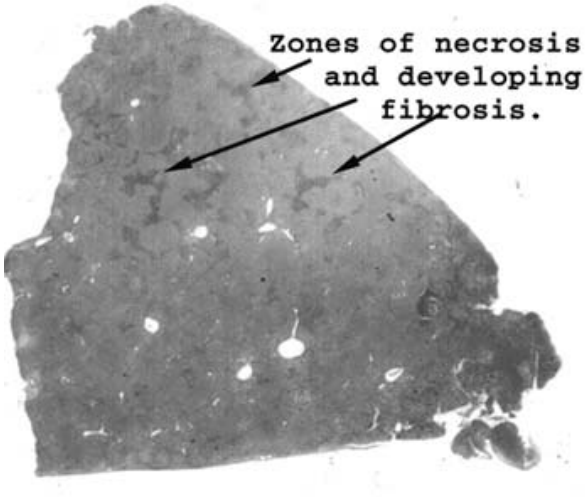
Again, the mottled appearance of the tissue tells you there is some diffuse and generalized process at work. I advise you to work your way down starting with the lowest power of magnification and see if you can identify anything that looks like a lobular pattern. Then go for high power and see if you can spot triads and figure out what happened here.

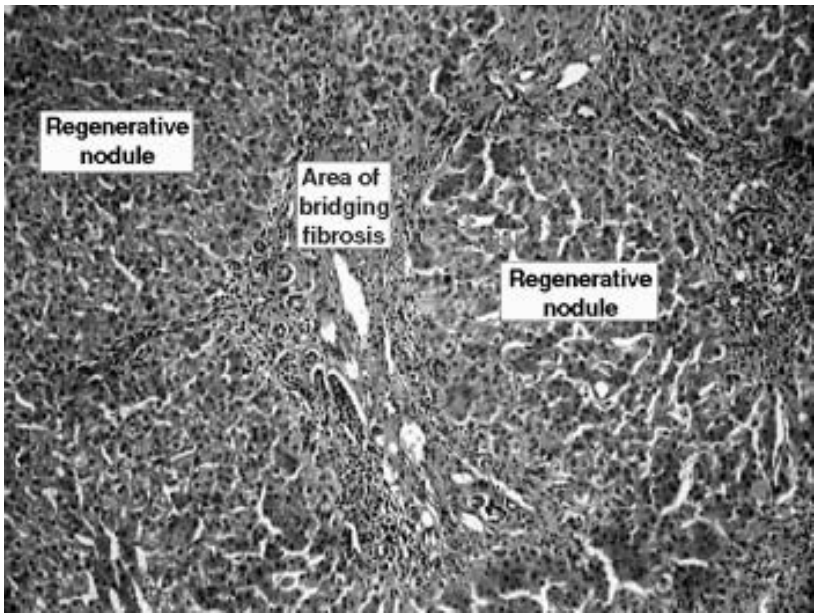
Your observations



Acute Yellow Atrophy is an old term, and not used much anymore. In this slide, so many hepatocytes have died and been removed, that it is hard to tell this is even liver. Most of what remains are bile ducts and triadal remnants. There is considerable inflammation and absolute absence of the usual lobular arrangement. If you are having trouble with this slide, you're in the majority; don't get too worried. This resulted from a toxic exposure of chloroform, but many other industrial volatiles can cause this same change. Clearly, this was an autopsy specimen.

Slide 41: Liver with acute and chronic cholangitis and fibrosis



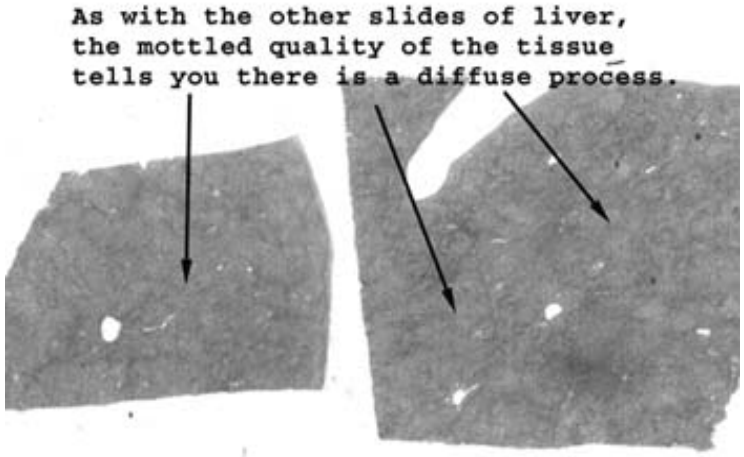


Here you can see the beginnings of cirrhosis. There is scarring, necrosis and a nodular pattern of regeneration.

Here the big changes are in the triads. This is a good example of the disruption of the normal architecture of the margins of the triads. Note the loss of definition of the "limiting plate" of the triads (the first layer of hepatocytes nestled right up to the triad is what is referred to as the limiting plate) with the marked degree of inflammation. There is early "bridging fibrosis" between the triads. This fibrosis represents the beginnings of cirrhosis. What are some of the causes of this condition?

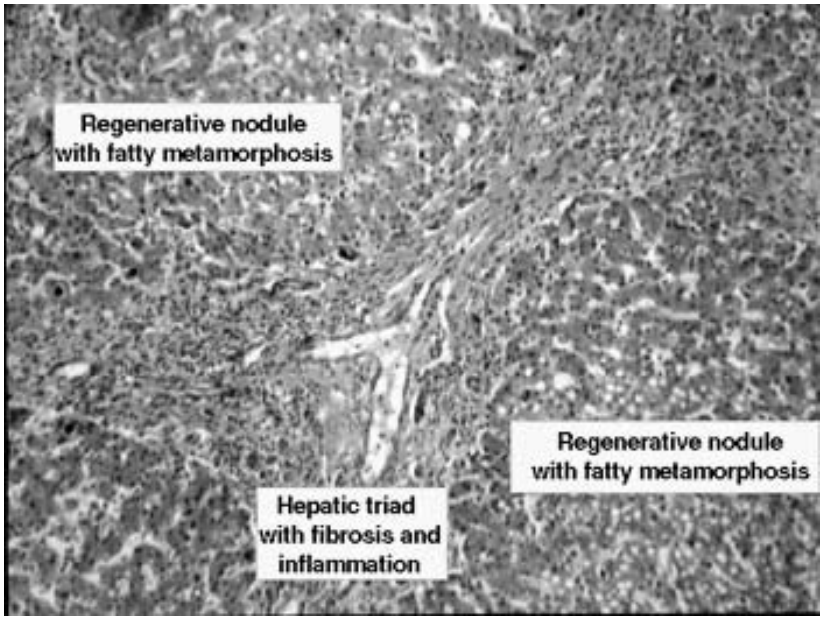
Your observations

Slide 42: Liver with cirrhosis



Here just looking at the tissue on the slide, you can see the evolving nodular pattern so characteristic of cirrhosis.

Your observations

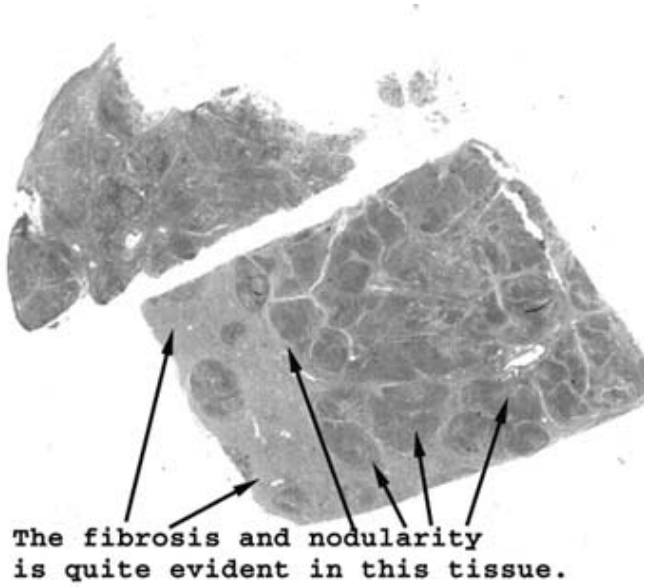


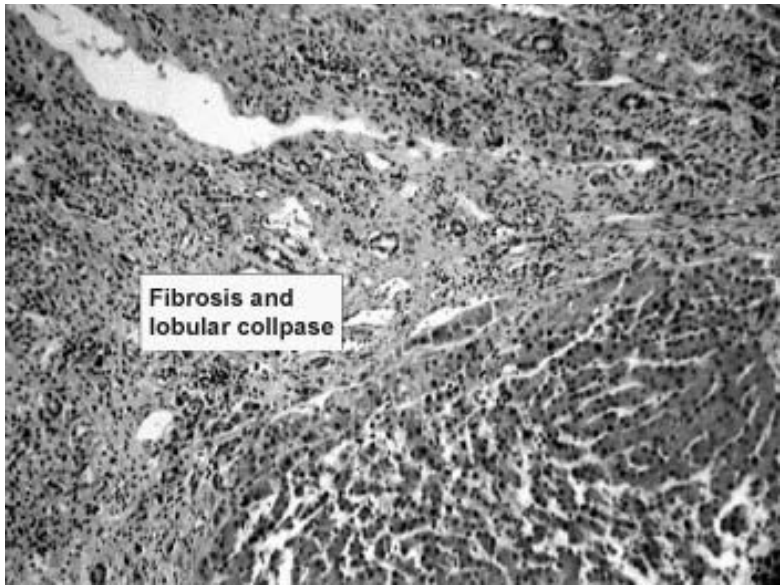
This slide shows all of the features of cirrhosis. You can probably see the degree of nodularity best by first looking at this slide on a white background before going to the microscope. Observe the "bridging fibrosis" between the triads and the loss of definition of the limiting plate of the triads. There is still much inflammation. Note the "regenerating nodules." These nodules are isolated from the biliary system and represent an effort by liver to repair damage, but it's clearly uncoordinated and ineffective. The deranged vascular flow will ultimately become a major problem for those with cirrhosis.

Slide 45: Liver with post necrotic cirrhosis

I'll bet you can't miss the nodularity and scarring in this example of cirrhosis.

Your observations

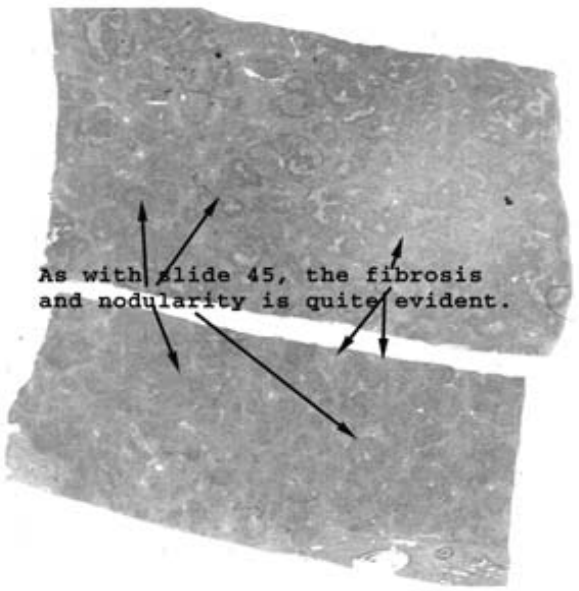




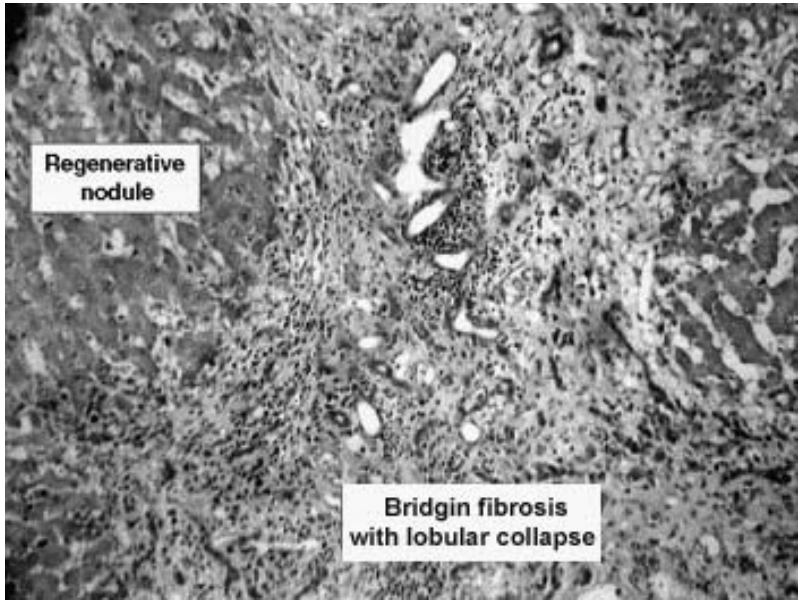
Here you will see large bands of scar tissue throughout the liver, and this feature is the hallmark of post necrotic cirrhosis. There is profound disruption of the expected lobular architecture, and some inflammatory cells should still be seen. But again, the vascular derangement will play havoc in this situation. What does the term "bile duct duplication" really refer to? Be sure you understand what is meant be the term "post necrotic" cirrhosis.

Slide 46: Liver with cirrhosis

Your observations



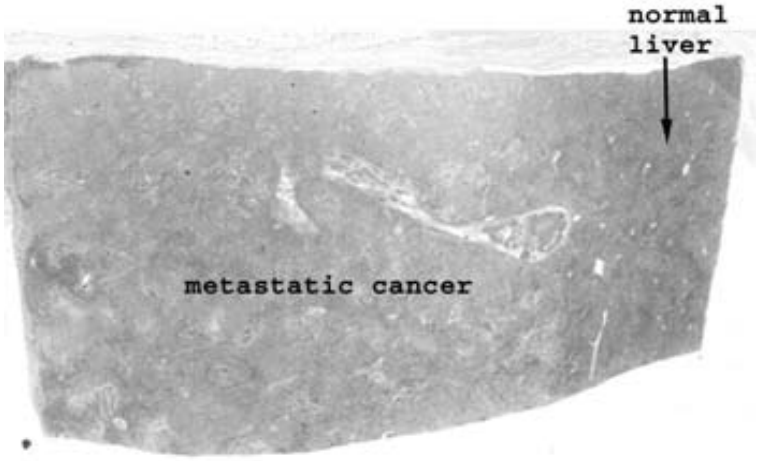
As with the other examples of cirrhosis, you can easily see the nodular pattern in this tissue.



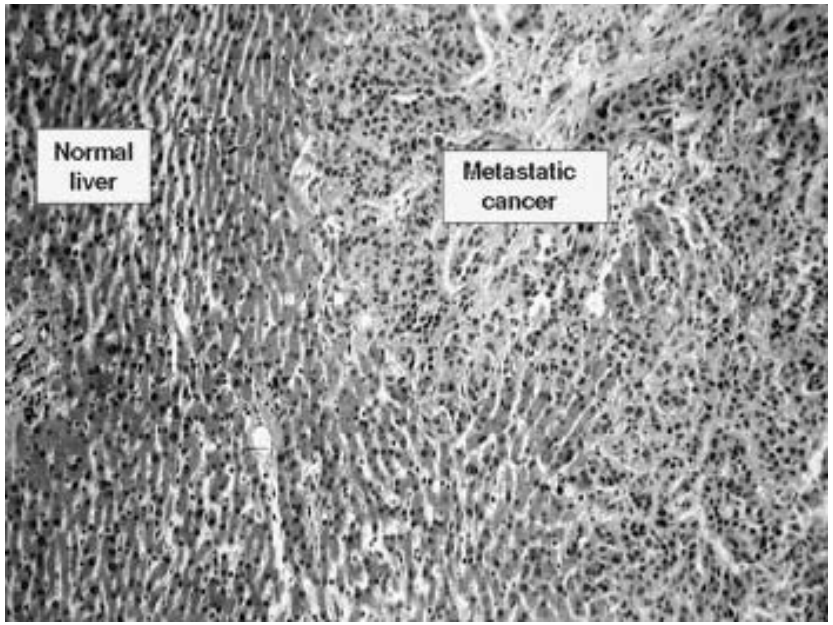
This liver is obviously shot! There is really very little of the lobular array left at all. You will see many inflammatory cells still at work removing the dead and dying hepatocytes. What could cause this degree of injury? What would the liver look like grossly?

Slide 47: Liver with metastatic cancer

Your observations

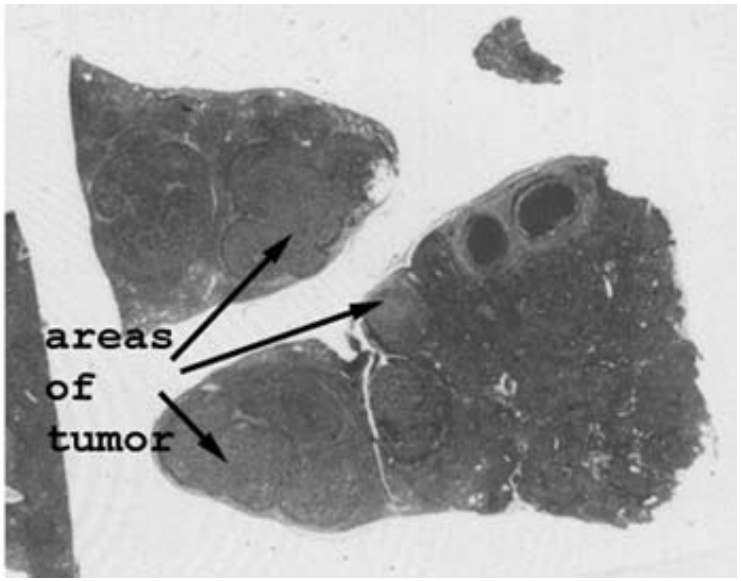


As with slides of this sort, look at the uninvolved liver first and then move to the region of pathology. The metastatic focus is pretty easy to recognize. See if you can detect a glandular or "Indian file" pattern.

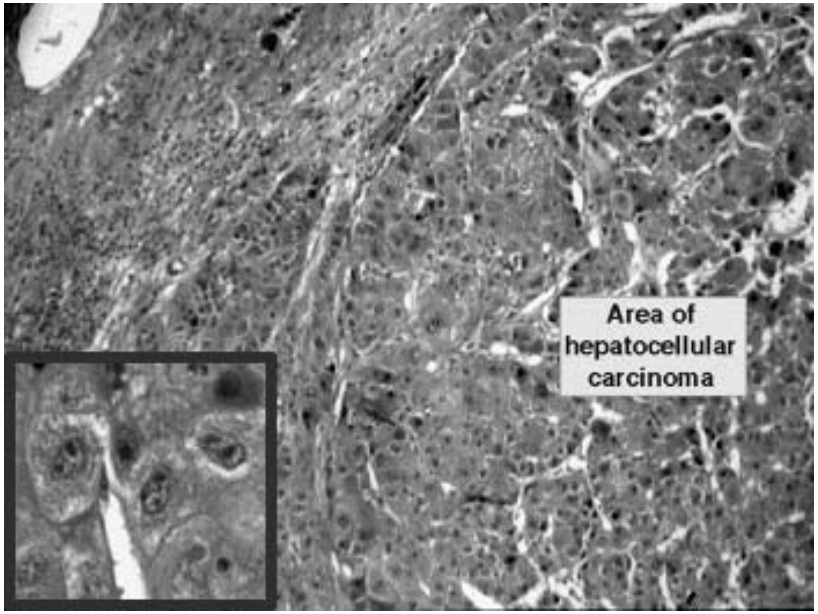


Again, looking at this slide on a white background will show the areas of cancer quite nicely. I believe this is an example of metastatic breast cancer. You will see rudimentary attempts to form glands by the malignant cells. Observe the advancing margins of the tumors. Compare the cytology of the foreign malignant cells to that of the surrounding healthy liver cells. Do you see vacuoles in the metastatic malignant cells?

Slide 63: Liver with hepatocellular carcinoma



I think it is possible to see the nodules of malignancy even with no magnification. If nothing else, you can see areas of the liver tissue are distinctly different from one another.



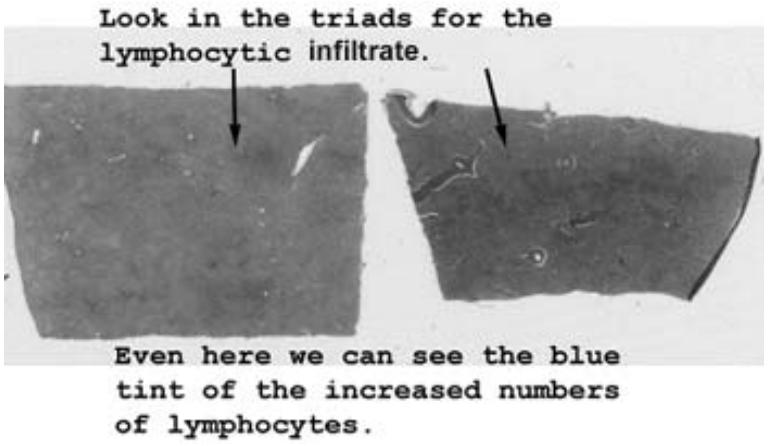
This cancer generally arises in a background of cirrhosis and represents a primary malignancy of the hepatocyte. You will see there is no lobular organization in the area of the tumor. Note the marked degree of nuclear atypia and the great number of mitoses. You are also likely to see many bizarre mitotic figures. There may be bile production by the malignant cells, but of course, there are no biliary hookups. This is a malignancy of hepatocyte origin, and is different from so called biliary carcinoma, which arises from the ductal elements of the liver (or pancreas for that matter).

The insert shows high power detail of the malignant hepatocytes.

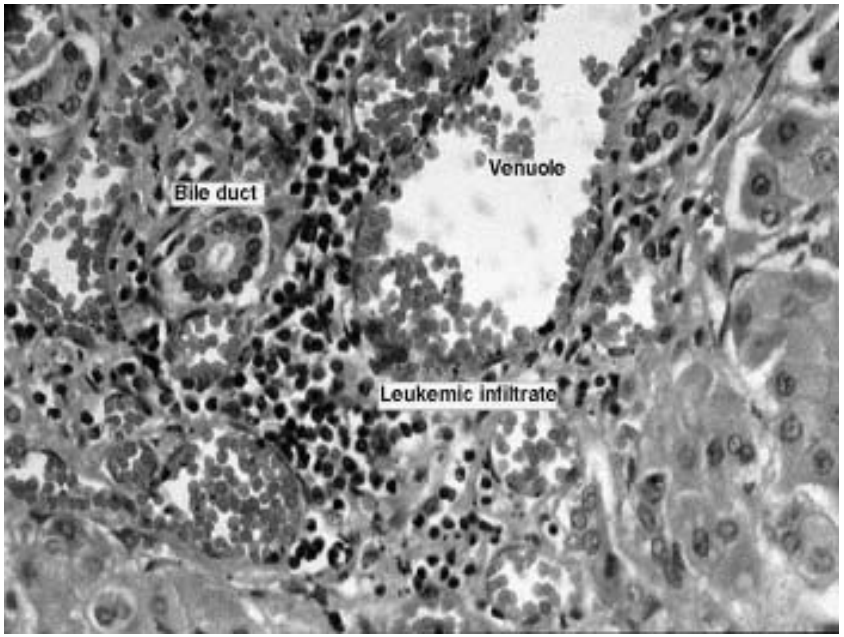
Your observations

Slide 69: Liver with chronic lymphocytic leukemia

Your observations



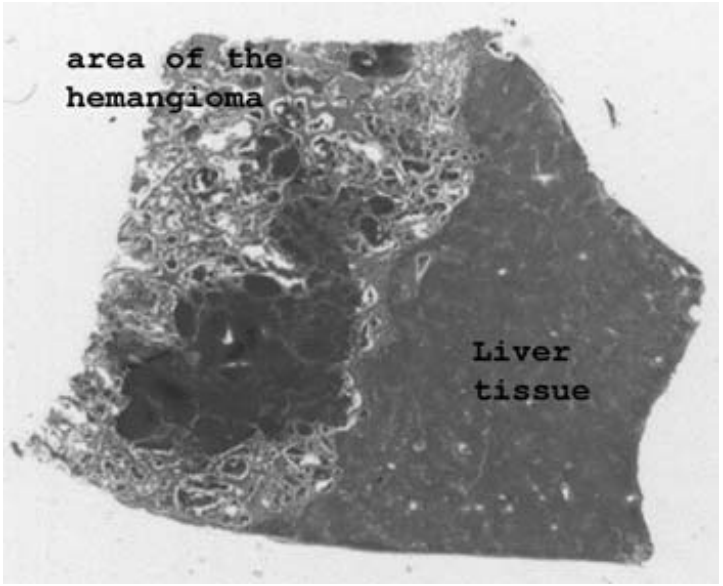
Can't really see much at this power of magnification. Look in the triads for the lymphocytic infiltrate.



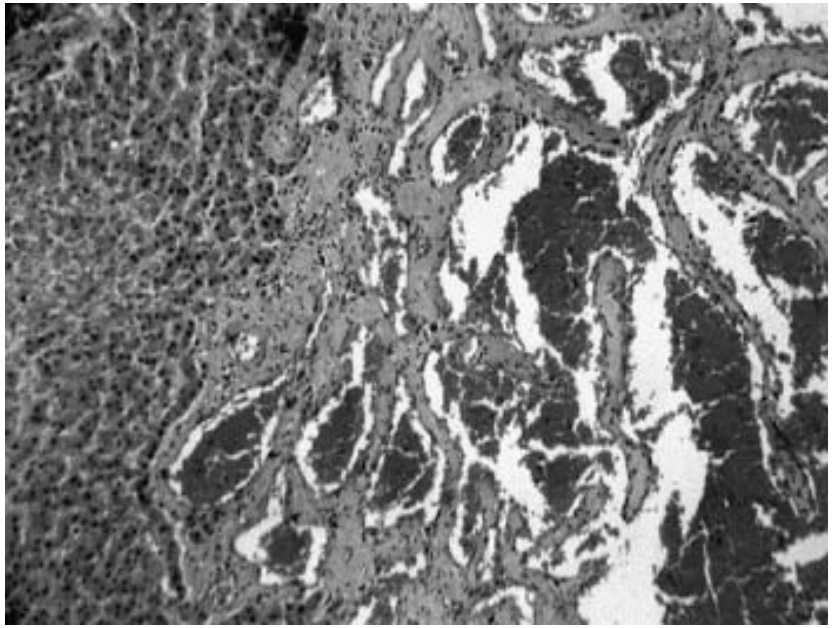
The changes here are subtle. You will see an infiltrate of, quite frankly benign looking, lymphocytes in the triads. We call this a "cold infiltrate" because the lymphocytes do not have a "stimulated" appearance and are not there as a response to some inflammatory process. These lymphocytes may lack the classical cytologic features of malignancy, but they are indeed malignant.

Slide 71: Liver with hemangioma

Your observations



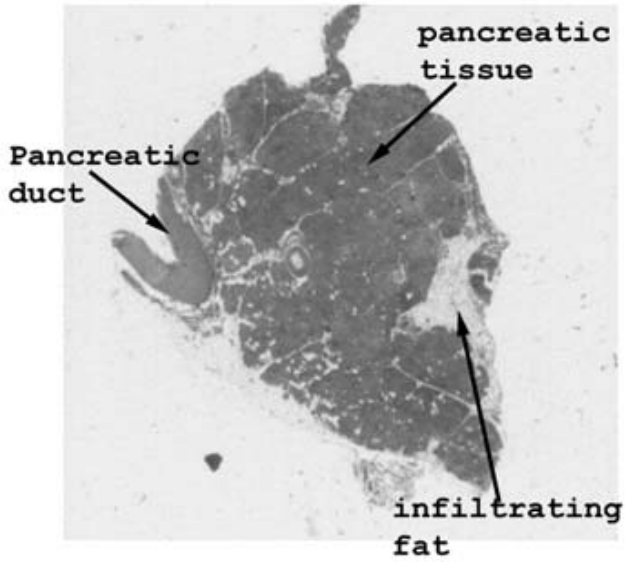
This should be obvious to the most casual of observers. One can easily see the altered area of the tissue with the many vascular channels filled with blood.



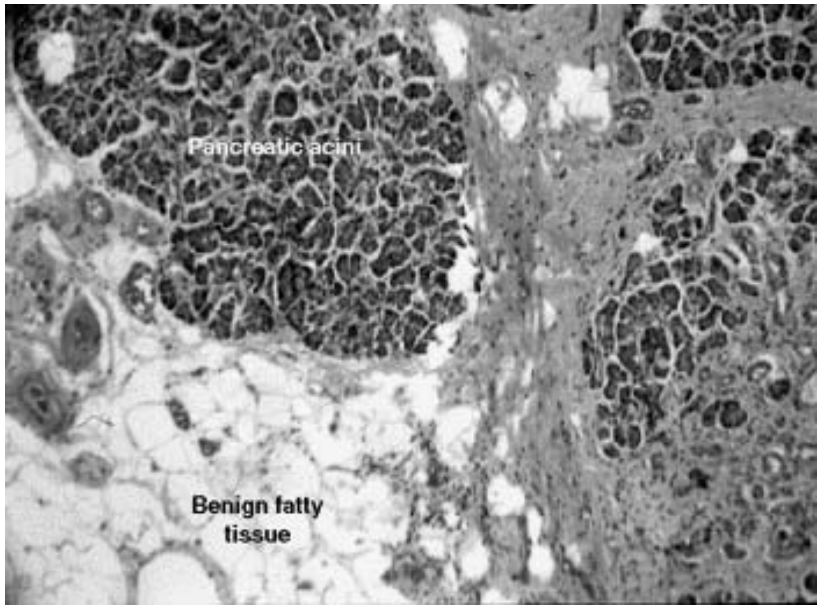
Just look at this slide on a white background, and you will have no trouble finding the area of abnormality. The vessels have cavernous lumens, and walls that look like hybrids between vein and artery. This hemangioma is benign and congenital. They can become a problem by thrombosing, bleeding or becoming infected. Most of the time they are quiet, and are incidental discoveries while surgery is going on for some other condition.

Slide 75: Fatty infiltration of pancreas

Your observations

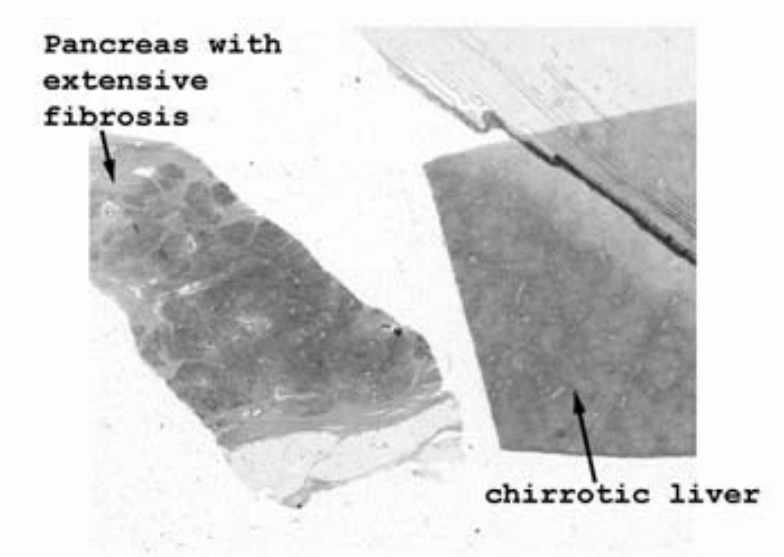


The changes of importance here are probably better seen in this scan of the tissue than by use of the microscope. Here you can see the "infiltration" of benign fat cells into the pancreas. That's all there is here.



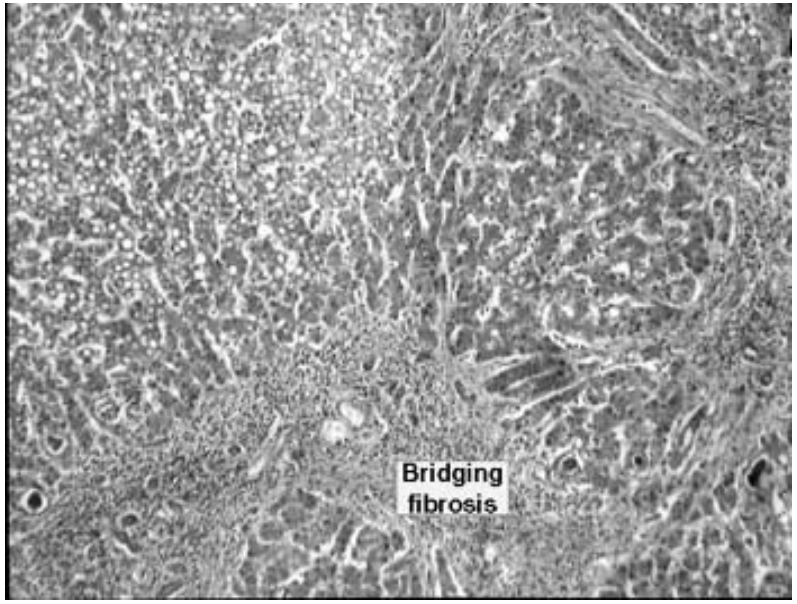
This is hard to pick up, because what is present in the pancreas is what is normally there; just more than usual. You should see mature fatty tissue extending into the lobules of the pancreas. The fat cells are not malignant, and this is not particularly pathological. We see this change in obese people. This condition is quite different from fatty metamorphosis which occurs in the liver. In fatty metamorphosis we see the effected cell accumulating a large lipid droplet. Slide #4 in your set shows a nice example. The main purpose here is to be sure you know the difference between fatty infiltration and fatty metamorphosis. Do you?

Slide 92: Liver with cirrhosis



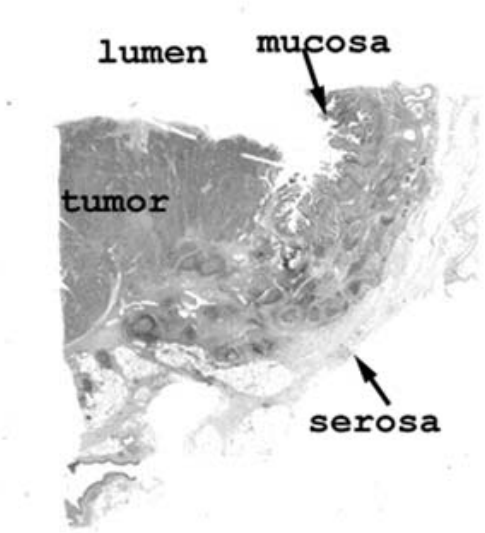
Even though this slide is generally faded, it is still possible to see the nodularity of the liver by just viewing it on a white background.

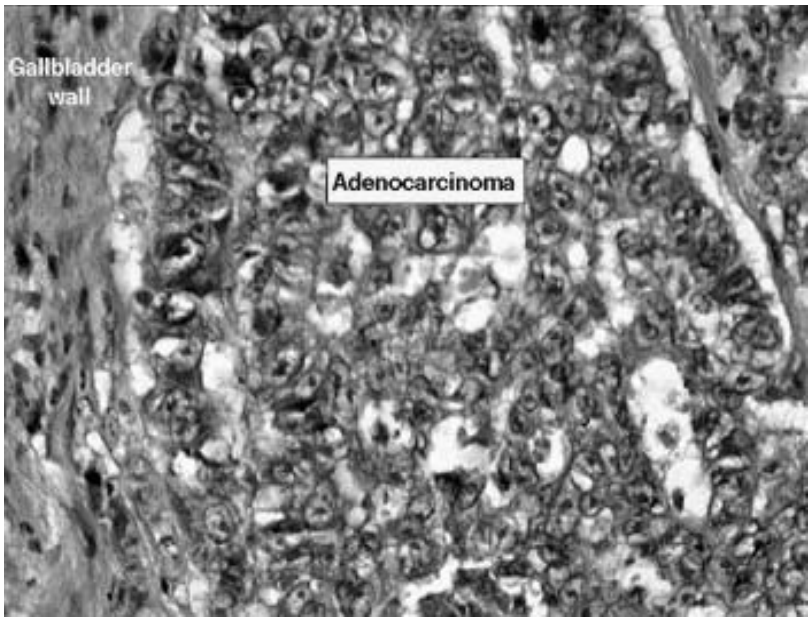
Your observations



This is an unbelievable example of cirrhosis! Look at the slide on a white background first to see the degree of nodularity. You will see the bridging fibrosis between triads with "triadal collapse," as well as a marked inflammatory infiltrate throughout this slide. What would you suspect to be the etiologic agent of this particular case? Hint: the combination of liver and pancreatic disease suggests a short chain hydrocarbon with toxic properties might be at work. (Ethanol perhaps?)

Slide 103: Adenocarcinoma of gallbladder



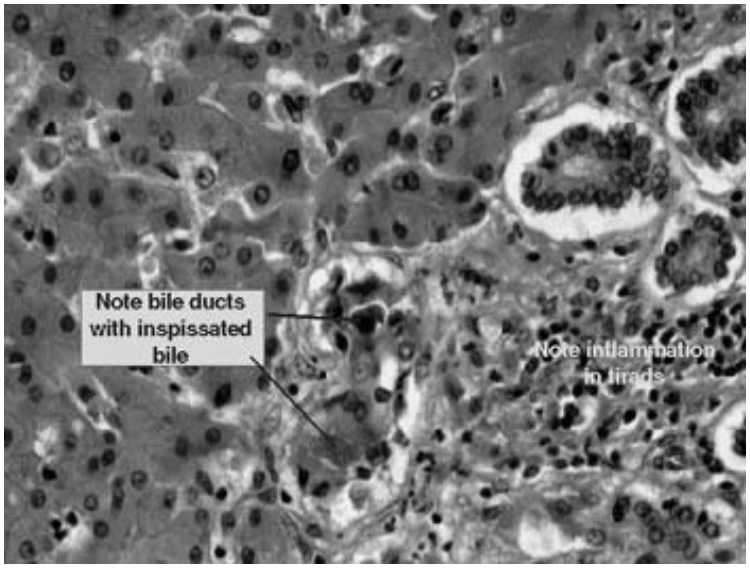


Your observations

Not much trouble seeing the cancer here. When you look at the tissue on the slide, you should be able to see the uninvolved mucosa, muscular wall and serosal surface. Use that area to get oriented and then move to the area of the adenocarcinoma.

I don't think there is much in the way of normal gallbladder left on this slide. It might help if you look around on your slide to find some to get oriented. The malignant cells of the neoplasm are very undifferentiated and are not forming much in the way of glands. Seeing the hallmark cytologic features of malignancy will be very easy. What are they? Predictable consequences of this condition?

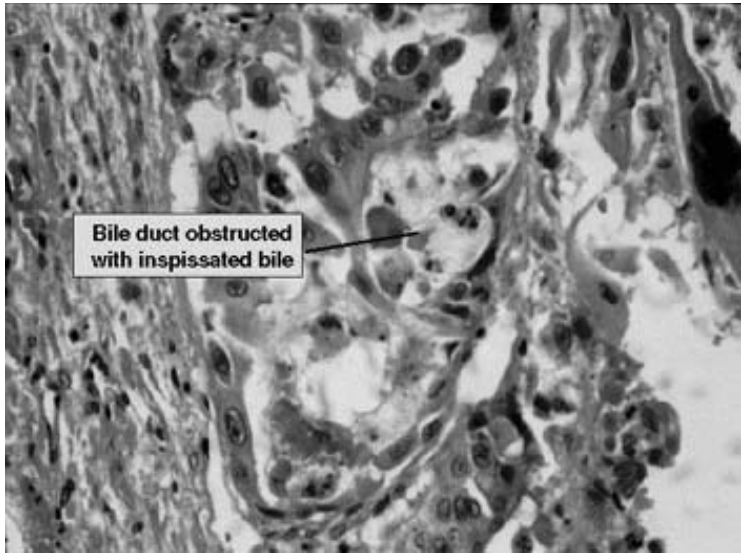
Slide 115: Biliary obstruction secondary to pancreatic carcinoma



You won't see any cancer in this slide. The malignancy is down in the lower end of the biliary system. You will see the bile ducts and canaliculi plugged with a glassy brown or deep red staining material. This is the inspissated bile. There will likely be some inflammation in the triads. The "clearing or halo" effect you will see around some of the bile ducts is an artifact of fixation, and not the pathology we are referring to. I have indicated an example on the picture.

Your observations

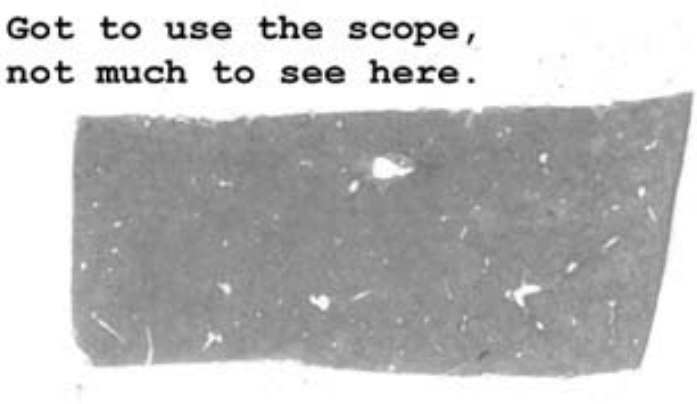
Slide 115: Biliary obstruction secondary to pancreatic carcinoma



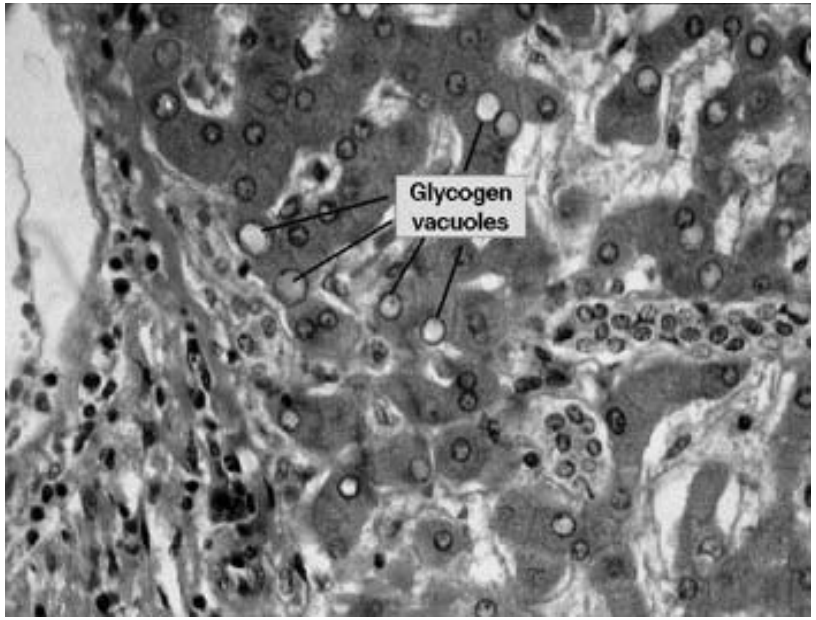
A higher power view of one of the triads. Note the "brick red" color of the inspissated material. Again, the artifactual separation of the ductal epithelium is very evident. This is a common artifact, and always looks like some kind of pathological process, but it's not.

Slide 117: Liver with glycogen vacuoles in hepatic nuclei

Your observations

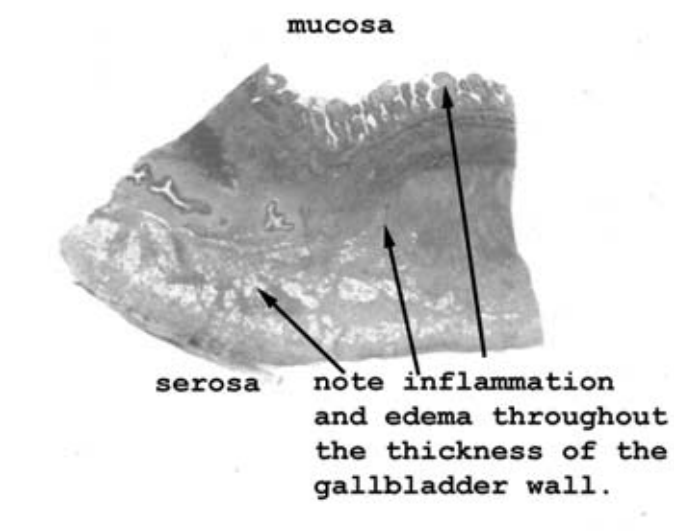


OK, I agree, this is a little boring here. You've got to use the scope on this one.



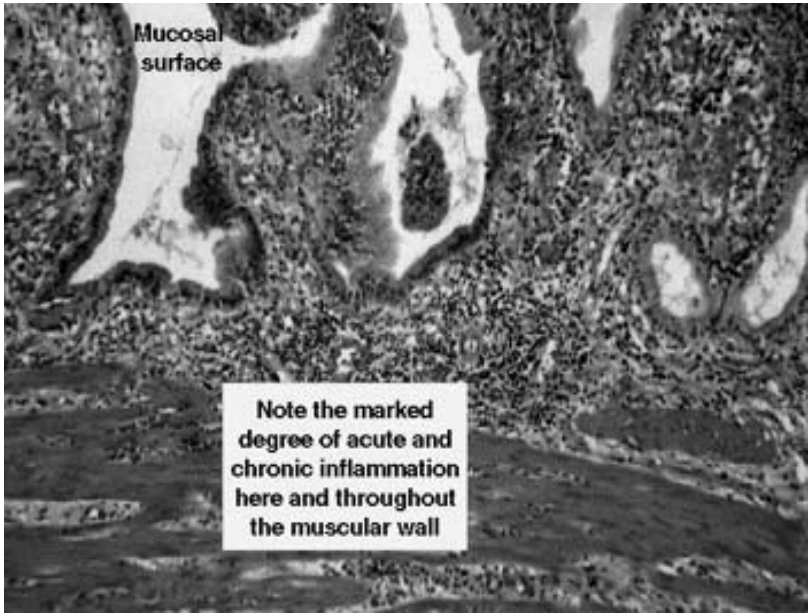
The picture pretty well says it all. You will see a wide eyed open looking nucleus with a very thin rim of chromatin at the margin. Don't think there is much else of great significance. What would this condition be associated with? Hint: think of a common and important disorder of glucose metabolism.

Slide 126: Gallbladder with acute and chronic inflammation



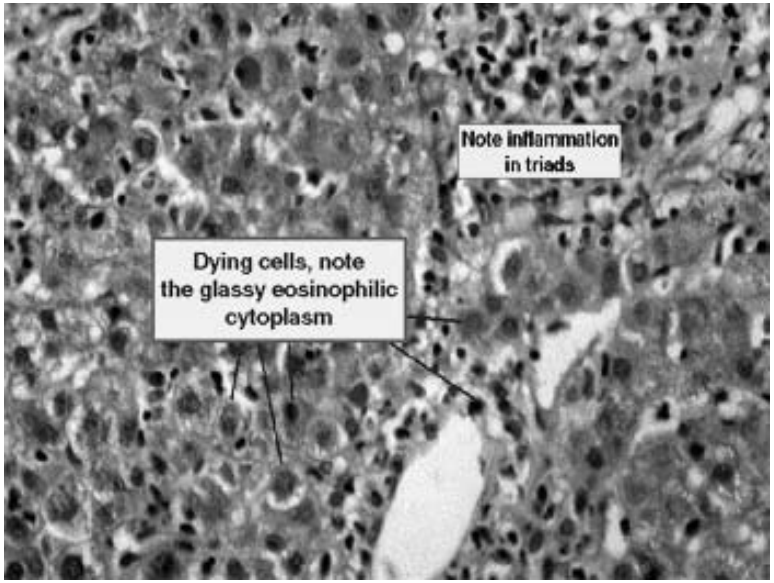
It's pretty obvious how markedly thickened and edematous the wall of this gallbladder is. Note the extensive inflammation throughout all layers of the wall.

Your observations



Are there ever numbers of acute inflammatory cells in the wall of this gallbladder! You will see a mixed infiltrate with both acute and chronic features. What defines the two different patterns? Look at the mucosa and the full thickness of the wall to get some idea of how inflamed this organ is. What are some of the causes and consequences of this condition?

Slide 132: Acute viral hepatitis



There are a number of features we look for to make the diagnosis of acute hepatitis, and this slide has them all. Note the "piecemeal (focal) necrosis" of the hepatocytes in the lobules. You will see little clusters of acute inflammatory cells in the lobules and in the triads. There may be some disruption of the "limiting plate" of the triads too. The limiting plate refers to the junctional zone (i.e. first layer of hepatocytes) between the triad and the liver lobules. You should also see some Kupffer cell hyperplasia, again a common finding in hepatitis, especially viral hepatitis. What exactly are the Kupffer cells? Hint: think reticuloendothelial system.

Your observations

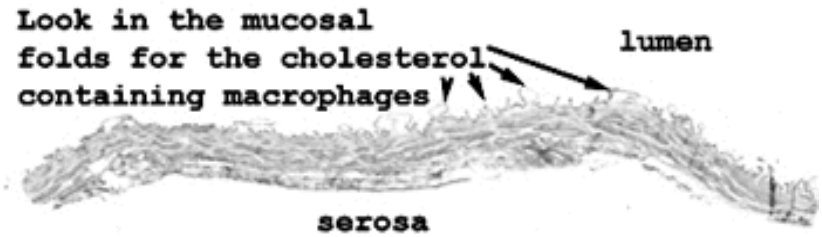
Normal liver for comparison

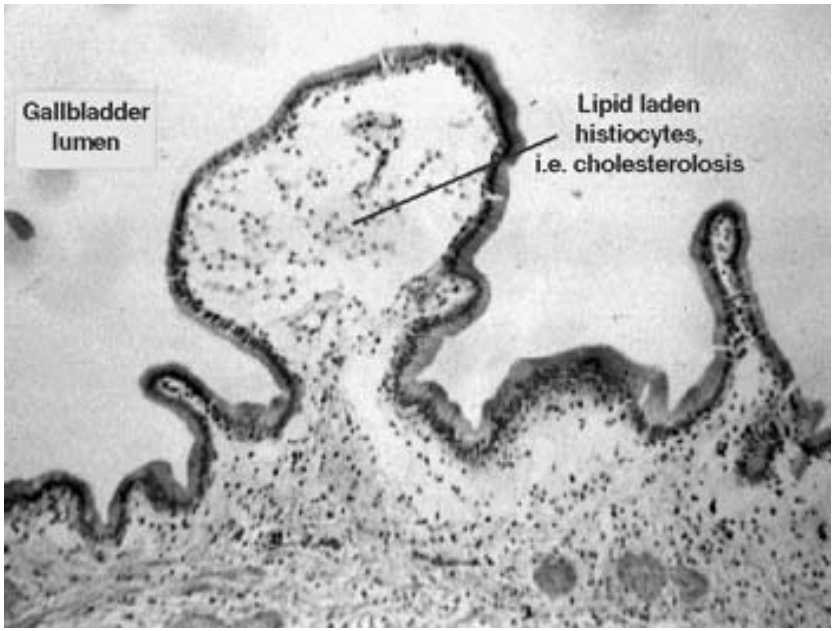
This is it. You know, normal liver.

Slide 137: Gallbladder with cholesterolosis

Your observations

Look in the little mucosal folds for the lipid laden histiocytes.





It helps to have an idea of normal gallbladder morphology to see what is wrong with this picture. You will see somewhat enlarged mucosal folds of the gallbladder, and in many there will be an infiltrate of foamy histiocytes. There is very little inflammation of the acute or chronic type here, and if there is any at all, it will be found in the muscular wall and serosal fat. This is a very common and benign process, and very likely is the starting point for some types of gall stones.

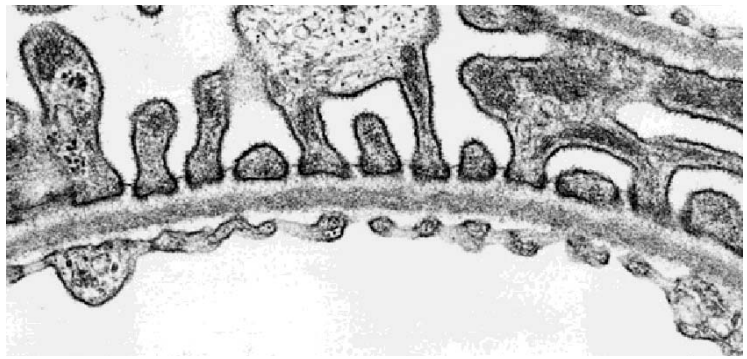
General and Systemic Histopathology
C601 and C602

Section 9 *Renal Disease*

Renal disease, and especially renal failure, can produce some of the most confusing and bewildering clinical symptoms of any organ system we will study. Because the kidney is involved with so many regulatory functions, presenting symptoms may vary from anemia to confusion or even pericarditis.

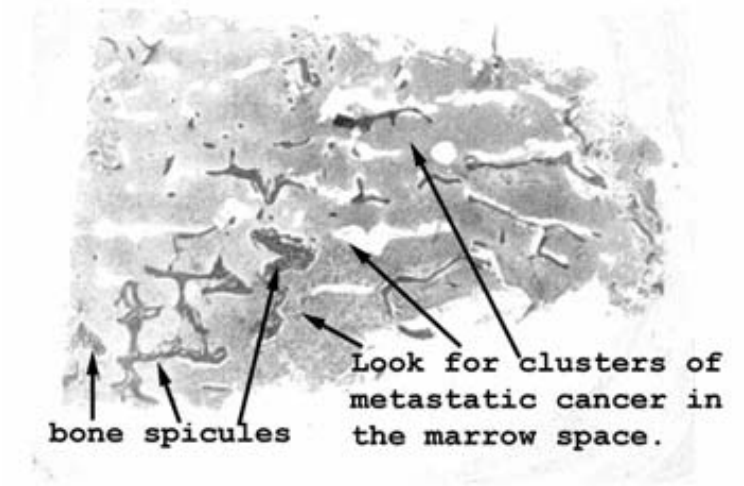
Renal disease is in large part a replay of microvascular disease. Antigen-antibody complex diseases, such as lupus erythematosus and post streptococcal syndromes will serve as our models for auto-immune injury. Diabetes will weigh heavily as a major cause in many aspects of kidney pathology. Remember that for all practical purposes, diabetes becomes a small vessel disease. The consequences of diabetes lead to damage of the glomeruli, interstitial tissue and even the tubular epithelium. It should come as no surprise that diabetic renal disease is the leading cause of renal failure in the United States.

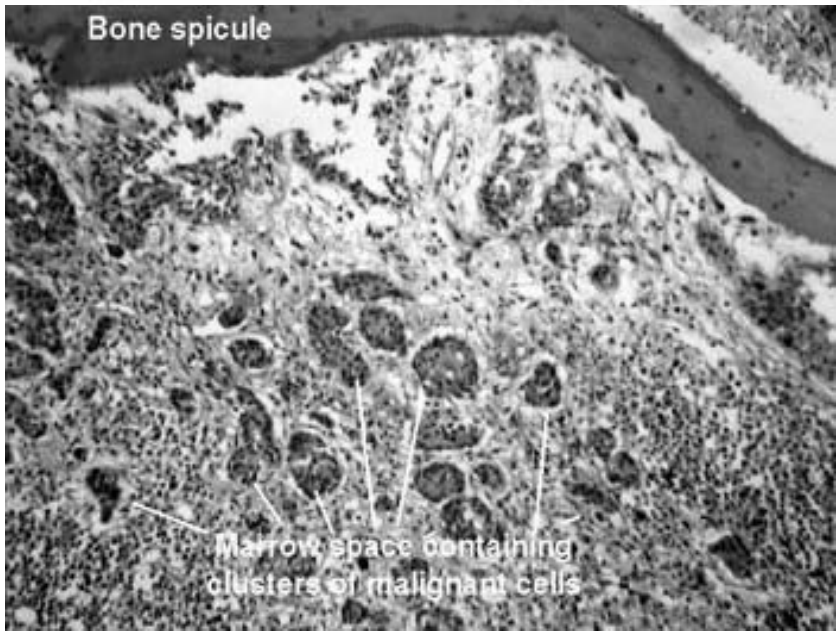
Considering infectious diseases, the kidney and lower urinary tract will show us time and again the problem of "opportunistic" infections. Finally, neoplastic disease of the urinary system is almost in a class by itself. We will see varied histologic appearances of renal cell carcinomas as well as widely varying clinical presentations. But even given the wide latitude of clinical presentations and histologic patterns of the tumors, if you know the basics of the physiology of the kidney you'll be able to puzzle your way through most situations.



Slide 23: Bone, Metastatic transitional cell carcinoma

Your observations

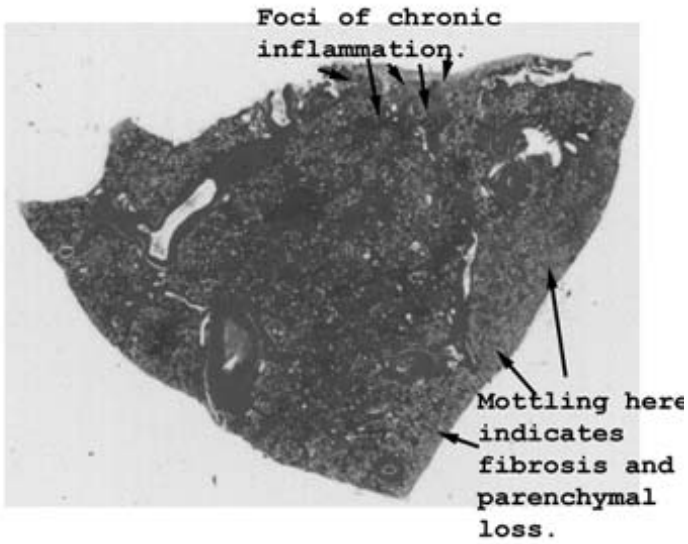




This slide shows metastatic "transitional cell carcinoma" in the bone marrow. What are the sources of "transitional cell carcinoma?" First, try to get oriented by finding some bone spicules and hematopoietic tissue. The malignant cells occur in clusters and closely resemble malignant squamous cells. Although these cells don't look too wild, they are not in the right place. Observe the "desmoplasia" (i.e. fibrosis) associated with the groups of tumor cells.

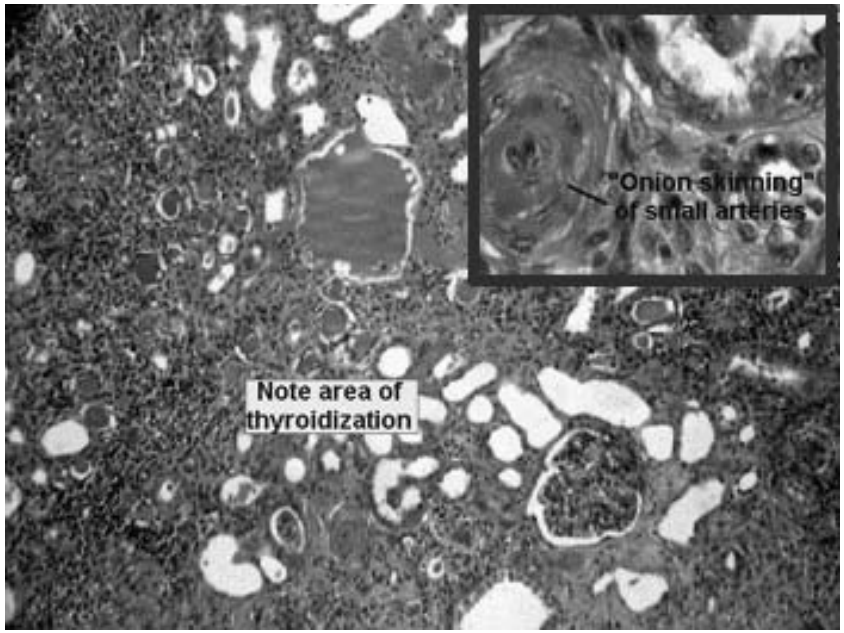
Note how "meaty" the bone marrow space is. Much of the hematopoietic space has been replaced by scar tissue and tumor.

Slide 79: Kidney with chronic pyelonephritis



Even with no magnification you can see the scattered blue staining that represents the large number of lymphocytes in the interstitial tissue. It is possible that you may be able to see little bright pink globs that represent the dilated, protein containing tubules.

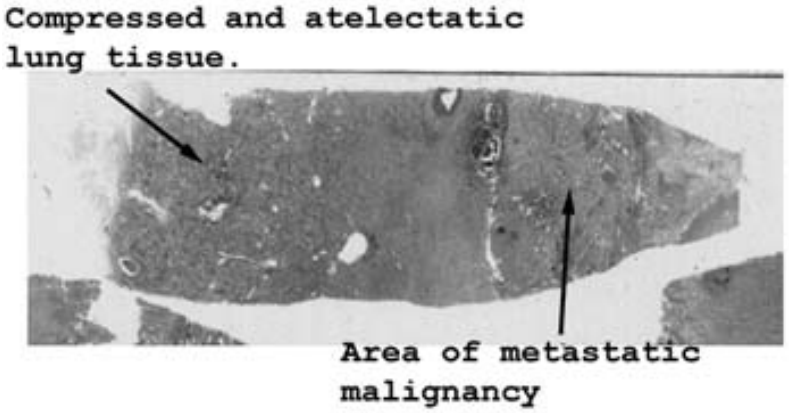
Your observations

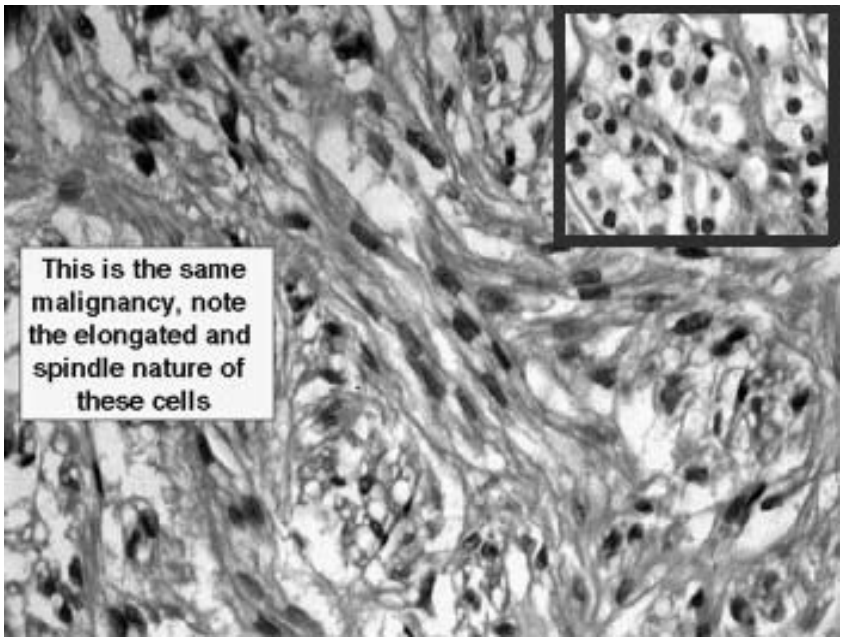


Note here the changes we call "thyroidization." You will see many chronic inflammatory cells in the interstitial tissue and dilated tubules containing pink staining proteinaceous goo, giving the appearance of thyroid colloid. You should note the scarring in the interstitial tissue in general and to some degree around the glomeruli. This is often associated with chronic ischemic injury of the kidney, which worsens as the process proceeds. Think diabetes and hypertension.

The insert (upper right) shows the arteriolar changes of hypertension that are throughout this section.

Slide 80: Lung with metastatic renal cell carcinoma, clear cell pattern





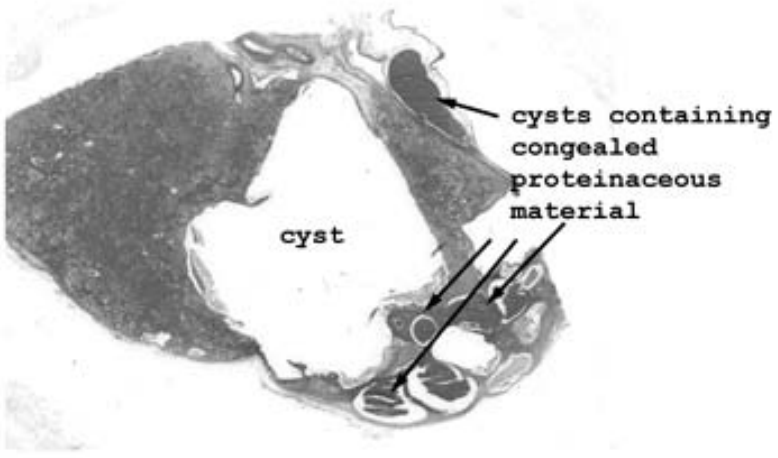
The appearance of this malignancy is a little atypical. Generally the metastases pretty faithfully reproduce the histological pattern of the primary lesion. Renal cell is probably the one tumor that most consistently breaks this rule. Here we see two patterns in the same metastatic focus; a spindle pattern and the more typical clear cell pattern.

This slide shows lung tissue that is essentially replaced with metastatic renal cell carcinoma. You will see clusters of cells with very clear, washed out appearing, cytoplasm. The cells appear in clusters that mimic the configuration of a renal tubule. The cells are clear because the lipid they once contained was "washed out" by the xylene during the processing of the tissue in preparation for sectioning.

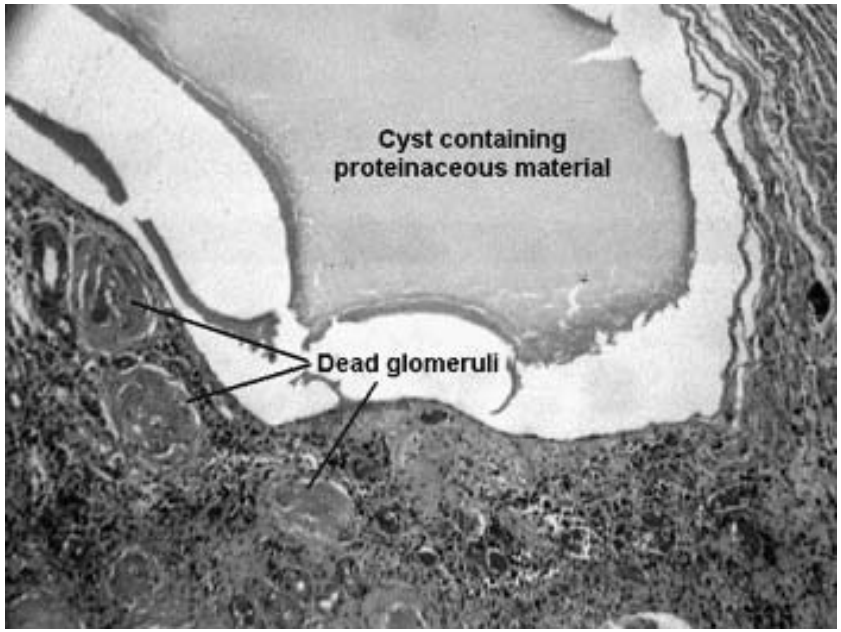
The insert (upper right) shows the more frequently seen “clear cell” pattern of this tumor.

Your observations

Slide 91: Kidney with polycystic renal disease



The cysts are so large and cause such deformity that it's almost hard to recognize this as kidney. Clearly there will be much in the way of inflammation associated with the renal tissue surrounding the cysts. In many situations such as this we will find a generalized chronic inflammatory infiltrate throughout the interstitial tissue.

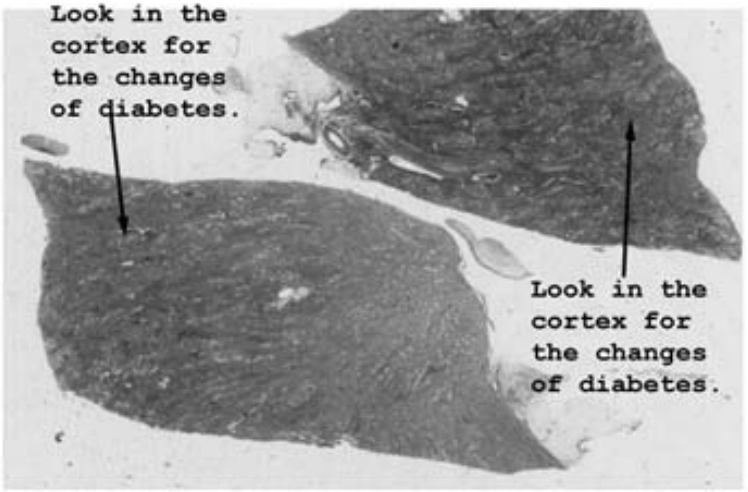


Note how little renal tissue there really is on this slide. The functioning tissue is squeezed into the spaces between the cysts. The cysts contain serous fluid and are obviously not connected with the collecting ducts. Chronic inflammation becomes a significant part of the problem as the cysts "grow." These kidneys can become ENORMOUS, but obviously consist almost exclusively of cysts filled with serous fluid. What are some causes of this condition?

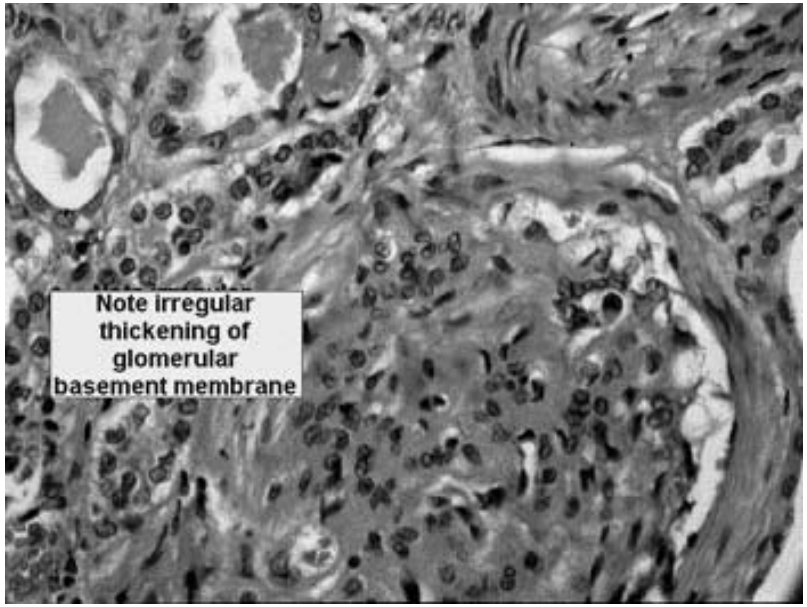
Your observations

Slide 95: Kidney with diabetic nephropathy

Your observations



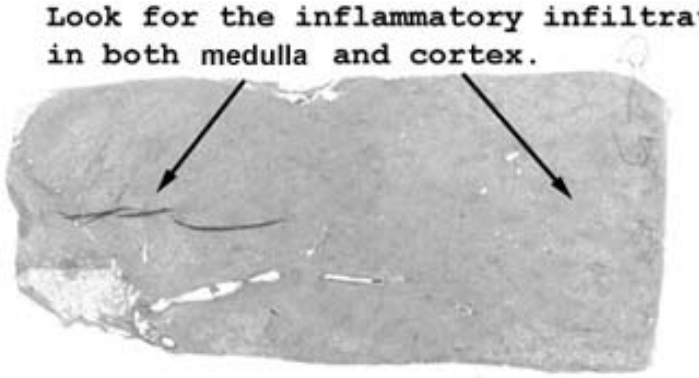
Not much to see grossly here. Most of the changes in this slide are to be found in the cortex.



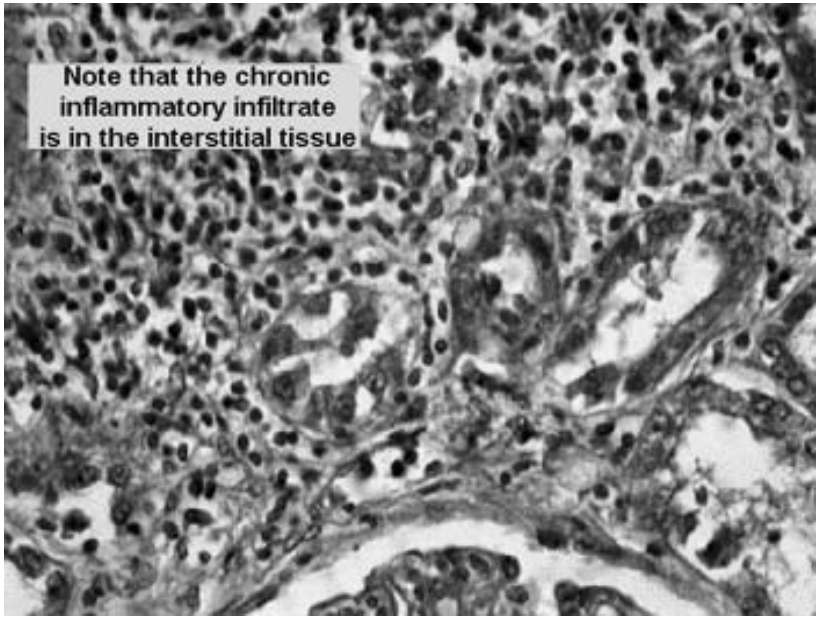
The glomerular changes present in this slide are one of the hallmarks of this disease. Note the irregular thickening of the basement membrane of the glomeruli and the hyalinized and thickened walls of both the afferent and efferent arterioles. You will also see some coexisting larger vascular disease and chronic pyelonephritis. Chronic infections and tissue hypoxia go hand in hand in this disease. The chronic pyelonephritis is a part of this picture, but does occur by itself. Know the difference between chronic pyelonephritis and diabetic renal disease.

Slide 113: Kidney with acute and chronic pyelonephritis

Your observations



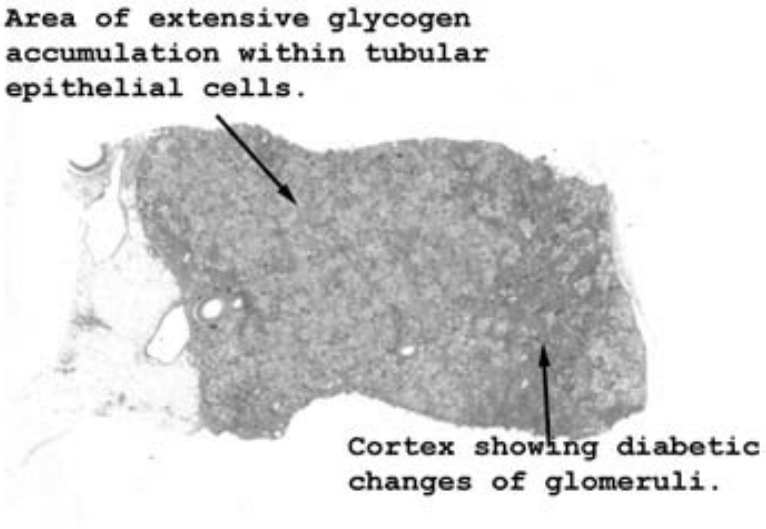
This slide shows an extensive mixed acute and chronic inflammatory infiltrate throughout the interstitial tissue. You will also see acute inflammatory cells in the lumens of many of the tubules. You know this kidney must have hurt.



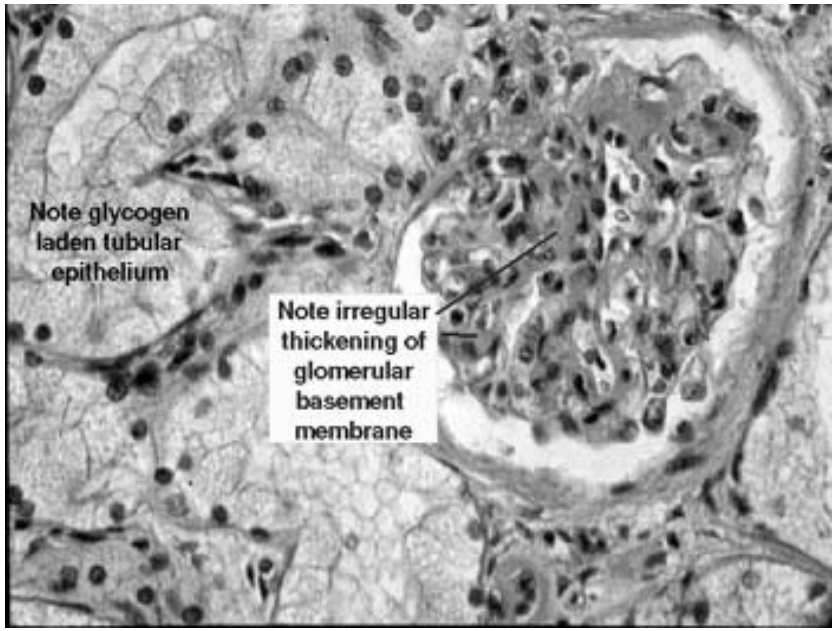
Note the marked degree of chronic and acute inflammation in the interstitial tissue. You will see some periglomerular fibrosis as well as marked changes in the epithelium lining the tubules. See if you can find any "casts" still in the tubules. What would they look like if they had been cleared in the urine? What do you think this person felt like? Fever? Peripheral WBC count? What organism is most likely, and how did it get here? What about antibodies stuck to the bugs? What would this mean if observed in the urine?

Slide 133: Kidney with diabetic nephropathy

Your observations

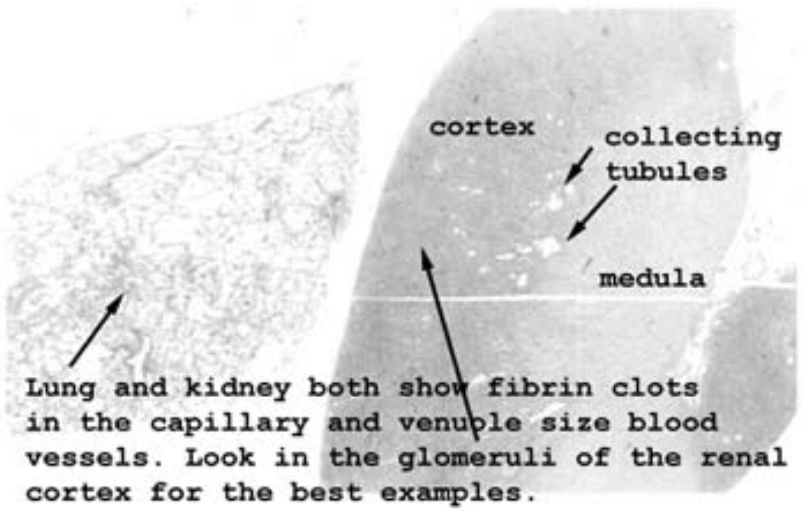


Even here you can see the differential staining of the tissue that reflects the extensive glycogen accumulation within the tubular epithelial cells.



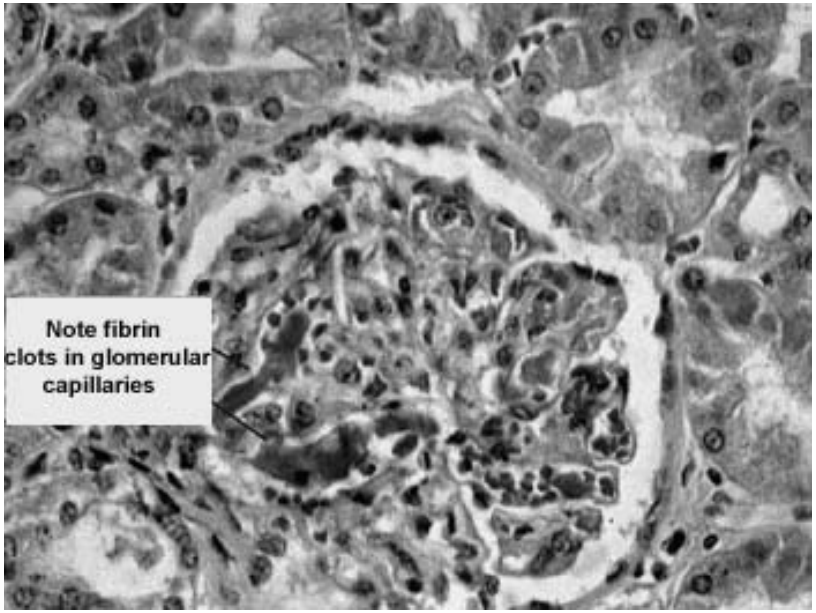
This slide shows an unusual change and at the same time one that is very common for diabetics. The vacuolization of the tubular cells is uncommon and reflects the tubular cell's attempts to recapture the sugar cleared in the urine. The material in these cells is glycogen. The glomerular changes are very common. Note the irregular thickening of the basement membrane of the glomeruli and the hyalinized and thickened walls of both the afferent and efferent arterioles. What is the name given to these changes? You will also see some coexisting larger vascular disease and chronic pyelonephritis.

Slide 135: Kidney with DIC



The best bet here is to look in the small vessels of the cortex, especially the glomeruli for the diagnostic changes. You're looking for thrombi composed only of protein. If you see what looks like thrombi with lots of RBC's in them, it's not what we're looking for.

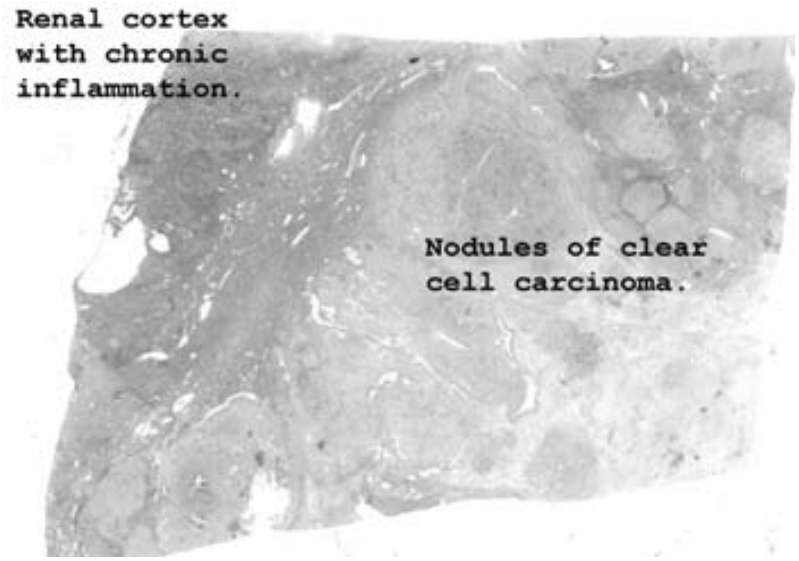
Your observations



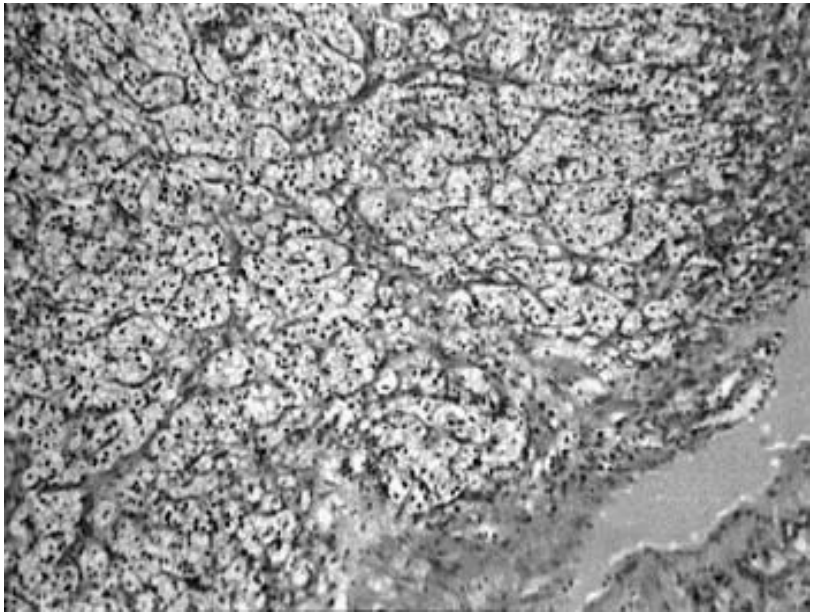
With disseminated intravascular coagulation (DIC), the person experiences "run away" intravascular blood clotting. This condition never just happens out of the proverbial blue. It is always a complication of something else that can trigger the clotting system, such as the leakage of amniotic fluid into the circulatory system in the course of some obstetrical disaster. As you might expect, there will be small thrombi in vessels throughout the body. This becomes an ischemic disease on the cellular level. People bleed with this condition because of the breakdown of the small vessels and consumption of the clotting agents. Causes are gram negative sepsis, massive trauma, OB disasters, etc.

Slide 145: Kidney with clear cell carcinoma

Your observations

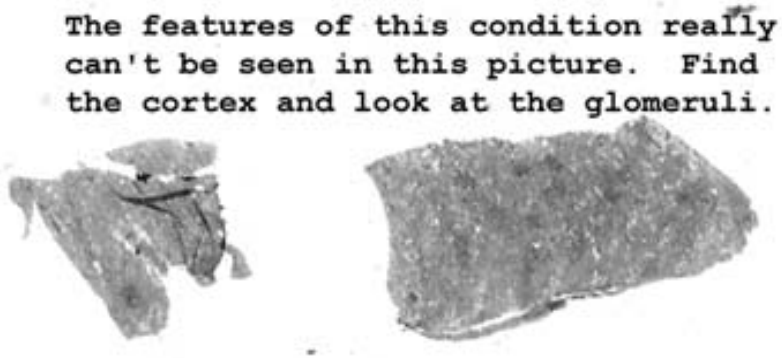


There should be no problem finding the area of tumor if you simply look at the tissue on a white background. Note the nodularity of the tumor. Also, there is quite a chronic inflammatory infiltrate in the surrounding uninvolved renal tissue.



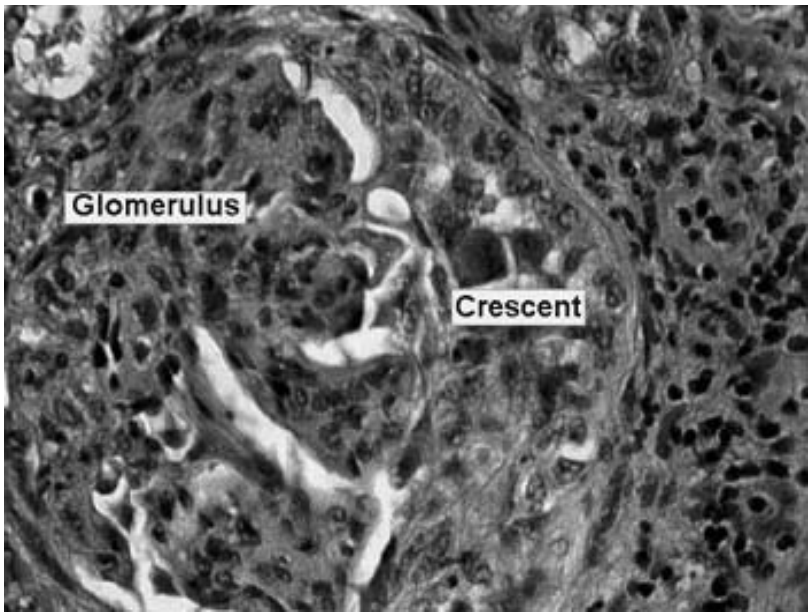
The entire field in this case is composed of the carcinoma. Note how the cells reveal a clear almost empty cytoplasm. These malignant cells contained a lipid droplet at one time, but it was "washed out" during the processing of the tissue. This is one of the most enigmatic tumors we know of. It can metastasize widely, but patients may go for years with it. It often uses the existing vasculature as a framework to grow on. You should see many mitotic figures.

Slide 164: Kidney with rapidly progressive glomerulonephritis



Again, I think you can appreciate the inflammatory infiltrate just by noting the focal and diffuse blue staining of the interstitial tissue. However, the most important finding here is the microscopic observation of the epithelial crescents within Bowman's space.

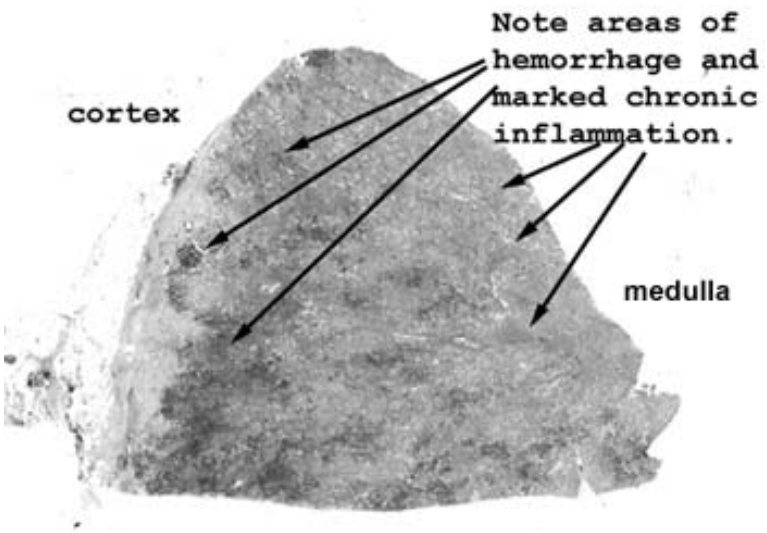
Your observations



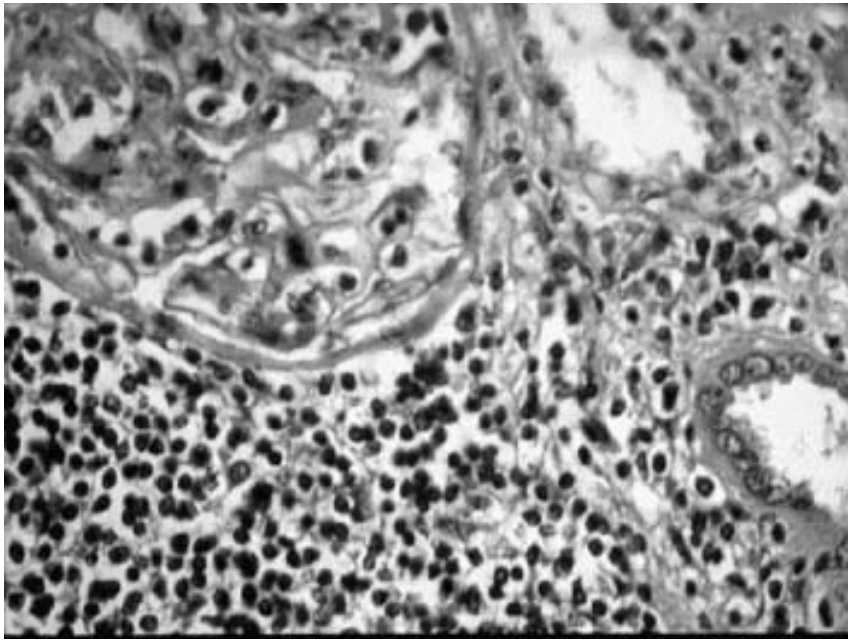
The hallmark of this disastrous condition is the proliferation of the parietal epithelium of Bowman's capsule. The proliferating cells grow into the shape of a "crescent" and may largely replace the space. The crescent is ONLY an indicator of the profound damage to the basement membrane. I doubt that the crescent itself contributes much to the progression of the disease. You should find evidence of marked glomerulonephritis in virtually all glomeruli.

Slide 175: Kidney with host vs graft reaction

Your observations



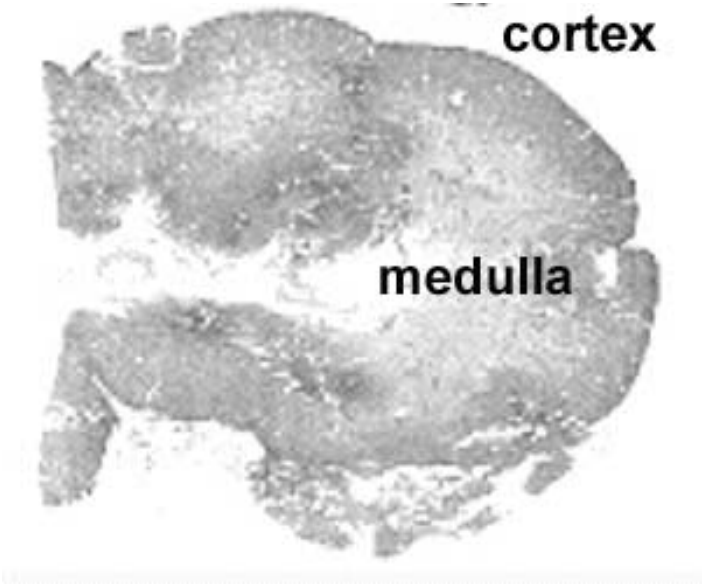
There should be no trouble seeing the disastrous changes of rejection in this slide. Note here the areas of hemorrhage and the diffuse blue coloration indicating the profound inflammatory infiltrate.



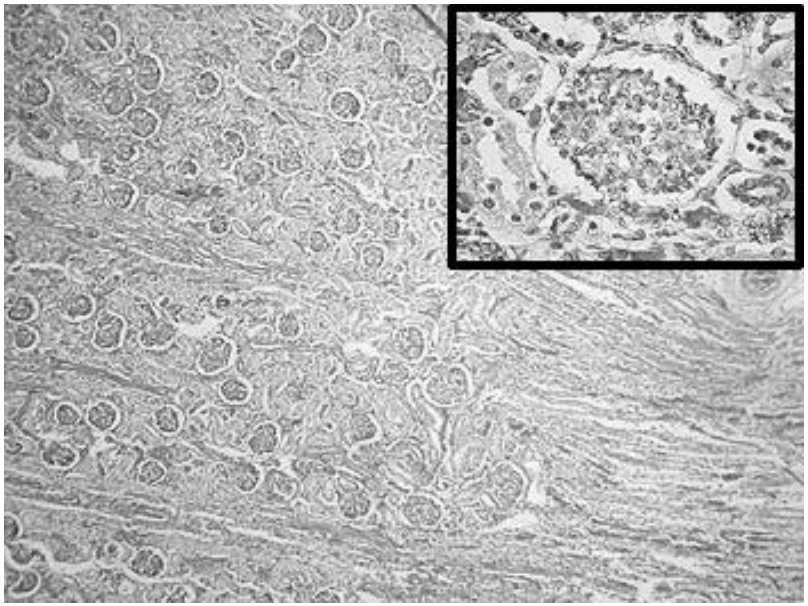
Look in the interstitial tissue and especially around the smaller blood vessels for the inflammatory infiltrate. This is a higher power view of one of the foci of inflammation and shows one of the smaller arteries with the characteristic inflammatory infiltrate.

Slide 219: 31 week gestational age fetal kidney

Your observations

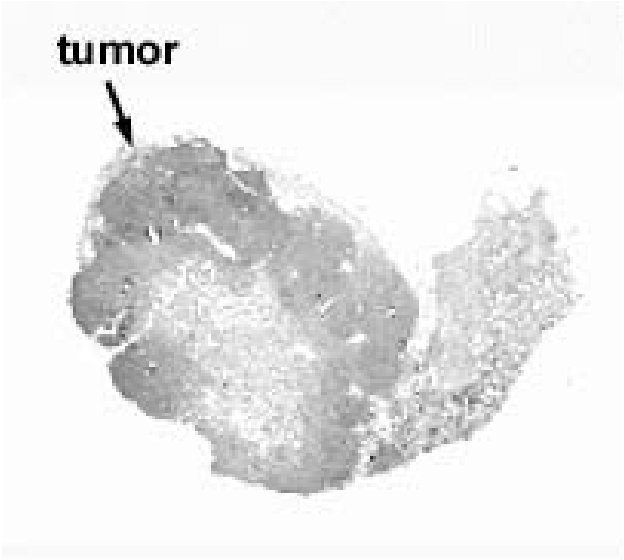


This is a section of fetal kidney, there's no particular pathology, it just shows third trimester renal development.

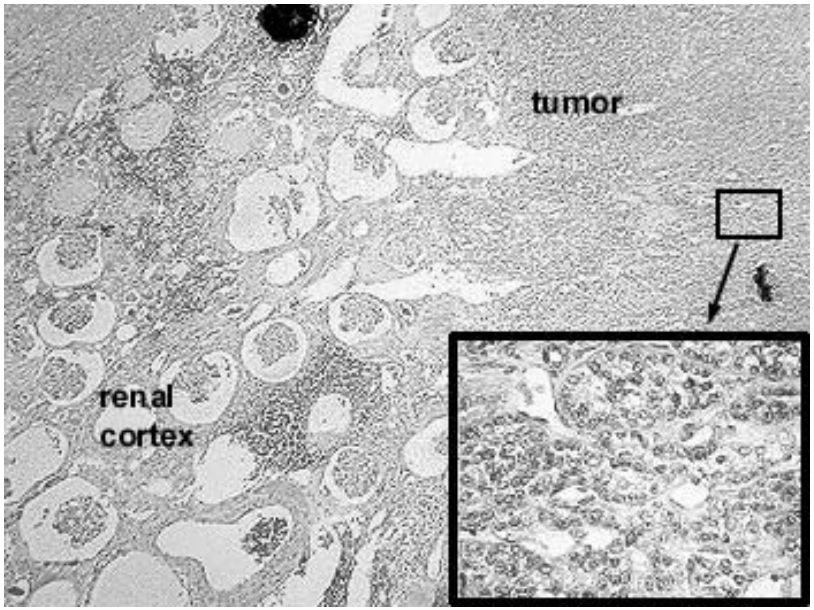


Slide 220: Kidney, papillary adenoma with chronic pyelonephritis

Your observations



This is kind of a perplexing slide. The adenoma is off to the left of the picture and rather marked chronic pyelonephritis is on the right. You will probably be able to see the thyroidization even without the microscope.



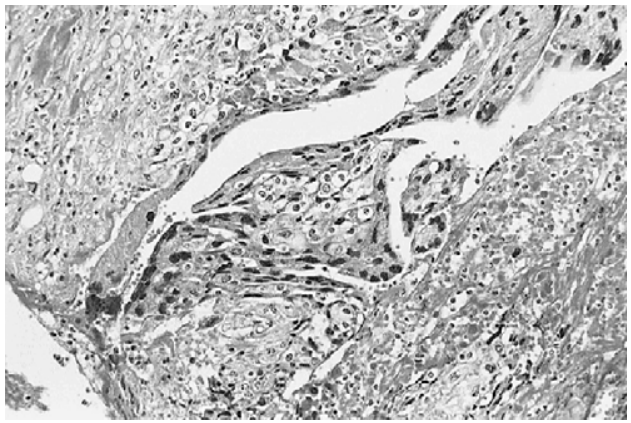
This will have the appearance of an adenocarcinoma, but the word is it's actually an adenoma. The cell of origin is the tubular epithelium and that's why the cells tend to group themselves into little tubes or rosettes. I doubt you will count any mitoses and the nuclear morphology is pretty bland.

General and Systemic Histopathology
C601 and C602

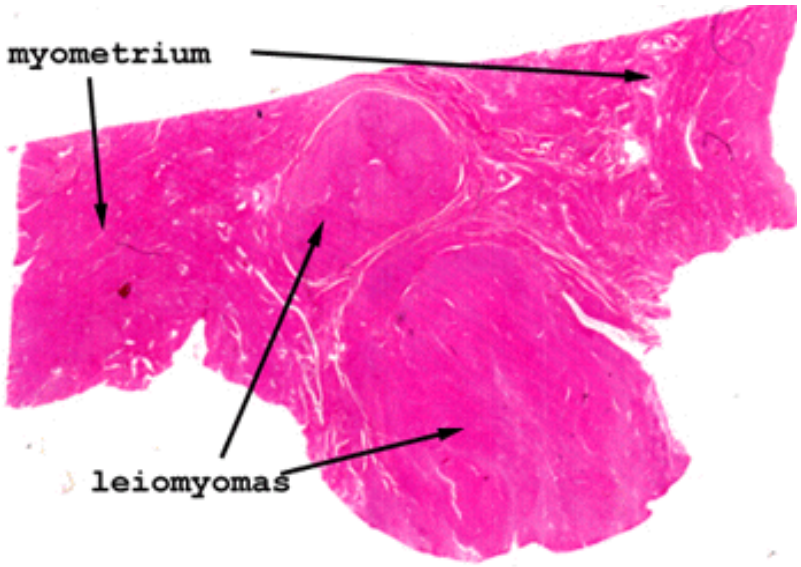
Section 10 *Reproductive System Diseases*

The reproductive unit is fairly sizable, but then it includes both male and female reproductive disorders. Obviously, study the parts that apply to the section we are on at the time. As is probably evident by this time, we have tried to include representative examples of common disease processes. I suspect by now you can recite these categories in your sleep, and perhaps you do. I am talking about the really big groups of disease, such as: infectious, neoplastic, traumatic, autoimmune injury, nutritional etc. In the case of pathology of the reproductive system, we will focus on infectious and neoplastic processes. Keep in mind that in some situations the two are very much connected. (I am referring to HPV virus and epithelial malignancies of the reproductive system.)

With regard to the male reproductive system, be sure you understand prostatic hyperplasia and cancer, prostatitis, testicular tumors and the difference between orchitis and epididymitis. Female reproductive disorders are a bit more involved. You will need to know about cervical cancer and dysplasia, ovarian tumors (benign and malignant), uterine tumors - both endometrial and myometrial - as well as a peculiar condition known as endometriosis. These conditions represent the basics, and if you master them you should be able to apply your knowledge to other related processes. Good luck.

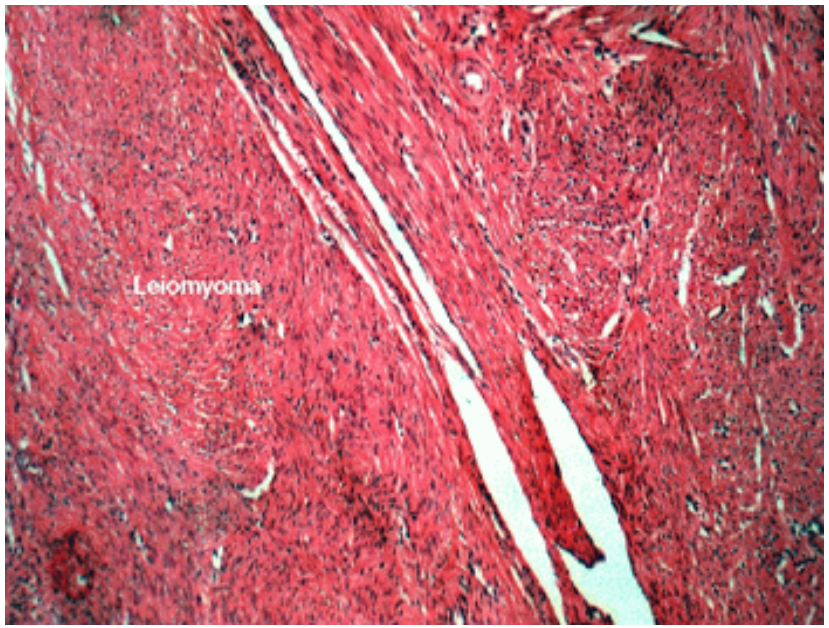


Slide 34: Uterus with leiomyoma



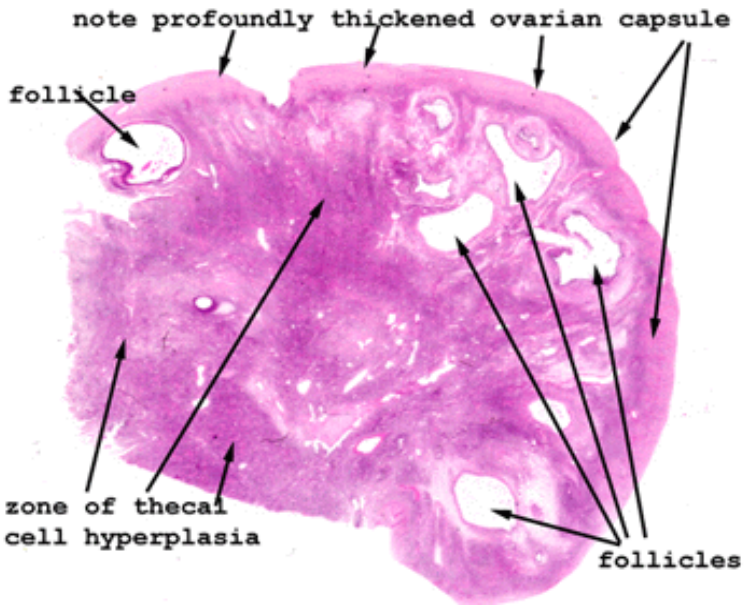
The multiple nodules of this benign smooth muscle tumor are readily apparent in this scan of the tissue. Be sure to look for a capsule and observe the whirl-like and interlacing quality of the clusters of cells.

Your Observations



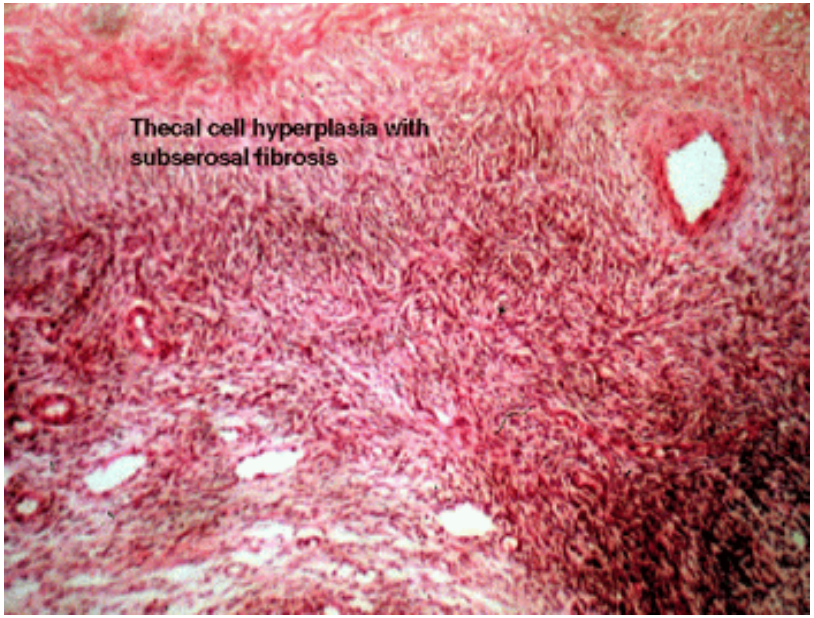
The picture pretty well says it all. You should look at this slide on a white or lighted background first to find the area of the tumor. This is a benign smooth muscle tumor and microscopically the cells are essentially identical to their "normal" counterparts in the surrounding myometrium. Look for the blunted ends of the elongated nuclei to distinguish these cells from fibroblasts. There should be no mitotic figures and no significant nuclear atypia.

Slide 37: Ovary with Stein-Leventhal Syndrome



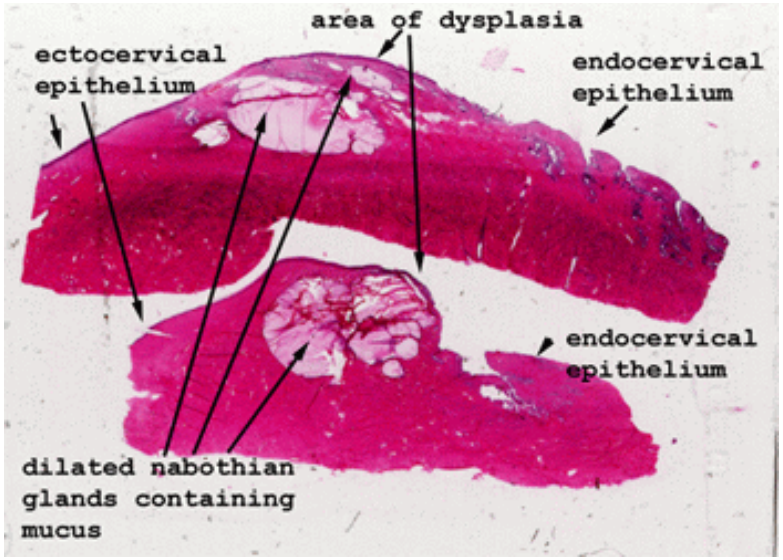
In this case it's probably easier to see the nature of the problem without the microscope. The scan at the left shows a markedly thickened capsule and many large and somewhat distorted follicles. Essentially, no eggs are making it out of this ovary. What do you think the consequences of the thecal cell hyperplasia are?

Your Observations



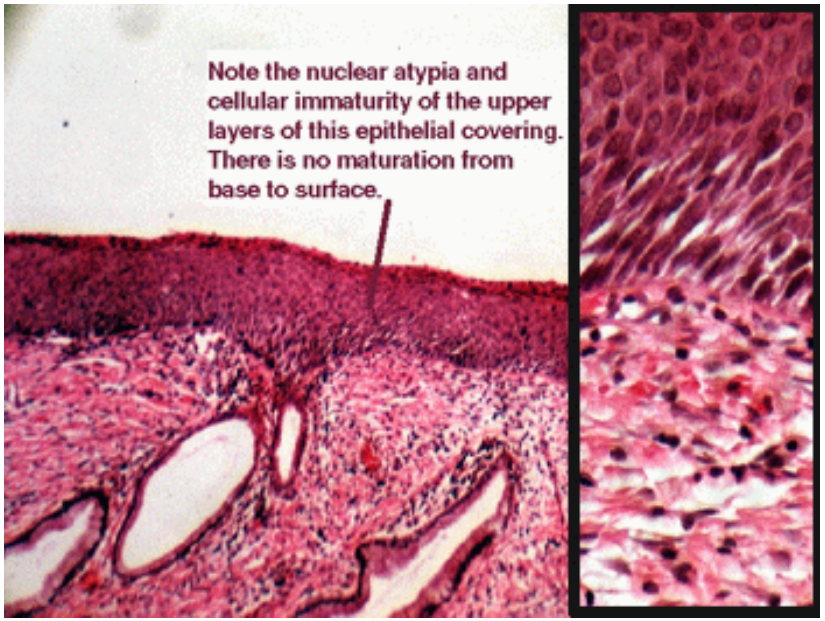
Here you will see a very thickened "capsule" in this ovary. This capsule in essence "traps" the developing eggs. There is no appreciable inflammation and no cellular atypia. You will see generalized areas of thecal cell hyperplasia. There are small follicles fairly deep in the ovarian stroma. See what you can find out about the physical appearance of women with this disorder. How might the appearance be explained in light of the changes in the ovary?

Slide 61: Cervical dysplasia



This can be a confusing slide if you don't get oriented first. In the scan at the left you can see both the endocervical and ectocervical regions. The big dilated cystic, mucin filled glands in the middle are glands of Naboth. We see these either in the endocervix or at the endocervical-ectocervical junction. Use them as a landmark to tell where you are. If you see squamous epithelium over these glands, it almost always represents squamous metaplasia. In this case, there's dysplasia as well.

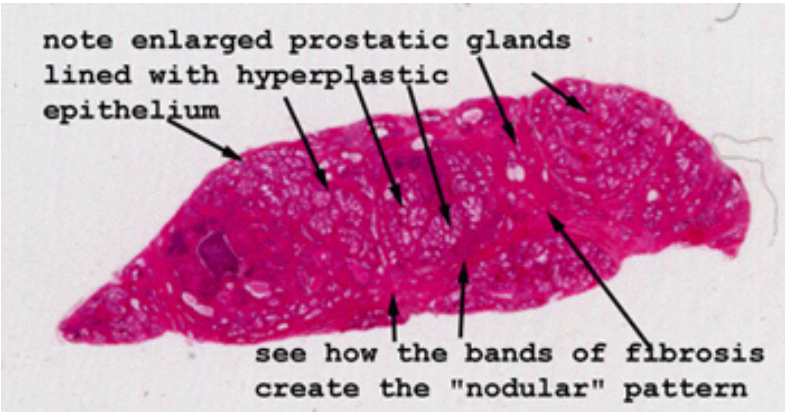
Your Observations



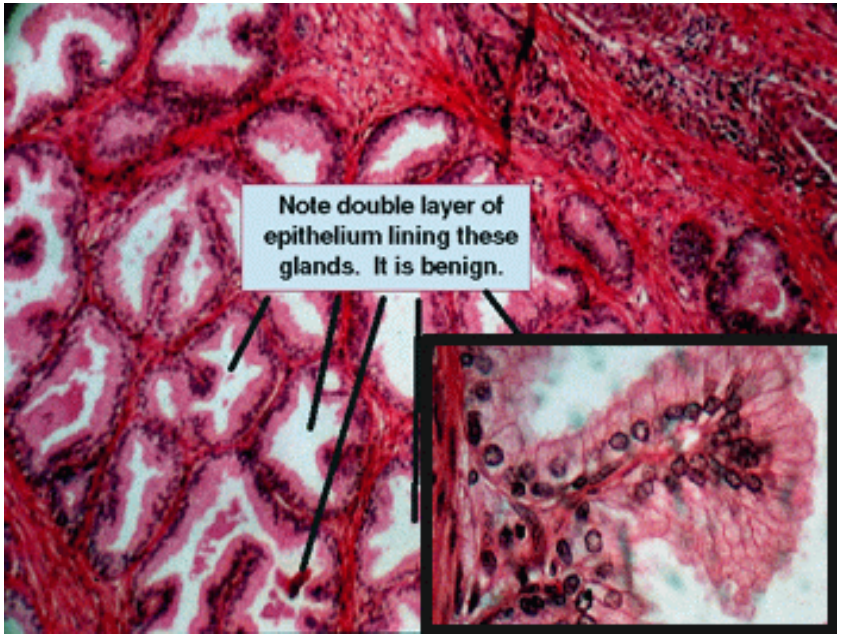
This picture pretty well says it all. This condition is viral in nature and some of the viral serotypes are known to be associated with the development of cancer. You will see immature basilar cells carried far up into the epithelial covering. There are many mitoses as well as generalized atypia of the nuclei. These change can look pretty disturbing on a PAP stain.

The right side of the image is a higher power view of the surface epithelium. Look for the immature basilar cells carried far up into the epithelial covering. There are many mitoses as well as generalized atypia of the nuclei.

Slide 85: Prostatic hyperplasia



Here you can easily see how the prostatic tissue is expanded with the mucin secreting glands. Note the fibrous tissue septal divisions. You are likely to see a number of lymphocytes within the stroma.

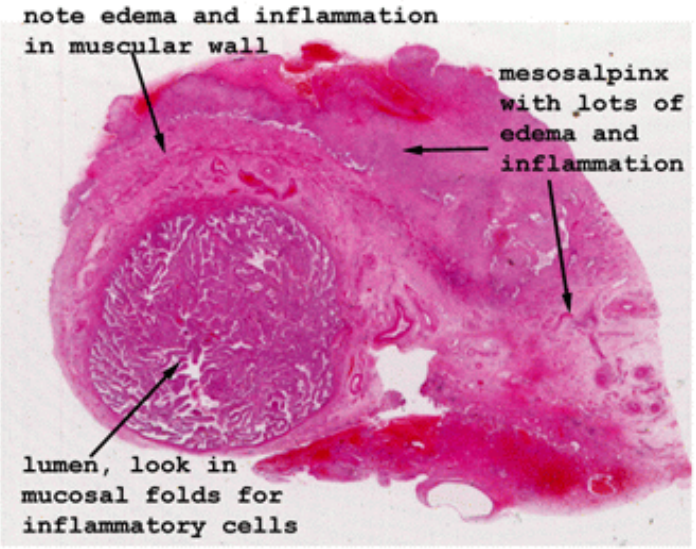


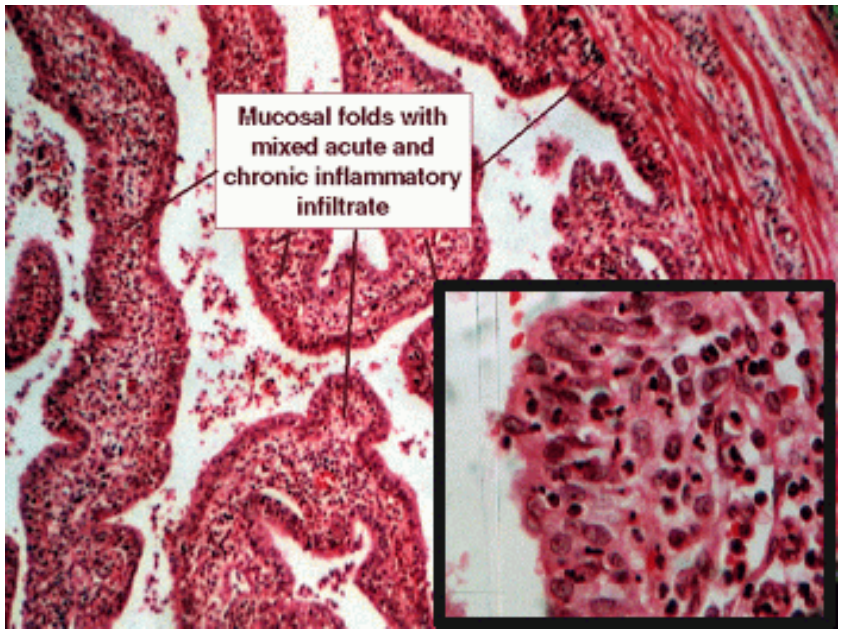
Note the serrated borders of the prostatic glands with the "piled up" and hyperplastic epithelial covering. You should be able to see a DOUBLE layer of epithelial cells in all the glands and there should be no mitoses. You will likely see some chronic inflammation in the interstitial tissue. Remember, this slide is almost certainly from an old man and more than one condition may be present.

The insert at the bottom right of the image shows a high power view of this benign proliferative process. Remember, look carefully for the double row of epithelium and note the absence of gland-within-gland pattern.

Your Observations

Slide 86: Fallopian tube with acute salpingitis





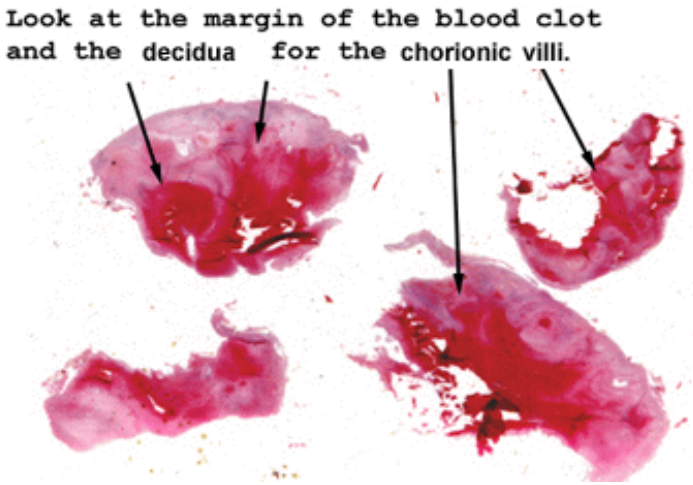
Look at how profoundly edematous all aspects of this fallopian tube are. We are going to focus on the mucosal folds, but the inflammatory features are present throughout this specimen.

Note the thickened and inflamed mucosal folds. You should see many acute inflammatory cells in both the wall of the fallopian tube itself and submucosal tissues. You might want to compare this sample to a normal slide to see how really thickened the wall and the mucosal folds are. This is most likely due to a bacterial infection although it could be chlamydial.

The insert in the lower right-hand corner shows a high power view of one of the mucosal folds. Here you can see the acute inflammatory infiltrate within the mucosal fold itself.

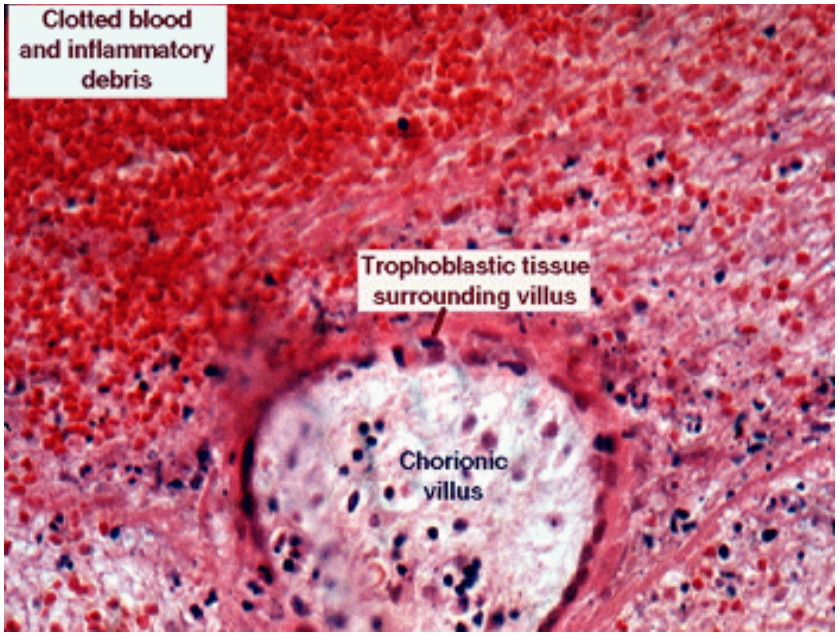
Your Observations

Slide 94: Uterine contents with chorionic villi



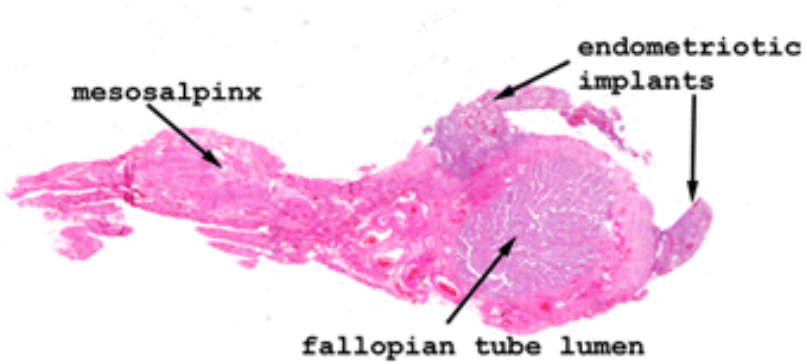
This is tissue from a spontaneous, first trimester abortion. There is a lot of inflammation and necrosis within the fragments of decidua. Look in the blood clot for the chorionic villi. You will not find them in the pink staining decidualized endometrium.

Your Observations



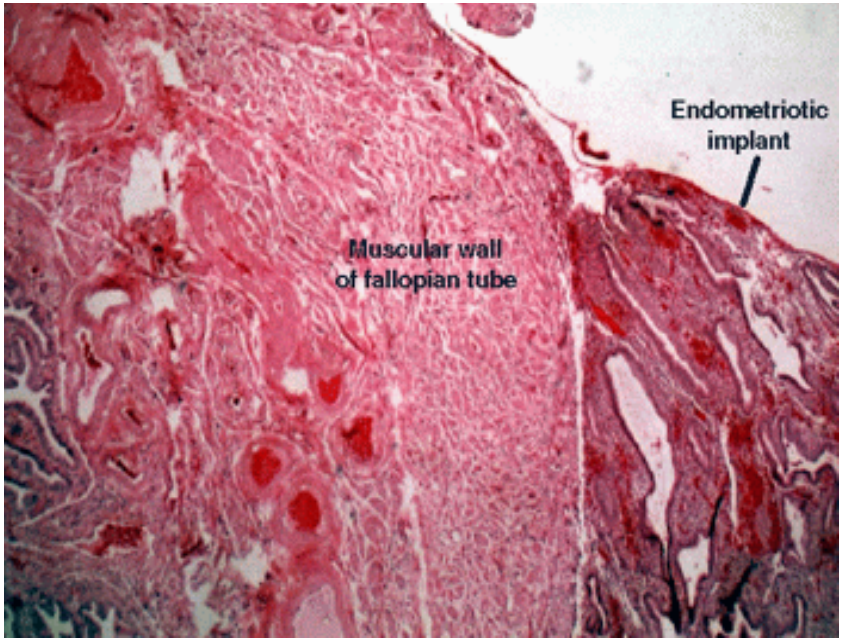
The chorionic villi are few and far between. This specimen is mostly blood clot but that's the way these specimens are. The villi should be small and fairly regular in shape and surfaced with both syncytiotrophoblasts and cytotrophoblasts. There will be lots of inflammation and necrotic debris. This is a spontaneous abortion and I do not know why the pregnancy was lost.

Slide 136: Fallopian tube with endometriosis



Endometriosis is a curious condition. One sees benign endometrial glands and stroma being seeded into the abdominal cavity and every now and then into the abdominal skin, particularly around the umbilicus. It's not malignant, but it sure gets around. The problems really come for the woman with this condition when she experiences her regular menstrual cycle. These foci bleed and under go some degree of necrosis and as you can imagine will cause a heck of a localized inflammatory reaction. These folks are in a lot of discomfort.

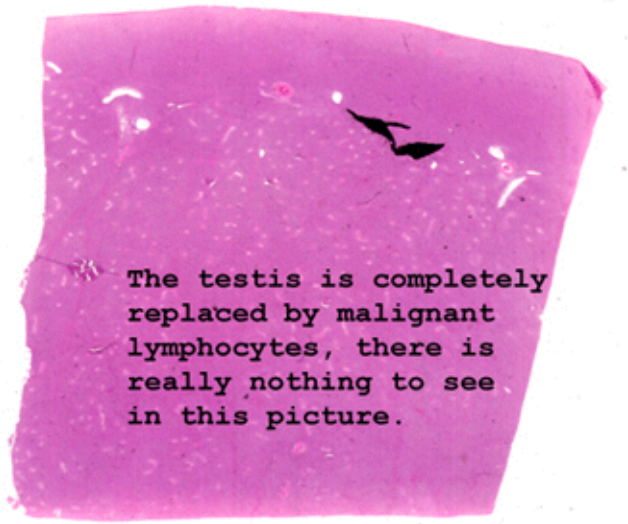
Your Observations



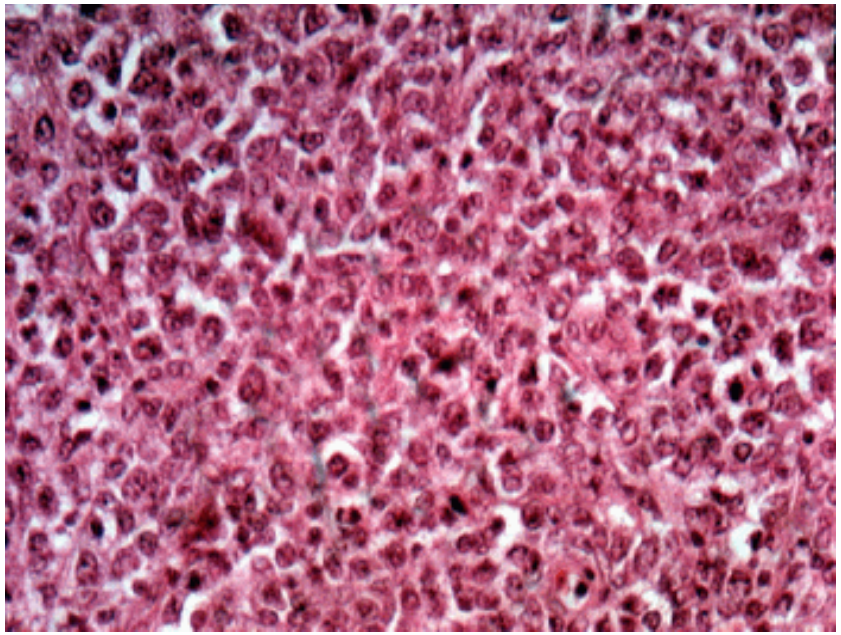
You will find benign endometrial glandular and stromal elements attached to the serosal surface of this fallopian tube. This is a very frequent problem which may lead to infertility because of the marked degree of scarring and deformity that occurs secondary to the repeated bouts of hemorrhage and inflammation at the implant site. We see it most commonly on the serosal surface of the abdomen and associated abdominal organs. But sometimes it can appear in the most unexpected places, such as in the skin around the umbilicus. How do you think this condition develops? What about the symptoms?

Slide 146: Testicular lymphoma

Your Observations



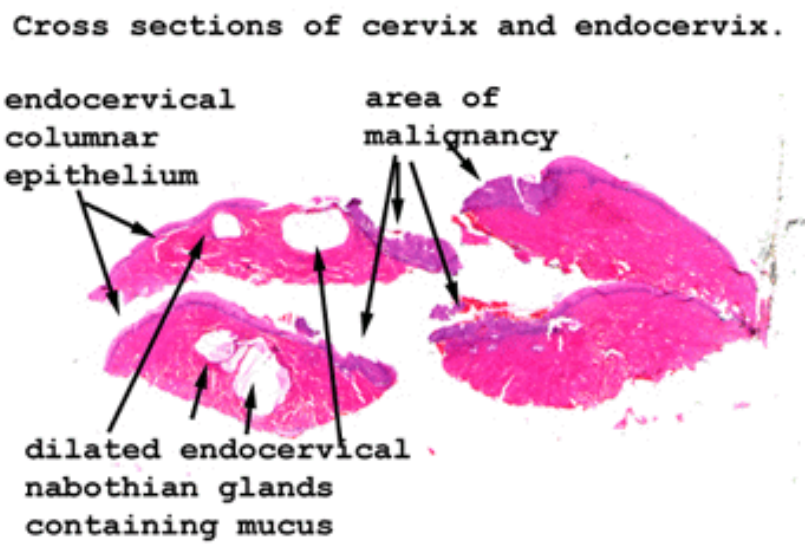
This slide is pretty much all malignant lymphocytes and I don't think there is anything even resembling testis. No, I'd never give you something like this as a quiz slide. Do the best you can with it.



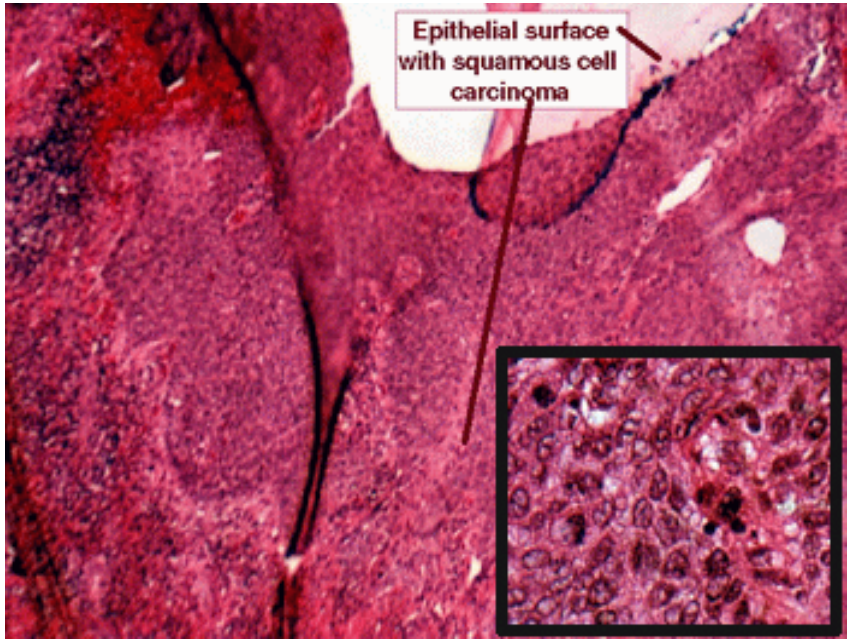
It would be impossible to tell the tissue source from the picture I have taken. Note the uniform infiltrate of monotonous lymphocytes throughout the entire specimen. Again, the object here is to be sure this tumor is not an embryonal carcinoma or version of seminoma, two common primary lesions of the testis. The treatments are completely different. Use this slide for comparison when studying the other testicular tumors we are about to see.

Slide 153: Squamous carcinoma of uterine cervix

Your Observations



As with slide 61, it's best to get the tissue oriented before going to your microscope. The dilated Nabothian glands should serve as a marker for the endocervix. The malignancy is on the ectocervical side. Can you identify areas of invasion?

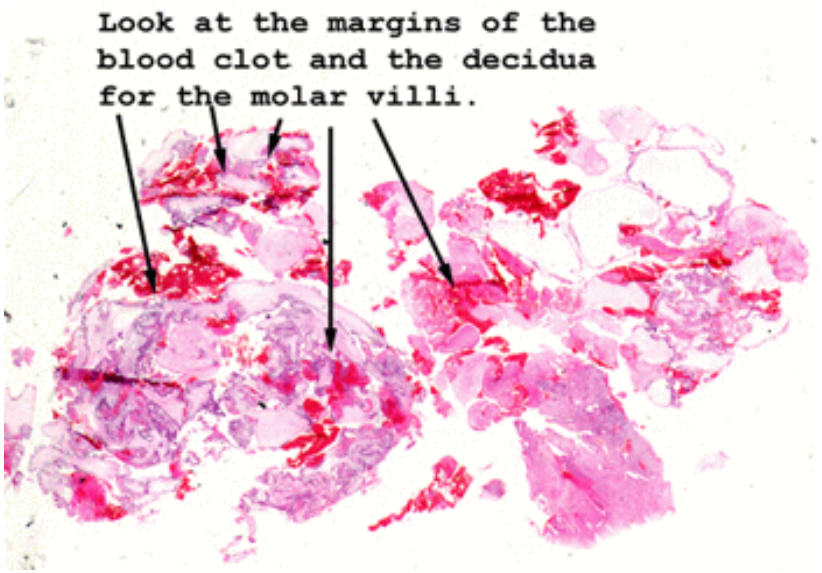


In this case, the cancer is not only in the mucosa, but can be found in the superficial lymphatics as well. Note the marked degree of nuclear anaplasia in the epithelial cells that are very close to the actual surface of the mucosa. There is no maturation at all. You should see numerous mitotic figures. There will be some inflammation which may obscure the process in some areas. Scan this with low power so you know where to concentrate your efforts.

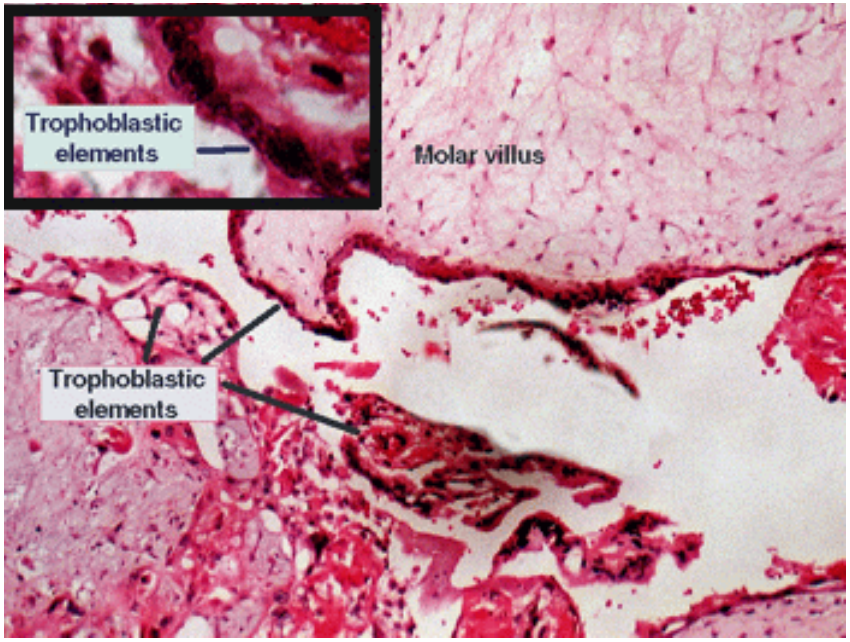
The insert shows a high power of the cytology of the malignant cells. Note the numerous mitoses and marked cytoatypia of the cells.

Slide 155: Hydatidiform mole

Your Observations



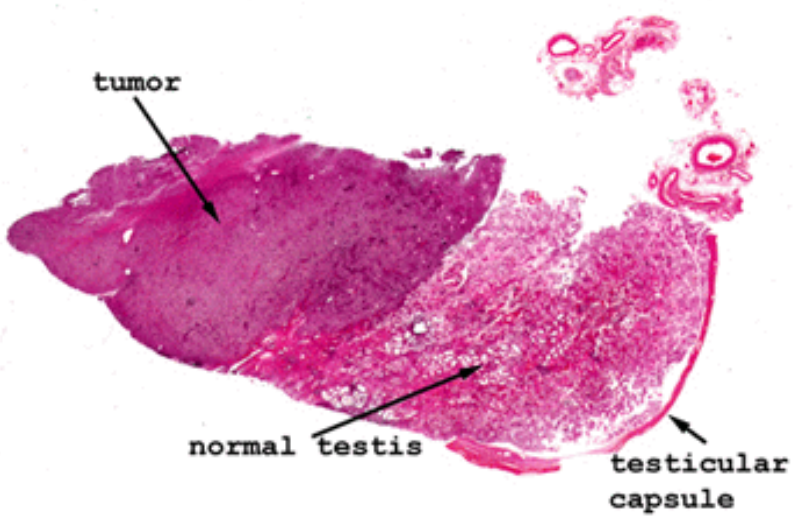
Look in the blood clot or at the margin of the clot and decidualized endometrium for these bizarre villi. You might want to compare these placental villi with those of the first trimester miscarriage in slide 94. There is quite a difference. Take note of the changes in the trophoblasts covering the villi.

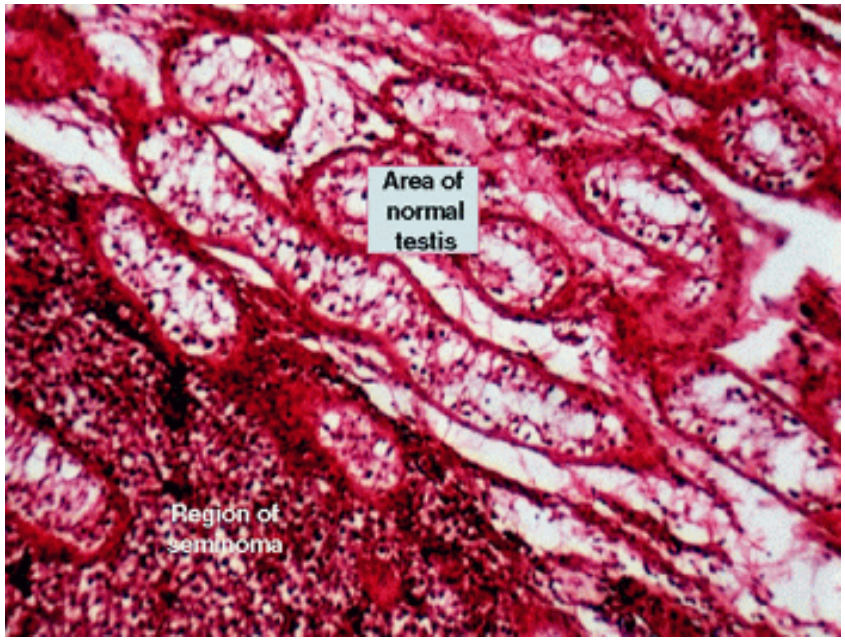


This is a classic "molar pregnancy." Note the large and abnormally shaped villi with edematous cores. These villi are covered with atypical trophoblastic cells growing as a syncytium. You may see a mitotic figure or two, but on the whole, the degree of anaplasia is not nearly as great as seen in a choriocarcinoma, the highly aggressive malignant counterpart of this lesion. There will be some necrosis and inflammatory debris mixed with the blood clot, but for the most part this is well preserved and very representative.

The insert, upper left-hand corner, details the trophoblastic elements.

Slide 162: Testicular seminoma



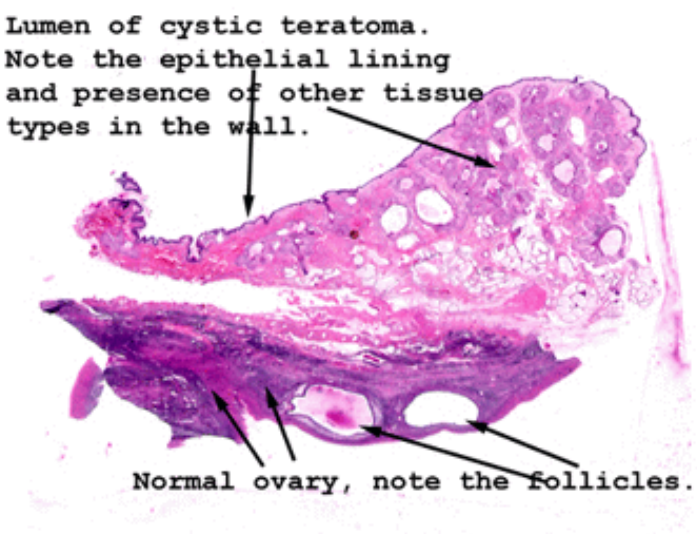


This scan shows quite nicely the area of tumor with the normal testis at the edge. See if you can recognize a tubular arrangement of the malignant cells. There will be a rather marked lymphocytic infiltrate as well. Sometimes this lymphocytic element is so pronounced that these tumor are occasionally mistaken for lymphomas.

This picture shows mostly normal testicular parenchyma with only a little tumor at the edge. Note the "watery" appearance of the cytoplasm of the malignant cells and their slight off center vesicular, "fried egg" looking nucleus. You may see the cells in little clusters something like seminiferous tubules. You will see the cells are very monotonous and bear some resemblance to lymphocytes. Because there is often a significant lymphocytic infiltrate along with this lesion, it is sometimes hard to distinguish from a testicular lymphoma. You will see some mitoses, and possibly some embryonic tissues mixed with the seminomatous elements.

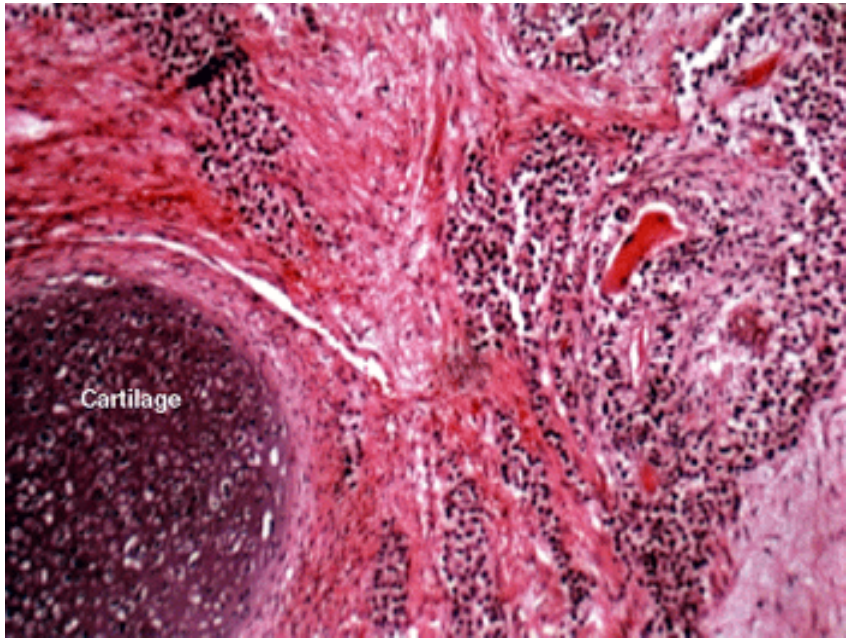
Your Observations

Slide 163: Ovarian teratoma



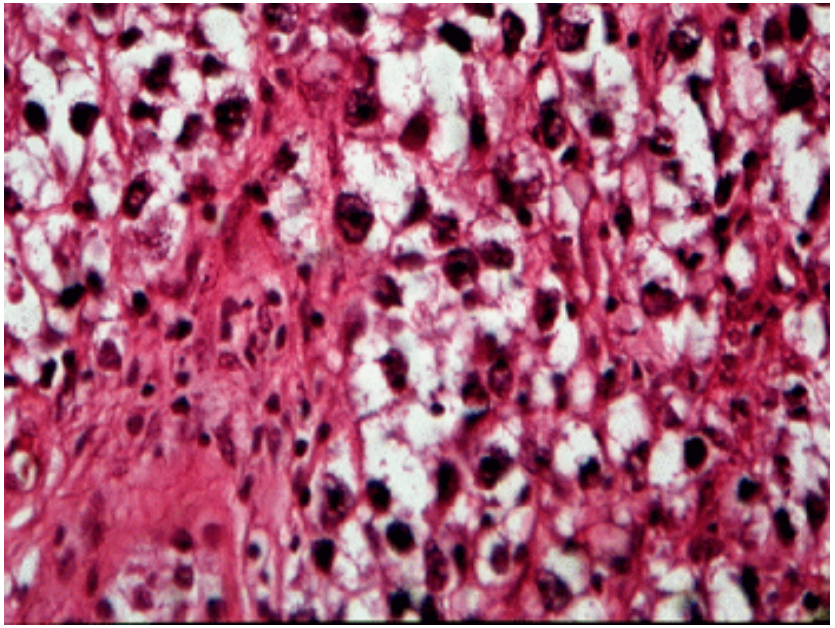
This picture nicely shows a portion of the ovary compressed at the edge of the cyst. The cyst lumen would be at the top of the picture. Note the many different kinds tissue in the wall of the tumor. Remember, this a benign lesion.

Your Observations



In this field you see some mature cartilage intermixed with other elements. These lesions are typically formed of benign tissue elements of all three embryonic germ layers. The most common constituent is skin, including both epidermis and dermis, but some of your slides include bowel and respiratory mucosa, and a few sections even had cerebellum. This degree of tissue diversity is probably not surprising given the origin of the tumor. Although these lesions are almost invariably benign in females, the testicular counterpart in a man is generally malignant.

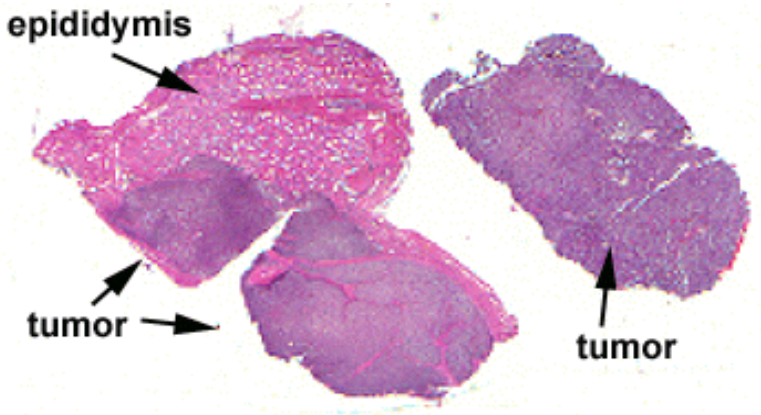
Slide 176: Lymph node with metastatic seminoma



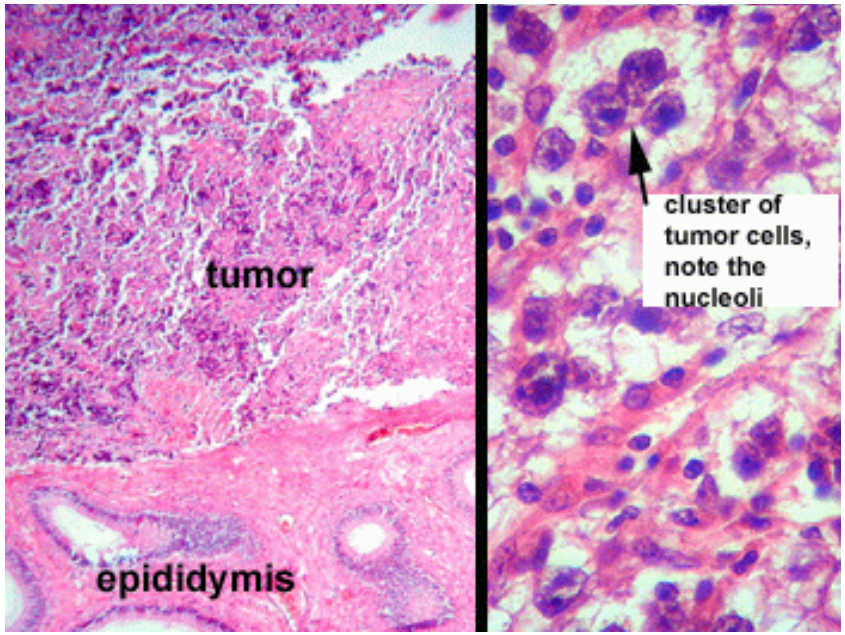
The seminoma cells may not be as easy to see as you think. Some will be very large and have vesicular nuclei and others may seem to disappear right into the lymphocytic background. The node is largely replaced so practically everywhere you look you should see tumor. Some of the smaller cells may resemble lymphocytes, a feature that sometimes makes it hard to diagnose if only a very small portion of the node is replaced. You have other such tumors in your set to compare this one with.

Your Observations

Slide 177: Seminoma of testis



In this slide there isn't a lot to tell you what the organ is. The epididymis should be recognizable, but I doubt there is an identifiable testicular tissue**.** Most of the section consists of the seminoma.

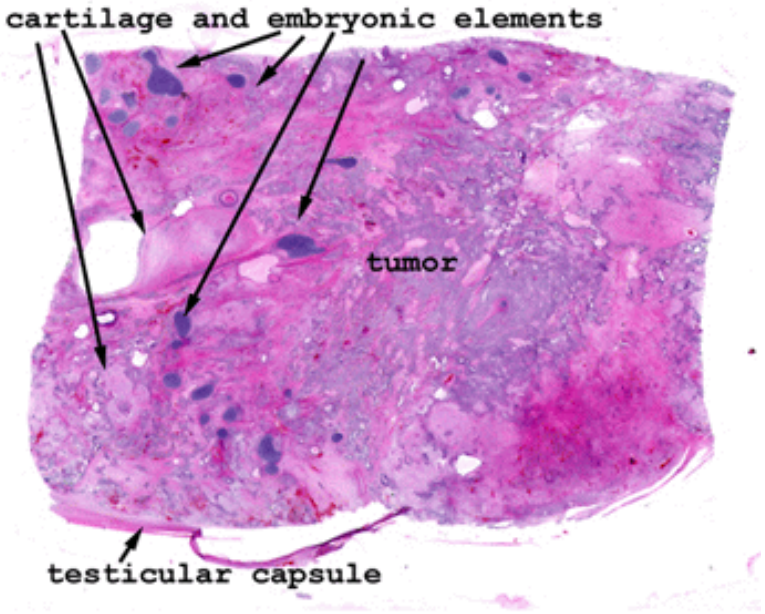


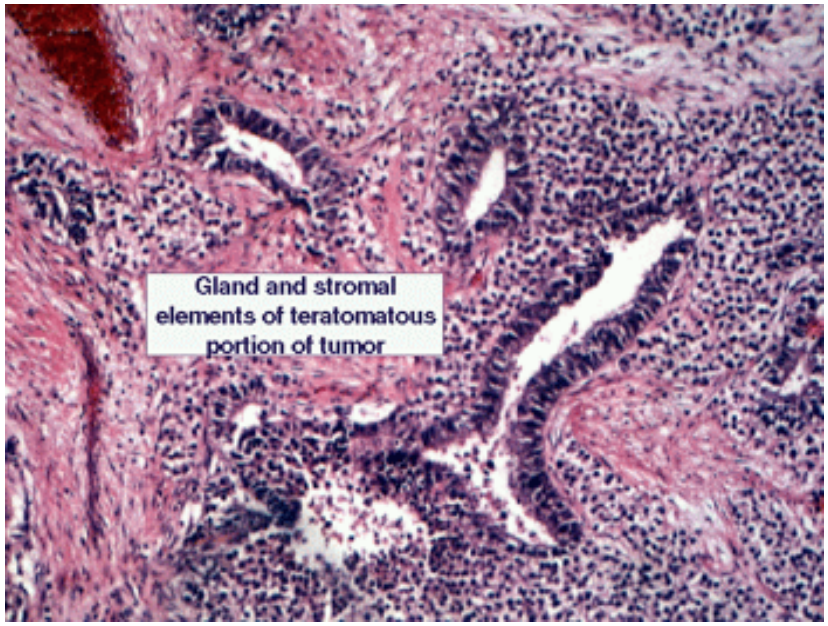
This split frame image pretty well shows it all. The tumor cells appear as very immature cells that one might see in the basal most layer of the seminiferous tubules. The nuclei are extremely large and many have gigantic nucleoli. The tumor cells are seen in clusters and you should see many lymphocytes within the tumor and the bands of fibrous tissue that divide it.

Where else can seminomas develop?

Your observations

Slide 178: Mixed lineage carcinoma of testis





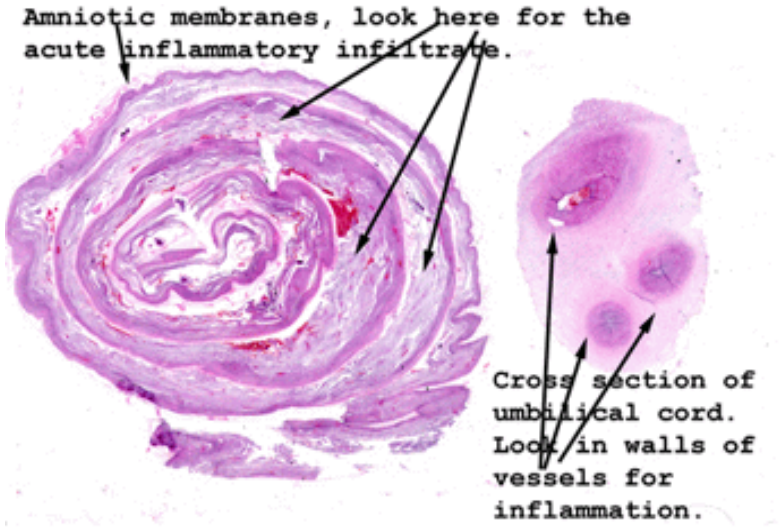
Even without any magnification you can see the tremendous variation in tissue types in this slide. I am not too sure you'll find much in the way of normal testis.

Note the multiple tissue types in this tumor. The picture reveals several gland-like structures lined by a columnar epithelium. There is an intervening stromal material composed of mesenchymal elements that look very embryonic and undifferentiated. This "embryonic" appearance gives rise to this lesion's name. You will see some mitoses and areas of necrosis with accompanying inflammation. In some of the slides, elements of a seminoma are also present.

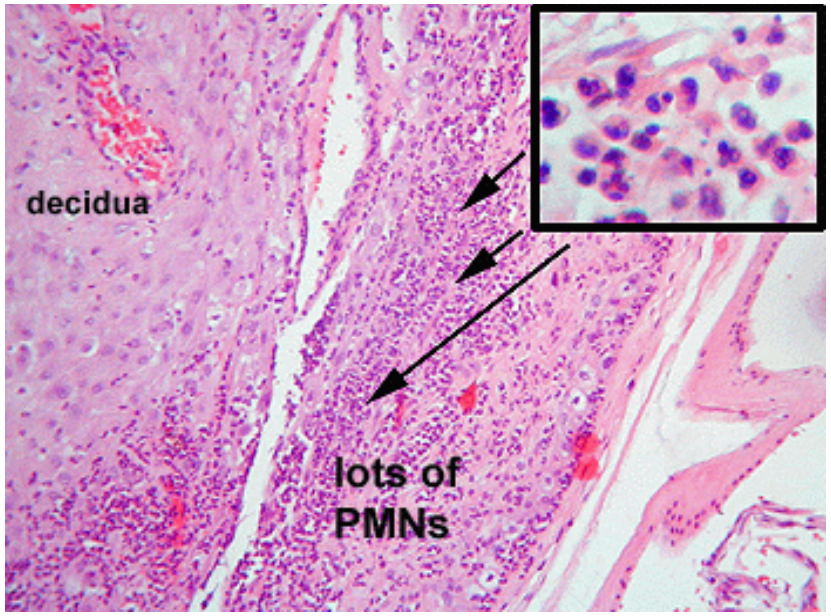
Your Observations

Slide 181: Amniotic membranes and umbilical cord with acute amnionitis

Your Observations

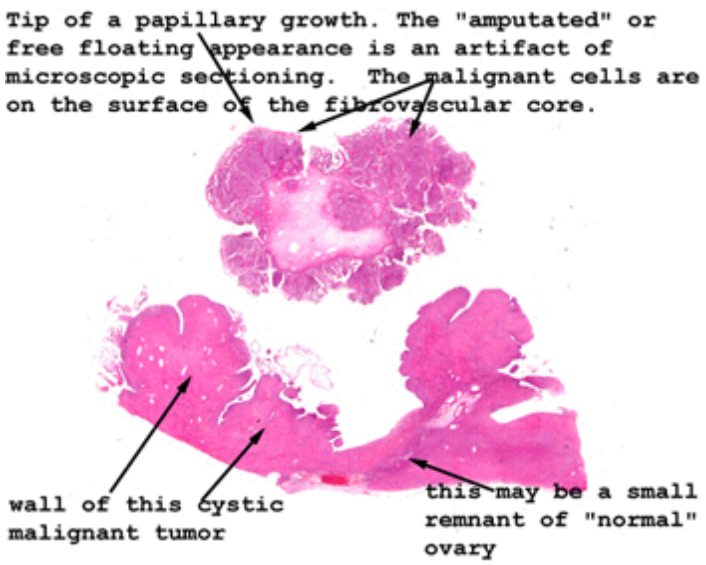


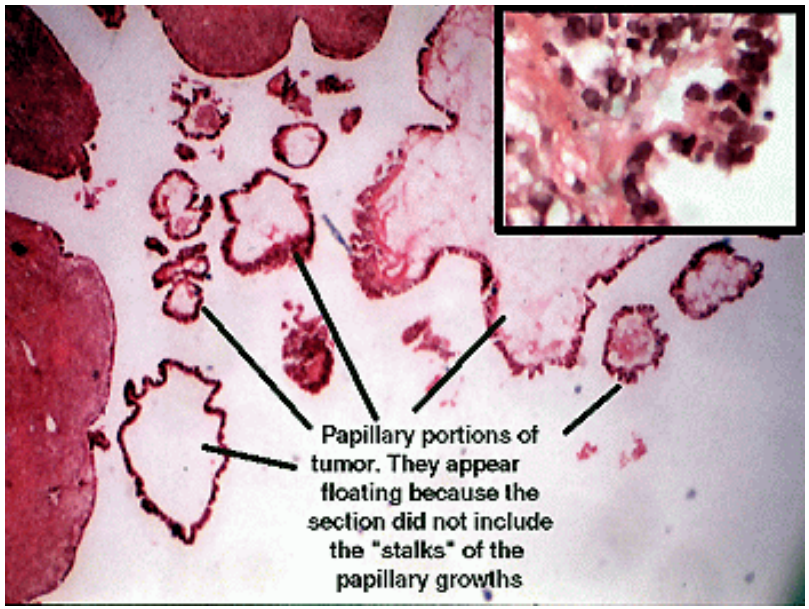
The coiled up thing to the far left is a section of amniotic membrane. Look at the margin of the membrane and the decidua for the acute inflammatory infiltrate. In the case of the umbilical cord, the acute inflammatory cells will be found in the walls of the vessels.



Here we see the great number of PMNs in the decidualized endometrium and amniotic membranes. Under normal circumstances, there should be none. The inflammation is due to an infection resulting from the prolonged period the amniotic membranes were ruptured. If delivery of the baby is very prolonged, it could lead to endometritis for the mother and a systemic infection for the newborn.

Slide 192: Ovary with papillary adenocarcinoma





Your slide consists of a very small strip taken from the wall of a very large cystic tumor. Don't waste a lot of time trying to find normal ovary, I'm not sure there is any.

The malignant epithelium is found lining the cyst and on the surface of the many papillary growths and extensions. The papillary "head" seen in the picture to the left appears to be "floating" because when the section was cut the stalk connecting it to the wall of the cyst was out of the plane of the section. Trust me, it was connected to the wall.

Look on the surface of this little "head piece" for the best examples of the malignant epithelium.

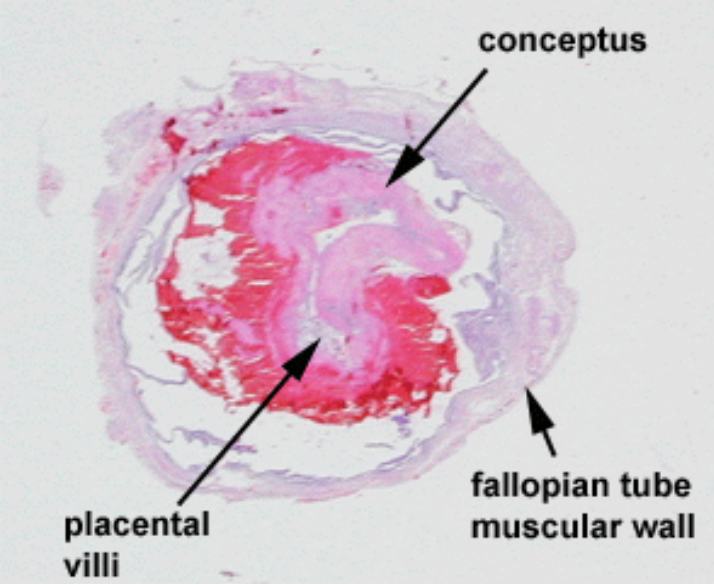
I am not sure how much normal ovary there is on this slide, but trust me it is ovary. The larger papillary projections will have a "detached" and free floating appearance because the microscopic sectioning process has created a "lobbed off" artifactual distortion. This happens frequently with objects that are tall and skinny or pedunculated. This tumor has arisen from the serosal epithelium, can spread widely in the peritoneal cavity and is often bilateral. The cancer cells are on the surface of the papillae.

The insert shows a high power view of the malignant epithelium on the surface of the papillations.

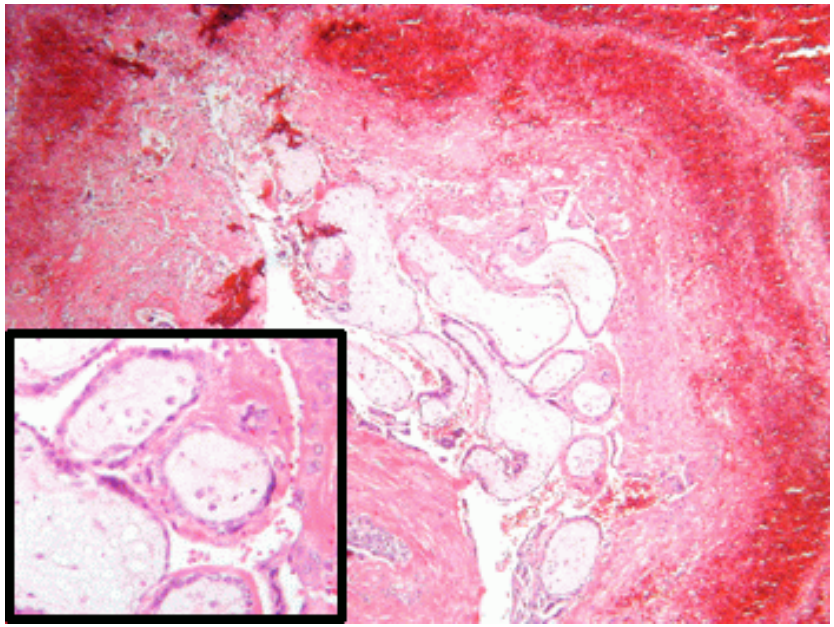
Your Observations

Slide 198: fallopian tube with tubal pregnancy

Your observations



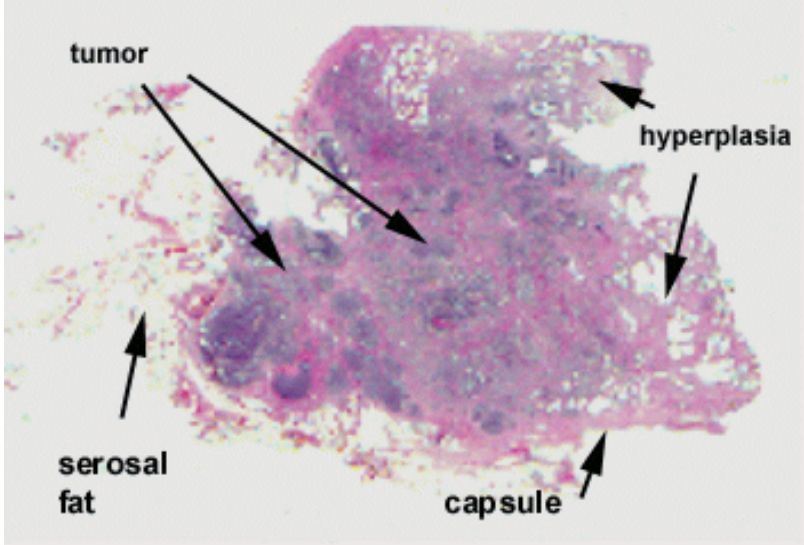
At one time, the conceptus occupied the entire lumen of the tube. You can see the area of fresh hemorrhage that was certainly the source of the pain that made this patient seek medical help. You're not likely to see any fetal tissue here, just the placental villi.



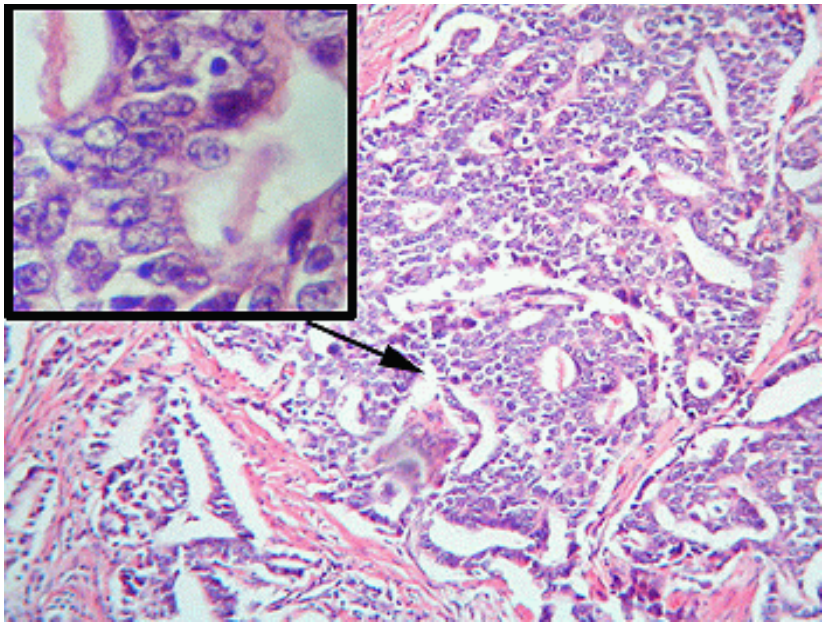
The placental villi within the remains of the conceptus.

Slide 200: Adenocarcinoma of protstate

Your observations



This section of prostate includes both areas of hyperplasia and malignancy. The adenocarcinoma should be obvious. Look for the bluer areas. Note the lobulation. You want to identify the capsule and scan around it looking for capsular invasion and perineural involvement.



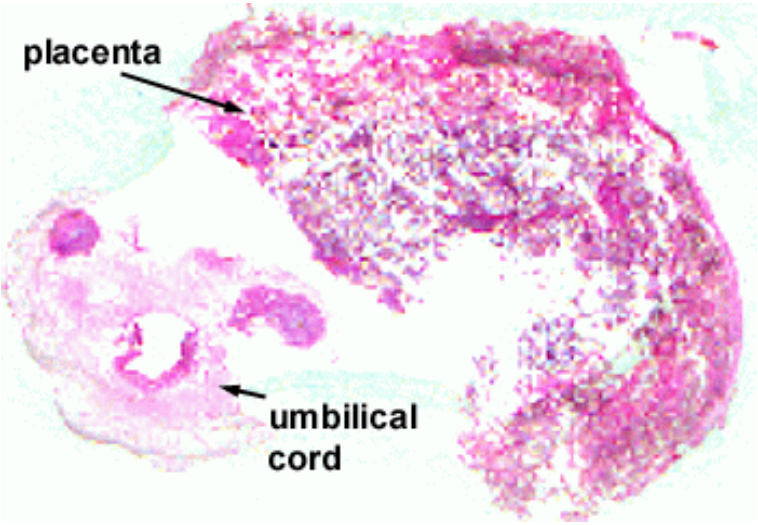
This section nicely shows the famous “gland-within-gland” pattern of the adenocarcinoma. The insert shows the cellular detail from the edge of one of these malignant gland forms. Note the angulation of the nuclear membranes and prominent nucleoli.

Be sure to check the capsule of the gland for invasion and pay attention to the little nerves in the surrounding fat. I don’t recall seeing perineural invasion, but it might be present on your slide.

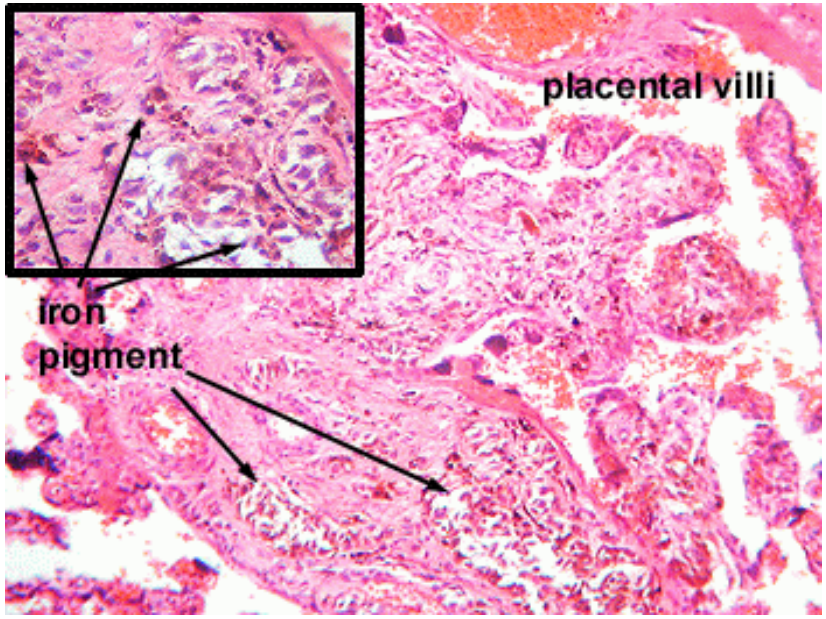
What about PSA? Would you expect it elevated in this case?

Slide 204: placenta, Rh incompatibility

Your observations



This slide includes both a section of placenta and umbilical cord. Look at it all, but the changes will be in the placental villi. We're looking for pigment deposition. It's iron and represents the leftovers from the RBC destruction brought about by the immune hemolytic process. Although this is an example of Rh incompatibility, other RBC antigens can also give rise to this condition. The key factor is that the antibody must be small enough to pass through the placenta and into the child's circulatory system.

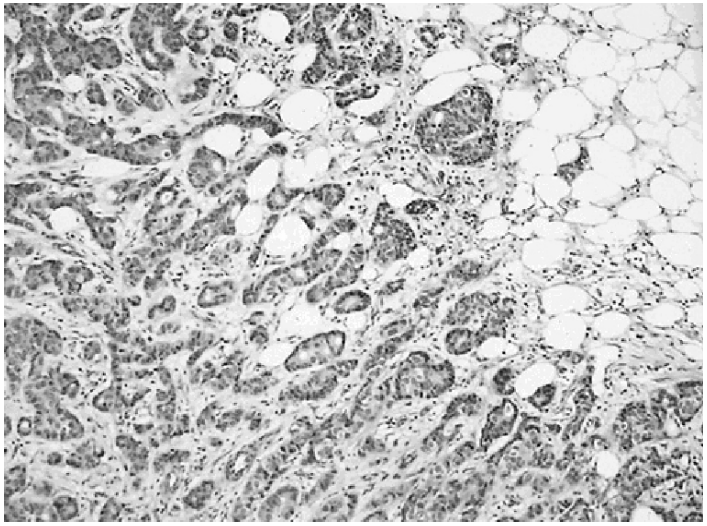


Look at the placental villi of with dark brown pigment; it's iron. This tells us there's been RBC hemolysis.

General and Systemic Histopathology
C601 and C602

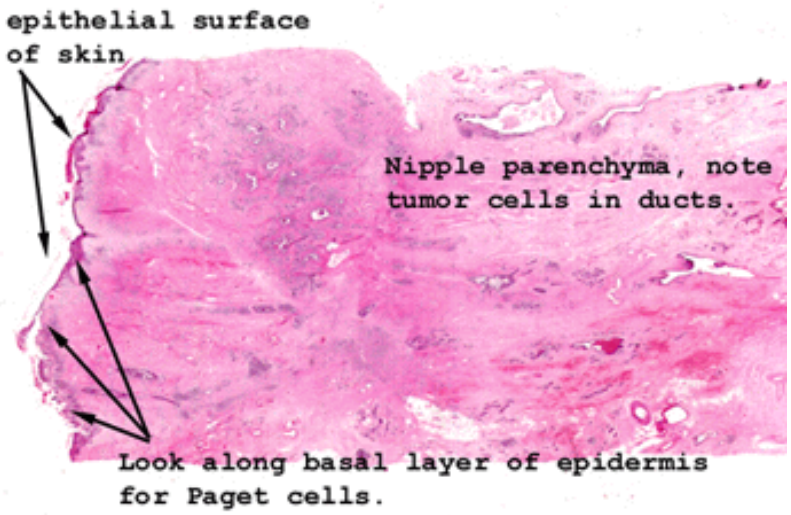
Section 11 *Disorders of the Breast*

Although the breast is subject to every major class of disease, by far cancer is the most significant condition we will study. Still you need to be familiar with inflammatory and traumatic lesions, as well as the common benign tumors. Even today a painless breast mass is often the cause of great concern. Sophisticated imaging techniques have certainly changed the evaluation of a breast lump, still the ultimate answer rests with the biopsy. In this unit we will be looking at conditions that present as masses or at least relatively well defined areas of abnormality. We will see various forms of breast cancer as well as several favorite methods and routes of spread. Although you won't be able to see the famous estrogen and progesterone receptors with the microscope, I might ask you something about them on a slide quiz. Furthermore, don't make the erroneous assumption that breast disease is restricted to women. You want to be sure you know what is meant by the term "gynecomastia" as well as its associated circumstances and agents.

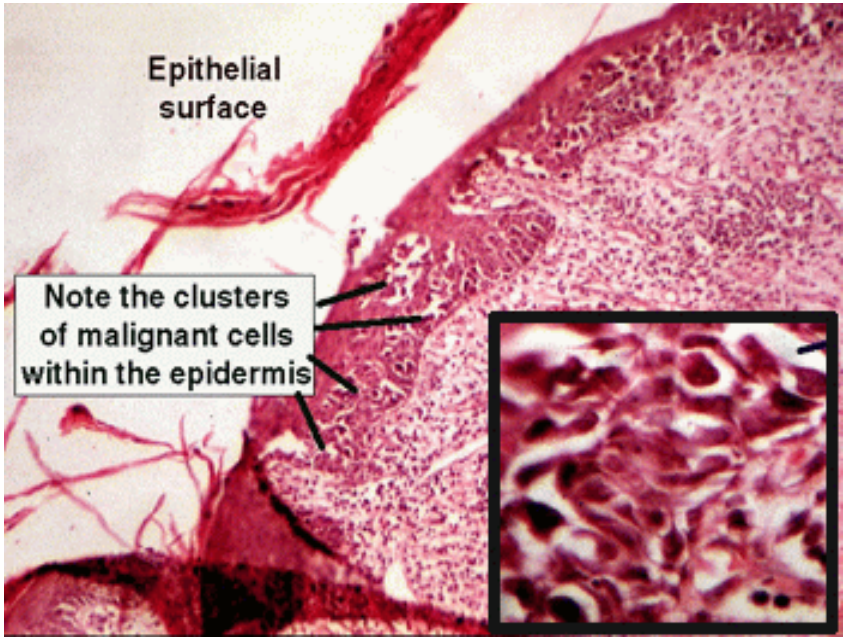


Slide 31: Breast Skin with Paget's Disease

Your observations



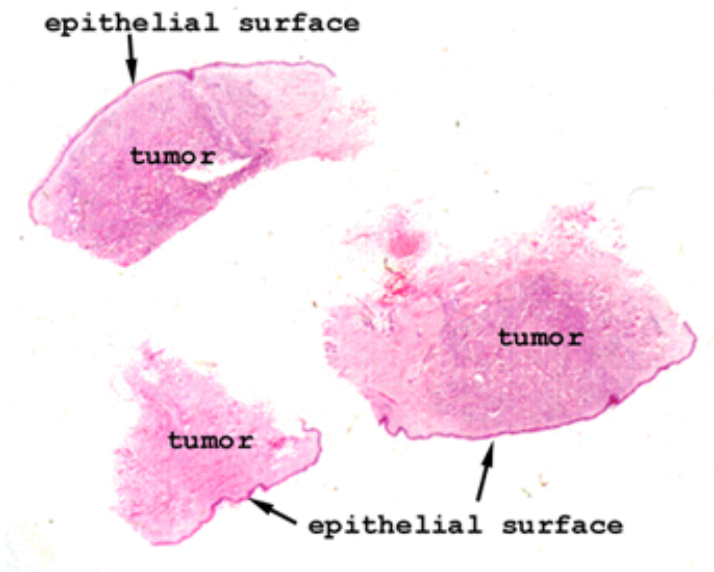
Here we have the condition of malignant duct cells growing up the major excretory ducts of the breast and out into the epithelial covering of the skin. You will actually see clusters of malignant cells in the epithelium itself. Look down in the breast to confirm the malignancy first. Sometimes this can be confused, microscopically with an early amelanotic melanoma. Grossly, this lesion is red and crusted and looks like a little focus of irritation on the nipple or areola.

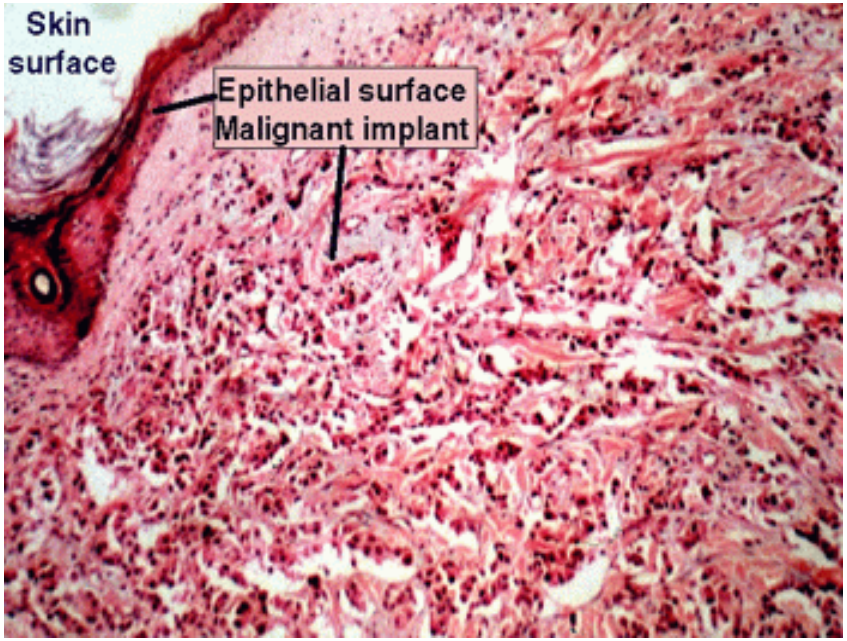


In this you will see clusters of the malignant ductal epithelial cells actually within the epidermis of the skin. These cells may look a bit like non-pigmented melanocytes, but they are indeed from the breast ducts. They have "migrated" along the basement membrane of the major breast ducts to end up in the skin. The cells you see here are not within dermal lymphatics, but rather the actual epithelial surface of the breast itself.

The insert is a higher power view of the clusters of the malignant ductal epithelial cells which have actually migrated upand out of the major breast ducts to proliferate within the epithelial layer of the skin.

Slide 33: Skin with metastatic breast cancer





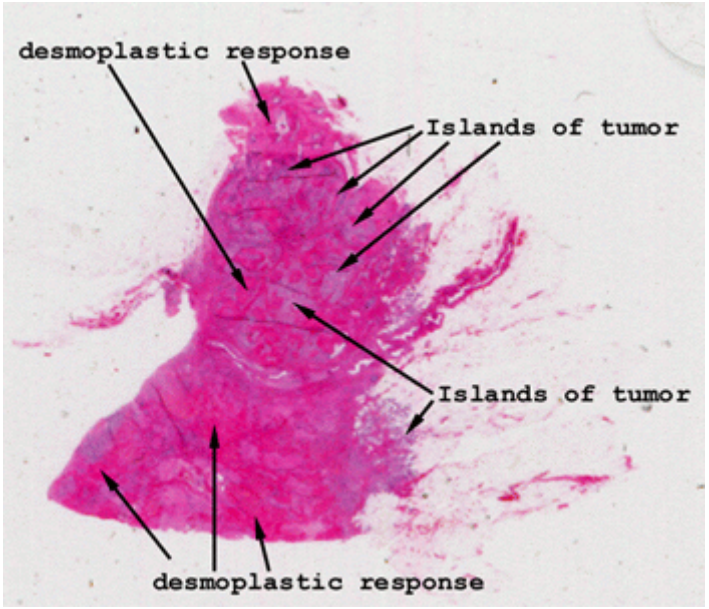
This situation is different from what we looked at in slide 31. here we actually see little dermal implants of metastatic breast cancer, not epithelial spread. These metastases can be from anywhere, unlike the situation of Paget's disease depicted in slide 31, where the spread is by direct continuity to the over lying nipple skin.

Note the difference between this slide and #31. The malignant cells are in the dermis and represent a distant metastases, not a direct "creeping type" spread from the breast ducts below the epidermis. This pattern is more typical of metastatic breast cancer. Take a look for the single file arrangement and "pseudoglandular" organization of this tumor. This pattern is highly characteristic which makes it possible to make a very good guess as to the primary when presented only with the metastatic tumor.

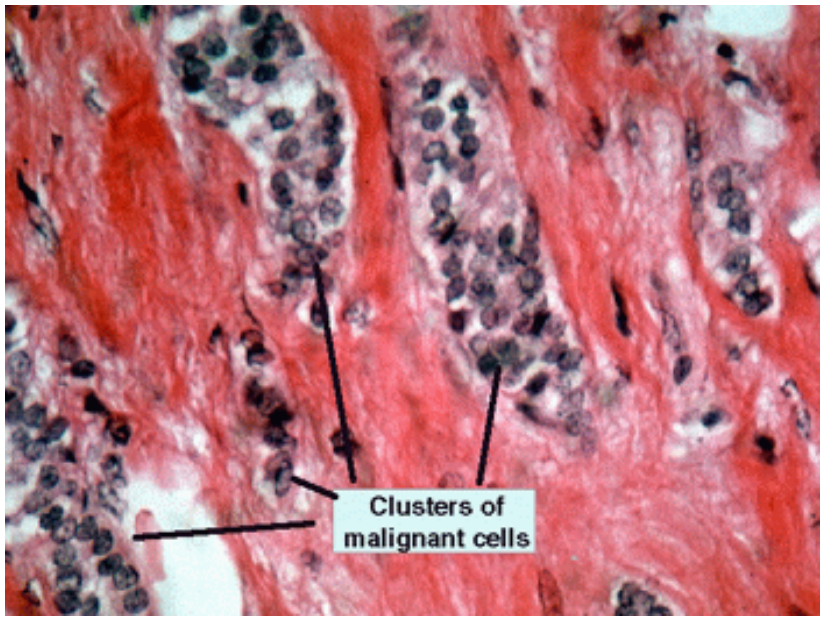
Your observations

Slide 51: Duct cell carcinoma of breast

Your observations

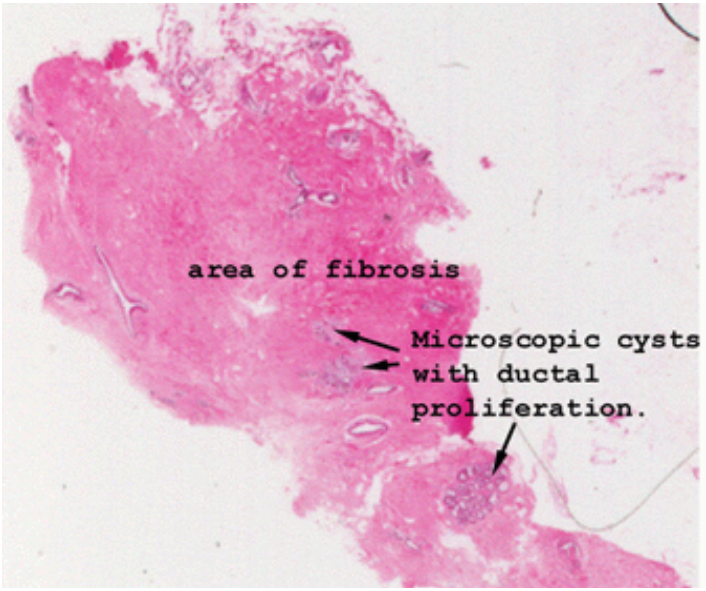


Breast cancer is one of those diseases that can induce a tremendous desmoplastic response. Here you will see many islands and clusters of malignant adenocarcinoma cells with an abundant intervening densely collagenized stroma.



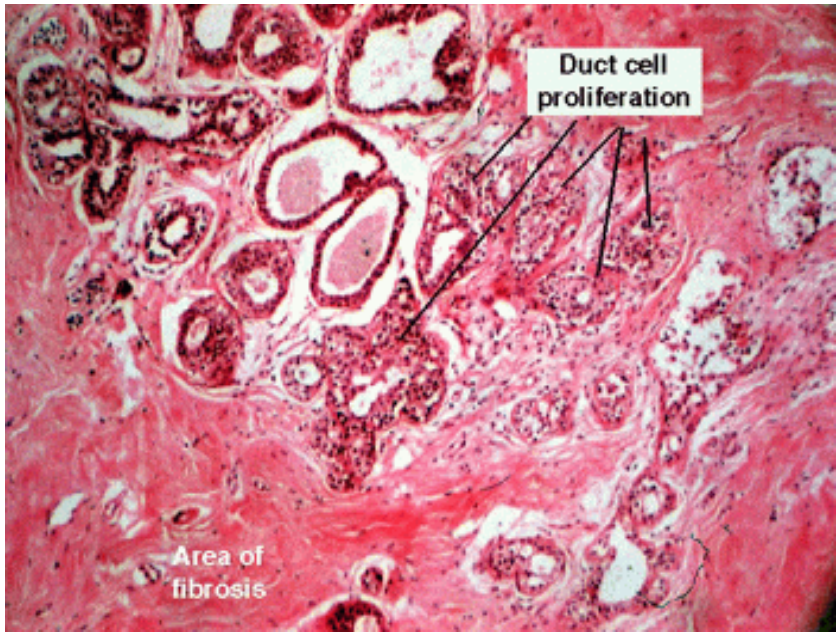
You will see strands, cords and single file ("Indian file") arrangement of the malignant cells in the breast connective tissue. Mitotic figures may be rare. Some gland-like arrangements will be present. There is not a real marked degree of nuclear atypia in these malignant cells, but they are cancer all the same. The single file arrangement is real important in recognizing this tumor. We use this arrangement to help with identification when this tumor has metastasized to a remote site. Note the degree of collagen production in response to this tumor. This is referred to as a scirrhous reaction and sometimes this tumor is referred to as scirrhous carcinoma of the breast.

Slide 73: Fibrocystic disease of the breast



This has got to be the most common condition of the breast leading to biopsy. It can present as a painless mass which is a very worrisome finding. Note the dilated ducts, fibrosis and ductal proliferation in this slide. Even without magnification you can see the smaller ducts, some of which are obviously dilated and contain inspissated material.

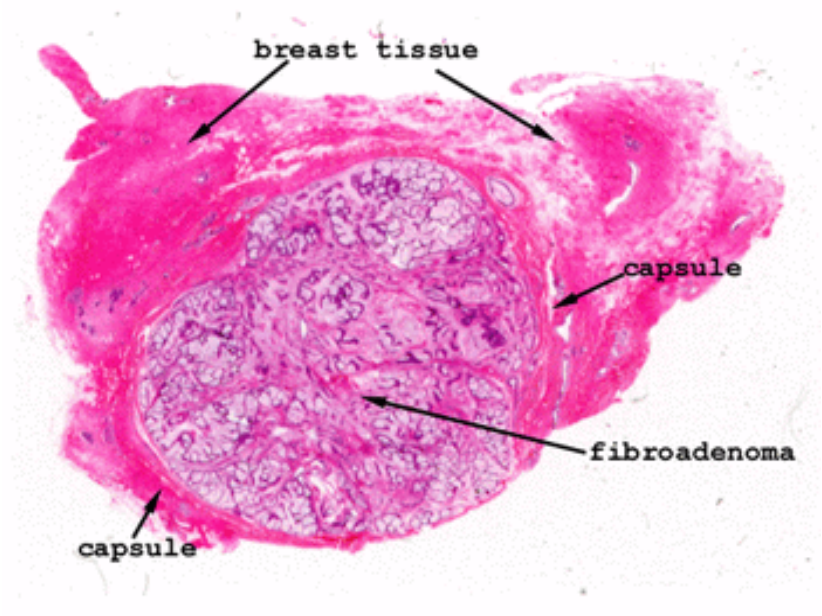
Your observations



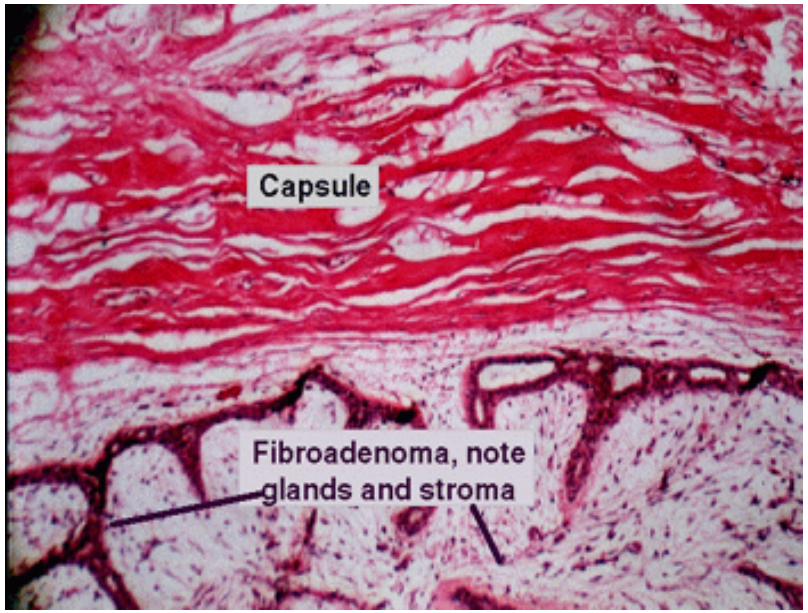
The name says it all with this disease. You should see fibrosis in the breast parenchyma with cystic dilation of the ducts. There will be ductal proliferation in many cases, a feature which is very evident in your sample. You may also see a chronic inflammatory infiltrate in the periductal areas. No changes of malignancy are present in this slide.

Slide 96: Fibroadenoma of breast

Your observations



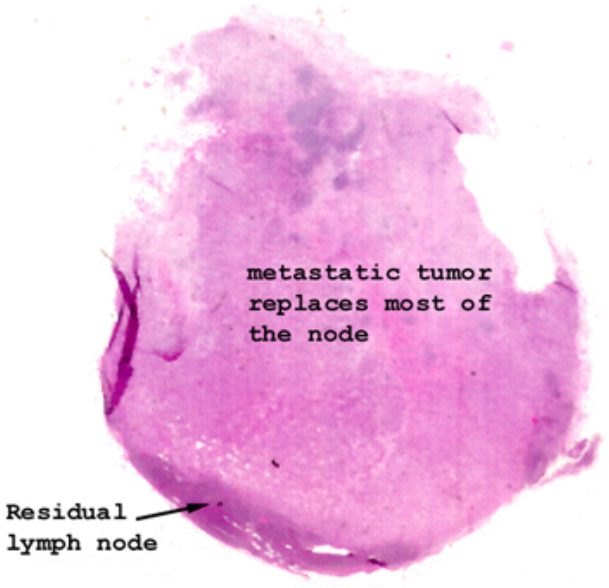
Just looking at this slide on a white background will show practically everything. Note how well circumscribed this lesion is. Here you can even see the glandular slits in the background of loosely woven fibroconnective tissue. These can be seen at any age, but tend to occur more frequently in younger woman. They are probably the most common benign solitary lesion of the breast.



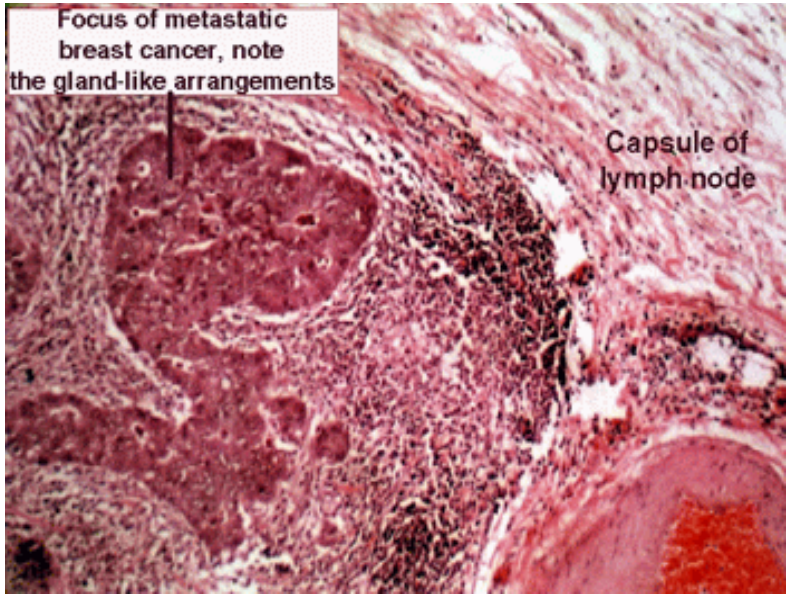
Note the well circumscribed margins of this benign lesion and its "biphasic" composition. You will see benign stroma with "glandular slits," or ducts, lined with benign epithelium. There may be some fibrosis and inflammation just outside the capsule of the tumor. Although this is probably the most common tumor of the breast, and is benign, it causes a tremendous amount of concern. It is, after all, a contender breast mass, and that's a cause of anxiety for every woman.

Slide 111: Lymph node with metastatic breast cancer

Your observations



Here you can see that most of the lymph node has been replaced by the tumor. Only a small amount of the uninvolved node remains along one margin.

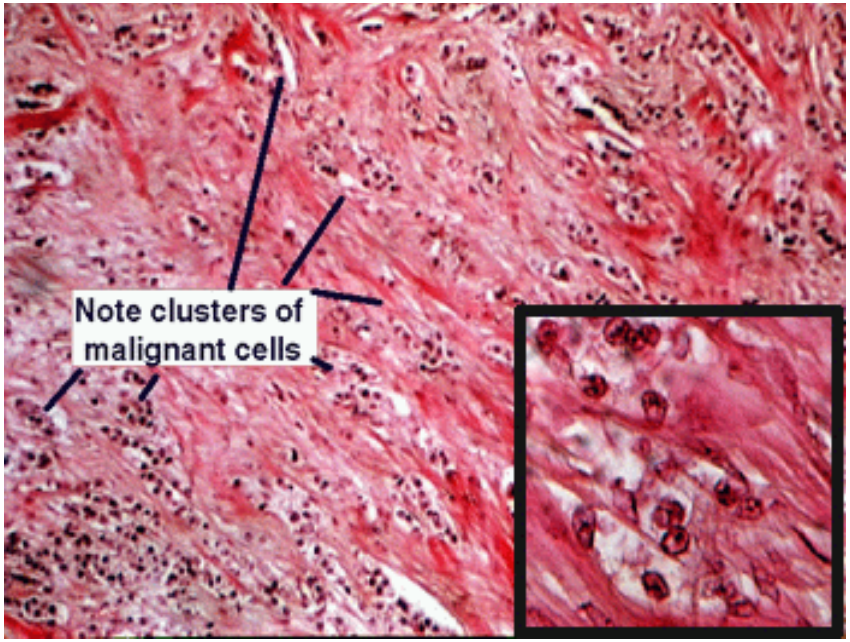


It would be almost impossible to tell just from the histology the source of the primary lesion in this case, but I do expect you to be able to make a good guess. Note the glandular pattern. See if you can tell where the tumor made its first invasion of this node.

Slide 158: Invasive duct cell carcinoma of the breast

Here we see a primary breast cancer, it just happens to be located near the skin surface. The typical features of a scirrhous carcinoma of the breast are present in virtually every field.

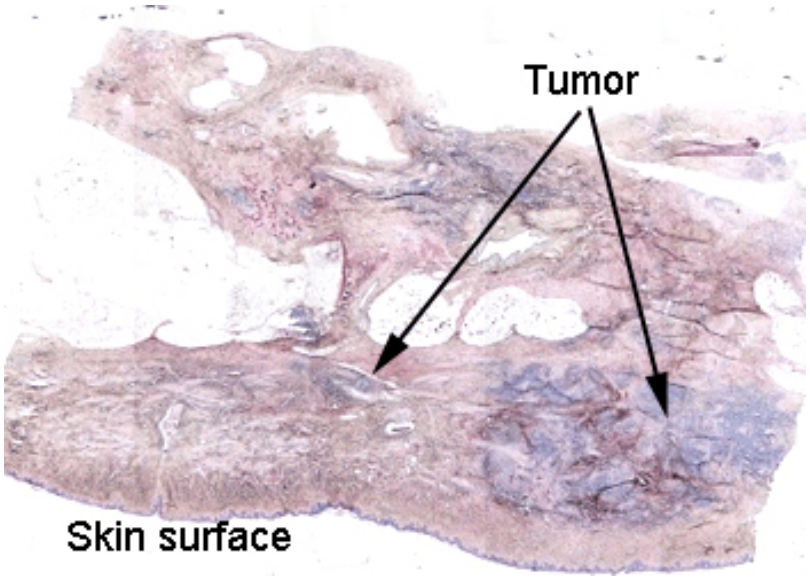
Your observations

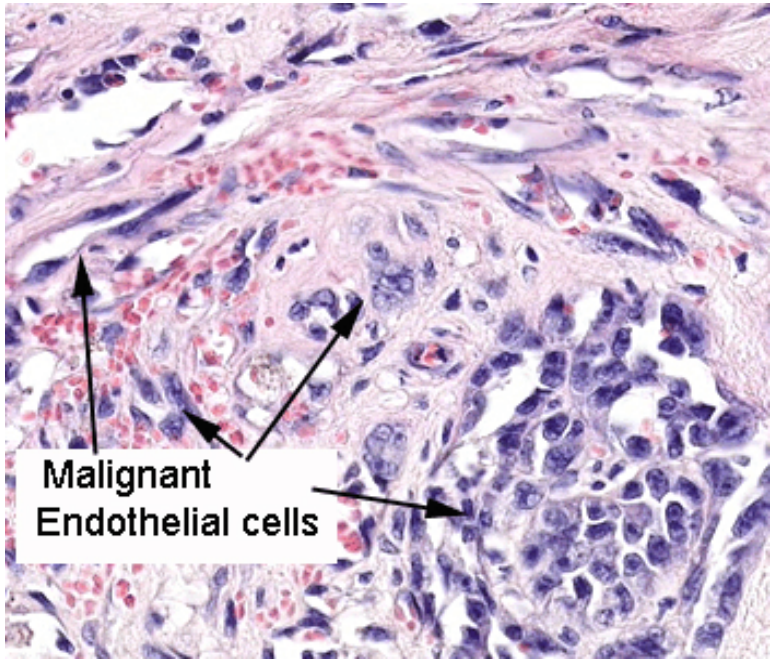


Like the other examples of cancer of the breast in your set, this one is invasive. You will see the malignant cells in the stroma in long clusters, glands and lines or files of individual cells. There will be few mitoses, and not much anaplasia, but this is cancer all the same. These cells may look like lymphocytes to you at first, but they are malignant ductal epithelial cells.

The insert is a high power view of several clusters of malignant cells. You can still see the malignant cells forming long clusters, glands and lines or files within the fibrous tissue stroma.

Slide 224, Angiosarcoma of Breast





This is an unfortunate example of second malignancy arising as a consequence of the treatment of the first one. This is an angiosarcoma that arose in the area of the previous cancer surgery, which was followed by irradiation.

Throughout this region you will see malignant endothelial cells, some aggregated into vascular structures. RBCs are within the vascular slits, and elsewhere they have been leaked into the surrounding tissue space.

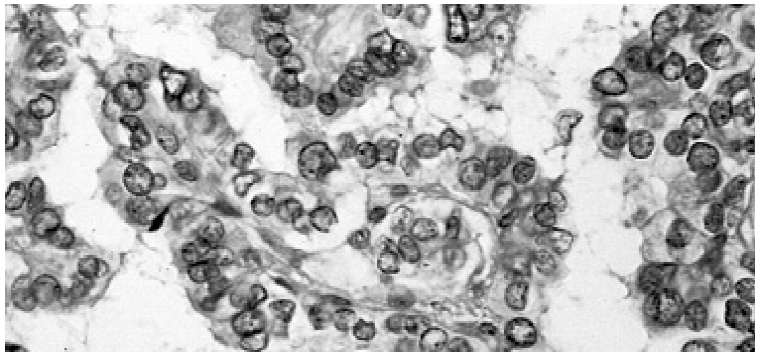
Your observations

General and Systemic Histopathology
C601 and C602

Section 12 *Endocrine Disorders*

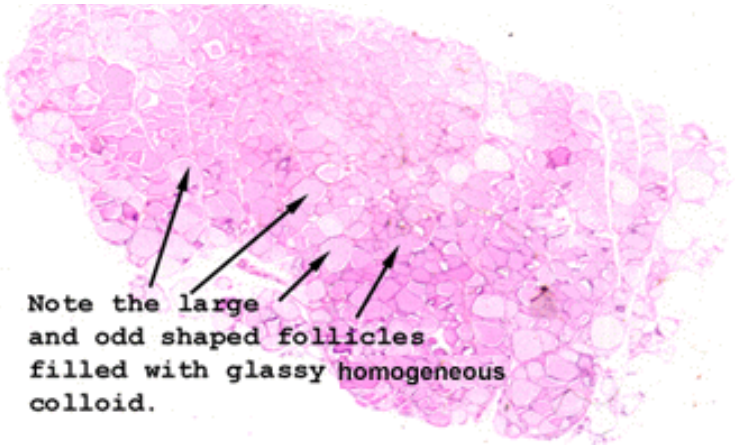
Disorders of the endocrine system are among the most challenging to diagnose, and yet the most fascinating of all medical conditions. The endocrine system is in essence a system of cellular communication, and abnormalities of one system can have ripple effects that affect many distant organ systems. I liken the whole physiological picture of the endocrine system to a three dimensional string structure known as a cat's cradle. As with the cat's cradle, when you shorten or lengthen one string the whole figure has to change to accommodate the new reality. With the endocrine system, excess or deficiencies of one hormone often leads to far reaching compensatory changes in many others. Because of this, it is sometimes difficult to tell for certain the initial or underlying problem. The endocrine system is one area in which the clinical laboratory can be extraordinarily helpful to you.

In this unit we will focus on thyroid, parathyroid, adrenal, endocrine pancreas and the pituitary. (Endocrine disorders of reproduction are dealt with in the reproductive unit.) Regarding the histology of endocrine glands, you may not think it is possible to tell if there had been a state of hyper or hypo-functioning, but in fact it is. We will be looking at histological changes in the thyroid, parathyroid and adrenal gland that will tell much about the level of active of these glands. In addition to states of hyper and hypo-activity of the glands, we will look at non-functioning benign and malignant tumors as well as combined or multiple glandular abnormalities. There's a lot of ground to cover.

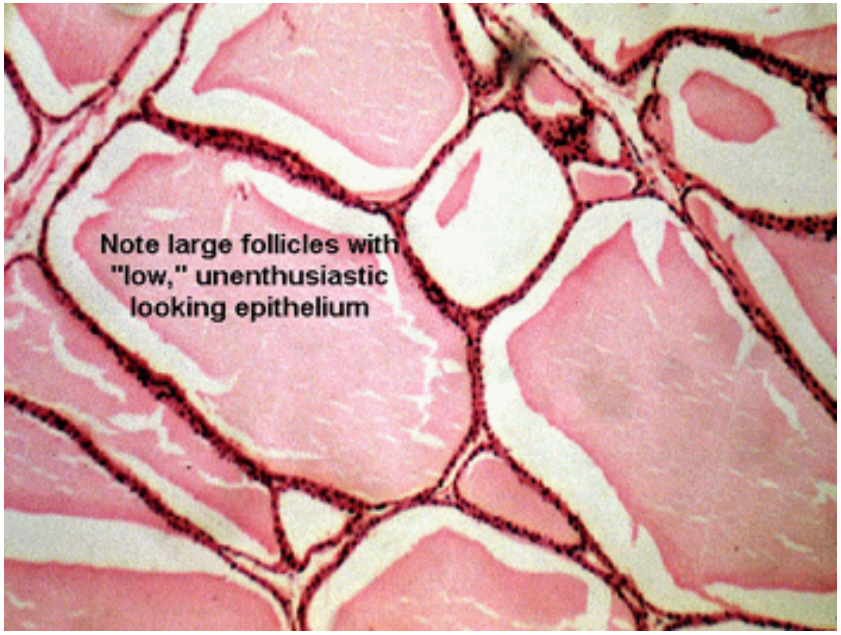


Slide 10: Colloid Goiter of Thyroid

Your observation

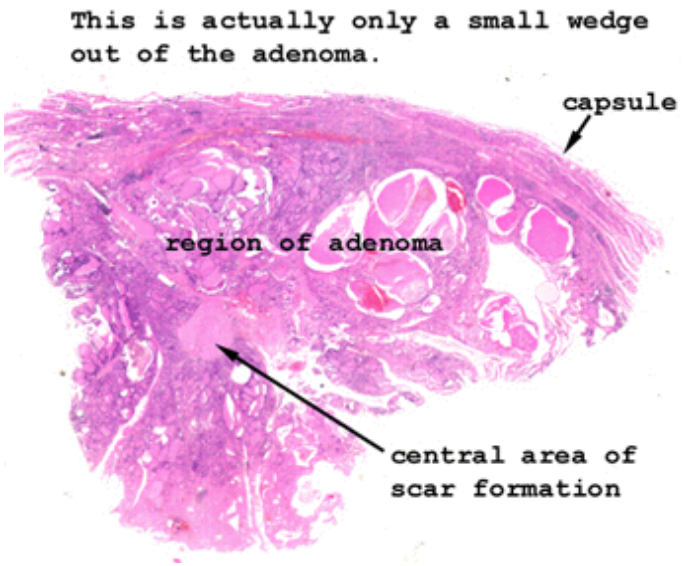


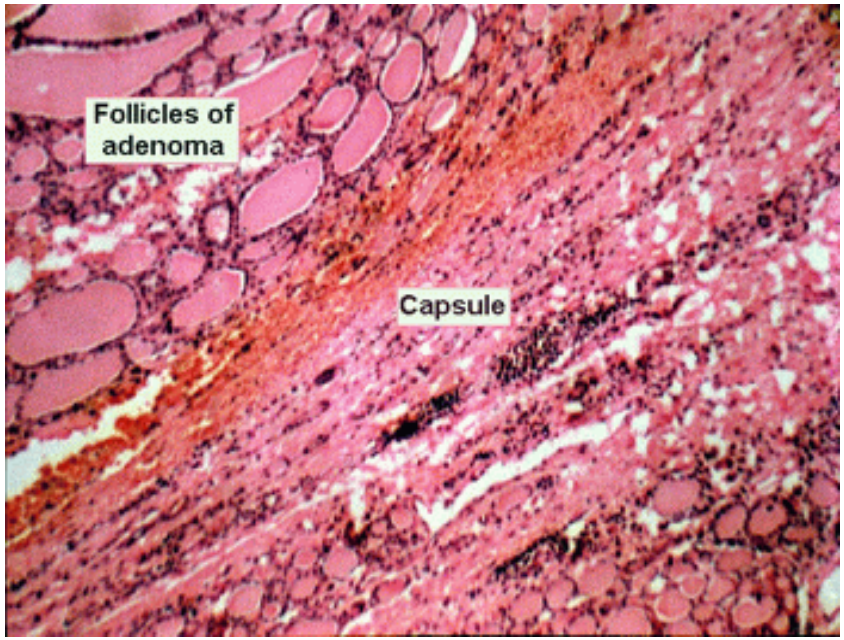
In this scan of the tissue you can easily see how enlarged some of the follicles are.



Note the large follicles filled with colloid. The follicles are lined by lazy looking follicular cells. This thyroid is fairly sleepy. You may see some inflammation in areas, but for the most part an inflammatory infiltrate is not a part of this lesion. The cleared areas at the edges of the colloid represent dehydration changes of the colloid during tissue processing, and not part of any pathology. What are some of the causes of this condition? What do you do to diagnose it? Will the thyroid function studies be abnormal? Would a needle aspiration help?

Slide 11: Follicular Adenoma of Thyroid



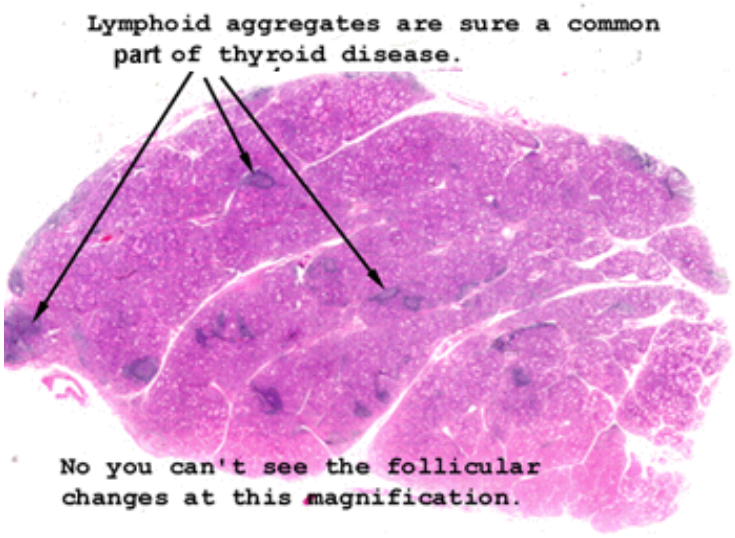


Your observation

The tissue on your slide is actually only a small wedge out of the intact and much larger lesion. You should be able to find part of the capsule and see the difference between the cells within the capsule and those outside. Yes you will see many inflammatory cells. The chronic inflammation seems to be a fairly consistent part of many forms of thyroid disease.

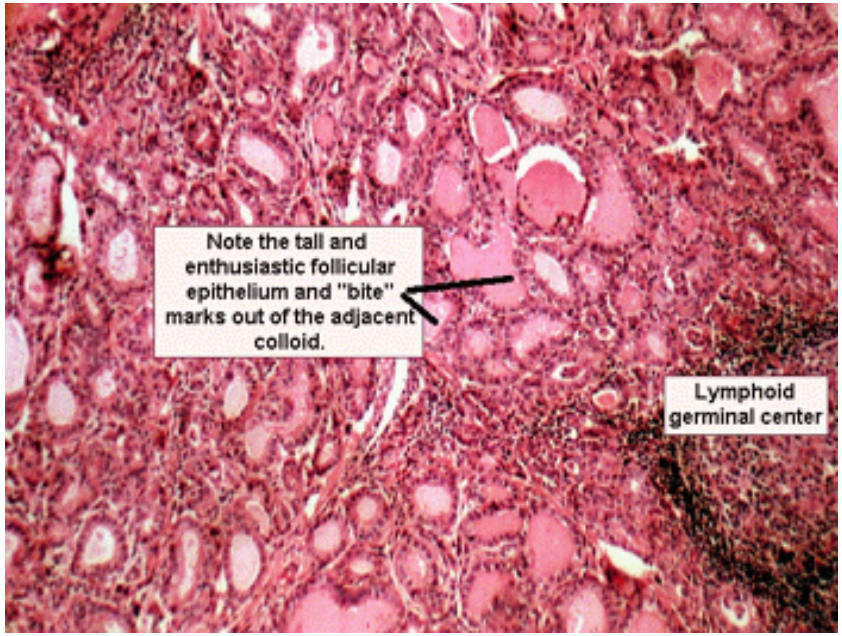
In this picture you see the edge of the adenoma with the capsule compressing the surrounding normal thyroid tissue. There will very likely be a few chronic inflammatory cells with some fibrosis around the adenoma, and elsewhere in this slide. How do we distinguish an adenoma from a malignant lesion in the thyroid? What features tell us this is benign? Does it have any malignant potential?

Slide 12: Treated Hyperthyroidism



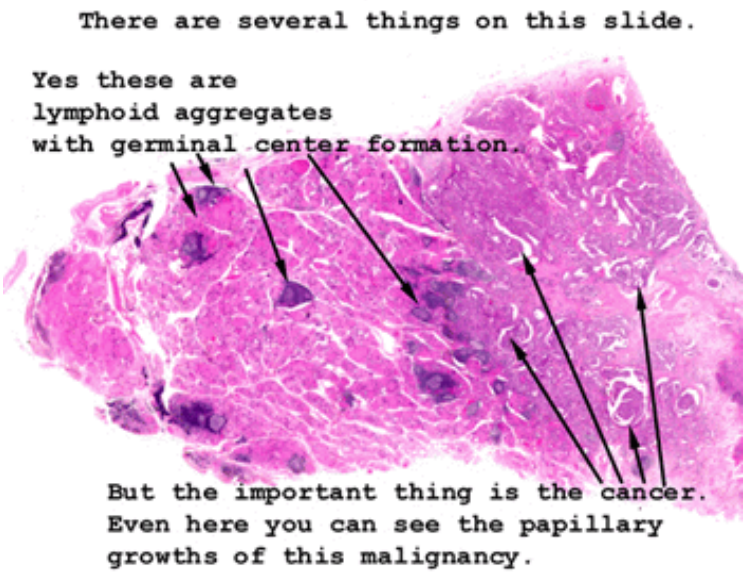
Your observation

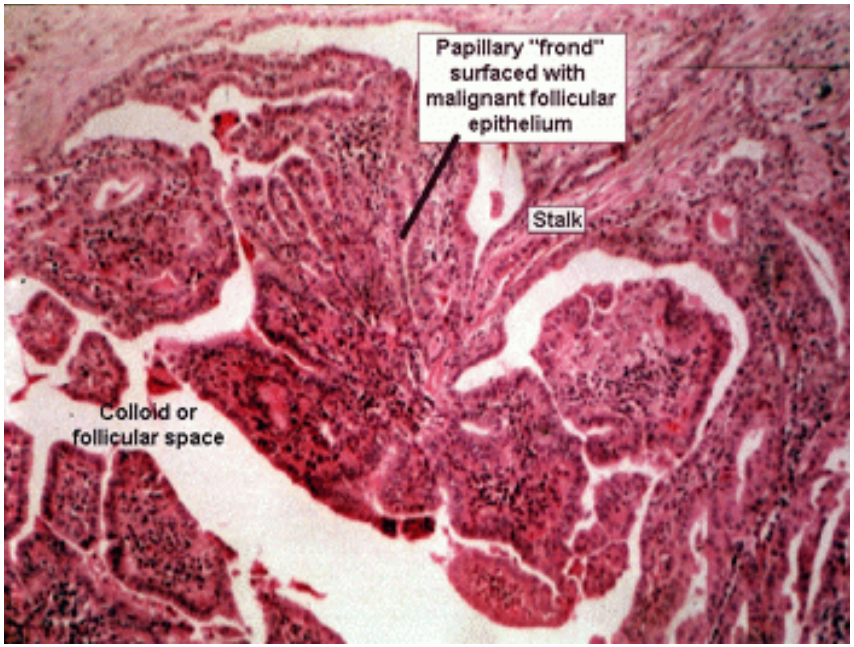
Even with no magnification you can easily see the lymphoid aggregates in the thyroid tissue. You may also be able to see areas of fibrosis.



You will see tall and inspired follicular cells lining the follicles. There will likely be "bite" marks out of the edge of the colloid (colloid scalloping), reflecting the degree of activity this gland has been driven to. Frequently, there will be some degree of chronic inflammation associated with such conditions, and this one shows a good deal. What would the thyroid function tests show? What are some conditions that lead to hyperthyroidism? Be sure you know the answers to these questions.

Slide 24: Papillary Adenocarcinoma of the Thyroid



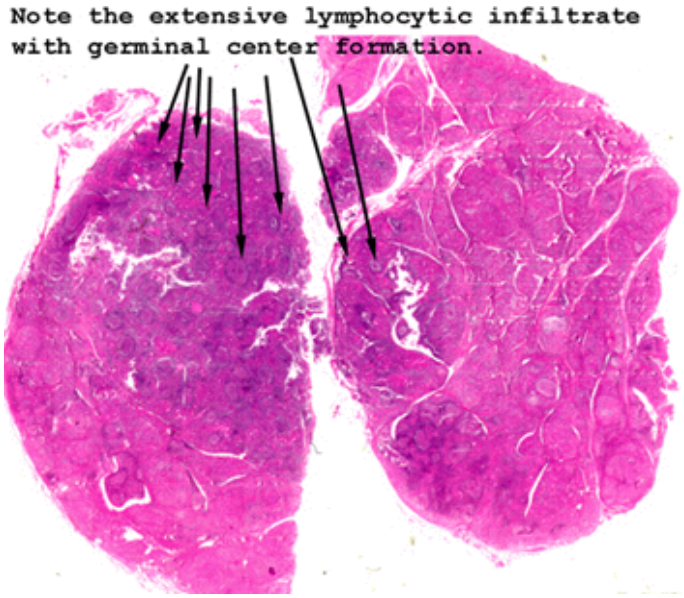


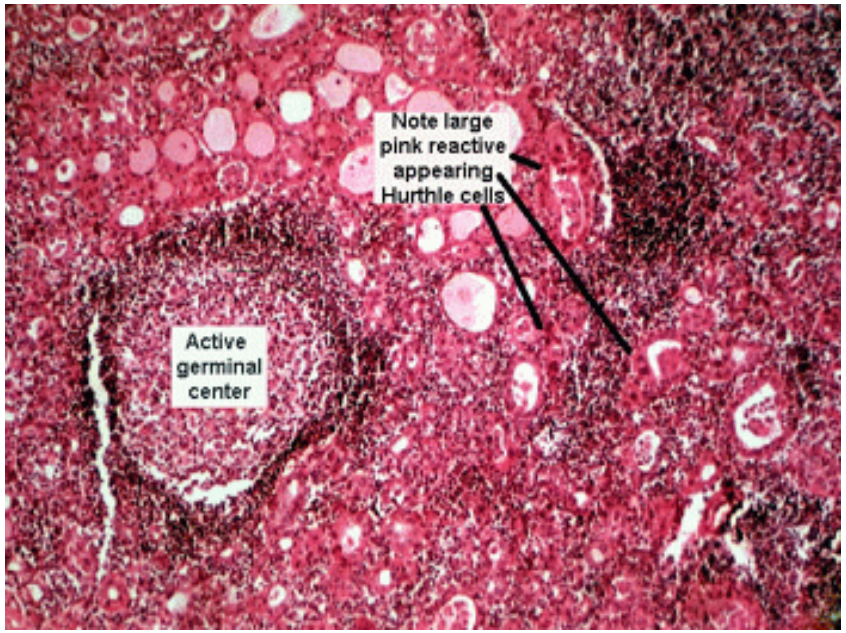
Note that you can actually see the areas of papillary carcinoma just by looking at the tissue on the slide. You will also see many lymphoid aggregates within the surrounding thyroid tissue. This may reflect some overall excitement on the part of the immune system or may indicate a coexisting thyroiditis.

This picture pretty well says it all. You will see papillary groups of fibrovascular tissue surfaced with cuboidal or columnar epithelial cells. The epithelial cells covering these papillary fronds are the malignant follicular cells. They perceive the space between the papillary groups as the follicular lumen, although they are not making much in the way of colloid. You will likely see some scarring and a few chronic inflammatory cells in association with the tumor.

Your observation

Slide 25: Hashimoto's Thyroiditis



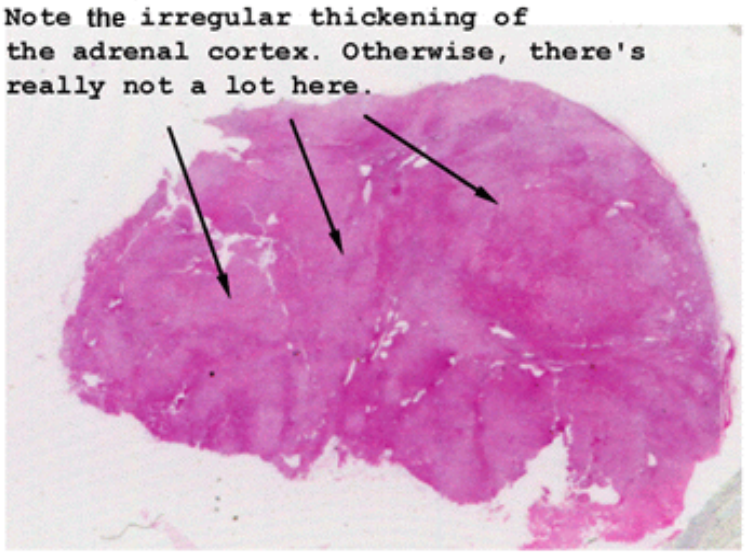


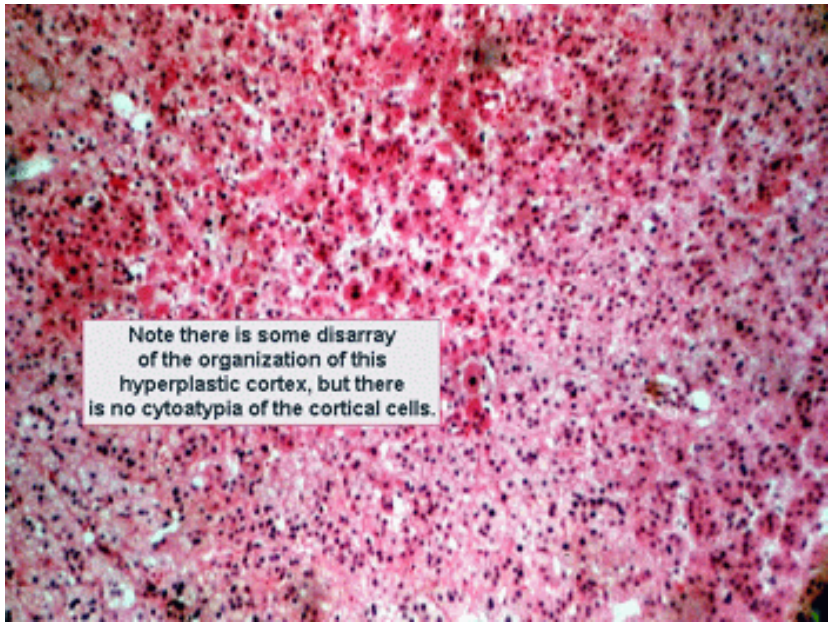
The key feature here will be the lymphoid aggregates with germinal center formation within the thyroid tissue itself. In the picture to the left, you can obviously see the clusters of lymphocytes as well as areas of fibrosis giving a lobulated look to the thyroid in general.

This is Hashimoto's thyroiditis. Note the chronic inflammatory infiltrate and especially the active lymphoid germinal centers within the gland itself. There is marked destruction of the gland. In areas of attempted regeneration you will see enthusiastic and stimulated follicular cells we call Hurthle cells. These are large, brightly pink stained cells that may or may not be seen in direct association with a follicle. KNOW THE ANTIBODIES that we use for diagnosis in this case. Check Bakerman for the important levels of anti-colloid and anti-microsomal antibodies. When this disease has run its course, what level of thyroid function do you think will remain?

Your observation

Slide 81: Adrenal Cortical Hyperplasia



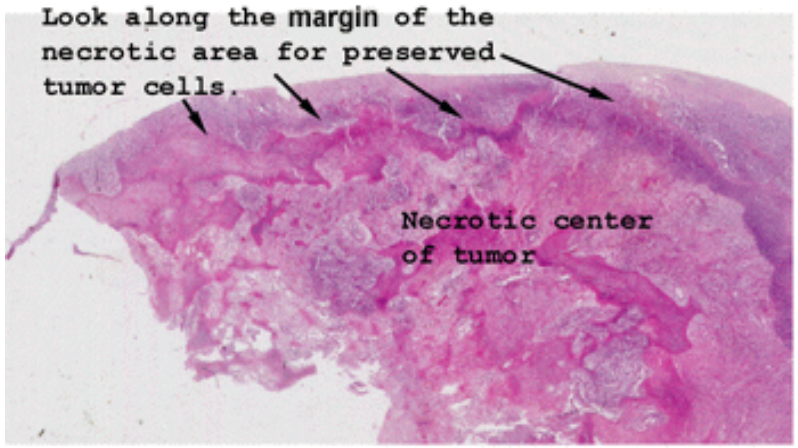


Your observation

This is a little tricky to see. There will be generalized thickening of the adrenal cortex and some "disarray" of the usual cortical architecture. The big question that comes up with this condition is why did happen?

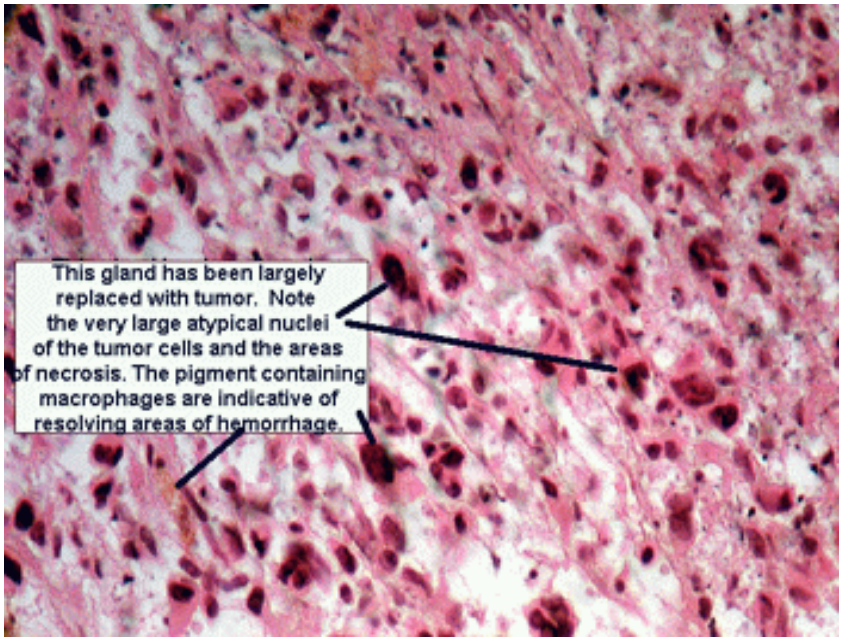
There is really not a whole lot to this slide. The cortex is markedly thickened and there are no well defined tumors or areas of necrosis. There is some "disarray" of the cortex, that is, it's hard to distinguish the three layers, but otherwise it is pretty much adrenal gland. You might want to look at the normal gland to see what the expected appearance should be.

Slide 82: Pheochromocytoma of Adrenal Gland



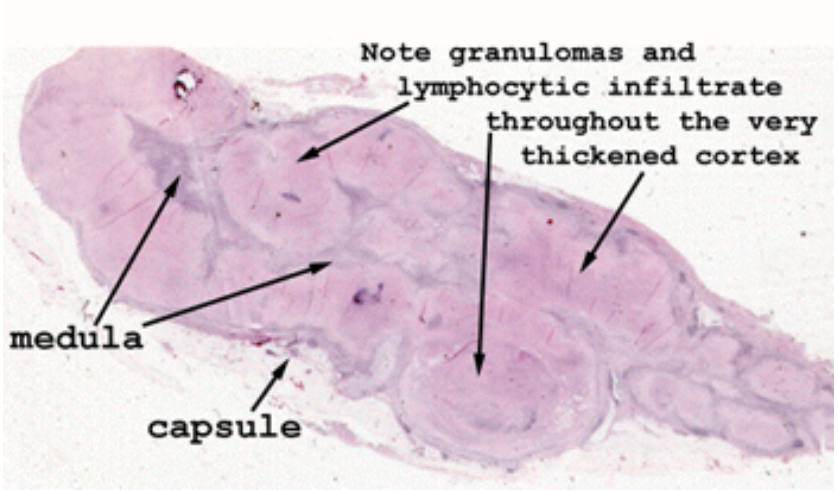
Along with hypertension, necrosis and hemorrhage is the story of this tumor. Understanding that will help aid with knowing why we see episodic swings in blood pressure in patients with this condition. Parts of the tumor die and suddenly release a large amount of epinephrine; up goes the blood pressure. It will be tough to find much viable tumor in this specimen, but it's there.

Your observation



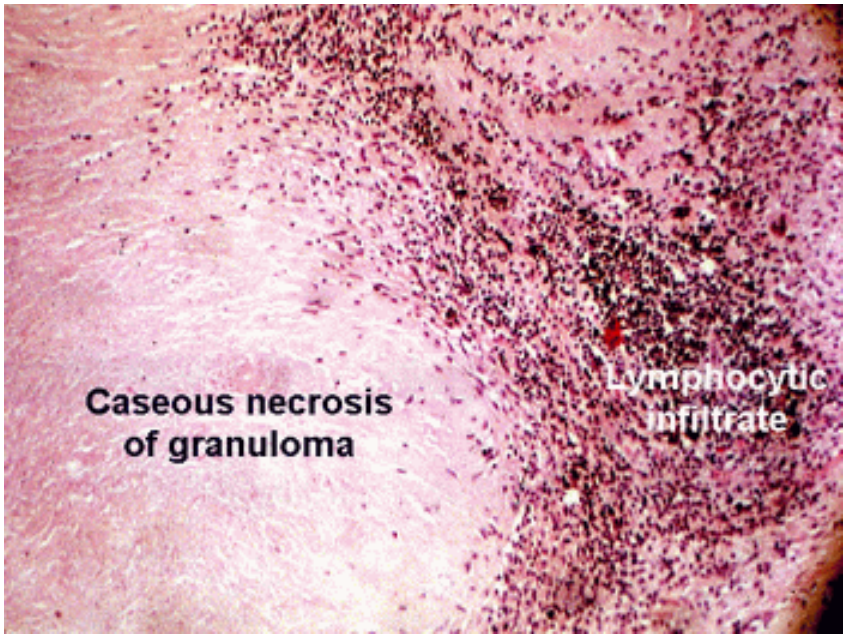
This is a hard slide to understand. There is a lot of necrosis, so don't bother with the central portion of the tissue. Also, I am not so sure there is much in the line of normal adrenal gland to get your "bearings" from. The necrosis is the hallmark of this lesion. Look around the edges for viable tumor cells. They will be large and have bizarre nuclear features. There will be lots of pigment, representing old hemorrhage with hemosiderin deposits. Read about this lesion before trying to tackle the slide.

Slide 97: Adrenal Tuberculosis



Your slide is a little faded, but there should be no trouble appreciating the destruction of the adrenal by tuberculosis. In the picture to the left you can easily see the generalized caseous necrosis. I suggest you start on the cortex and work your way into the specimen. At least for a bit you'll know where you are on the slide.

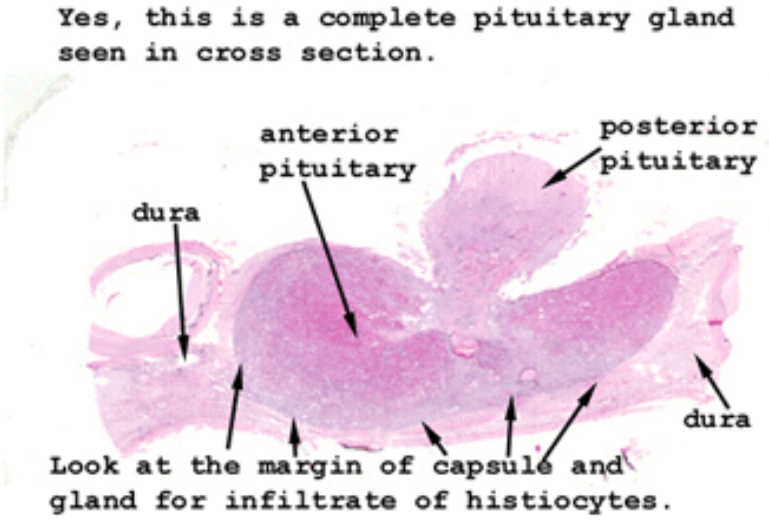
Your observation



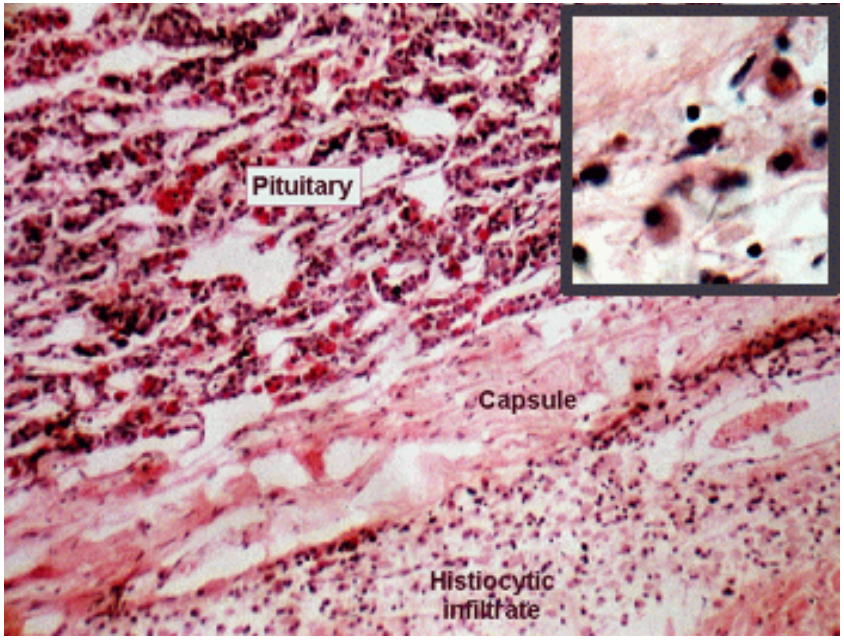
Observe the granuloma with caseous necrosis at its center. There are a few giant cells, but the principal remaining inflammatory pattern is of non-specific chronic inflammation. You will see lymphocytes and plasma cells comprising the majority of the inflammatory pattern. At one time, this was a very common cause of adrenal failure and subsequent Addison's disease. Today, adrenal insufficiency secondary to destruction of the gland is more often the result of metastatic cancer. Even so, destruction of the gland is not the most common cause of Addison's disease. Do you know what is?

Slide 102: Pituitary with Histiocytosis

Your observation



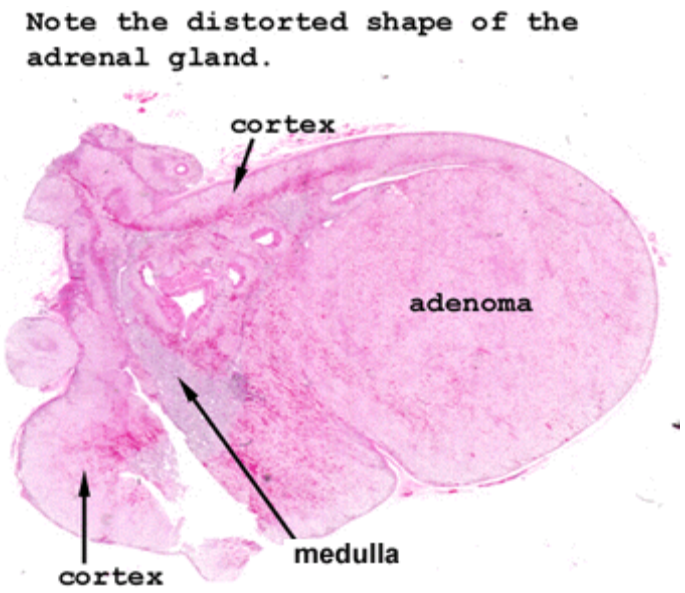
Look at this, a complete cross section of a pituitary gland! We want to concentrate on the area right at the edge of the gland for the infiltration of the histiocytes.

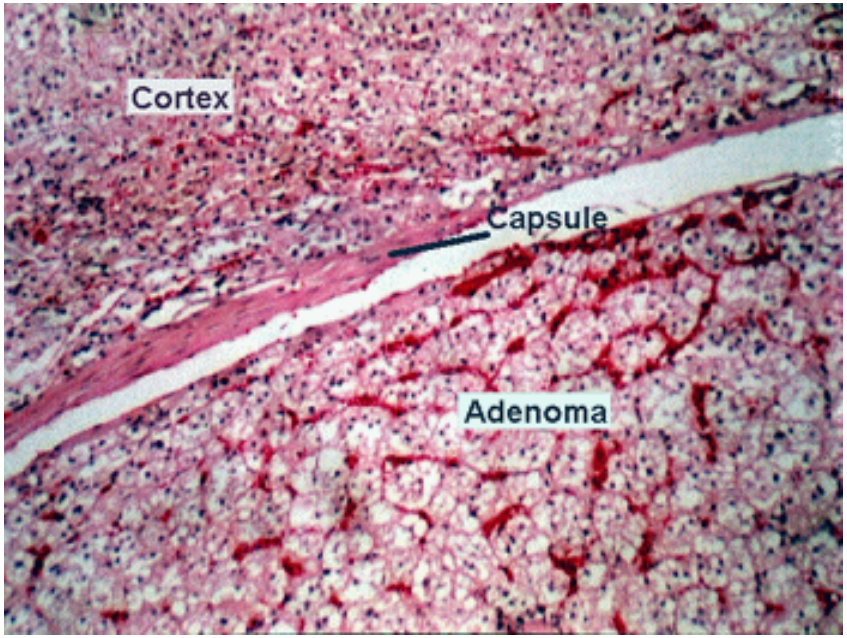


The histiocytic infiltrate in this case is around the capsule of the gland. It is kind of subtle, and you may want to check on the histology of the normal gland to appreciate the difference. The histiocytes do not look particularly aggressive, but they continue to slowly reproduce and cause organ failure.

The insert in the upper right-hand corner of the image shows high power detail of the histocytic infiltrate surrounding the capsule of the pituitary.

Slide 109: Adrenal Cortical Adenoma



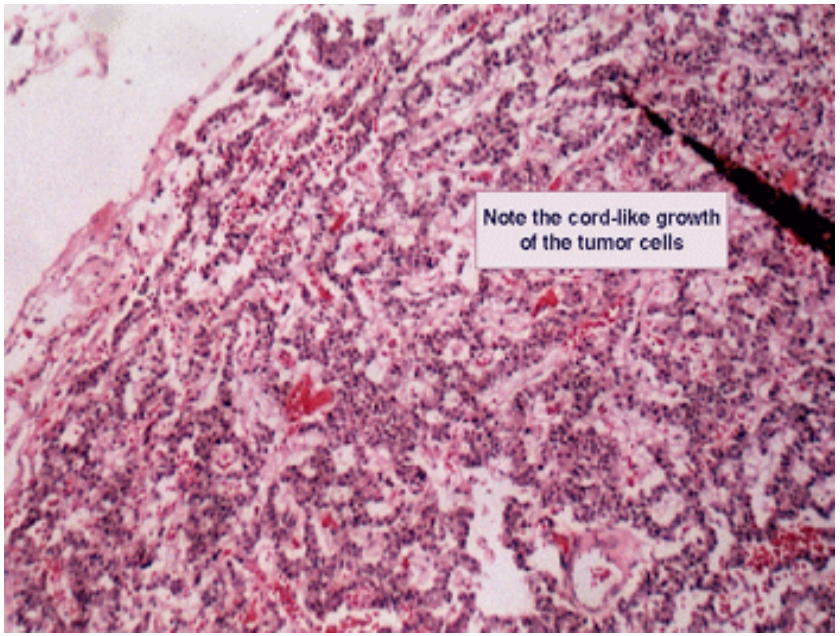


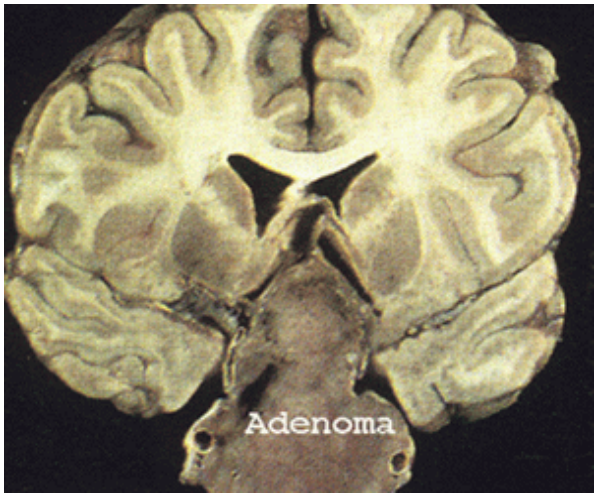
Your observation

No trouble seeing the adenoma here. As with all the other slides, I suggest you look at the normal part of the gland first and then move to the area of the tumor.

These adenomas can become quite large, so your slide may only have a small part of it. See if you can find the capsule to get your bearings. The tissue within the capsule will not look very much different from that outside. Basically, the microscopic examination confirms the benign nature of this lesion. I doubt that anyone could tell they were looking at an adenoma if only a small part of this tumor were to be shown in a picture. You would need the whole thing to see it.

Slide 149: Pituitary adenoma





This gross photo of the brain with the adenoma was initially published in Laboratory Medicine, volume 29, number 10, page 612. It had been submitted as one of the photographs in the 1998 Art and Science of Medicine Photography contest. It was taken and submitted by Dr. James M. Gulizia of Brigham and Women's Hospital, Boston.

This picture is of a "benign" pituitary adenoma. Although biologically benign, it is sure in the wrong place and can be lethal just because of its location. You will see clusters and cords of the tumor cells, and it may be tricky to distinguish the tumor from the surrounding normal pituitary. Does the term "tumor" apply here? You should see no mitoses.

Your observation

Section 13 *Blood Smears*

Looking at blood smears is always a little tricky. First, this is one of the few situations in which you may actually need to use your oil immersion lens. Please be careful. It's easy to run it through a slide. Knowing where to look on the slide can make all the difference between being able to see what's there, and simply being frustrated. You want to be way out on what we call the "feathered edge" of the slide. That is, you want to be almost off the shallow end of the blood smear, not in the middle of the slide. In most cases, the label is at the thick end of the slide, so head as far as you can in the other direction. You want to be right out where the little pointy ends of the blood smear disappear into nothing. You need to find an area where the RBCs just barely touch each other, or are free swimming. If you are looking at an area where the RBCs are piled on top of one another and the WBCs are dark and small, keep going to the thinner end of the slide.

When you study a smear, remember there are three formed elements to assess, as well as what can be learned from the background. No matter what you have been told about the condition the slide represents, always look at the RBCs, WBCs and platelets. The degree of blue staining in the background can also give you an indication of the amount of protein in the blood. The darker blue the background, the more there is. Again, be sure you are looking in the far reaches of the feathered end of the slide.

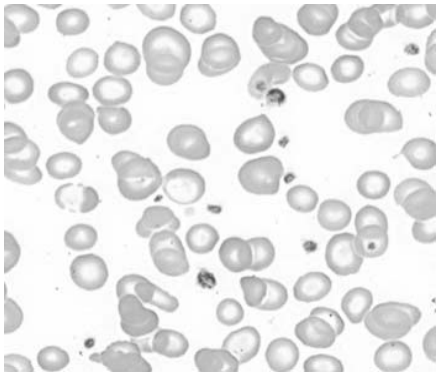
Some of the peripheral smears for the cases in this section are found only online, while others are both in your slide box and online. Be sure you use your scope for the ones you have in your slide box. You will have a slide quiz covering the blood smears, and it will be a real glass slide you will need to diagnose using your microscope, not the computer monitor.

These are real clinical cases. Good luck.

Case 1, virtual slide: A 69-year-old man with hematuria.

Your observations and answers to the questions.

This 69-year-old man complains of gross hematuria of several days duration. He claims to have had bloody urine several times over the past 3 years, but nothing like he is experiencing now. He also has arthritis and claims to take up to 8 aspirin a day. Here are his labs:



WBC 17,800			RBC 2.90	Unrinalysis
	Percent	Abs	HGB 7.1	Pink/cloudy
NE	86.5	H 11.0	HCT 21.6	9.030 sg
LY	7.3	L 0.9	MCV 74.5	1+ protein
MO	4.4	0.6	MCH 24.5	pH 5
EO	0.4	L 0.1	MCHC 32.9	3+ Hgb
BA	1.4	H 0.2	RDW 21.0	RBC: many
			PLT 484	WBC: many
			MPV 8.0	

PT = 11.5 sec
PTT = 28 sec
ESR = 114 mm/hr
FE = 17
TIBC = 470 ug/dl

Ferritin = 5 ng/ml
Stool hemoccult +

This is an online case so you'll need to use the virtual microscope function to review this smear. Describe what you see and then answer the following questions.

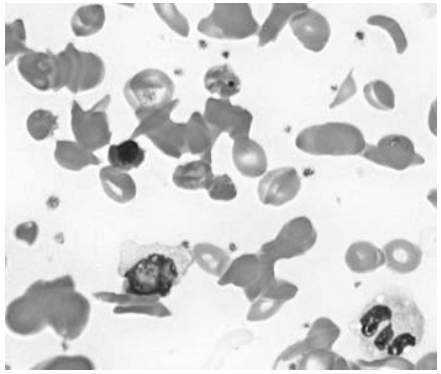
- Likely cause of his anemia?
- What kind of anemia?
- RBC morphology?
- Other labs?
- Why is the stool occult blood positive?

Case 2, virtual slide and glass slide: A 22-year-old black man with abdominal pain.

Your observations and answers to the questions.

This 22-year-old black man complains of severe abdominal pain and fever. He has a history of similar episodes, some requiring hospitalization. He also believes he has some form of 'kidney' problem.

Physical exam reveals a slight man of small stature who is in considerable distress. No significant physical findings are present, and no spleen is palpated. Here are his labs:



WBC 12,400			RBC 3.2	Sickle Dex +
	Percent	Abs	HGB 9.3	
NE	71.8	8.9	HCT 27.5	
LY	21.6	2.7	MCV 85.7	
MO	4.7	0.6	MCH 28.9	
EO	0.4	L 0	MCHC 33.7	
BA	1.5	H 0.2	RDW 15.7	
nRBC 5/100 wbc			PLT 304	
			MPV 7.7	

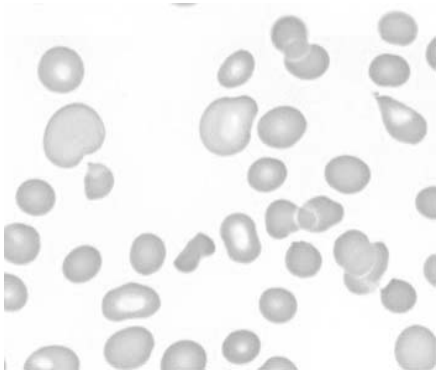
For this case, there is both an online version of the slide and a real glass slide in your slide box. Describe what you see and then answer the following questions.

- What is the basic defect with this man's red blood cells?
- Expected clinical course of homozygous and heterozygous states?
- Additional laboratory tests?

Case 3, virtual slide: A 19-year-old college students complains of ease of fatigue.

Your observations and answers to the questions.

This 19-year-old white college student complains he can no longer complete his daily 10 mile jog. He develops extreme fatigue at about 5 miles. He's also noted bruises around his ankle and has recently had several nosebleeds. In retrospect, he feels his symptoms have slowly been coming on for about 2 months. Physical exam reveals a slight man of small stature who is in considerable distress. No significant physical findings are present, and no spleen is palpated. Here are his labs:



WBC	0.5 X 10^3		RBC	2.61	Anti-HBsAg +
	Percent	Abs	HGB	8.2	TIBC 350 ug/dl
NE	2.3	0	HCT	23.2	FE 180 ug/dl
LY	96.5	0.5	MCV	89.2	Ferritin 100 ng/ml
MO	0.7	0	MCH	31.5	
EO	0.5	0	MCHC	35.3	
BA	0	0	RDW	13.1	
			PLT	23 X 10^3	
			MPV	10.2	

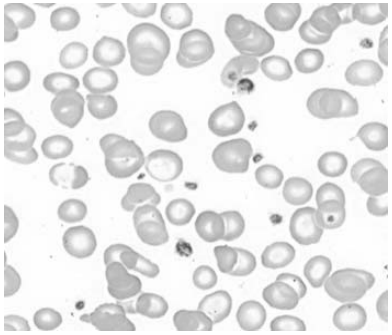
This is slice online only, so use the virtual microscope. Describe what you see and then answer the following questions.

- What is the abnormality in this peripheral smear?
- Possible etiologies?
- Criteria for diagnosis?
- How would the bone marrow biopsy help with the diagnosis?

Case 4, virtual slide: A 27-year-old black female with a fever.

Your observations and answers to the questions.

This 27-year-old black woman was admitted with fever, renal failure and possible mental status changes. She was well until 3 days ago when she contracted a 'mild cold'. Her fever began yesterday, her urine output has diminished markedly and family says she is profoundly depressed. Her past history is unremarkable and she taking no medication.



WBC	25 X 10^3	RBC	2.62	Macros	Mod
	Percent	HGB	5.5	Micros	Mod
NE	93.5	HCT	18.3	Poik	Marked
LY	4.4	MCH	21.1	Polychrome	Many
MO	0.8	MCHC	30.3	Schistocytes	Many
EO	0.3	RDW	27.5	Spherocytes	Many
BA	1.0	PLT	115 X 10^3	nRBC	65/100 WBC
		MPV	7.2	Retic Ct	17.1
				Bilirubin (T/I)	2.0/1.8

Review this slide by using the virtual microscope. Describe what you see and then answer the following questions.

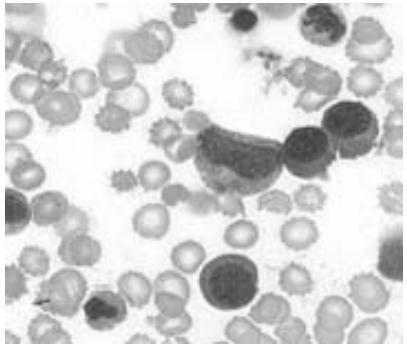
- Abnormality in the peripheral blood smear?
- Possible etiologies?
- Examples of conditions with these changes?
- Your differential and what labs help make the real diagnosis?

LDH 448 IU/L	PT 11.5 secs
BUN 60	PTT 28.0 secs
Creatinine 3.5	Fibrinogen 350
Coombs direct: Neg	FSP 20-40
Coombs indirect Neg	

Case 5, virtual slide: 56-year-old man with frostbite.

Your observations and answers to the questions.

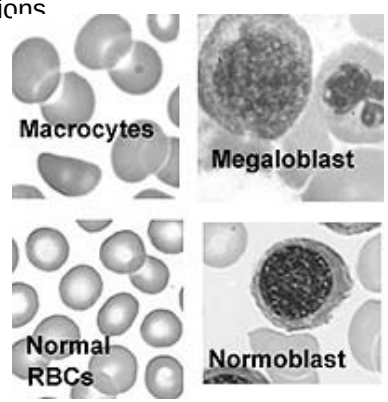
This 56-year-old, chronic alcoholic, man is brought to the emergency room with hypothermia and frostbite involving his toes and fingers. He was found down in the street with no shoes or coat. It is mid-January and the outside temperature is 18°F. He smells strongly of alcohol.



WBC	3.3 X 10^3		RBC	2.22	Retic	1.0 %
	Percent	Abs	HGB	8.5	Bilirubin (T/D)	1.8/0.2
NE	38.5	L 1.3	HCT	23.7	LDH	10,000
LY	44.4	H 1.4	MCV	126.8	Fe	200ug/dl
MO	16.7	H 0.6	MCH	38	Blood alcohol	286mg%
EO	0.3	L 0	MCHC	35.7		
BA	0.1	0	RDW	16.4		
			PLT	109 X 10^3		
			MPV	8.0		

This is an online slide of **bone marrow smear** and you will need to see the slide using the virtual microscope. Describe what you see and then answer the following questions

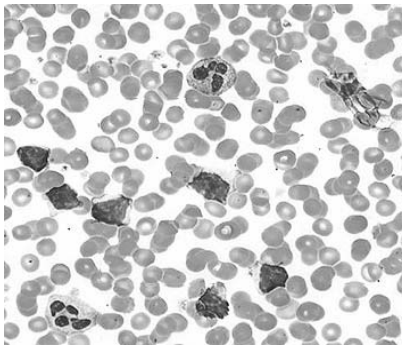
- Why does this man have macrocytes?
- What's with the LDH?
- What other tests do you need?
- See how a bone marrow is done.



Case 6, virtual and glass slide: This 70-year-old man complains of fatigue.

Your observations and answers to the questions.

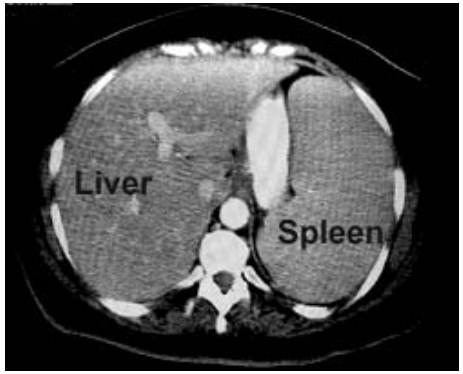
This 70-year-old white man complains of fatigue, decreased exercise tolerance and what describes as a "pulling" sensation in his abdomen. He has always been in good health, is able to walk several miles a day and lives alone. Physical reveals a well developed and well nourished man who is slightly pale and looks a little younger than his stated age. He has enlarged and non-tender cervical lymphadenopathy and spleen tip is easily palpated at the level of the umbilicus. The liver seems enlarged.



WBC 107 X 10^3	RBC 2.76
Percent	HGB 10
NE 7.8	HCT 29.8
LY 78.6	MCV 108
MO 13.6	MCH 36.1
EO 0	MCHC 33.4
BA 0	RDW 15.0
Many Smudge cells	PLT 26 X 10^3
	MPV 6.9

For this case there is a real glass slide and online virtual slide for you to review. Describe what you see and then answer the following questions.

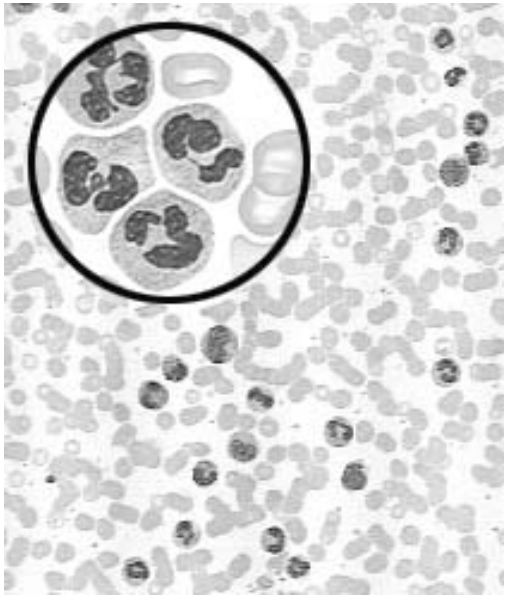
- What's wrong here?
- Why the anemia and thrombocytopenia?
- Do you think the MCV is accurate?
- What organs are affected by this condition?
- Morphologic criteria for the disease?
- How to distinguish CLL from ALL?



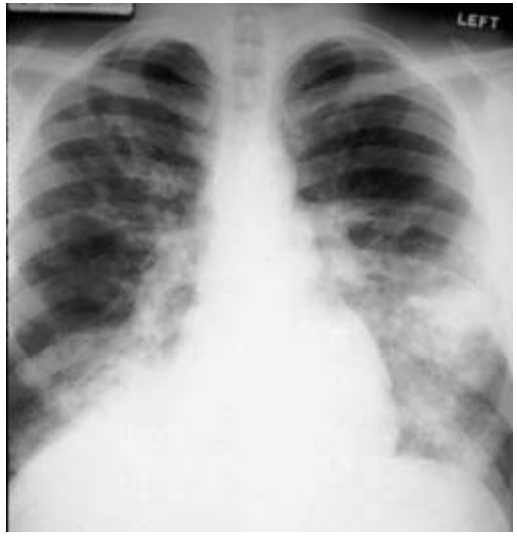
Case 7, 60 Year-old woman complains of cough and shortness of breath.

Look at the pictures here and online and see if you can figure out what's going on. Answer the questions below.

This 60 year-old woman complains of fever, shortness of breath and cough. Her cough is productive of a yellow sputum. Physical exam reveals a pale, slight woman with mild cyanosis of the nail beds. Rales are heard in the base of both lung fields.



WBC	35.9 X 10^3		RBC	3.81	
	Percent	Abs	HGB	10.7	LAP = 250 (20-100)
NE	85.5	30.8	HCT	31.7	
LY	6.2	2.2	MCV	83.2	
MO	4.3	1.5	MCH	28.1	
EO	3.7	1.3	MCHC	33.8	
BA	0.3	0.1	RDW	15.6	
Bands observed			PLT	375 x 10^3	
Dohle bodies seen			MPV	9.8	



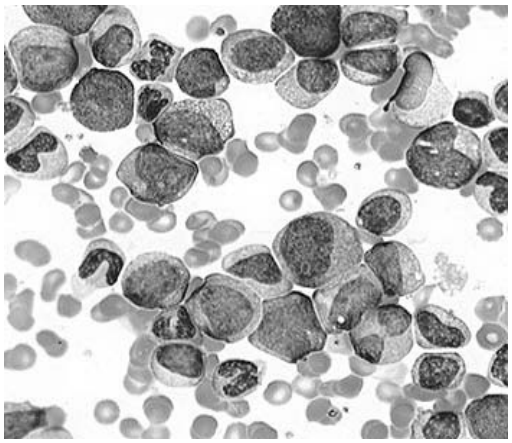
There is no slide to look at, but there are a few questions.

- What's with the LAP (leukocyte alkaline phosphatase)?
- What about the Dohle bodies?
- What findings of the CBC favor a leukemoid reaction over leukemia?
- For that matter, what is a leukemoid reaction?
- Would you expect this person to be PH[1] chromosome positive?

Case 8, Glass slide and virtual slide: A 32-year-old white man is referred because of abnormal CBC.

Your observations and answers to the questions.

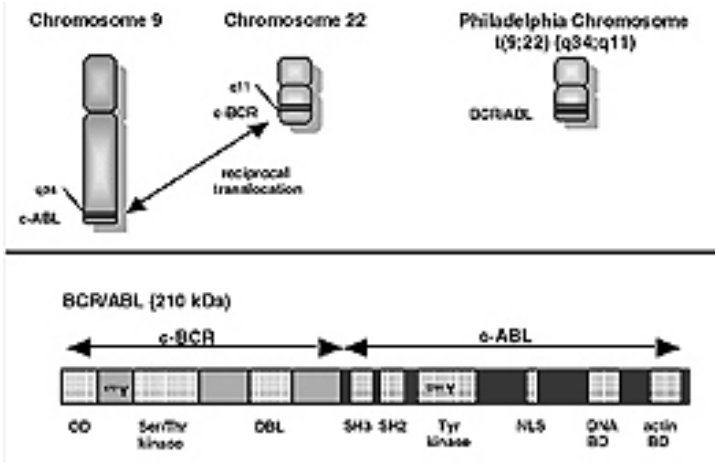
This 32-year-old white man was referred because of an abnormal CBC that was part of his pre-employment physical at a local school. His only complaints were weight loss and fatigue. Physical exam reveals a pale, thin and apprehensive young man. He experienced mild LUQ abdominal pain during the exam, and his spleen was enlarged. No adenopathy was observed.



WBC	89.1 X 10^3		RBC	2.85
	Percent	Abs	HGB	8.4
NE	89.5	79.8	HCT	23.9
LY	5.6	5.0	MCV	83.8
MO	2.3	2.0	MCH	29.6
EO	2.6	2.3	MCHC	35.3
BA	0	0	RDW	15.8
Many immature cells			PLT	565 X 10^3
LAP = 5 (20-100)			MPV	8.4

For this case, there is a real glass smear and virtual microscope slide to review. Describe what you see and then answer the following questions.

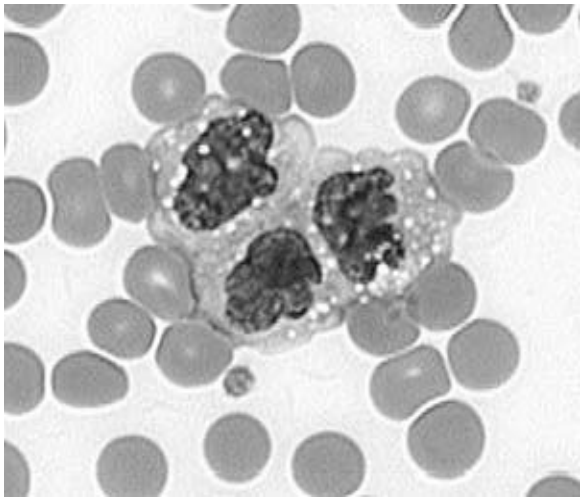
- Define a myelproliferative disorder (MPD).
- What's the most likely diagnosis here?
- How would you confirm it?
- What is the PH[1] chromosome?
- In what cells do you find it?
- What would the marrow look like?
- What's with his big spleen?
- What would a serum vitamin B_{12} show?



Case 9, glass slide and virtual slide: This 48-year-old man complains of fever and oral ulcers.

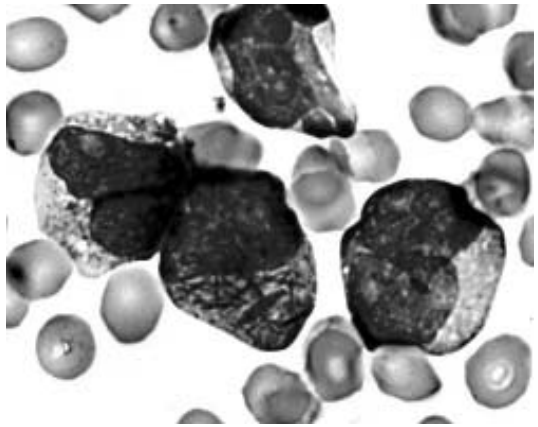
Your observations and answers to the questions.

This 48-year-old man is seen for a fever of 3 days duration and oral ulcerations, bleeding gums and a sore throat. He also indicates ease of fatigue and bruisability. Physical exams reveals an apprehensive, pale man with oozing gums, oral ulcerations and numerous bruises of the lower legs. He is febrile, has a tachycardia and an increased respiration rate. There is no oragnomegaly and no adenopathy.



WBC	47 X 10^3	RBC	3.08	Uric acid	10 mg/dL
	Percent	HGB	10.4	LDH	250 IU/L
NE	19.7	HCT	24.9		
LY	1.8	MCV	80.8		
MO	40	MCH	33.7		
EO	0	MCHC	41.6		
BA	0	RDW	15.6		
Blasts	38.5	PLT	119 X 10^3		
		MPV	7.0		

For this case, there is a real glass smear and virtual microscope slide to review. Describe what you see and then answer the following questions.

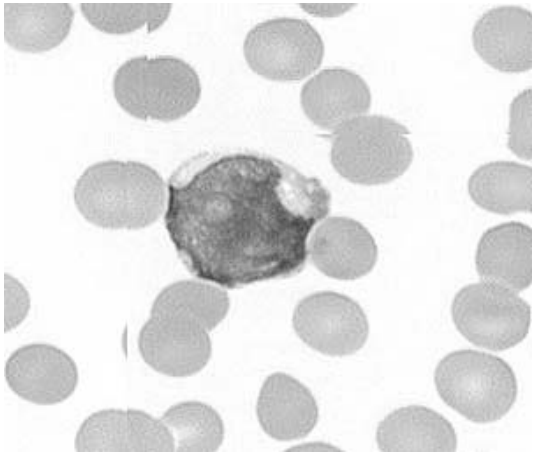


- What is a leukemia?
- What is the FAB classification scheme?
- To what group of leukemias does it apply?
- What do you think the bone marrow looks like?
- What is an Auer rod and what does it mean?
- See them in the picture? (Roll the cursor)
- How to distinguish ALL form AML?
- Why the oral ulcers and ease of bruising?
- What blood and urine tests will help distinguish acute monocytic leukemia from acute granulocytic?

Case 10, glass slide and a virtual slide: A 5 year-old girl comes for a pre-school physical exam.

Your observations and answers to the questions.

This 5 year-old girl comes for a pre-school physical exam. Her mother indicates she has been listless, complains of headaches, arm and leg pains. Physical exam reveals a well developed, well nourished pale child. There is slight splenomegaly and hepatomegaly with generalized enlarged lymph nodes. Scattered petechiae are seen on the legs.



WBC 18 X 10^3

	Percent	Abs
NE	6.2	1.08
LY	90.5	16.2
MO	2.8	0.5
EO	0.5	0.1
BA	0	0

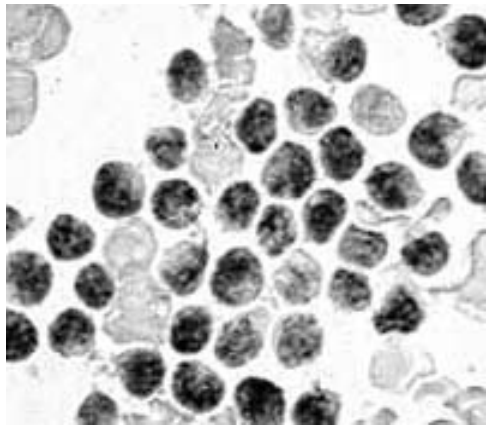
Immature lymphs

RBC 2.76
HGB 6.6
HCT 19.1
MCV 84.4
MCH 29.9
MCHC 35.5
RDW 17
PLT 26 X 10^3
MPV 7.4

Tdt = positive
CD10 (Calla) = positive

For this case, there is a real glass smear and virtual microscope slide to review. Describe what you see and then answer the following questions.

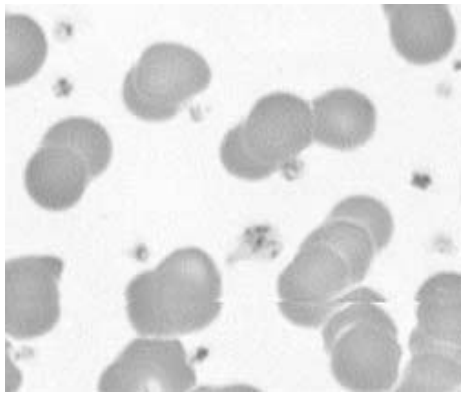
- What features of the lymphocytes suggest they are malignant?
- What clinical features of this girl suggest this is a leukemia?
- How do we distinguish ALL from AML?
- What will the bone marrow show?
- Would you expect the cells to be positive for PH^1 chromosome?
- What treatments exist for this condition?
- Why should one be cautious of uric acid levels during treatment?
- Prognostic indicators for this disease?



Case 11, virtual slide: A 56 year-old woman with a positive hemoccult test.

Your observations and answers to the questions.

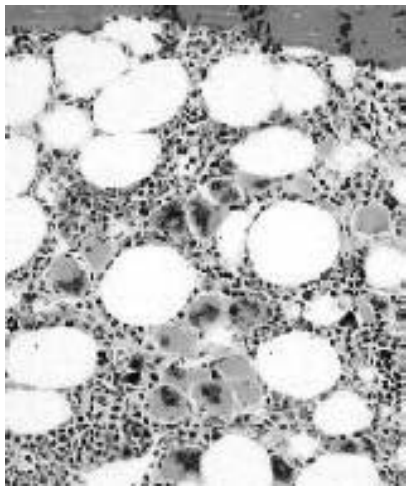
This 56 year-old woman is being seen because she had a positive screening occult blood test. She is well apart from mild hypertension, supposedly treated with diuretics. Two weeks ago she reports suffering a thrombosed superficial varicose vein in her left leg. Physical exam reveals a slightly over weight woman with blood pressure of 150/95.



WBC	6.5 X 10^3		RBC	4.13
	Percent	Abs	HGB	12.7
NE	52.8	3.5	HCT	37.3
LY	34.3	2.2	MCV	90.4
MO	9.0	0.6	MCH	30.7
EO	3.6	0.2	MCHC	34.0
BA	0.3	0	RDW	12.3
			PLT	>1 X 10^6
Stool is heme positive			MPV	7.3

This is an online blood **smear**, so you will need to use the virtual microscope. Describe what you see and then answer the following questions.

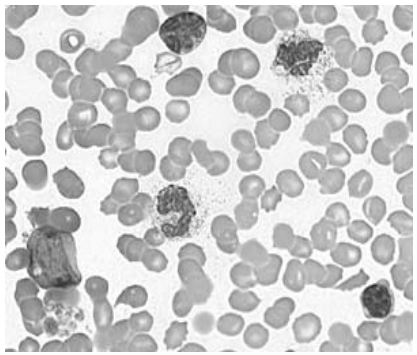
- What indicates this patient has a myeloproliferative disease?
- Are these findings specific for any one in particular?
- What are the guidelines for essential thrombocytosis?
- What would show the thrombocytosis is not reactive?
- Would you expect normal platelet function tests?
- Why heme positive stools?
- What other complications do you need to be ready for?



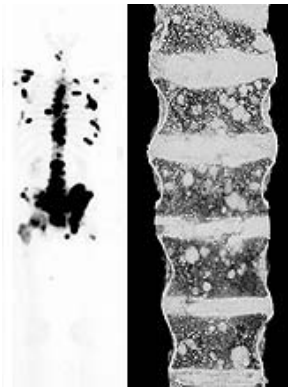
Case 12, glass and virtual slide: This 78 year-old man complains of lethargy and back pain.

Your observations and answers to the questions.

This 78 year-old man complains of lethargy, and is known to have a five-year history of prostate cancer. He also gives a history of recent onset back and leg pains. At the time of diagnosis of his prostate malignancy, his PSA was not elevated, although several regional lymph nodes were positive for metastatic malignancy.



WBC	6.1 X 10^3	RBC 2.76	Alk Phos = 430 U/L
	Percent	HGB 10	Calcium = 11.5 mg/dL
NE	41	HCT 29.8	PSA = None detected
LY	36	MCV 101	
MO	12	MCH 36	
EO	4	MCHC 33	
BA	2	RDW 17	
NRBC	5	PLT 68 X 10^3	
Immature cells seen		MPV 8.2	



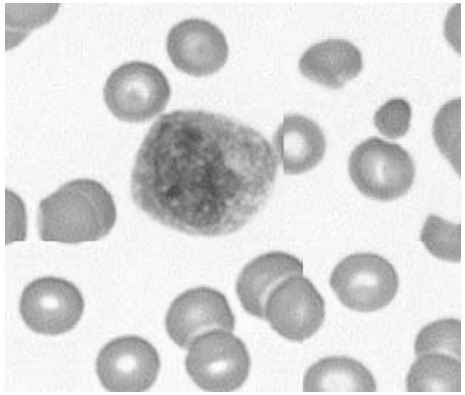
For this case, there is a real glass smear and virtual microscope slide to review. Describe what you see and then answer the following questions.

- What can explain the peripheral blood findings?
- What is the association with the history of prostate cancer?
- What is with the non-detectable level of PSA?
- What can be judged from the bone scan to the right?
- Is he experiencing a primary malignant transformation of his bone marrow?
- Where are the NRBCs and immature cells coming from?

Case 13, glass and virtual slide: This 20 year-old female college student complains of a sore throat.

Your observations and answers to the questions.

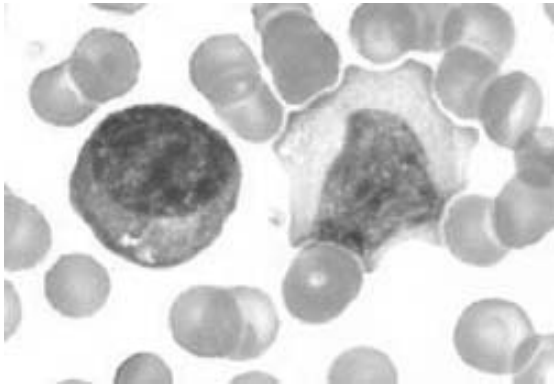
This 20 year-old female college student has been in good health all her life, but developed a fever and sore throat 2 days ago. Physical exam reveals a red and injected throat with tonsilar enlargement and exudate. There are several enlarged and tender cervical lymph nodes.



WBC	8.4 X 10^3	RBC	4.5	Cold Agglutinin	Neg
	Percent	HGB	13.2	Heterophile	Pos
NE	42	HCT	42		
LY	30	MCV	80		
MO	10	MCH	25.2		
EO	3	MCHC	27.2		
BA	1	RDW	10.1		
Atypical lymphs	14	PLT	210 X 10^3		
		MPV	7.2		

For this case, there is a real glass smear and virtual microscope slide to review. Describe what you see and then answer the following questions.

- This woman's blood smear is consistent with what?
- Are the cellular changes diagnostic?
- The agent?
- What's with the heterophile test?
- Anything more specific?
- What of potential long-term complications?
- Short-term concerns?

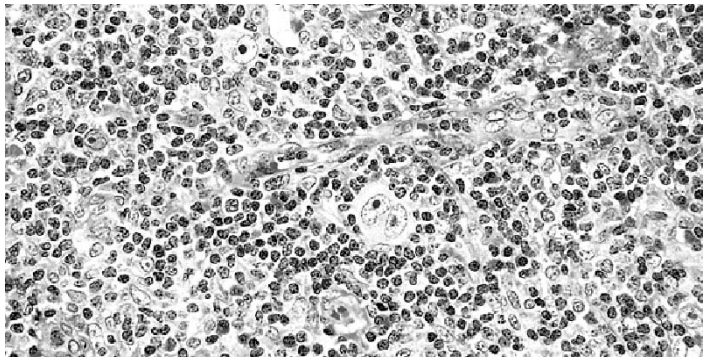


General and Systemic Histopathology
C601 and C602

Section 14 *Disorders of the Lymph Nodes*

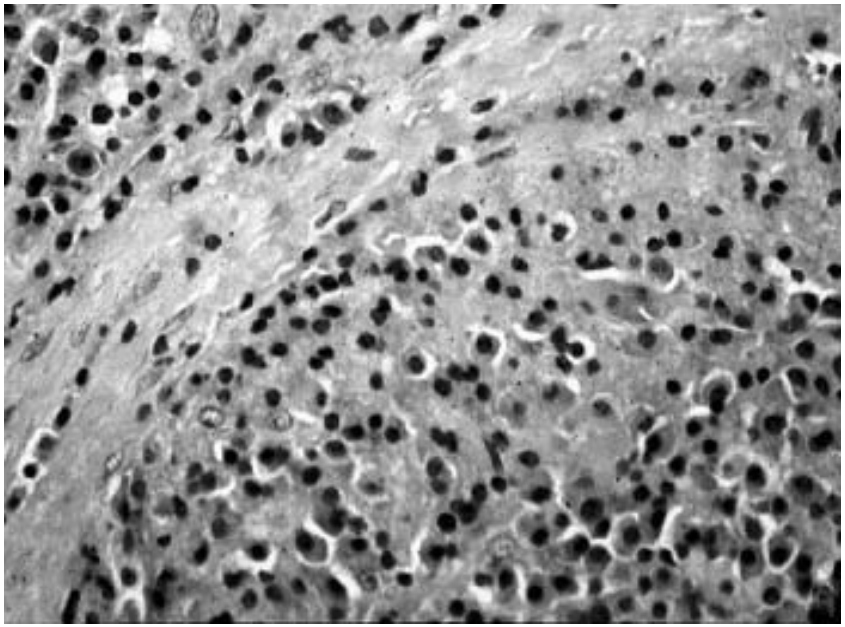
Remember that the lymph nodes are designed to catch a lot of "floating" and foreign material, so they frequently become secondarily involved in many conditions. Furthermore, we are going to look at situations in which proliferative conditions of the lymphatic system involve organs as an "innocent bystander." There are a number of organs that may not leap to mind as harboring a great deal of lymphatic tissue; consider for example the bowel. The most common primary malignant tumor of the small bowel happens to be a malignant lymphoma.

By now, it should be ingrained in your thinking to look at a slide on a white background before putting it on the stage of the microscope. It's doubly important in the case of lymph nodes. This visual assessment will often provide much information about the extent of replacement or involvement of the node with whatever process afflicts it. Also, when assessing a lymph node, keep in mind the node should have a characteristic microscopic architecture. That is, a capsule, subcapsular sinuses, cortical tissue and cortical sinuses, and so forth. The description and understanding of what is meant by "either complete or partial effacement of a lymph node" is not only crucial to recognizing the underlying disease process, it is crucial to your grade. Questions about this term will come up on the test, and you can bet when you are asked to diagnose a slide with a malignant lymphoma, I'm going to be looking for the appropriate terminology in your write-ups. Although there are a number of slides in this unit, I'd recommend taking a little extra time, and possibly going over your observations with a friend. Good luck.



Slide 30: Solitary Plasmacytoma

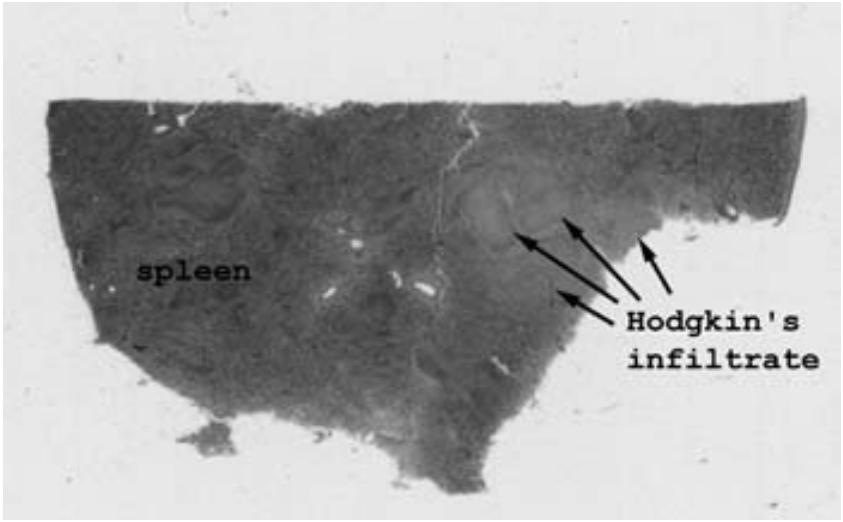
I am not too sure you will be able to tell the tissue of origin here, but it is spleen. These tumors can occur in many different organs, liver, spleen and bone marrow being most frequent. The plasma cells in this lesion may be active, and if so produce a monoclonal gamma globulin or portion of gamma globulin. (Be sure you understand what is meant by an electrophoretic spike.) On occasion no spike is seen in the serum and the reason is that the protein being elaborated is so small that it is cleared in the urine. Checking the urine for a gamma globulin spike is always a good idea in plasma cell tumor.



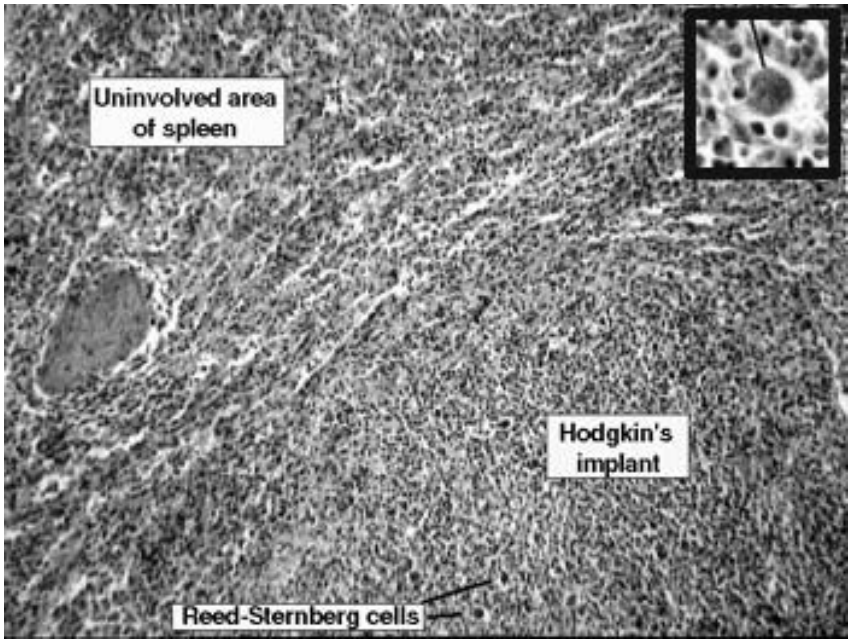
The story here is simply plasma cells. Essentially every cell in the field is a plasma cell. As I try to emphasize above, it's the protein they are making that needs to be watched and understood.

Your observations

Slide 57: Hodgkin's Disease in Spleen



The areas of splenic involvement are pretty obvious here, but this isn't always the case. Look at the uninvolved spleen first to get oriented and then focus on the areas of tumor.



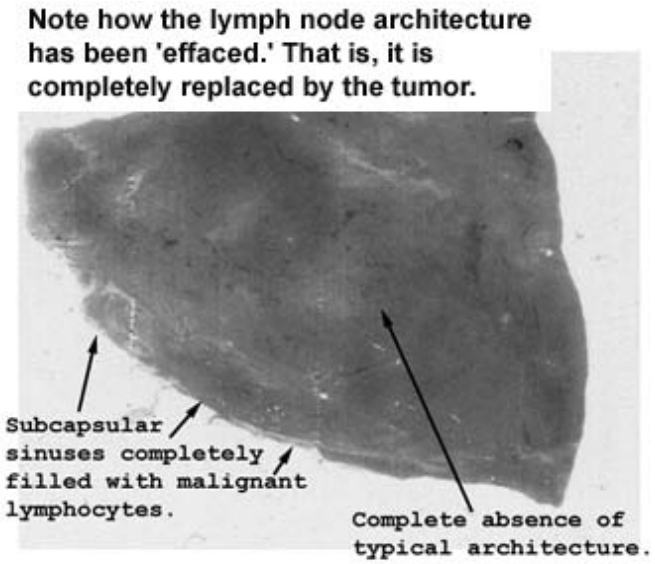
The involvement with Hodgkin's is easy to see in this slide, although this is not always the case. You should be able to find Reed-Sternberg cells within this splenic implant. Remember that when trying to identify them, it is essential that they are in "their proper background." That is to say that they are seen with the Hodgkin infiltrate consisting of lymphocytes, plasma cells and especially eosinophils. There are many cells seen in a reactive lymph node that will mimic the Reed-Sternberg cell. Before identifying anything as one of these diagnostic cells, be sure it is in its proper setting!

The insert in the upper right of the image shows a typical Reed-Sternberg cell.

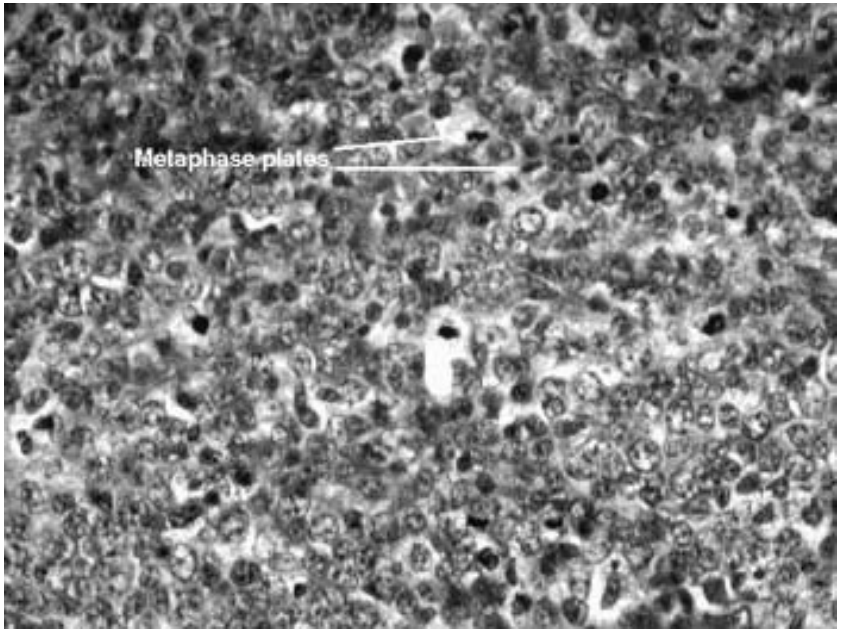
Your observations

Slide 60: Malignant Lymphoma

Your observations

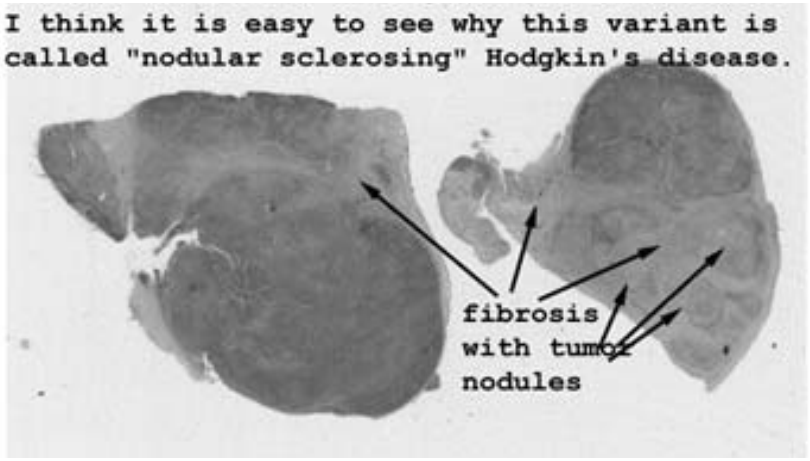


Here you can see the generalized replacement of the lymph node architecture with a diffuse infiltrate of lymphocytes. OK, maybe you can't tell they are lymphocytes by looking at the picture at the left, but when you use your microscope you'll see them.



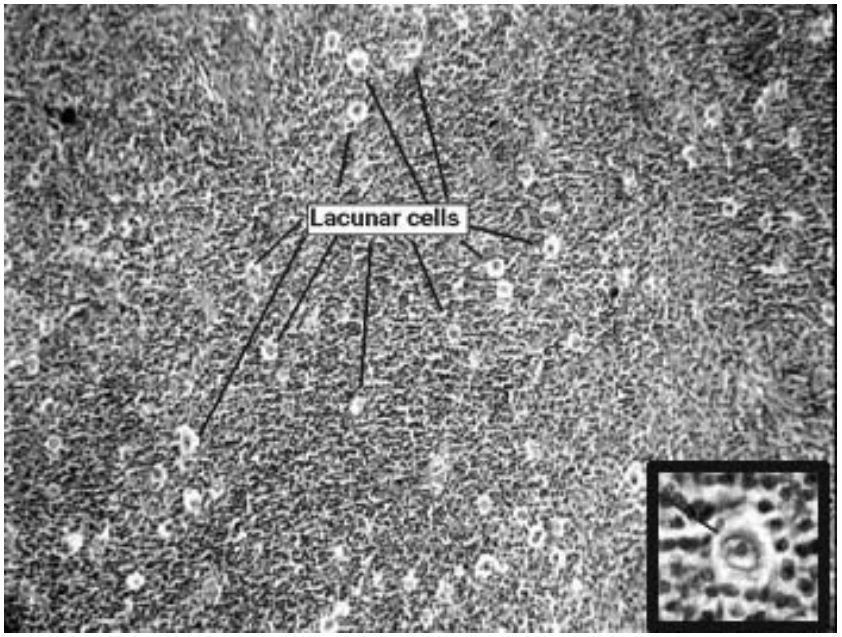
The picture says it all here. Remember to look for cleaved nuclei. Does this slide show a diffuse or nodular pattern? Can you identify the cell type? If not, don't be too worried, even for someone who has had a fellowship in the discipline, it isn't always possible. But I do want you to give it a try. Remember, EFFACEMENT of the nodal architecture.

Slide 62: Hodgkin's Disease in a Lymph Node



You sure can see the nodules and fibrosis in this form of Hodgkin's Disease.

Your observations

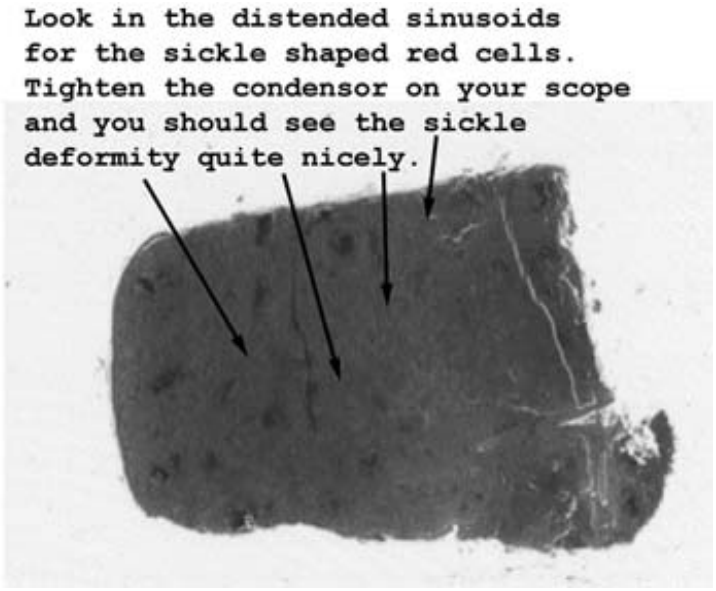


You will have no trouble finding lacunar cells in this slide. Lacunar cells are seen in abundance in nodular sclerosing Hodgkin's disease. Scan the slide first on low power and you will see them everywhere. Like Reed-Sternberg cells they must be in the proper background. They definitely are in this case. This is as a good time to review the kinds of Hodgkin's disease. What is meant by "A" and "B" symptoms? Stages?

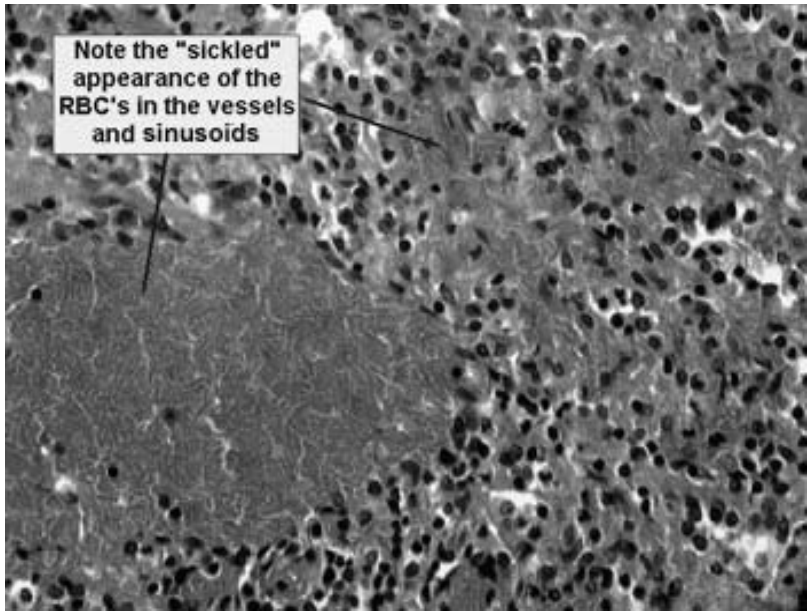
The insert in the lower right of the image shows a lacunar cell in detail.

Slide 67: Spleen in Sickle Cell Crisis

Your observations

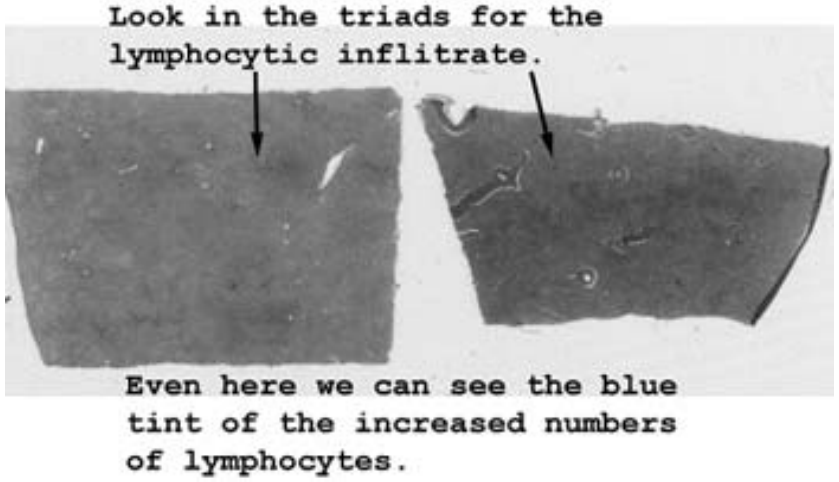


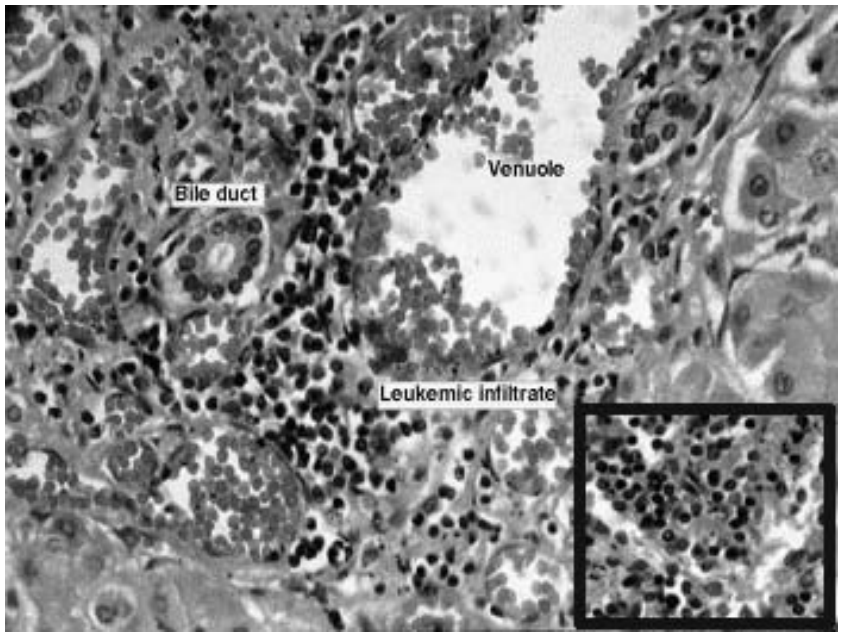
It is certainly possible to see the distended and congested sinusoids and vessels of the spleen in this picture. That's where you want to look for the deformed and packed in RBC's.



Note the sickled RBC's in the sinusoids. If you tighten the condenser you will see the sickled cells nicely outlined.

Slide 69: Liver with Chronic Lymphocytic Leukemia





Look for the malignant infiltrate in the triads of the liver and in the sinusoids of the spleen.

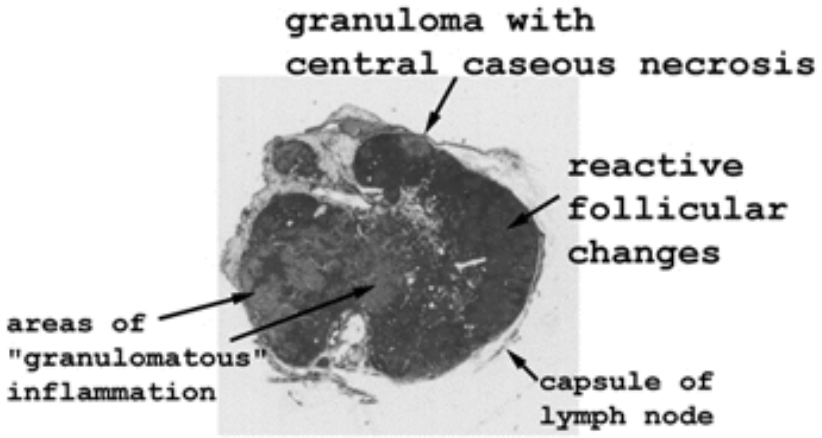
The changes here are subtle. You will see an infiltrate of, quite frankly benign looking, lymphocytes in the triads. We call this a "cold infiltrate" because the lymphocytes do not have a "stimulated" appearance and are not there as a response to some inflammatory process. These lymphocytes may lack the classical cytologic features of malignancy, but they are indeed malignant.

The changes in the spleen are shown in the insert in the lower right of the image. Again you will see a bland looking diffuse infiltrate in the parenchyma as well as "cuffing" of lymphocytes around some of the vessels. It would be good to look at sections of a normal adult spleen first to know what it is supposed to look like. Then concentrate on the areas around the smaller blood vessels.

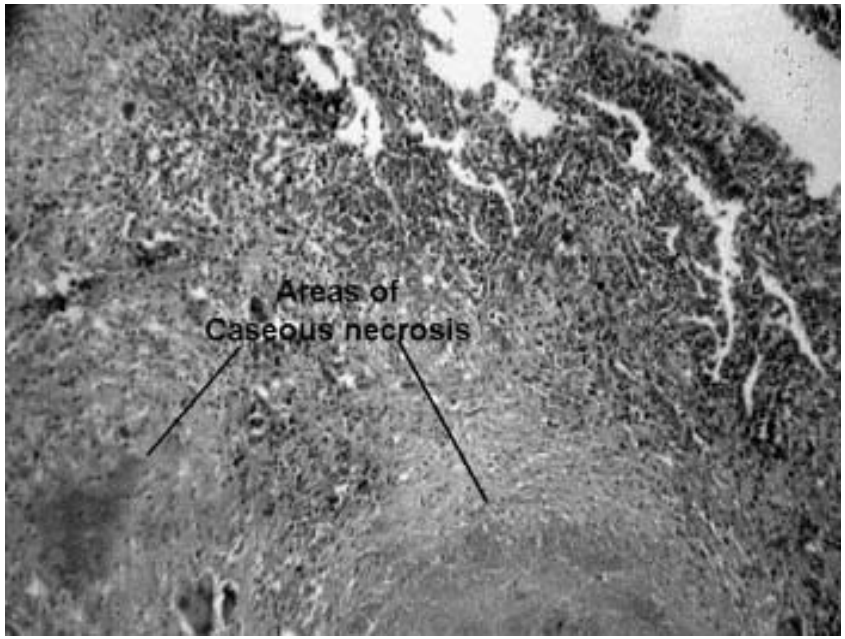
Your observations

Slide 77: Pulmonary hilar lymph node with tuberculosis

Your observations



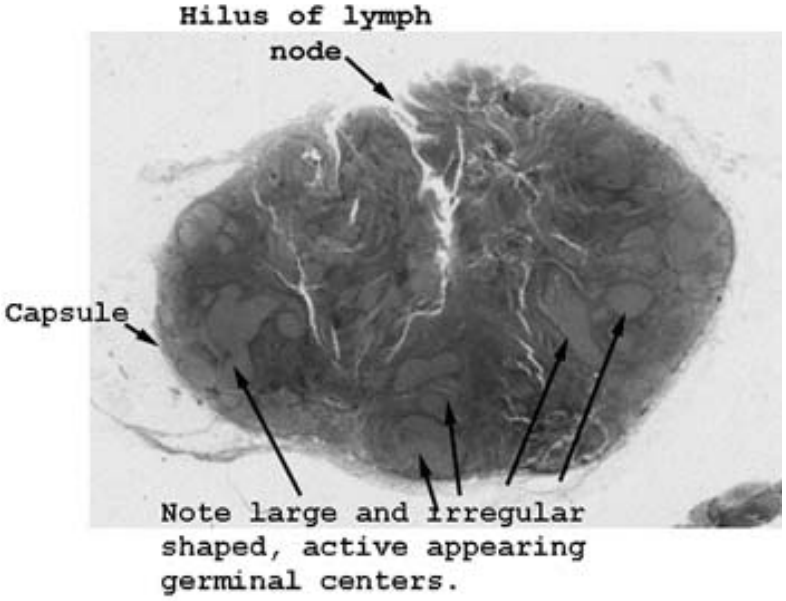
Although this slide is a bit faded, you should be able find the areas of granulomatous inflammation. In some areas there are well developed granulomas with giant cells.



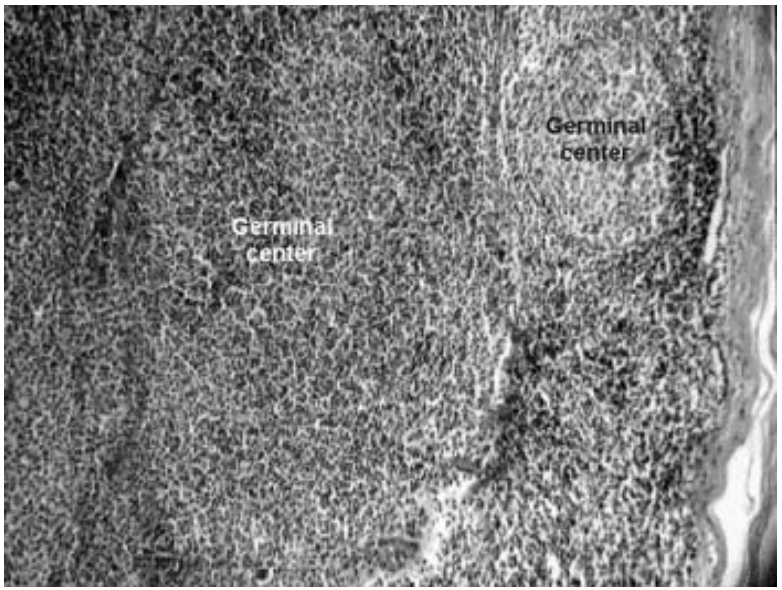
By this stage, you should be pretty familiar with the microscopic anatomy of a granuloma. The granuloma structure is the same as seen in slide 76, but the slide is a little better stained. This is a pulmonary hilar lymph node showing a granuloma and many giant cells. It is from the person that also gave you your pulmonary example, slide 76. It demonstrates quite nicely the body's reaction to tuberculosis.

Slide 84: Lymph Node with Reactive Hyperplasia

Your observations



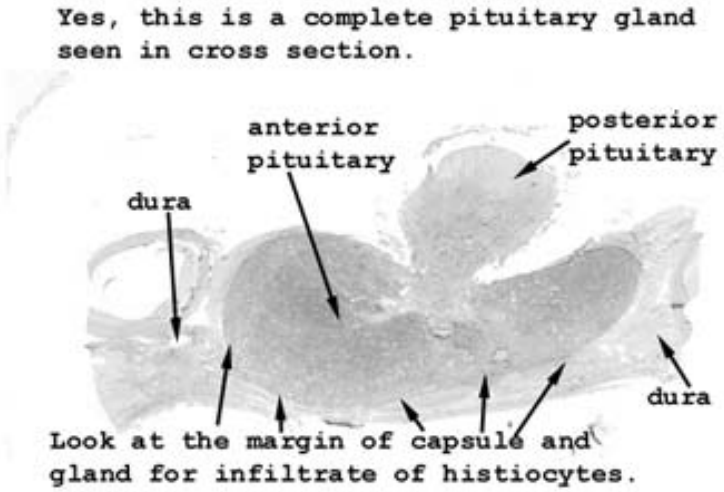
Please observe here that the lymph node is essentially intact. You can easily see the capsule and the other elements of a healthy lymph node. You will, however see, considerable reactive hyperplasia of the follicles.



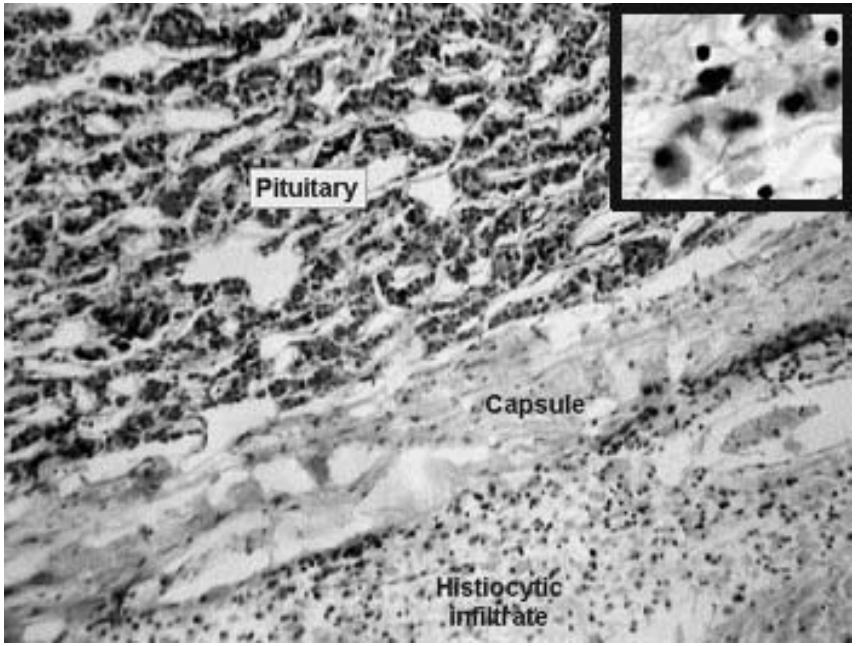
This node has the classical features of follicular hyperplasia. You will see many large and to some extent odd shaped germinal centers. These changes are reactive, not neoplastic, even though the germinal centers are distorted and look fairly wild. All the cells that should be present are here, and there is NOT a monomorphic pattern or infiltrate. You will see the sinuses are open, and there is no EFFACEMENT of the nodal architecture. This is a reactive and not malignant lymph node.

Slide 102: Pituitary with Histiocytosis

Your observations



Look at this, a complete cross section of a pituitary gland! We want to concentrate on the area right at the edge of the gland for the infiltration of the histiocytes.

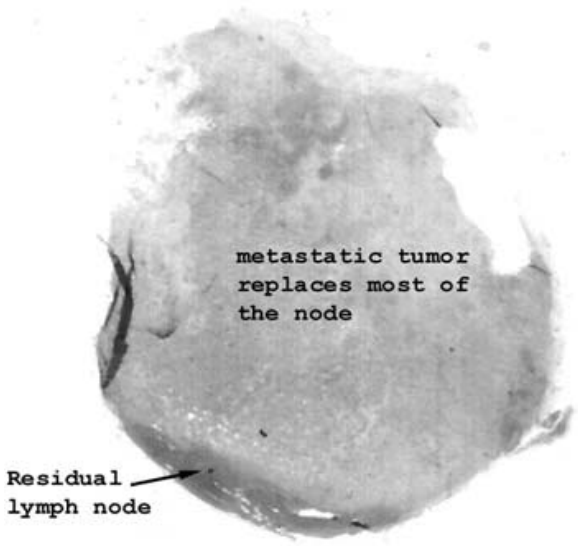


The histiocytic infiltrate in this case is around the capsule of the gland. It is kind of subtle, and you may want to check on the histology of the normal gland to appreciate the difference. The histiocytes do not look particularly aggressive, but they continue to slowly reproduce and cause organ failure.

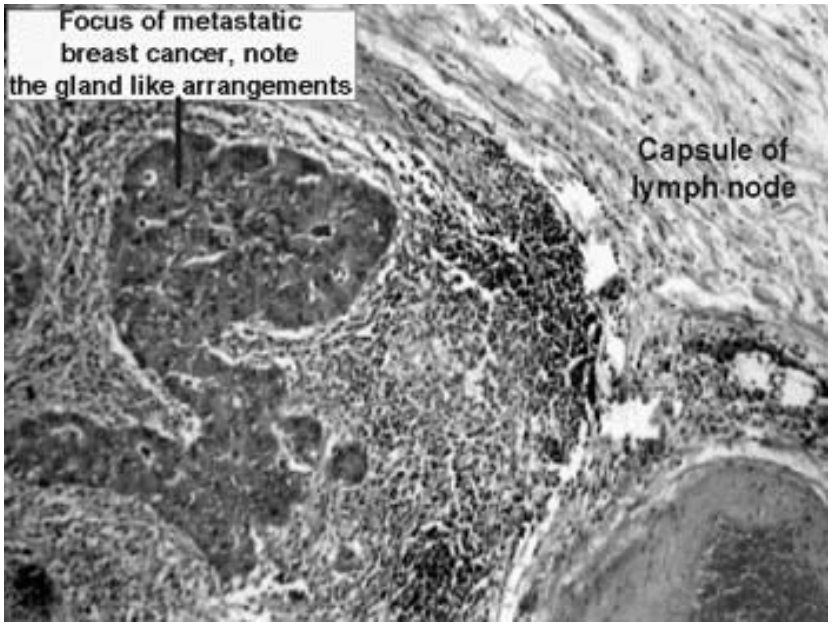
The insert in the upper right of the image shows a detail of several of the histiocytes seen in the capsule of this pituitary.

Slide 111: Lymph node with metastatic breast cancer

Your observations



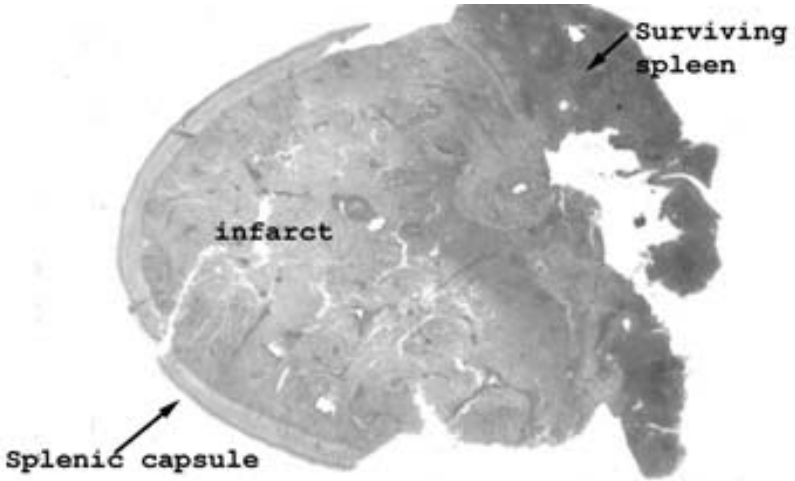
Here you can see that most of the lymph node has been replaced by the tumor. Only a small amount of the uninvolved node remains along one margin.



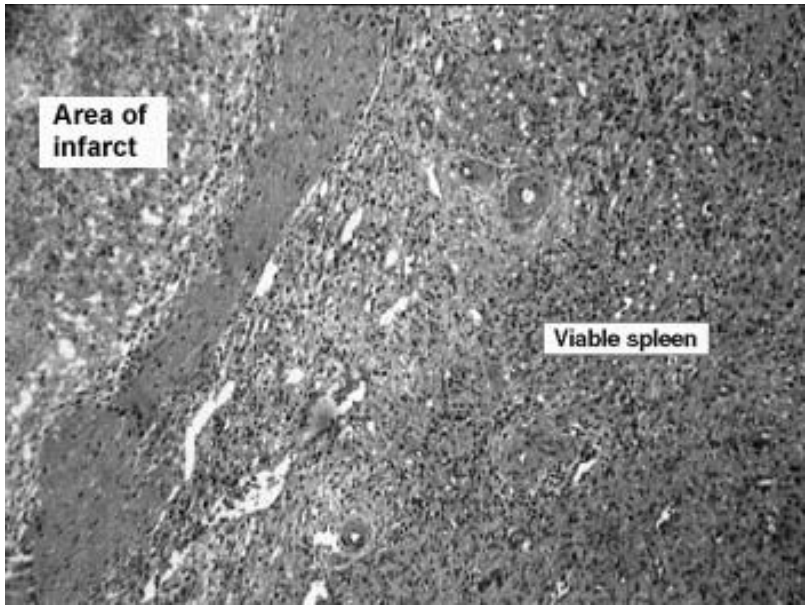
It would be almost impossible to tell just from the histology the source of the primary lesion in this case, but I do expect you to be able to make a good guess. Note the glandular pattern. See if you can tell where the tumor made its first invasion of this node.

Slide 114: Splenic Infarction

Your observations



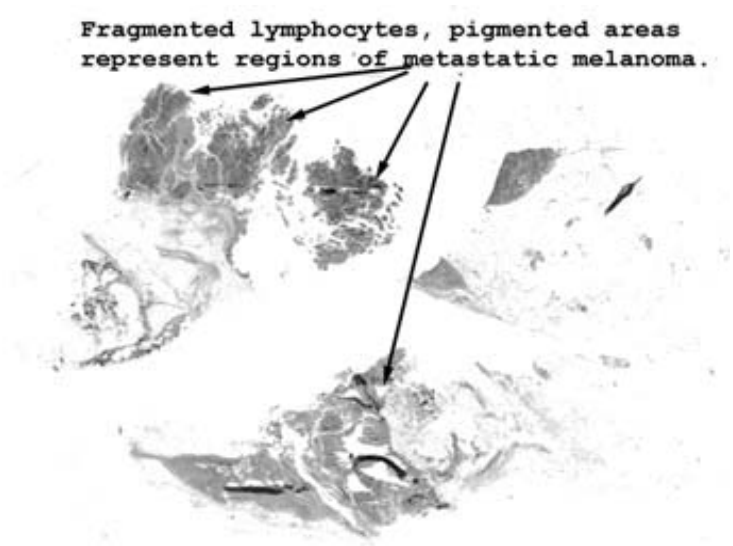
This picture shows you the business end of this slide. The infarct represents most of the tissue. I suggest you start at the edge of the normal tissue and move into the area of the infarction.



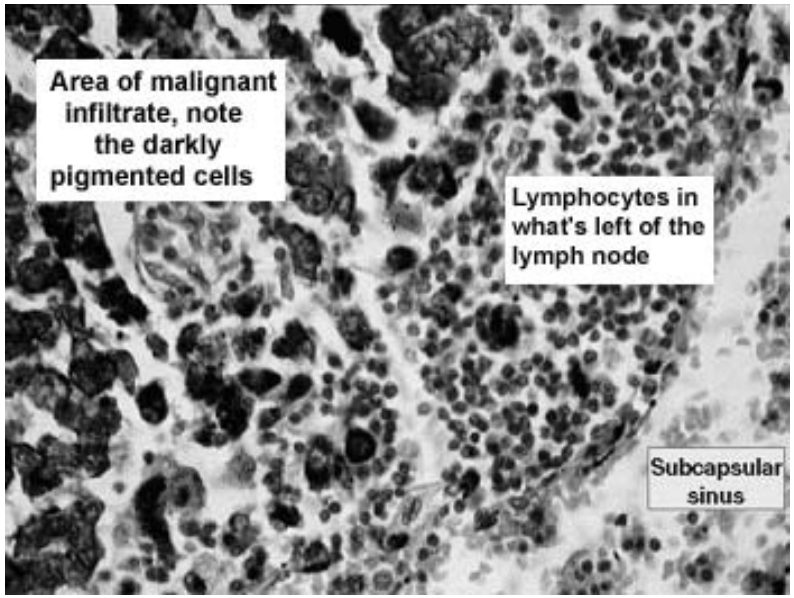
The picture pretty well says it all here. You should be able to find the area of infarction just by looking at the slide on a white background. Seeing this much hemorrhage in a splenic infarct is a little unusual as the arterial supply is what we refer to as an "end organ" type. One typically sees an anemic (white) infarct in the spleen, but in this particular case there is some hemorrhage. Why do you think this is so?

Slide 118: Lymph Node with Metastatic Malignant Melanoma

Your observations



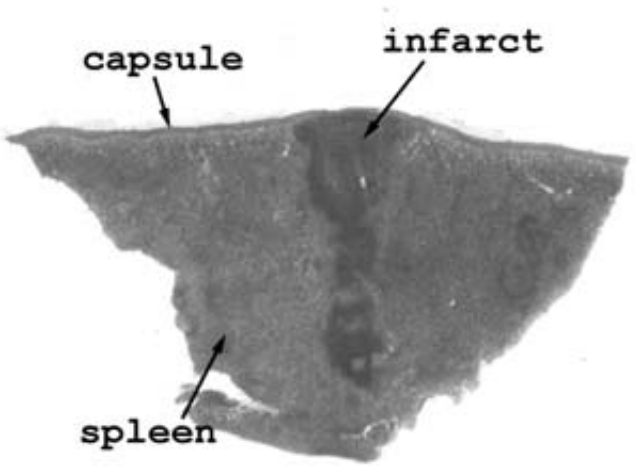
Although fragmented, you can see the area of involvement in this lymph node.



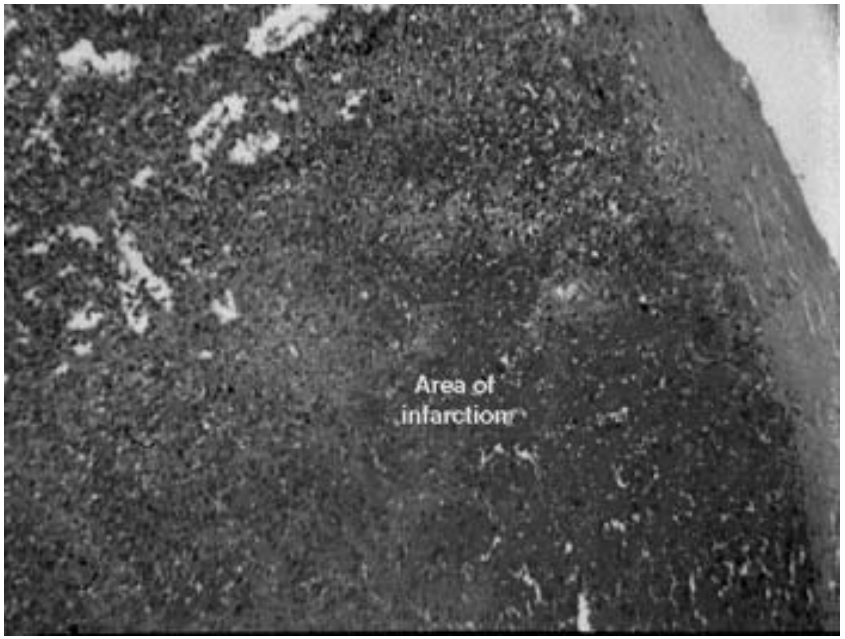
Again the picture pretty well says it all here. You will see a node partially replaced with groups of cells that clearly don't belong there. Many contain abundant dark brown pigment. In general I advise that you look at the subcapsular sinuses and pericortical sinuses for the first evidence of metastatic involvement. Of course, in this case, it is no problem to see the altered histology and the process is considerably advanced.

Slide 123: Splenic Infarction

Your observations



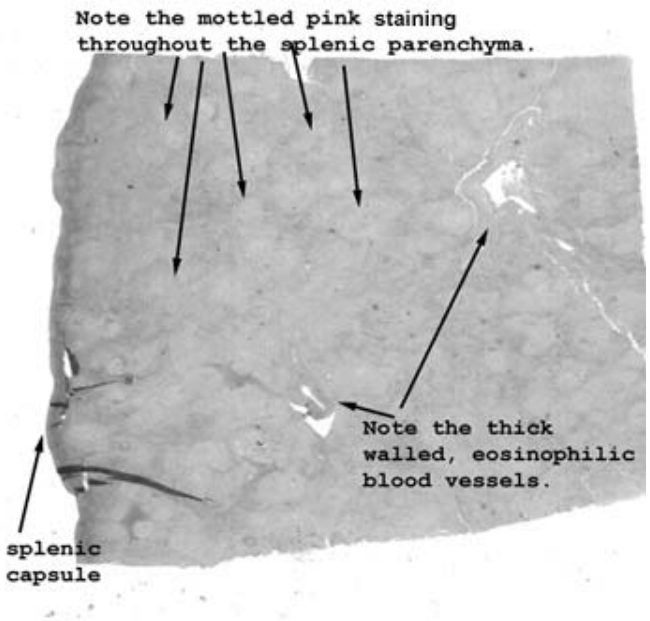
Is this little infarct wedge shaped or what? Again, I think you will easily find the area of the infarct just by looking at the tissue on the slide.



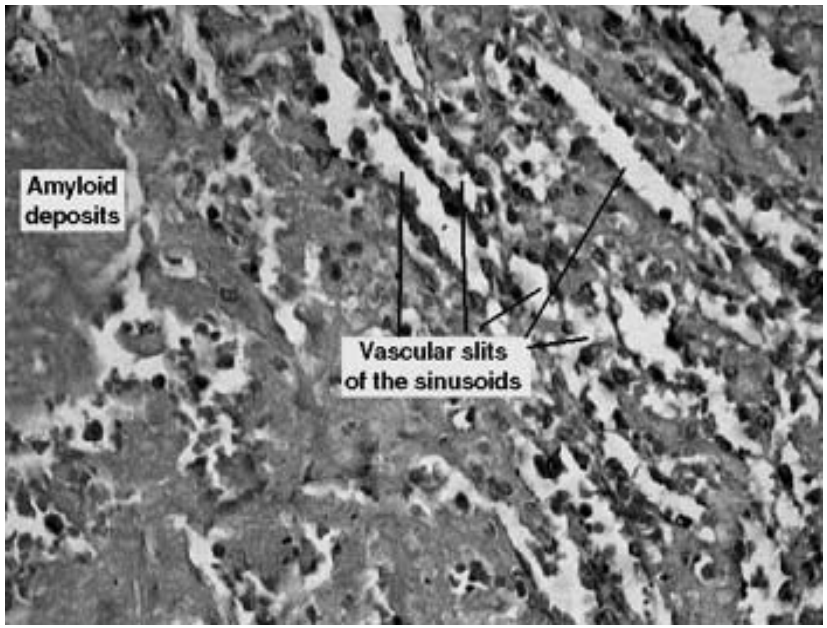
Holy cow! Would you look at this. I keep saying the infarcts in spleen are anemic, and here this thing is hemorrhagic. Well, can't be right all the time in medicine. Most of the time splenic infarcts are anemic because the spleen has an "end artery" system of vascular supply, just like the kidney. But here we have a hemorrhage, possibly due to some degree of trauma of leakage from neighboring sinusoids. When this infarct finally scars down, it will look very much like the expected ones.

Slide 124: Spleen with Amyloidosis

Your observations

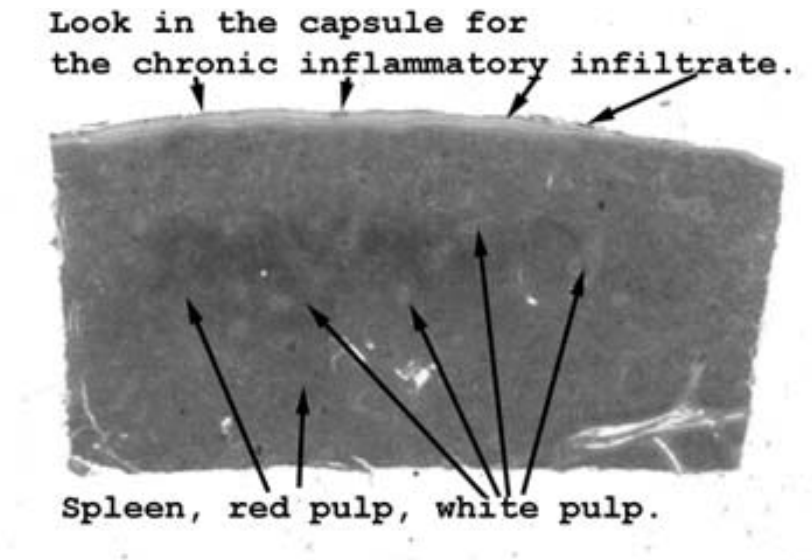


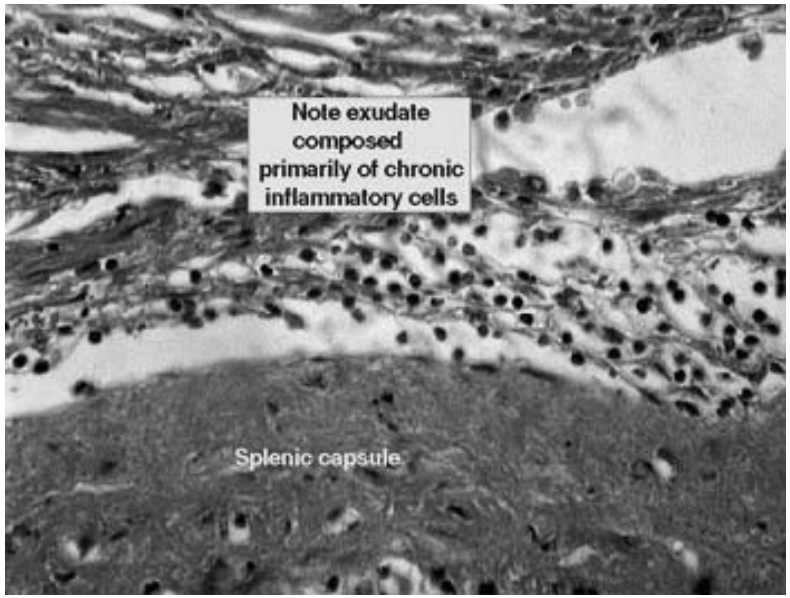
Just looking at this slide, it's easy to understand how functionless it must have been. I think it's easy to see the extensive parenchymal deposition of the amyloid protein. That's what you're looking for.



Not much to add to the picture. The amyloid material is diffusely spread throughout the splenic parenchyma. You might want to compare this slide to a normal spleen to see how involved it is. Take this time to consider all the places you can see amyloid accumulate. What are the basic forms of amyloidosis?

Slide 130: Chronic Splenitis



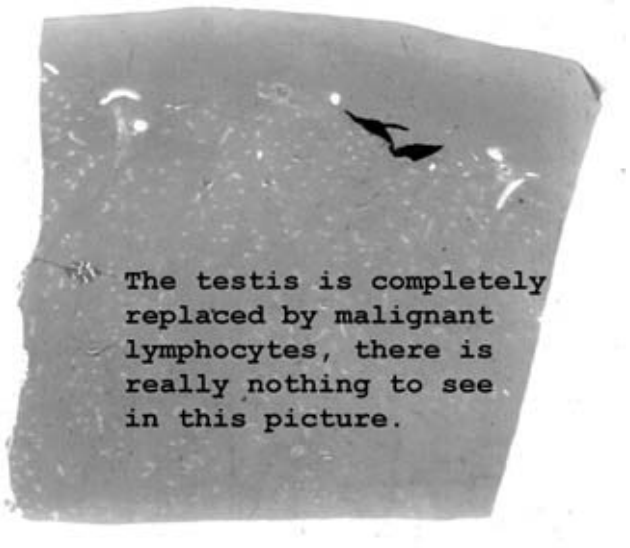


The story of fibrosis and chronic inflammation is in the capsule of this spleen.

Look in the capsule and subcapsular tissue for the lymphocytic infiltrate. What conditions do you suppose would be associated with this ailment? Any symptoms in particular?

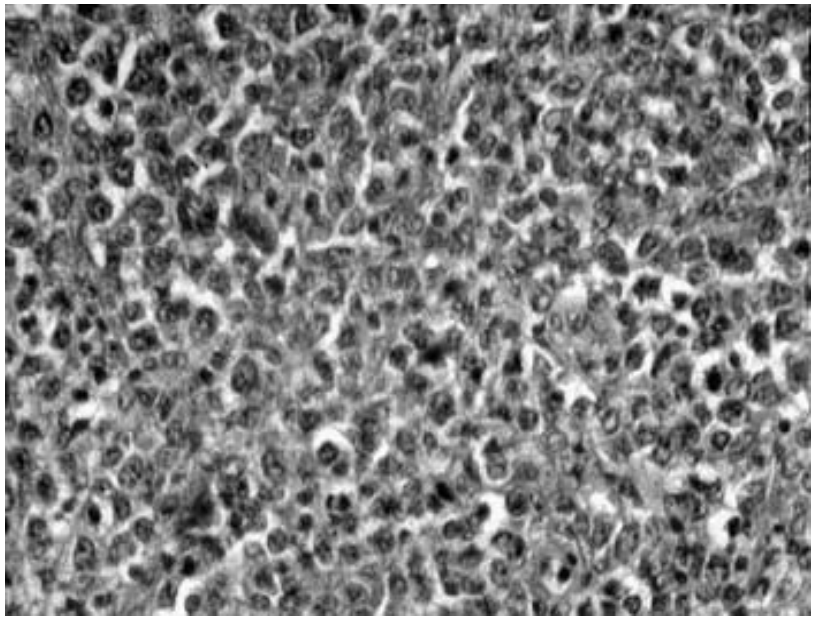
Your observations

Slide 146: Testicular Lymphoma



Trust me that this is from a testis. I see nothing on the slide to help with the identification of the tissue, but I am sure you can appreciate the profound degree of replacement of the tissue with the malignant lymphocytes.

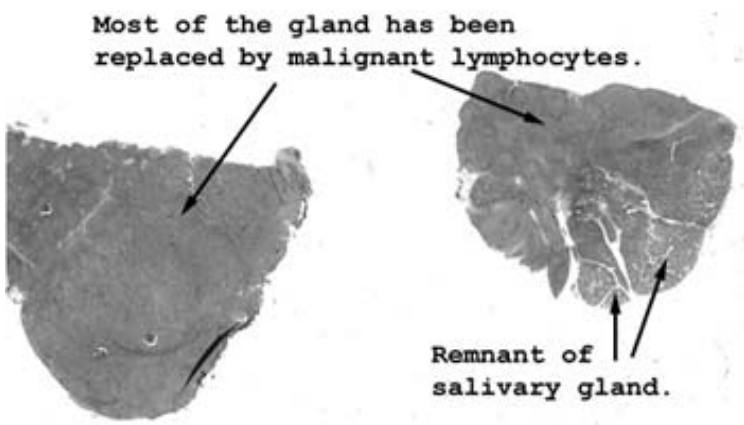
Your observations



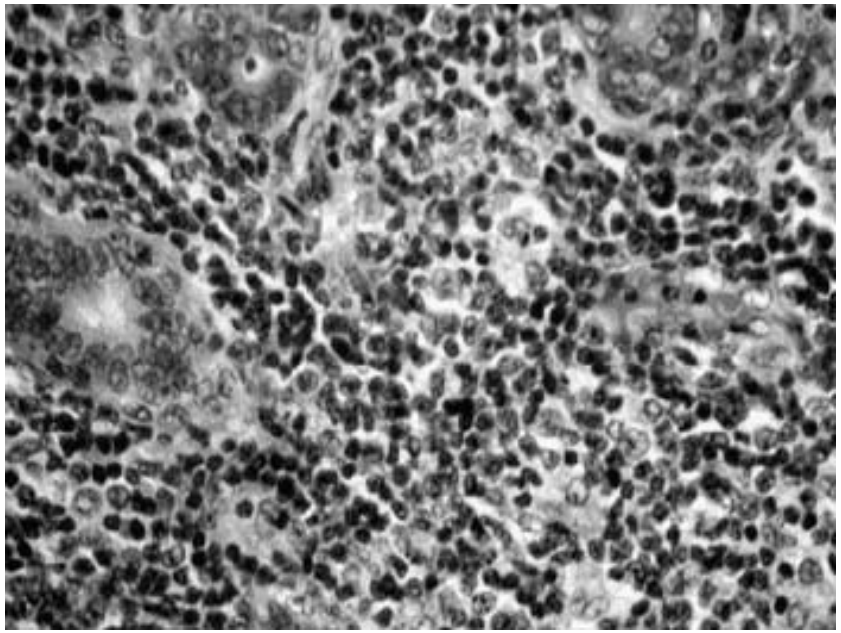
I am not too sure there is anything approaching "normal" testis on this slide. It would be impossible to tell the tissue source from the picture I have taken. Note the uniform infiltrate of monotonous lymphocytes throughout the entire specimen. Again, the object here is to be sure this tumor is not an embryonal carcinoma or version of seminoma, two common primary lesions of the testis. The treatments are completely different. Use this slide for comparison when studying the other testicular tumors we are about to see.

Slide 160: Malignant Lymphoma of Salivary Gland

Your observations



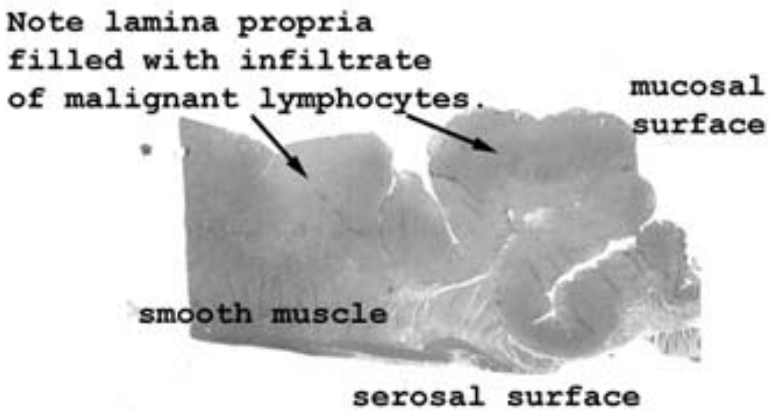
There is a tiny bit of normal salivary gland on this slide. As you will see, the majority of the gland has been replaced by the lymphoma.



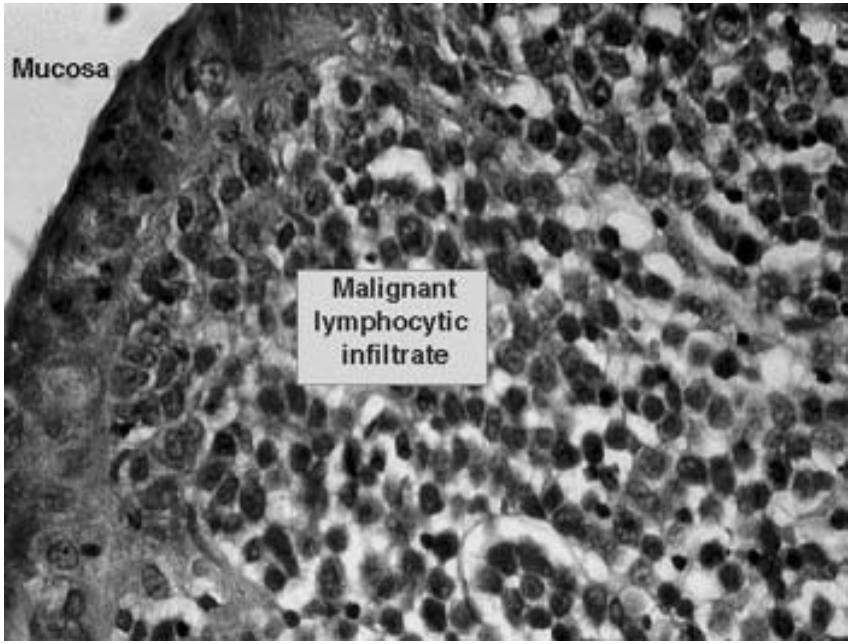
Look at the edges of the fragments of tissue and you should be able to spot some salivary gland in one of the fragments. You will see everywhere else, a sea of lymphocytes with a "diffuse" infiltrative pattern replacing the entire gland. These are medium sized lymphocytes and many show nuclear "cleaves or grooves." In addition to malignant lymphomas, there are several conditions in which one sees a profound lymphocytic infiltrate of the salivary gland. Can you think of any? Maybe associated with ocular manifestations?

Slide 167: Intestinal Lymphoma

Your observations



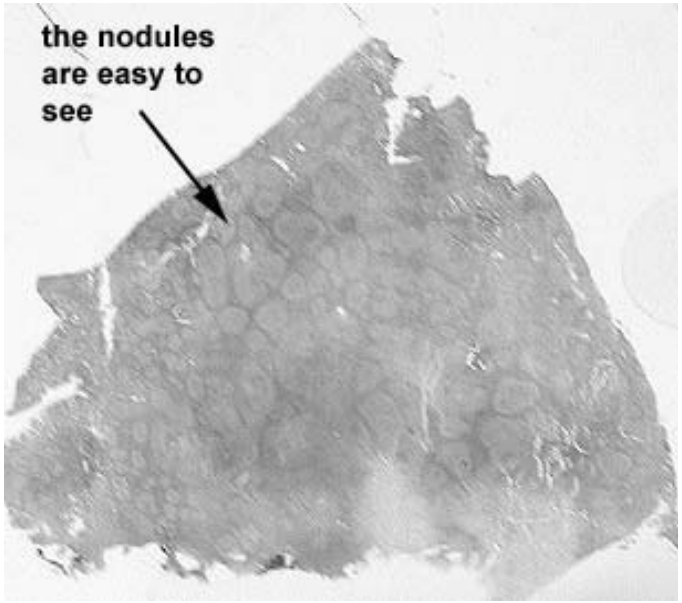
It's a lot easier to see the changes in this slide than in #142. Here you can actually see the infiltrative pattern of the tumor.



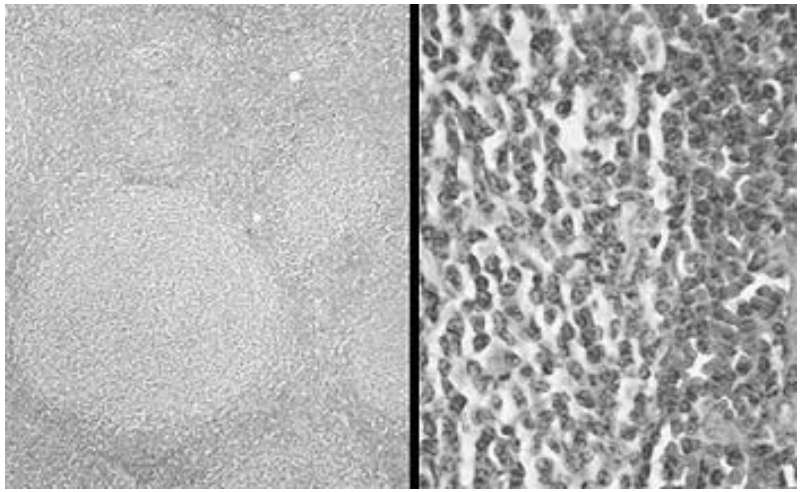
This is the second example of an intestinal lymphoma. The features are essentially the same as in slide 142. See which is the better example in your set and spend time with that one. You will see the malignant lymphoid infiltrate in the submucosa and possibly extending through the muscular wall. Note the monomorphic nature of the malignant lymphocytes. The distinction of nodular and diffuse does not apply here; these terms only have reference in lymph nodes themselves.

Slide 197: Lymph node, malignant lymphoma

Your observations



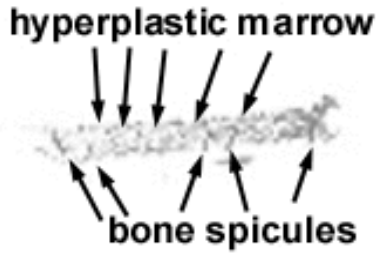
It's not that hard to see the nodularity of this lymphoma. Again, take into account that the entire nodal architecture has been effaced and replaced with the malignant infiltrate



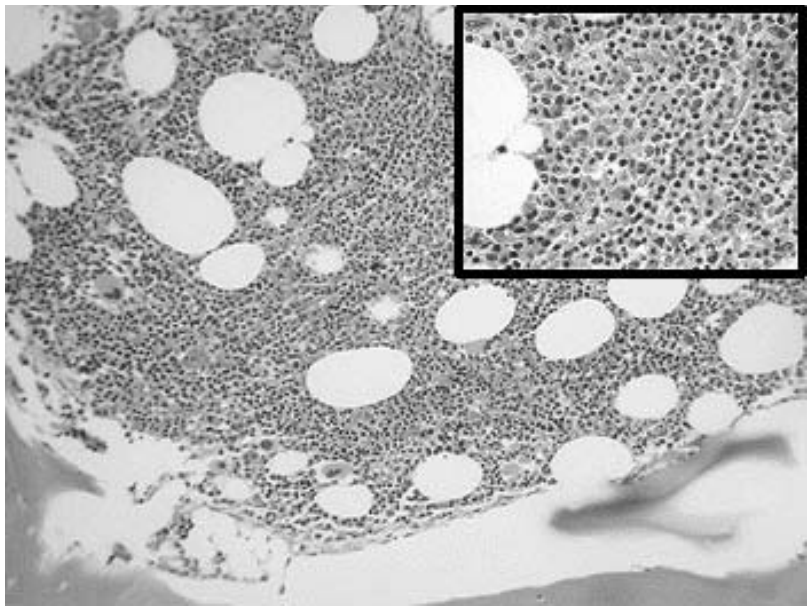
At low power they do look a bit like germinal centers, but take a closer look. There's no cellular differentiation and the entire node is replaced with a clonal proliferation from a single malignant lymphocyte.

Slide 205: hyperplastic bone marrow

Your observations



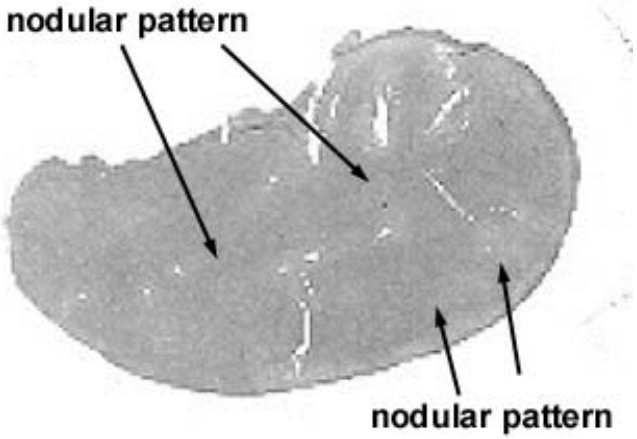
Recall the expected adult cellularity of the bone marrow is 50:50. That is 50% myeloid tissue and 50% fat. Here we see something more like a 80:20 cell:fat ratio.



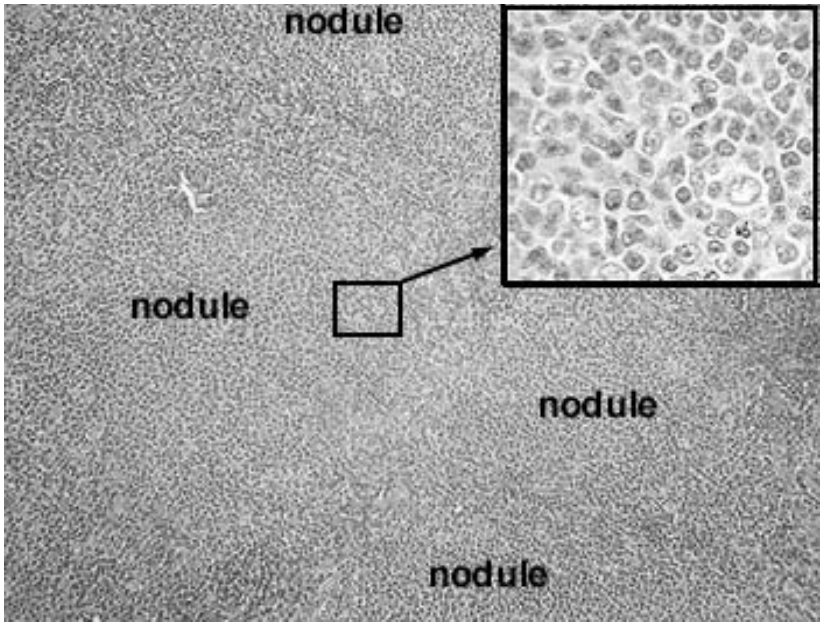
The bone marrow elements mature normally, it's just that there's a bunch of them. What sorts of things could lead to this?

Slide 206: Lymph node, follicular lymphoma

Your observations



Hold this slide up to the light and you'll have no trouble seeing the nodular aggregations. Even though there is nodularity, there is still uniform effacement of the expected nodal architecture. That is to say, the expected microscopic organization of germinal centers, sinusoids and the like has been completely replaced by the monomorphic growth of the malignant lymphocytes.



Here you can see the nodular, or follicular-like, arrangement of the malignant lymphocytes. Even though they superficially look like germinal centers, there is no maturation of cells and nothing healthy about the organization.

General and Systemic Histopathology
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Section 15 *Diseases of the Immune System*

In this laboratory we will be looking at examples of diseases that begin as, or principally involve, abnormal activation of the immune system. Clearly, the immune system participates to a degree in all forms of disease, most of the time on behalf of the good guys. Here we will see what can happen when our tissues become the object of interest and destruction by our own immune system. We will see examples of both direct assault and what might be termed "innocent bystander" injury. This would be a good time to review the topic of hypersensitivity and the four classes of this type of injury. In a most distilled form the categories are:

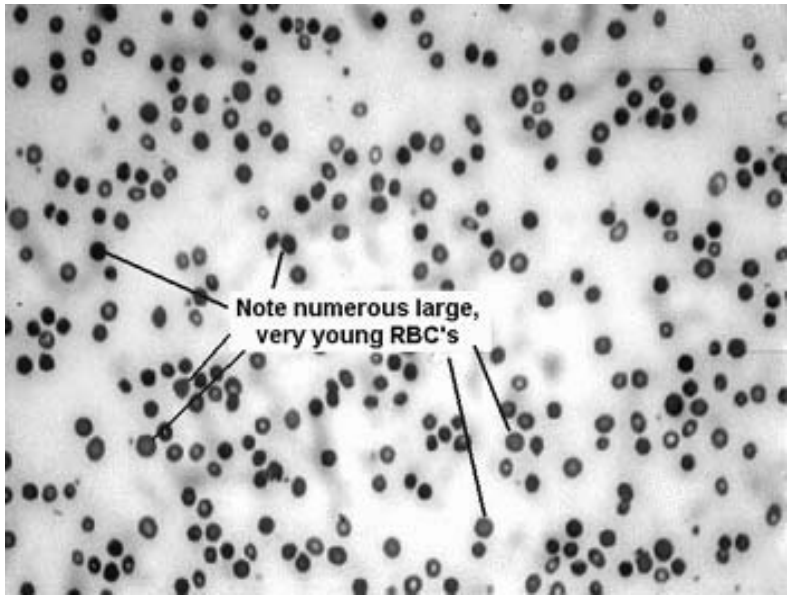
Type I IgE mediated histamine release.
An example would be an anaphylactic response to a bee sting.

Type II Antibodies produced to "self antigens."
For example lupus erythematosus or an autoimmune hemolytic anemia.

Type III Antigen-antibody complex disease.
In this instance, the antigen is "non-self," but the complexes are passively absorbed onto bodily tissues and immune system destroys the "innocent bystander." An example would be streptococcal induced glomerulonephritis.

Type IV T-cell mediated hypersensitivity.
The best example I can think of is tuberculosis

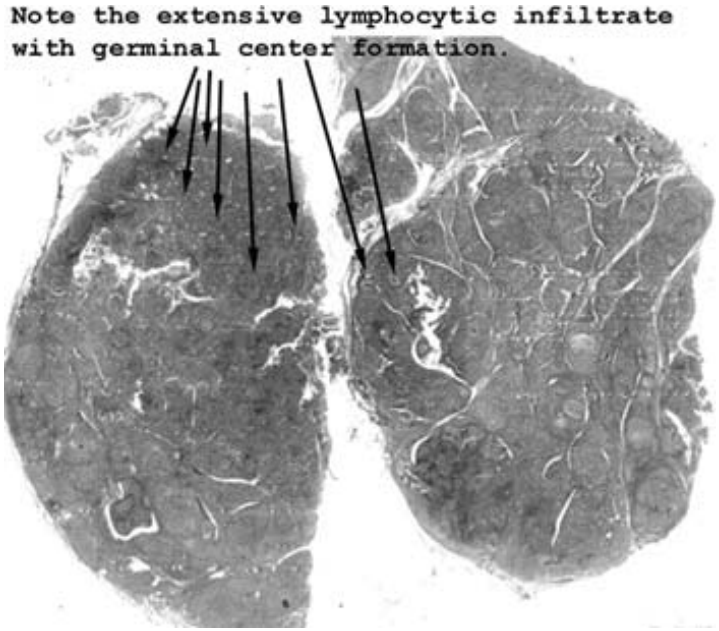
Hemolytic Anemia



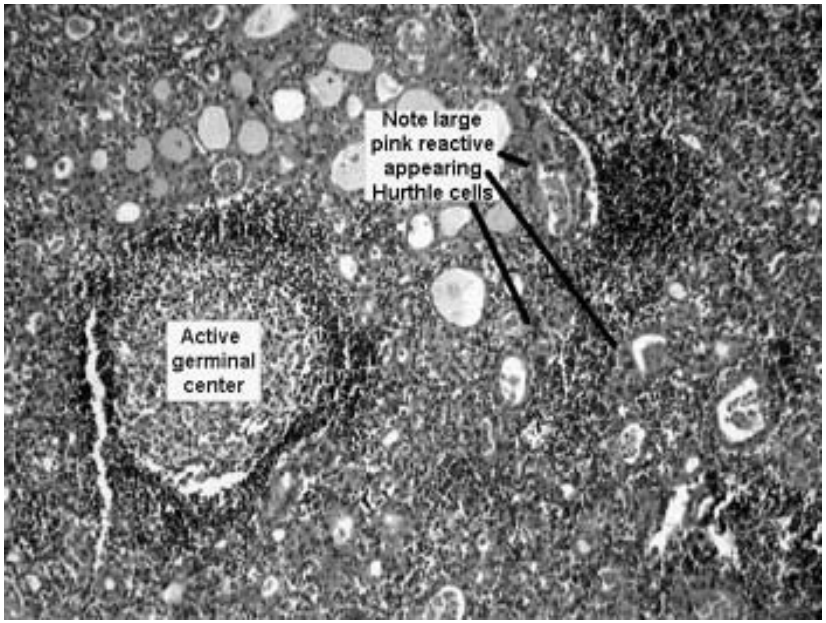
The red cells in this slide are really chewed up. You will see many odd-shaped and fragmented cells as well as a few target cells. You will see some rather large red blood cells with a distinct purple quality to the cytoplasm. These are very young red cells known as reticulocytes. The reticulocyte gets its name from the fact that a fine reticulum of RNA remains in it for a few days after being expelled from the marrow. This RNA content gives the purple caste to the cytoplasm. We use this aspect of the youngest RBC's to determine the rate of introduction of new red blood cells into the circulation. By extension, the number of reticulocytes also gives us a good idea of the rate of turnover (i.e. life span) of the red blood cells. Of course, you can only make these determination from the "corrected reticulocyte count." Be sure you know the difference between just the regular reticulocyte count and the much more important corrected reticulocyte count. What is it corrected for? Hint, remember reticulocyte number is expressed as a percentage of red blood cells.

Your observations

Slide 25: Hashimoto's Thyroiditis



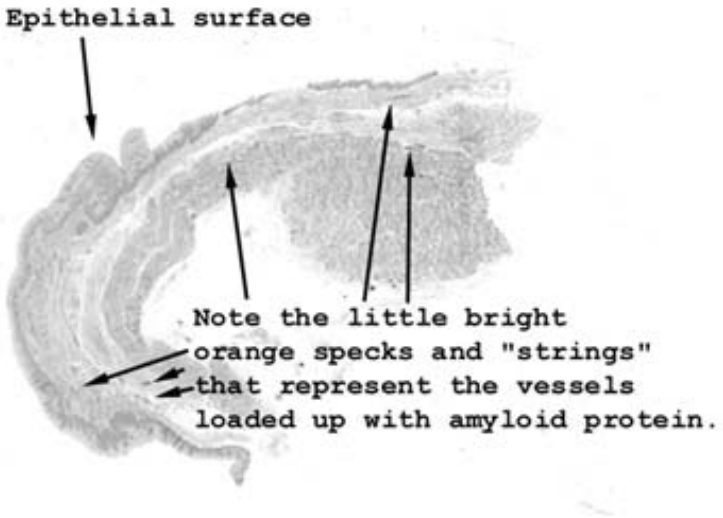
The key feature here will be the lymphoid aggregates with germinal center formation within the thyroid tissue itself. In the picture to the left, you can obviously see the clusters of lymphocytes as well as areas of fibrosis giving a lobulated look to the thyroid in general.

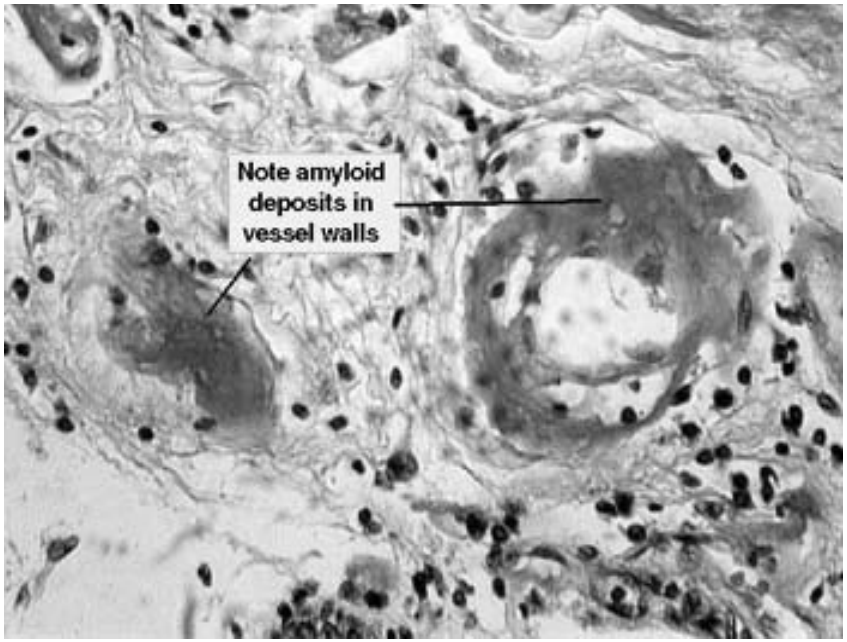


This is Hashimoto's thyroiditis. Note the chronic inflammatory infiltrate and especially the active lymphoid germinal centers within the gland itself. There is marked destruction of the gland. In areas of attempted regeneration you will see enthusiastic and stimulated follicular cells we call Hurthle cells. These are large, brightly pink stained cells that may or may not be seen to be in direct association with a follicle. KNOW THE ANTIBODIES that we use for diagnosis in this case. Check Bakerman for the important levels of anti-colloid and anti-microsomal antibodies. When this disease has run its course, what level of thyroid function do you think will remain?

Your observations

Slide 169: Skin with Amyloidosis, Congo Red Stain





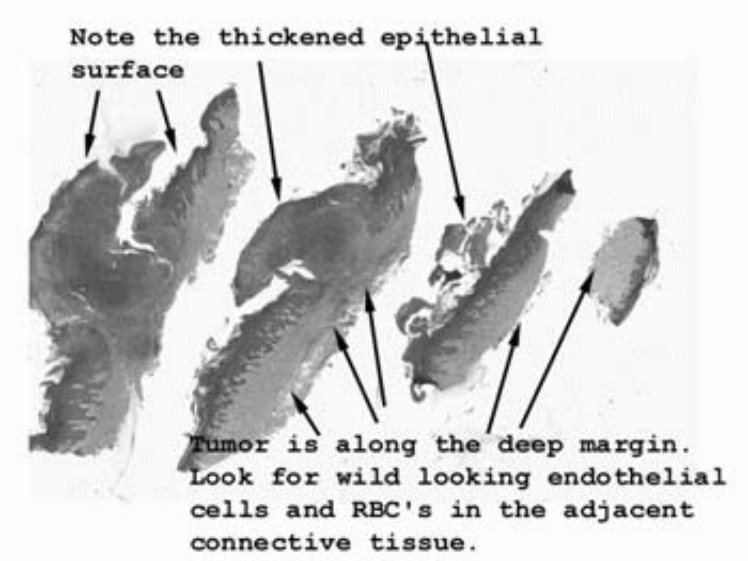
You want to look at the vessels in the dermis. The amyloid deposits will be in the walls.

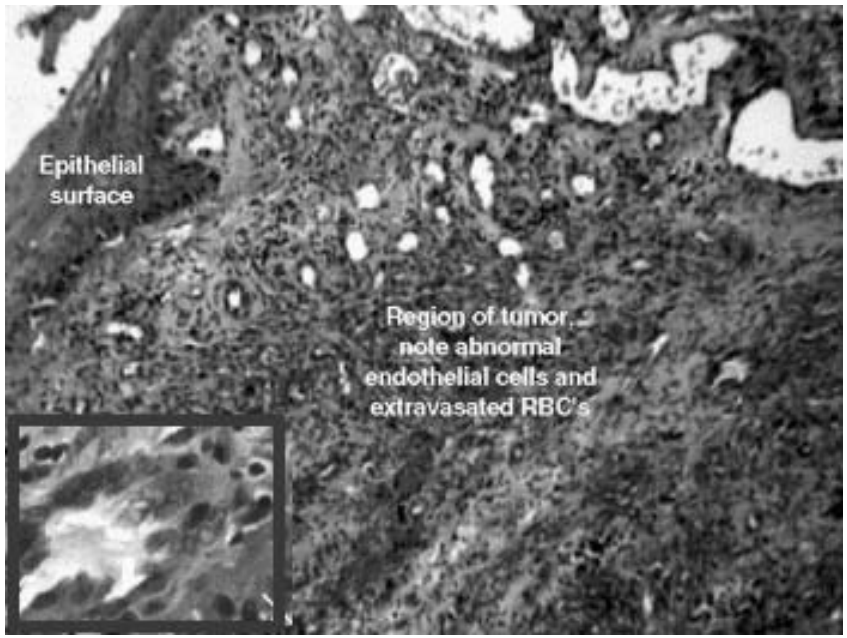
Your observations

This slide is stained with congo red stain, a dye that binds to the amyloid protein. Look in the vessel walls of the dermis for this fibrillary orange staining material. You won't see it to any great extent in the general connective tissue of the dermis.

Compare this slide to 168 to see the difference the congo red staining makes.

Slide 190: Kaposi's Sarcoma of the Skin





Your observations

Here we have multiple serial sections of the skin biopsy. Once you've scanned the entire slide, look in the dermis for the characteristic malignant endothelial cells.

Yes, this biopsy is from an AIDS patient. Note the extravasated RBC's in the surrounding connective tissue and the bizarre and very disturbed looking endothelial cells that comprise this lesion. You will see many very abnormal "fibroblast" looking cells, but these are really bizarre endothelial cells. You will also see some dark brown or black pigment in the background and possibly in some of the histiocytes. This pigment is actually iron from the red blood cells that have previously broken down. An iron stain, such as a Prussian Blue, would really highlight this feature.

The insert in the lower left of the image shows a detail of the malignant cells making up the vessels and the extravasated red cells.

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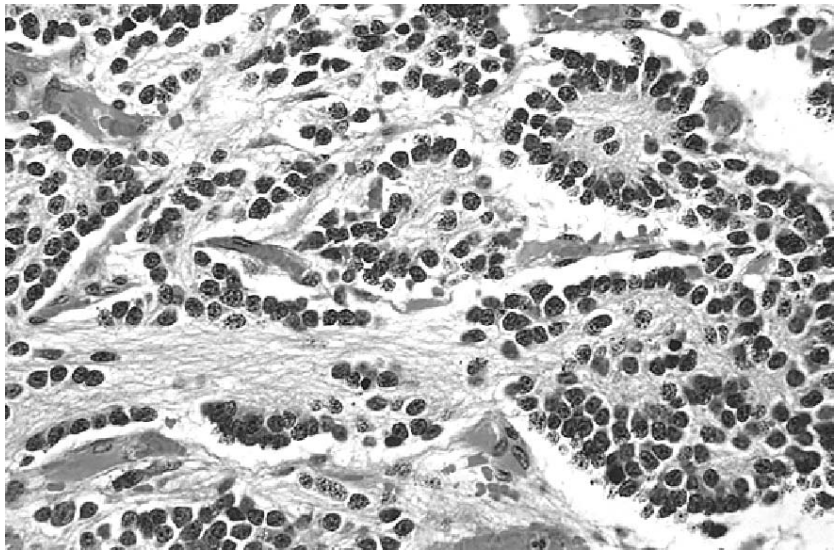
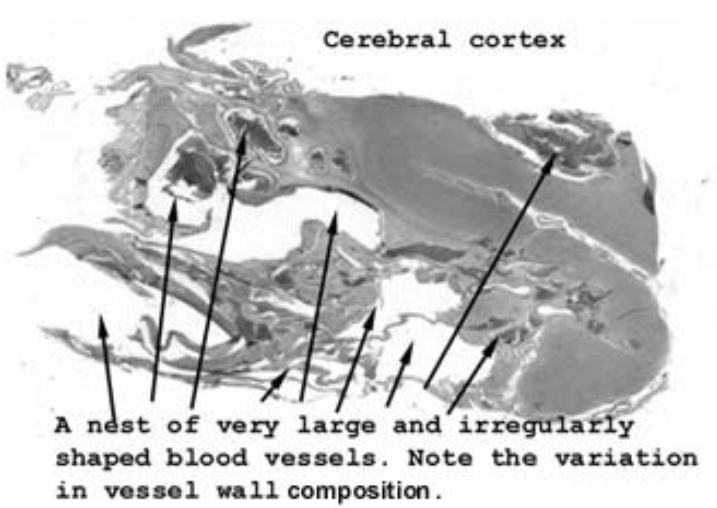
Section 16 *Pediatric Pathology*

As surprising as it might sound, we really know little of the physiology and maturational processes of childhood and adolescence. In fact, and unfortunately so, it's not obvious to most people that children are not just smaller versions of the adult form of Homo sapiens. They suffer from different types of illnesses ranging from infections to neoplasia. Many genetic conditions become evident in early childhood, but not all with obvious manifestations. Because children are naturally curious, accidental injury becomes a significant element in their lives. And most unfortunately, their limited ability to defend themselves make them obvious targets of abuse. We simply don't have the time or resources to explore all aspects of pediatric pathology, still the cases that have been chosen should provide a good grounding in the basic patterns of pediatric illness and the juvenile response to various forms of injury.

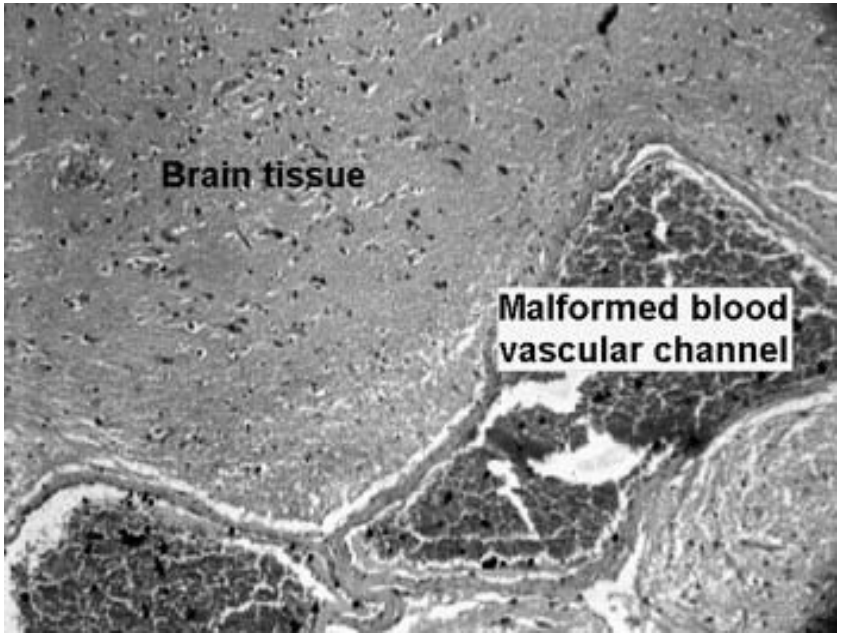


Slide 83: Arteriovenous Malformation in the Brain



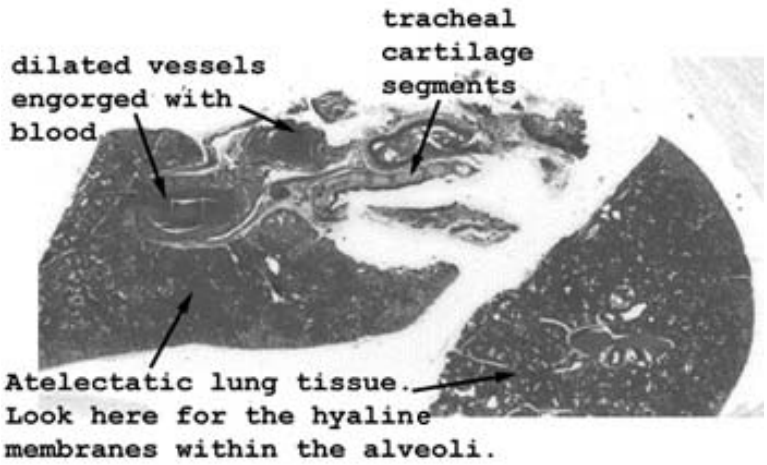
The many malformed vascular channels are quite evident in the picture to the left. These lesions are apt to bleed, as the presence of this specimen in our study attests to. No this is not a surgical specimen.

Your observations



Here you will see many large and malformed blood vessels that have a "hybrid" wall structure. In some areas the wall resembles a vein and in others an artery. Look for an elastic interna. One would never expect to see vessels of this size with such peculiar wall structure within the brain. This represents a congenital deformity and can cause death at any age. The vessels are subject to leakage or rupture and this subject in fact died with an intracerebral hemorrhage.

Slide 89: Infant lung with hyaline membrane disease



The lung tissue here is quite "meaty," and may not even appear as lung to you. Fetal lung looks much like this, although in this case there is extensive atelectasis along with the accumulation of the alveolar proteinaceous material. See how many aspects of pulmonary histology you can identify in this slide.

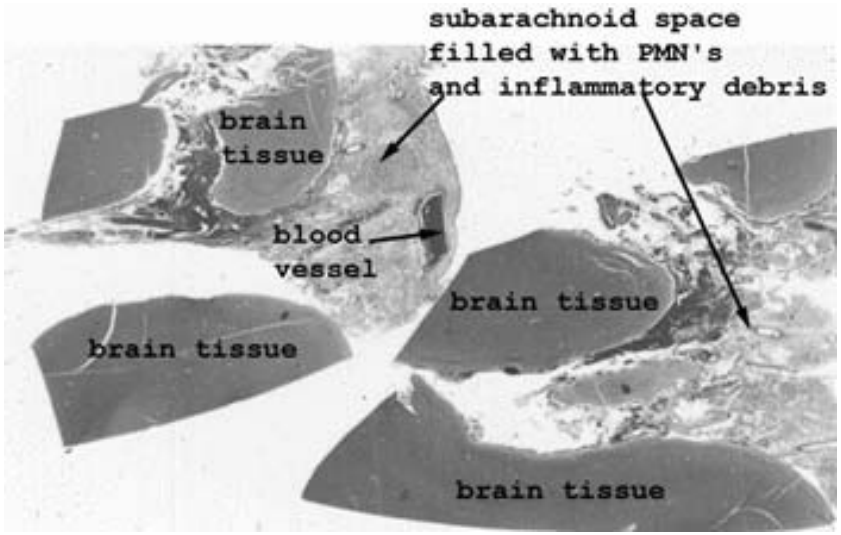
Infant lung looks considerably different from adult tissue. Note how much more cellular and thick walled the alveoli are. The vessels are quite congested. The "hyaline membranes" are deposits of pink staining proteinaceous material in the alveolar spaces. They are not continuous, but appear as half moon shaped deposits. They are hard to see at first, but once you have picked them up, they will start to appear all over the slide. What caused this condition? Do adults have something similar?

A higher power view of one of the hyaline membranes is shown in the insert, upper right corner. Note how the histological appearance of infant lung is so much different from that of adult pulmonary tissue. Here you can see how much more cellular and thick walled the alveoli are and how cuboidal the alveolar lining epithelium appears. This cuboidal nature of the epithelium is not a function of the disease, rather reflective of the degree of immaturity of the lung tissue.

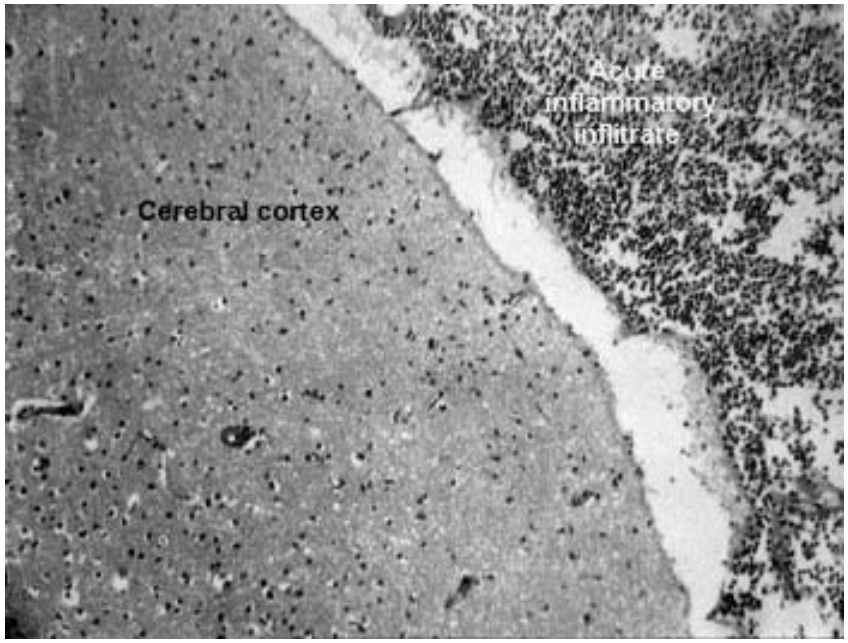
Your observations

Slide 90: Acute meningitis

Your observations

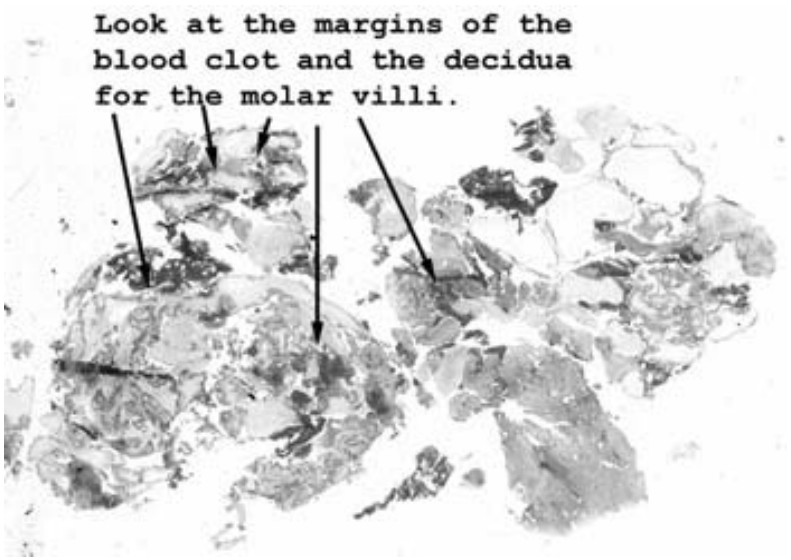


Here you see the unbelievably expanded subarachnoid space containing numerous polymorphonuclear leukocytes. What do you suspect the exudate looked like grossly?



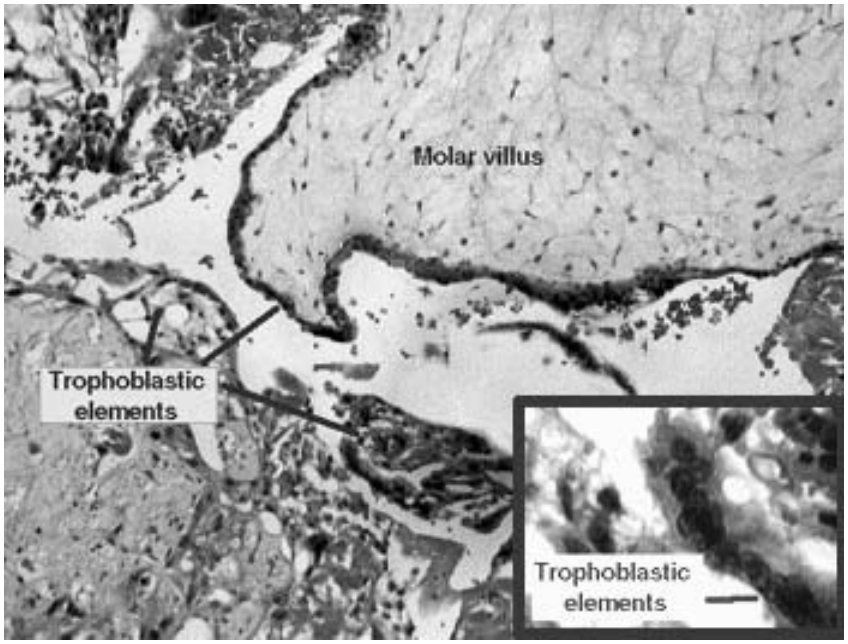
This slide shows a profound acute inflammatory infiltrate associated with Hemophilus influenza meningitis. The organism most likely gained entrance into the subarachnoid space by way of the blood stream. The child with this condition died shortly after being admitted to the hospital, despite vigorous antibiotic therapy. Unfortunately, the child was not brought in until he was virtually moribund. You should have no trouble finding the polymorphonuclear leukocytes in this slide.

Slide 155: Hydatidiform mole



Look in the blood clot or at the margin of the clot and decidualized endometrium for these bizarre villi. You might want to compare these placental villi with those of the first trimester miscarriage in slide 94. There is quite a difference. Take note of the changes in the trophoblasts covering the villi.

Your observations



This is a classic "molar pregnancy." Note the large and abnormally shaped villi with edematous cores. These villi are covered with atypical trophoblastic cells growing as a syncytium. You may see a mitotic figure or two, but on the whole, the degree of anaplasia is not nearly as great as seen in a choriocarcinoma, the highly aggressive malignant counterpart of this lesion. There will be some necrosis and inflammatory debris mixed with the blood clot, but for the most part this is well preserved and very representative.

The insert, lower right, is a higher power view of the trophoblastic element of this molar pregnancy.

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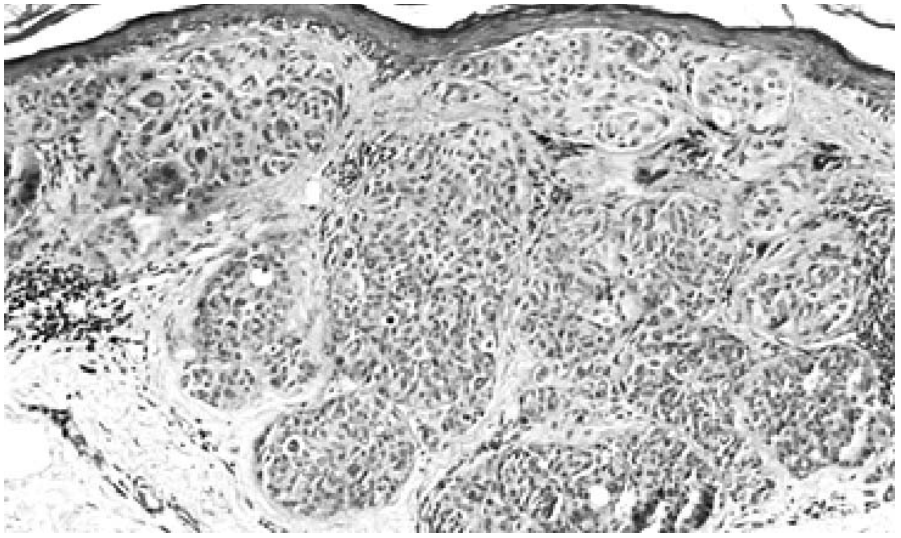
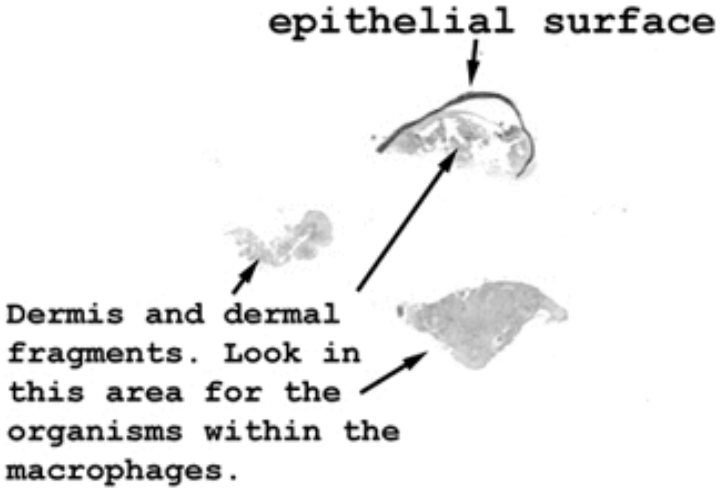
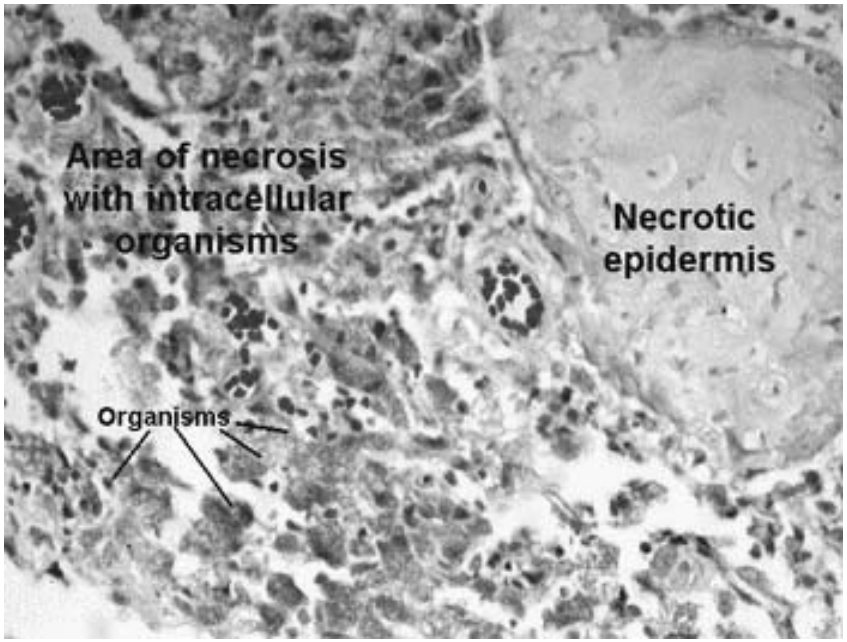
Section 17 *Disorders of the Skin*

The skin is a much more complex organ than most people think, and this includes many physicians. It's involvement in normal physiology goes far beyond just holding us together and serving as a barrier to the outside world. Obviously it's involved in temperature regulation, fluid and electrolyte balance (at least secondarily), antigen processing and even vitamin metabolism. Because it is one of our principal points of contact with the outside world, it is subject to many environmental stresses. These stresses may produce fairly diagnostic changes or in some cases out-right diseases. We will look at a number of lesions as well as ways in which the skin tries to adapt to changing environmental influences. Principal among these is solar induced injury, and resultant skin malignancies. But we must keep in mind that the skin will also reflect underlying, and often quite distant, medical problems. We will see examples of metastatic cancer to the skin, as well as immunologic and infectious injury. Although our collection may be somewhat limited, we will look at representative examples of most forms of injury of the skin, and you should be able to apply what you learn to most other cutaneous disorders. Hang in there.



Slide 17: Skin with leishmaniasis





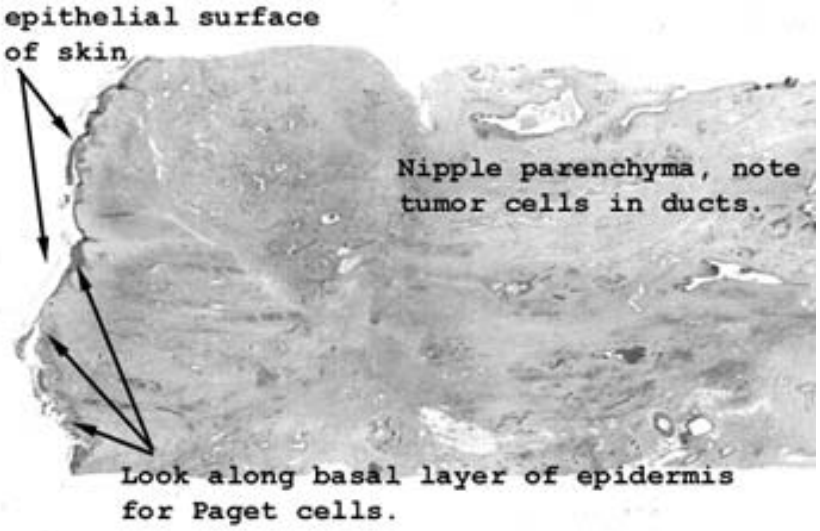
This specimen consists of little fragments of skin and it's difficult to get oriented. You want to be looking in the dermis for histiocytes containing the organisms. There is a lot of necrosis along with the inflammatory infiltrate.

This slide is not H&E stained. We used a stain to highlight the organisms. In some slides there is an ulcer with granulation tissue in the base. Look in the dermis and you will see an infiltrate composed largely of mononuclear cells. The organisms are in the monocytes, and appear as small dots with a cleared area or "halo" around them. They are quite small. Some may appear in the tissue, but I think this reflects rupture of the cells, possibly even as a tissue processing artifact. This slide is to further your education, and I'll tell you right now I don't have a sample of this in my quiz slide collection.

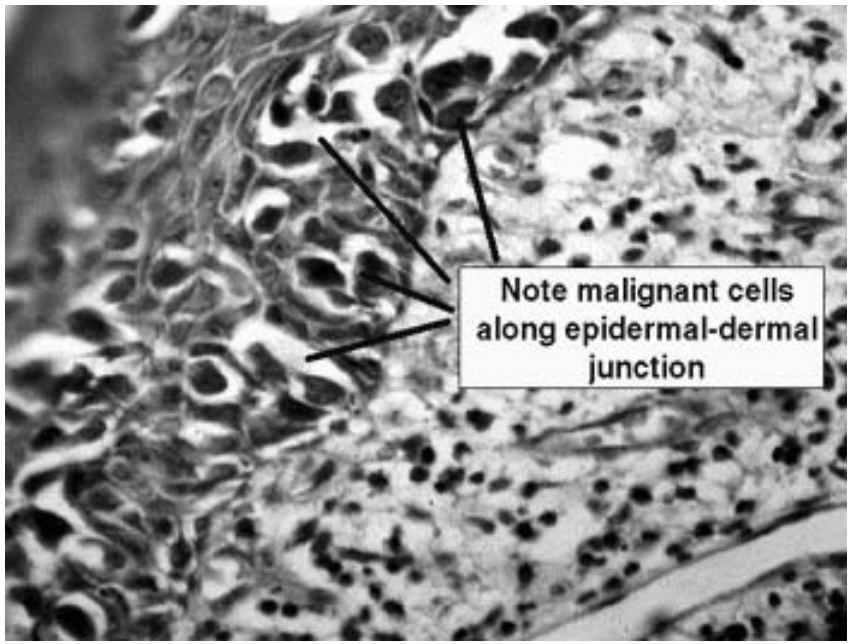
Your observations

Slide 31: Breast skin with Paget's Disease

Your observations

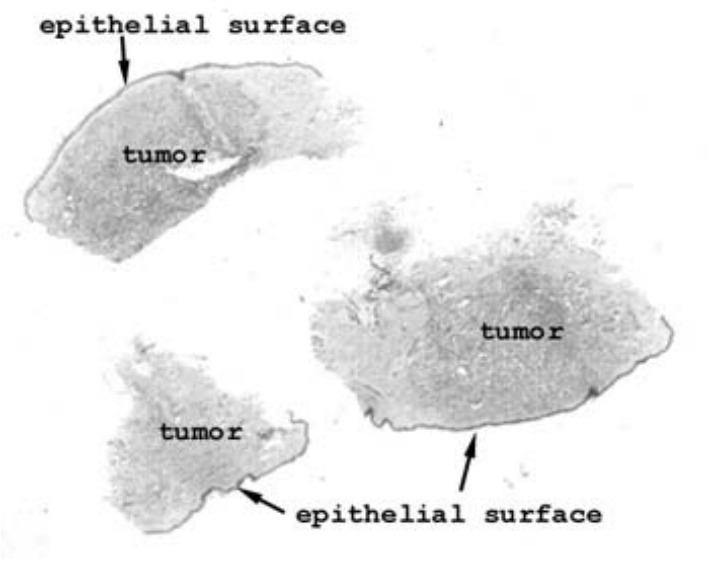


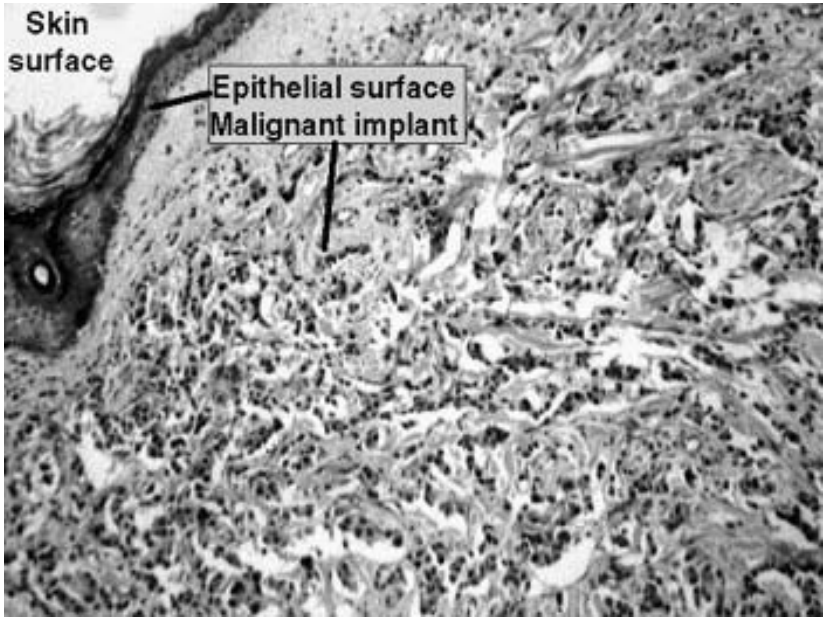
Here we have the condition of malignant duct cells growing up the major excretory ducts of the breast and out into the epithelial covering of the skin. You will actually see clusters of malignant cells in the epithelium itself. Look down in the breast to confirm the malignancy first. Sometimes this can be confused, microscopically with an early amelanotic melanoma. Grossly, this lesion is red and crusted and looks like a little focus of irritation on the nipple or areola.



Here you see a higher power view of the clusters of the malignant ductal epithelial cells which have actually migrated up and out of the major breast ducts to proliferate within the epithelial layer of the skin. These cells may look a bit like non-pigmented malignant melanocytes, but they are indeed from the breast ducts. The cells you see here are not within dermal lymphatics, but rather the actual epithelial surface of the breast itself.

Slide 33: Skin with metastatic breast cancer





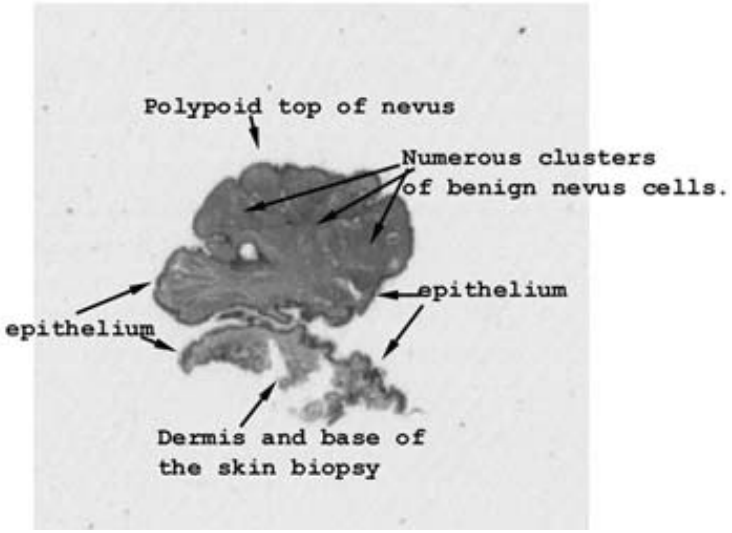
This situation is different from what we looked at in slide 31. Here we actually see little dermal implants of metastatic breast cancer, not epithelial spread. These metastases can be from anywhere, unlike the situation of Paget's disease depicted in slide 31, where the spread is by direct continuity to the overlying nipple skin.

Note the difference between this slide and #31. The malignant cells are in the dermis and represent a distant metastases, not a direct "creeping type" spread from the breast ducts below the epidermis. This pattern is more typical of metastatic breast cancer. Take a look for the single file arrangement and "pseudoglandular" organization of this tumor. This pattern is highly characteristic which makes it possible to make a very good guess as to the primary when presented only with the metastatic tumor.

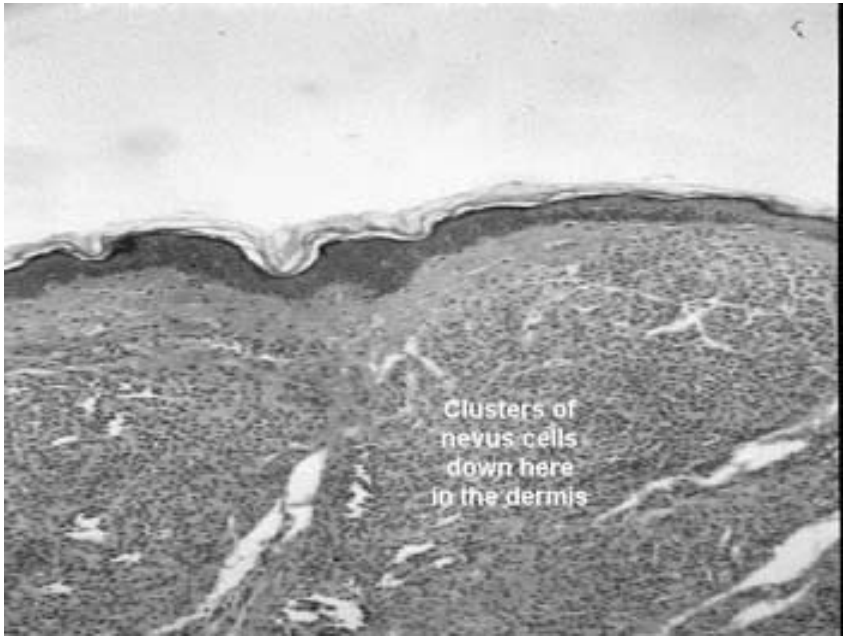
Your observations

Slide 52: Skin with Intradermal Nevus

Your observations

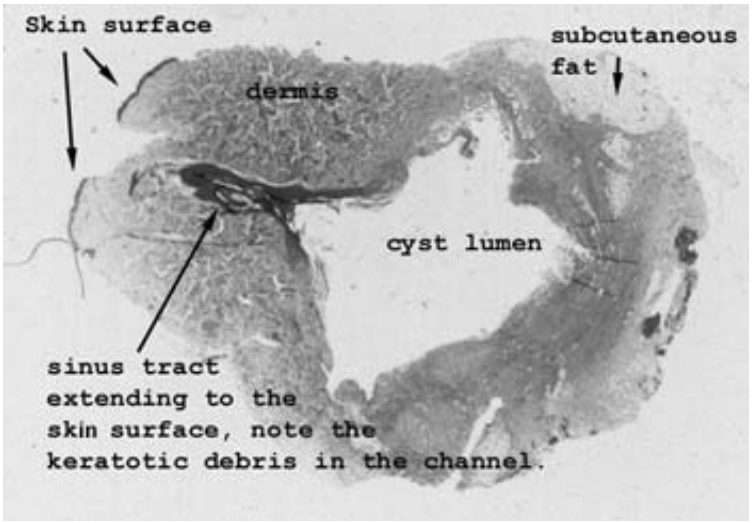


This picture is a nice cross section of a piece of skin with a polypoid shaped nevus extending from the skin surface. Not all nevi acquire this polypoid configuration but a fair number do. Your section may not include the stalk, sorry.



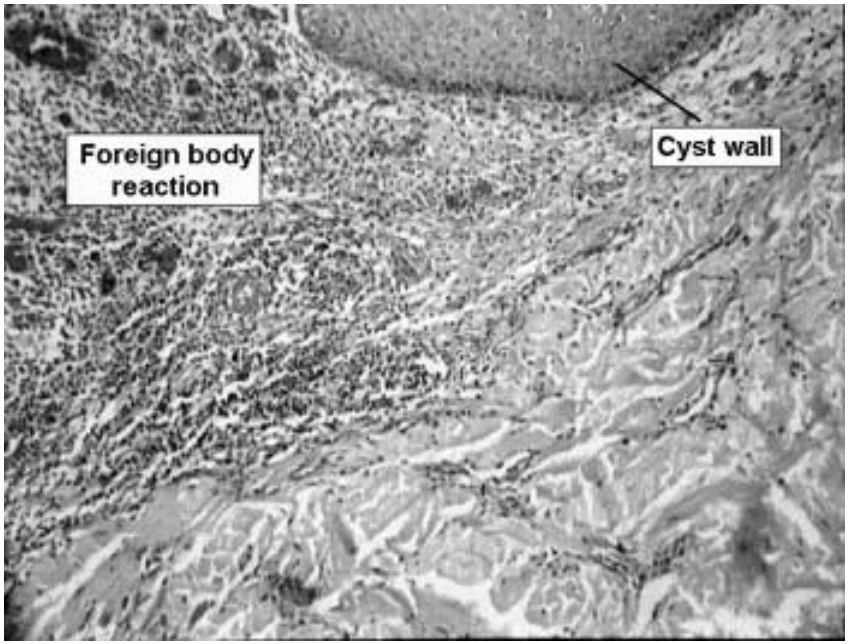
Note the clusters of benign nevus cells in the dermis. There is maturation "from surface to base," and by this we mean the nevus cells look more and more mature as you scan from the epidermal covering to the deeper dermis. You will see no mitotic figures and there is no cytoatypia of the nevus cells. If there had been nevus cells in the epidermis what would have the lesion been called? No the answer is not melanoma.

Slide 65: Ruptured Epidermal Inclusion Cyst



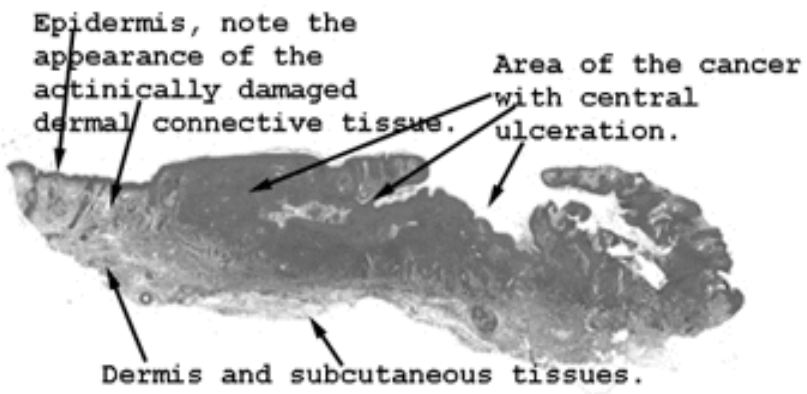
Here it's easy to understand the nature of this lesion. We have a benign cyst, lined by stratified squamous epithelium, present in the dermis. This probably came into being as a puncture wound in the skin which drove a small piece of epidermis down into the dermis. Rather than dying and being removed, it survived and formed the cyst. In thia case we even see a little sinus tract communicating to the skin surface.

Your observations



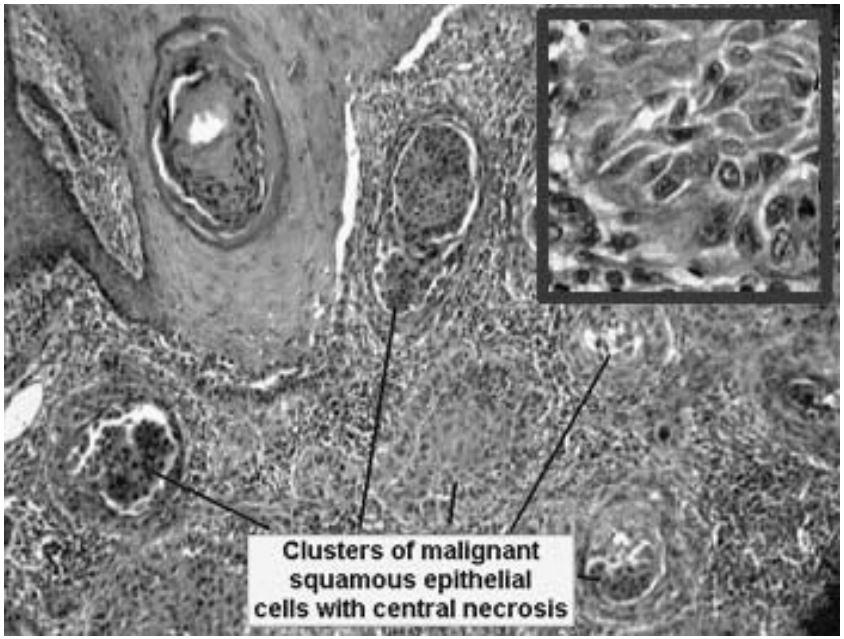
Note the cyst lining composed of keratinized squamous epithelium. You should be able to find the foreign body reaction at the edge of the cyst, and may even be able to discern the site of rupture of the cyst wall. What are the giant cells reacting to? How would a cyst of this type form? Try slide 152 for another example, and answers to these questions.

Slide 87: Squamous Cell Carcinoma of Skin



Here you can see the malignancy in the center of the skin biopsy. Please take the time to look at the surrounding skin first. You will see there is rather significant solar damage to the dermal connective tissue and very likely there will be dysplasia of the epithelial covering as well.

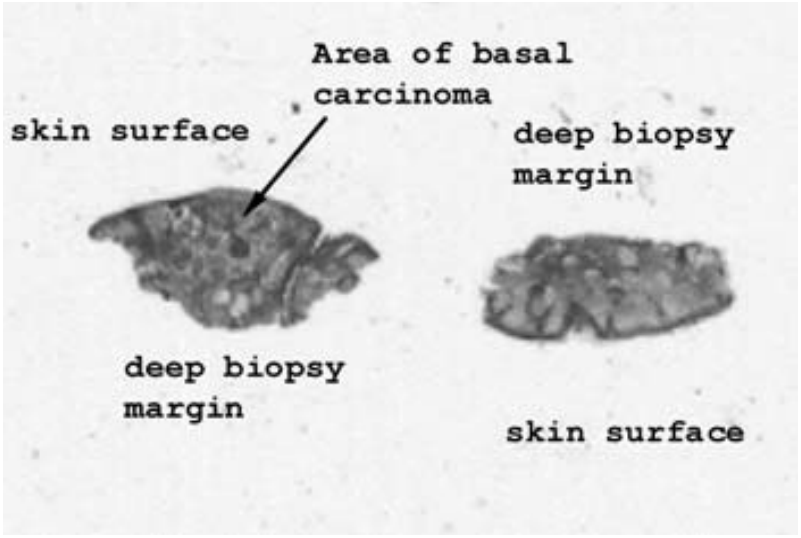
Your observations

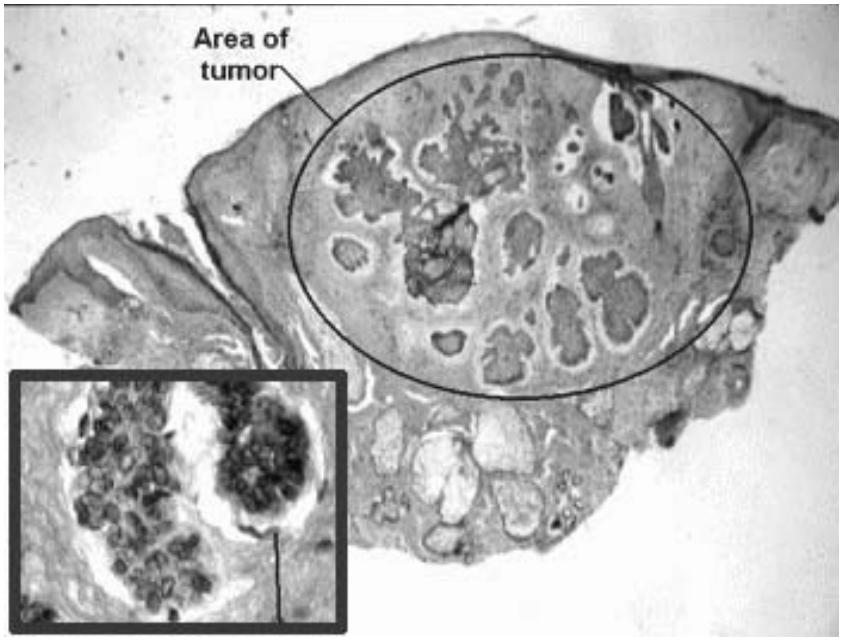


You will see groups and clusters of malignant squamous epithelial cells extending into the dermis, and many reveal whirl like clusters of desquamated squamous cells centrally. Some of these groups have areas of necrosis, and you will see a mixed acute and chronic inflammatory infiltrate in many areas.

The insert in the upper right of the image shows a detail of the malignant squamous cells. The insert picture is from the edge of one of the clusters of cancer cells.

Slide 93: Basal Cell Carcinoma of Skin





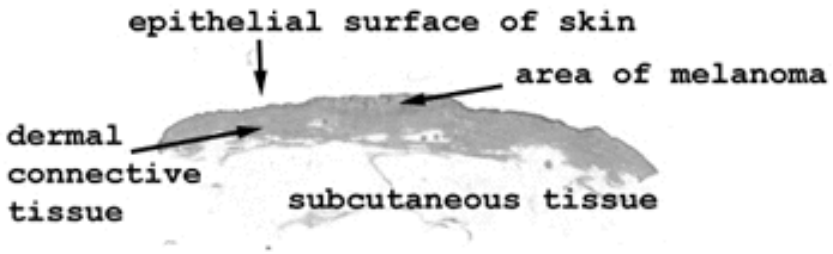
Even in this blurry scan of the tissue, you can see the little nests of basal cell carcinoma.

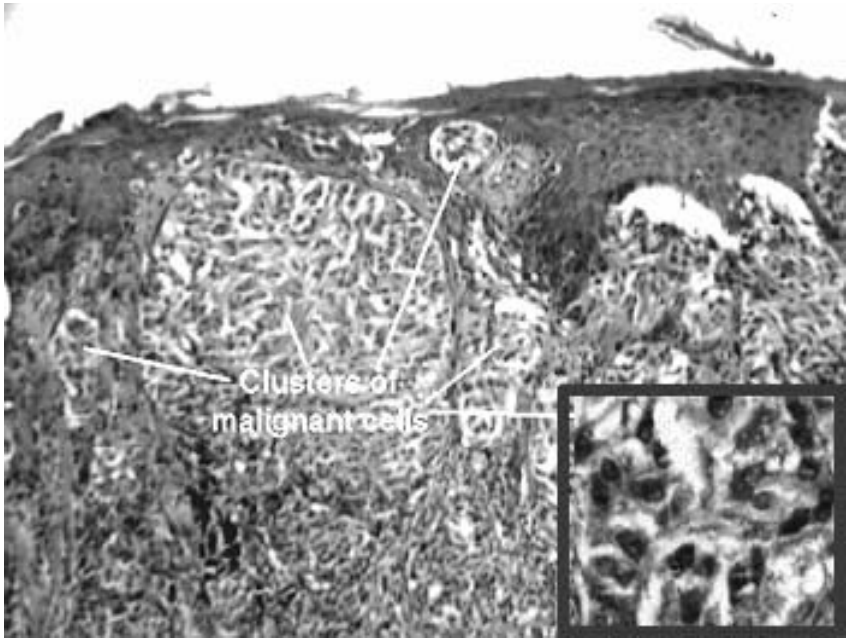
Basal cell carcinoma is one of the most common skin malignancies in humans. They are directly associated with sun exposure and solar damage to the skin. They are found most often on the face. In fact, something like 80% of them are found above a line from the corner of the mouth to the lower tip of the ear. They are of fairly low invasive potential and generally expand by radial growth. They may involve local, contiguous structures, but almost never metastasize, unlike their malignant squamous cell counterparts. Although some basal cell carcinomas show varying degrees of "skin appendage maturation," that is to say they may look like a little hair shafts or sebaceous glands, the hallmark histological feature is the peripheral palisade arrangement of the cells in the individual clusters. The outer layer of cells line up like a little picket fence, and this feature is a dead giveaway as to what you are looking at.

The insert, lower left, shows a detail of one of the clusters of basal cell carcinoma.

Your observations

Slide 116: Skin with malignant melanoma





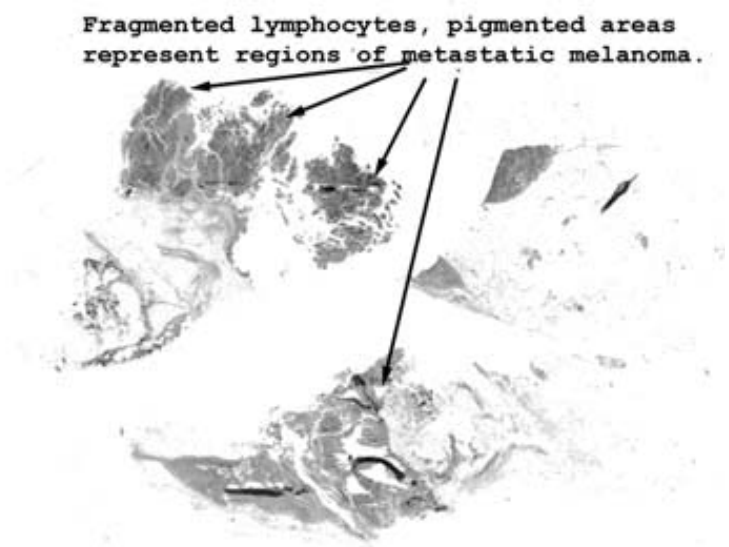
Although this is just a little shave biopsy of skin, you can easily see the central area of thickening where the melanoma is.

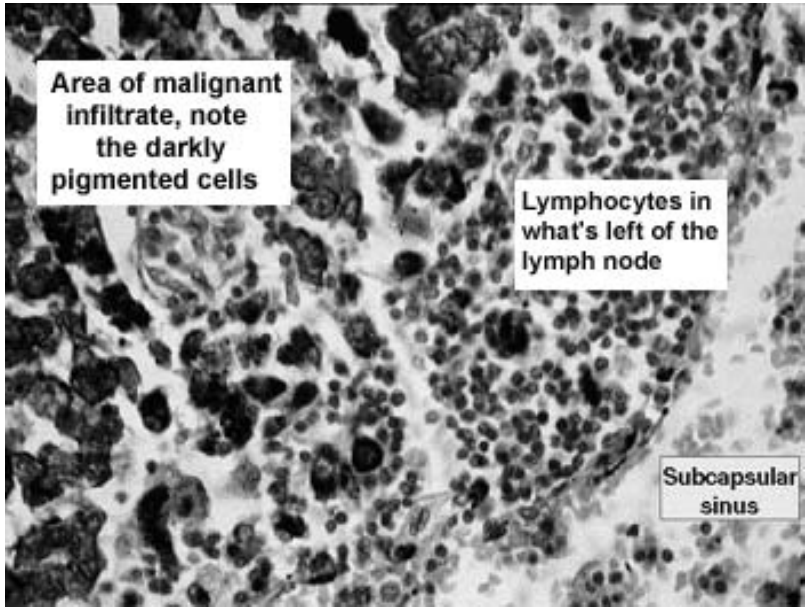
The skin in this slide shows clusters of malignant melanocytes in the dermis. Observe the lack of "cohesion" of the cells. Nuclear features of malignancy should be obvious, and many cells will show abundant pigment. There is no "maturation from surface to base" in this lesion, an important consideration in distinguishing this from its benign counterpart, a "nevus." Depth of penetration is a critical part of "staging" this lesion.

The insert, lower right, shows detail of the malignant melanocytes.

Your observations

Slide 118: Lymph Node with Metastatic Malignant Melanoma



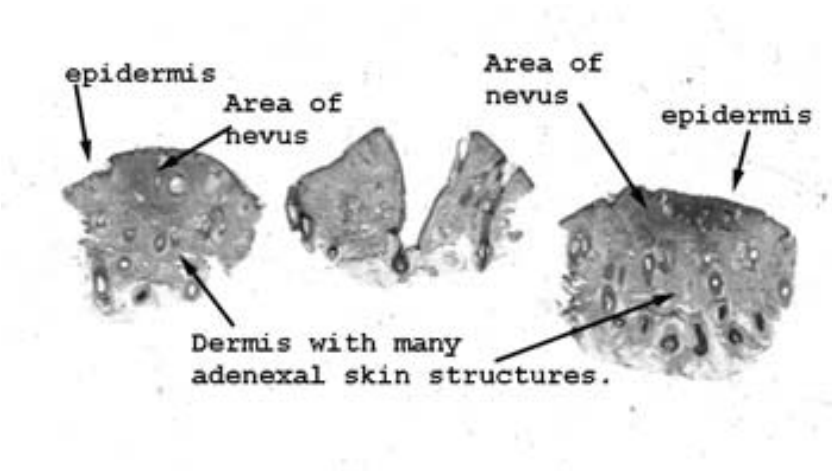


Your observations

Although fragmented, you can see the area of involvement in this lymph node.

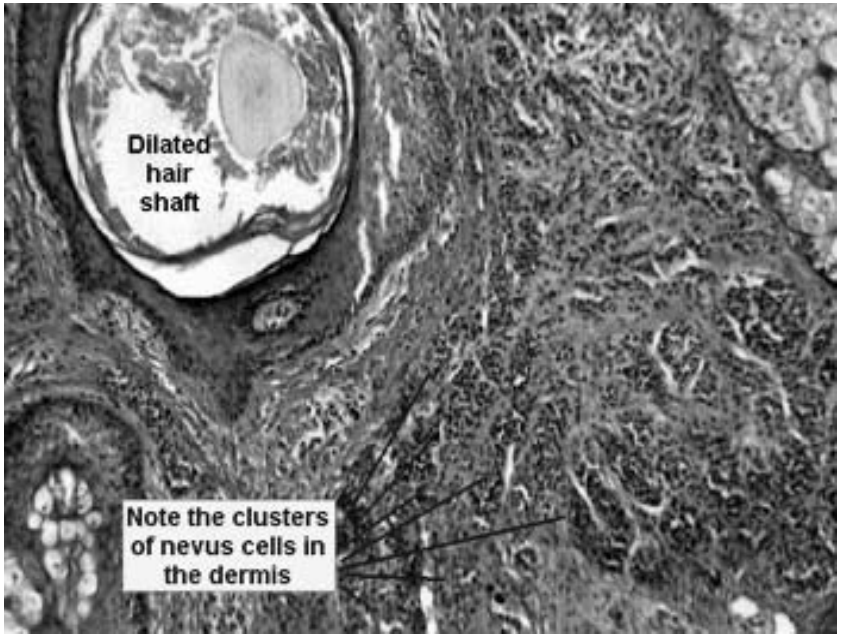
Again the picture pretty well says it all here. You will see a node partially replaced with groups of cells that clearly don't belong there. Many contain abundant dark brown pigment. In general I advise that you look at the subcapsular sinuses and pericortical sinuses for the first evidence of metastatic involvement. Of course, in this case, it is no problem to see the altered histology and the process is considerably advanced.

Slide 150: Intradermal Nevus of Skin



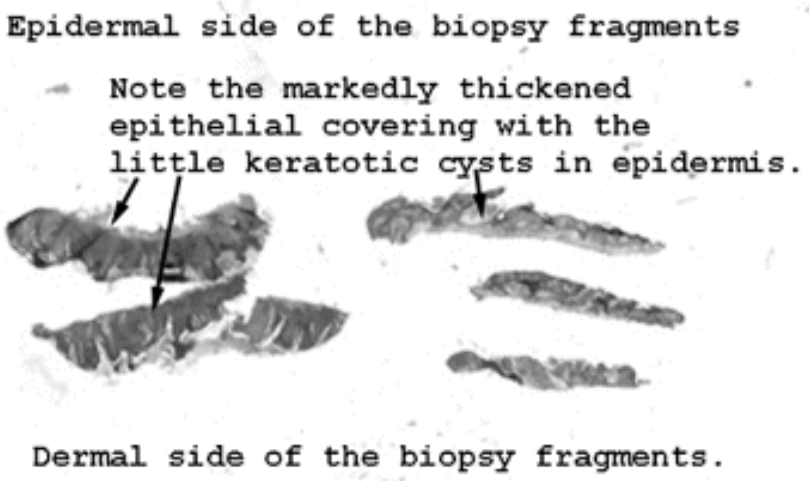
Again, it's fairly easy to spot the lesion just by looking at the slide before going to your microscope. You will see a number of hair shafts and sebaceous glands, some of which are bit deformed due to the presence of the nevus. Even so, this lesion is still benign.

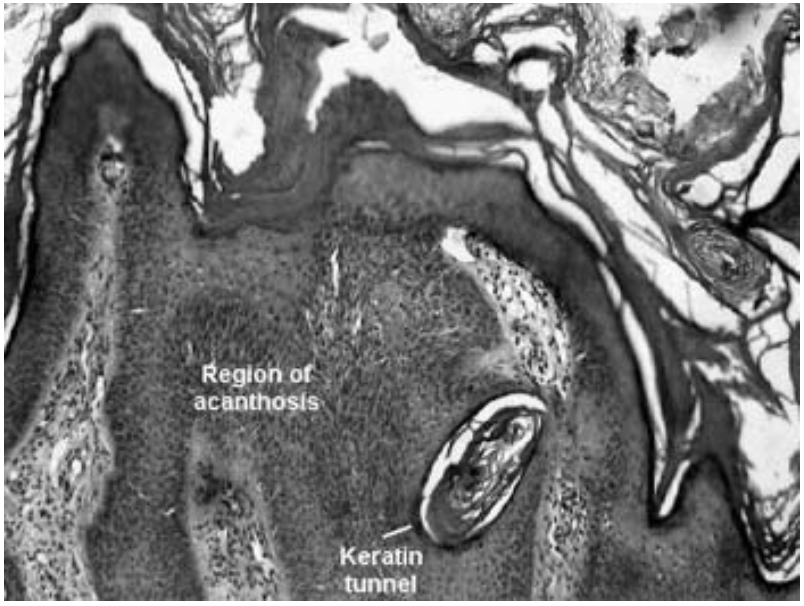
Your observations



In this case you will see clusters and theques of benign nevus cells in the dermis. You should be able to see there is "maturation" of the cells as one goes from the surface of the lesion to the base. You will find no mitosis and there is no cytoatypia of the nevus cells. How would you distinguish this lesion from a malignant melanoma?

Slide 151: Seborrheic Keratosis of Skin



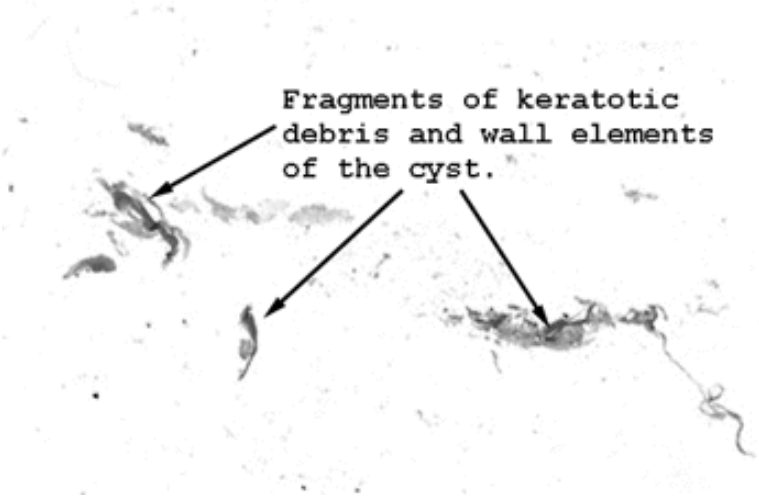


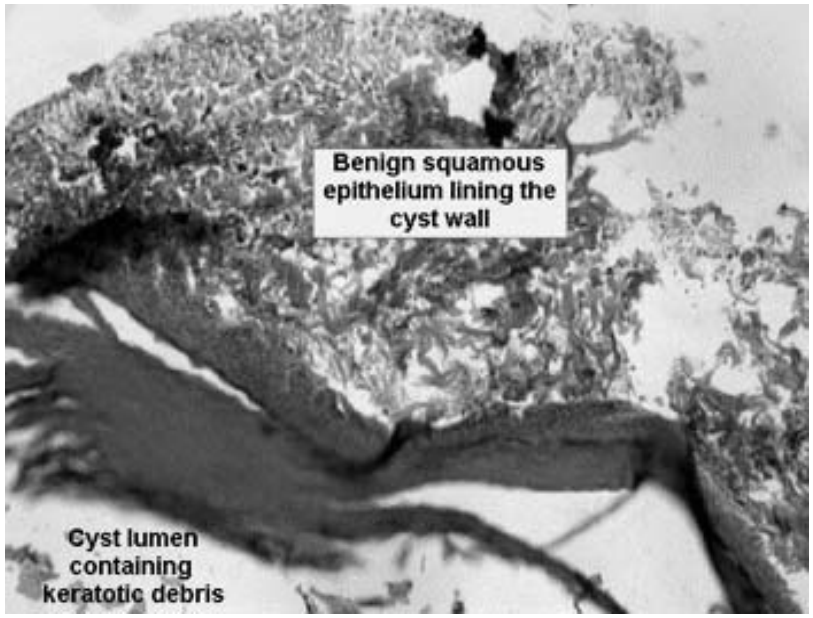
It's not real easy to see what we're looking for in this biopsy, although once you recognize it, you'll be surprised how abnormal the epidermis can look. The thickening of the epidermis involves pretty much the whole surface. This is a very common skin abnormality.

This may fool you by looking a bit like cancer, but it's not. This is a very common lesion. You have seen them very likely as dark brown greasy looking spots on the face, and especially around the temple, of older people. Note the hyperkeratosis and acanthosis, that is to say the thickening and hyperplasia of the acanthotic region and keratotic layers of the epidermis. You will also see what appears to be little keratin inclusion cysts in the thickened epidermis. These are often referred to as "pseudohorn" cysts and keratin tunnels. Even though this lesion may look a little spooky, it is really not. Why do you suppose this is not considered malignant?

Your observations

Slide 152: Ruptured Epidermal Inclusion Cyst of Skin





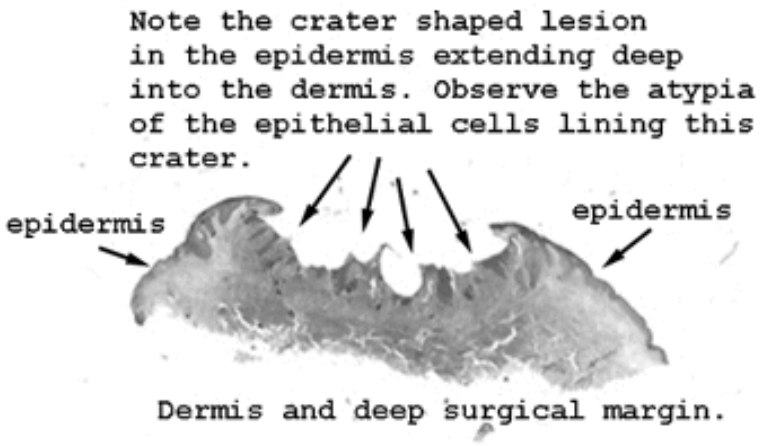
OK, there isn't much to this one, but it's pretty common for us in the clinical lab to receive a specimen that looks like this.

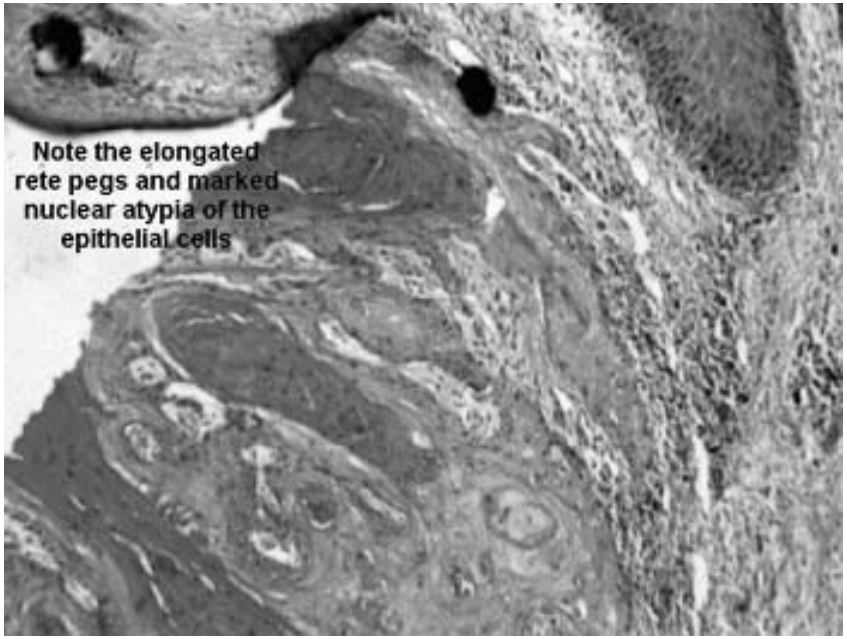
Generally the surgeon just pulls out fragments of the wall of the cyst and bits of its contents. Take note of the lining and keratotic matter.

These are very common lesions of the skin, and may result from the implantation of a small fragment of viable epidermis into the deeper layers of the dermis or subcutaneous tissues. The lesion is just as it sounds, a cyst composed of epidermal elements. The cyst lining is composed of benign squamous epithelium, and the lumen eventually fills with shed keratotic matter. If these rupture, the keratin debris is considered "non-self" by the immune system, and there follows a significant and often rather painful foreign body type inflammatory reaction. Because of the swelling associated with the reaction to the keratin from a ruptured epidermal inclusion cyst, the person considers the lesion to have "grown" dramatically almost over-night. As you can guess, this is very worrisome, and most folks come right in to have it looked at, thinking it must be cancer because of the rapid "growth."

Your observations

Slide 154: Keratoacanthoma of Skin



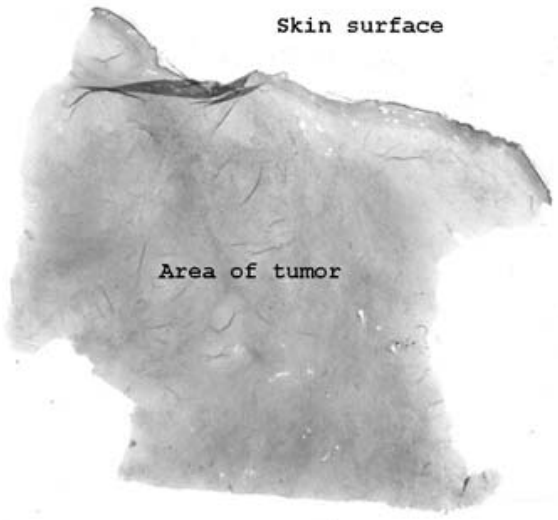


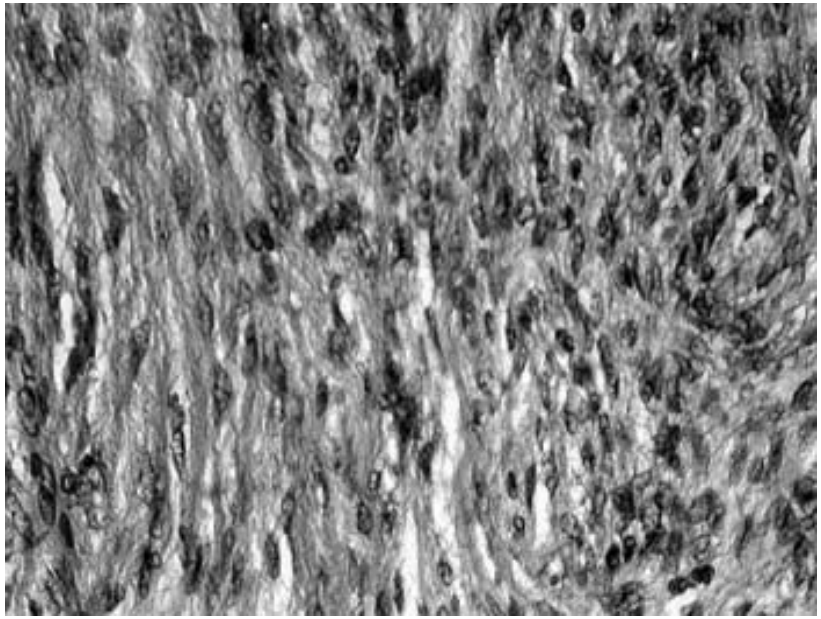
This is an absolutely classic appearance for this lesion; at least in two dimensions. Deep central crater, lined by highly atypical cells. As always, start at the very edge of the biopsy to get oriented as to more or less normal skin. Take note of the degree of actinic degeneration within the dermis. Then move to the lesion itself. Stay on low power to get the overall feel of this condition.

This is an important lesion to know, it's very common and almost always on sun exposed parts of the body. The backs of the hands and helix of the ears are very common sites. This lesion is difficult to distinguish from its more aggressive, invasive squamous cell carcinoma cousins. Although long thought to be some benign variant or transitional form of squamous tumor, we now consider this to be a low grade, locally invasive form of squamous cell carcinoma. Note the "cupped shaped" nature of the lesion. To see this important diagnostic feature, you will need to look at the slide on a white background. Other important microscopic features include keratin "pearls," and an advancing margin along the base of the lesion. There is no question, the cells of this tumor look a good bit wilder than they behave, still removing is the way to go.

Your observations

Slide 156: Dermatofibrosarcoma Protuberans of Skin



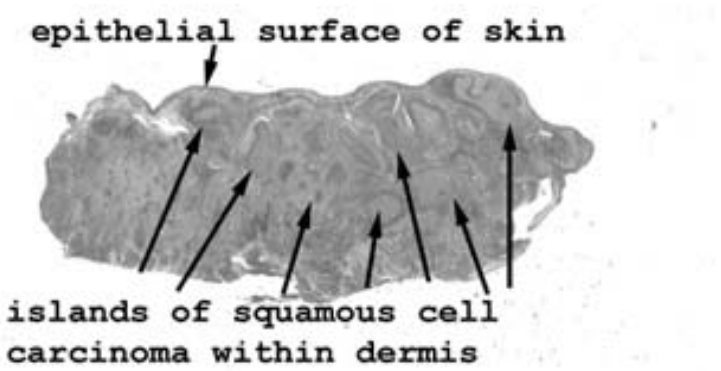


I don't think you'll have any trouble seeing the tumor here.

This is one of the most enigmatic and unpredictable tumors of soft tissue. It generally arises in the dermis, spreads locally and may metastasize to distant organs. Although fairly slow growing, it is relentless. This is generally considered a localized form of fibrosarcoma, although it may become aggressive in some circumstances. Note the highly atypical fibroblasts and especially the "woven mat or storiform" pattern of the groups of cells. This pattern creates the appearance of a coarsely woven mat, kind of like the type you would wipe your feet on at the front door of your home. You will definitely miss this important diagnostic feature of this lesion if you go straight to your high power objective. Cruise first on low power to see this aspect of the tumor.

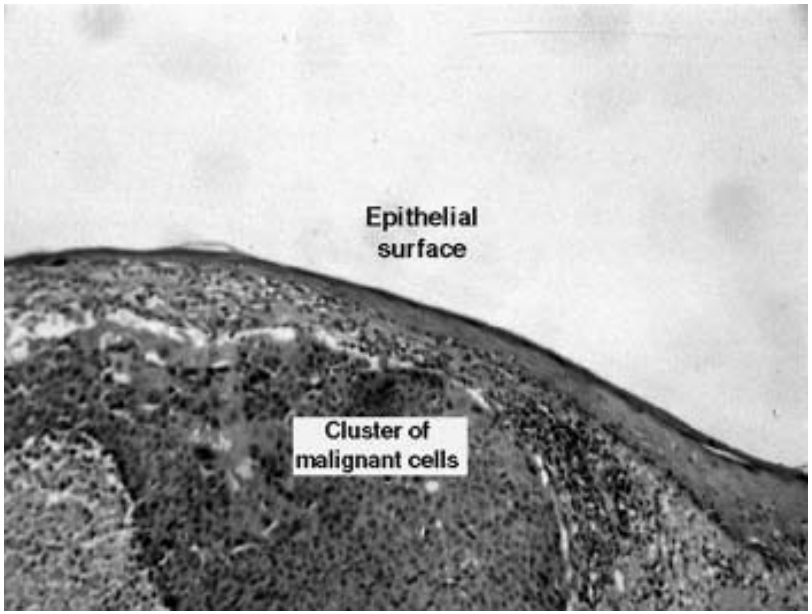
Your observations

Slide 157: Skin with recurrent squamous cell carcinoma



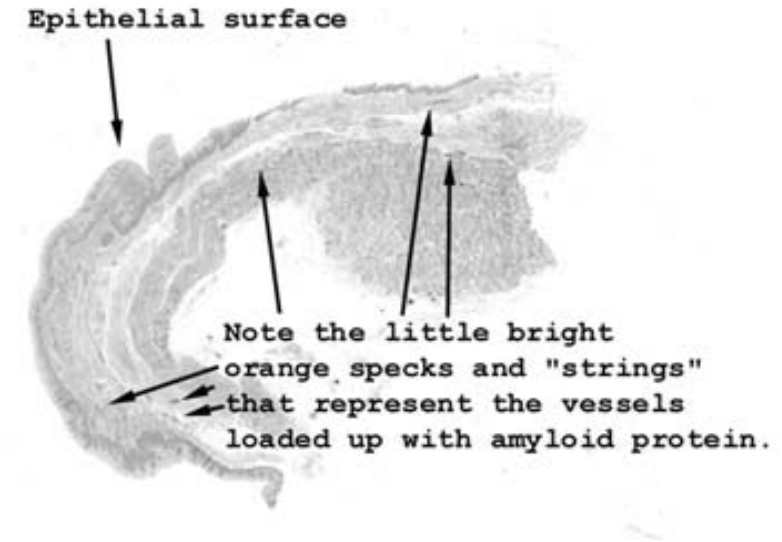
Here you see the groups of malignant cells within the dermis but seemingly having no connection to the epidermis. What's the explanation?

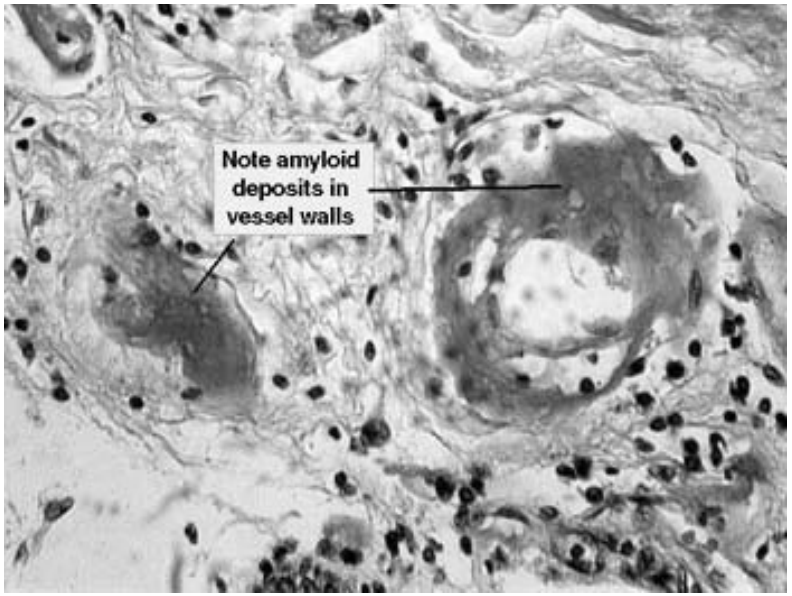
Your observations



The picture of this slide could be in focus a little better, but it's what we have. Note the epithelium does not show changes of nuclear atypia nor cancer. The squamous cancer is in the dermis, and represents a recurrence from a previously removed malignancy. On your slide, you should be able to see the hallmark nuclear features of cancer i.e. angulated nuclear margins, hyperchromasia and reduced nuclear to cytoplasmic ratio. Look for "intracellular" bridges between the malignant cells.

Slide 169: Skin with Amyloidosis, Congo Red Stain





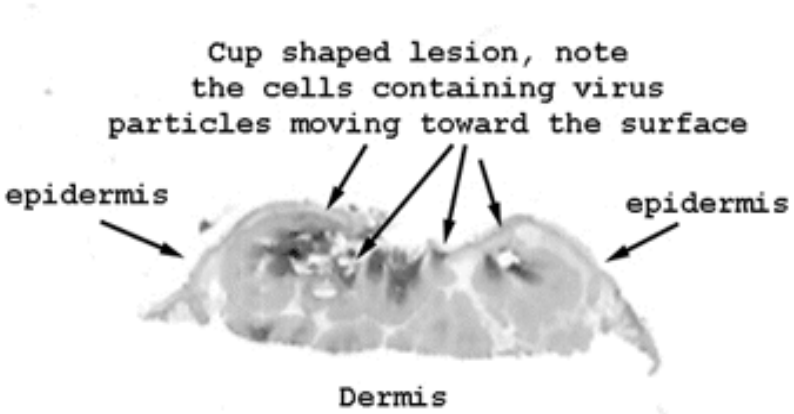
Your observations

You want to look at the vessels in the dermis. The amyloid deposits will be in the walls.

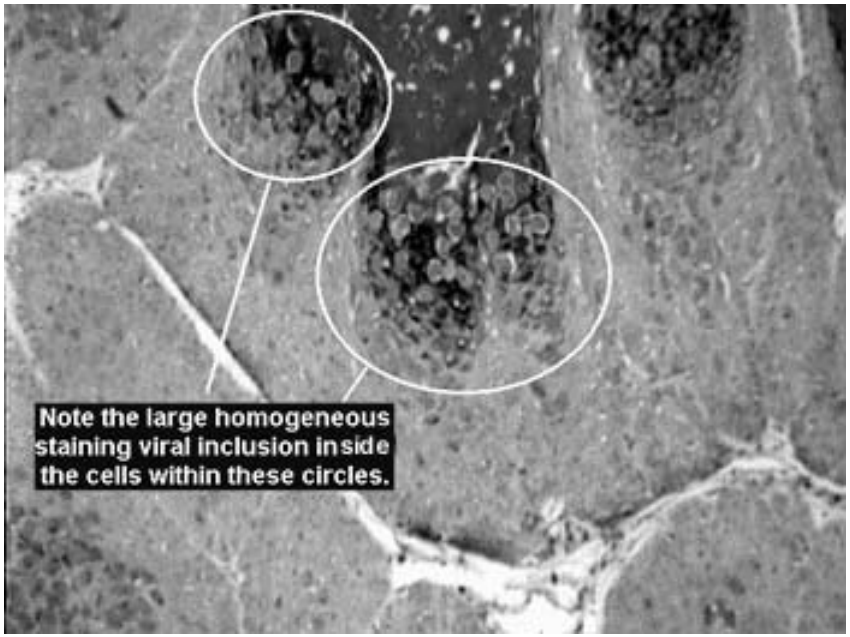
This slide is stained with congo red stain, a dye that binds to the amyloid protein. Look in the vessel walls of the dermis for this fibrillary orange staining material. You won't see it to any great extent in the general connective tissue of the dermis.

Slide 185: Molluscum Contagiosum

Your observations

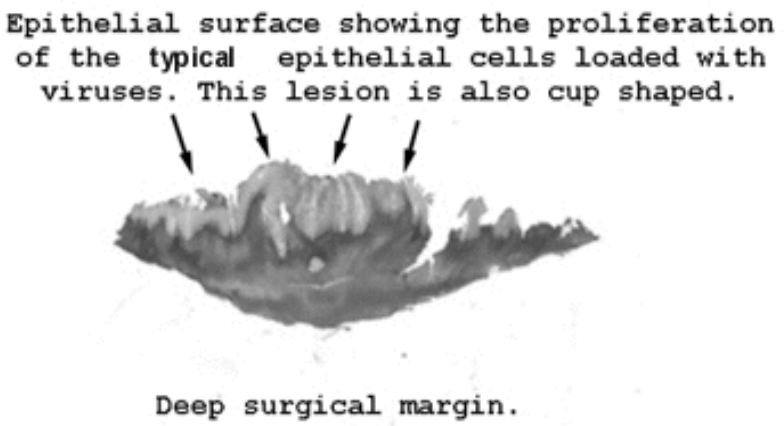


Again, a fairly common skin lesion. As with so many, note the cup shaped nature of the lesion. See if you can find the viral inclusions.



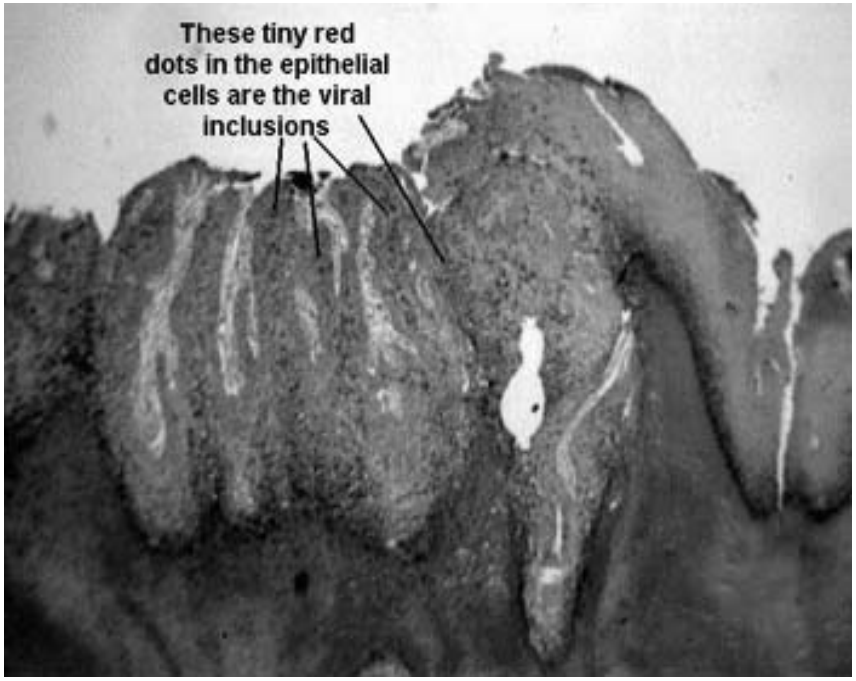
Another cup shaped lesion of the skin. Note the granules in the epithelial cells of the lesion, you should be able to see a color change from surface to base. As you know, these are the little packets of the molluscum virus.

Slide 186: Verruca Vulgaris (A Wart)



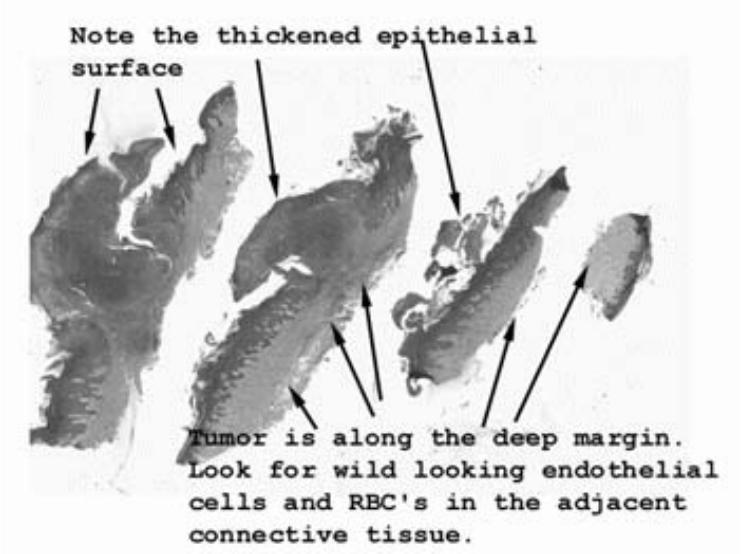
This slide consists almost exclusively of epidermis. There is very little dermis, still this specimen shows nicely the features of one of the most common viral induced skin lesions.

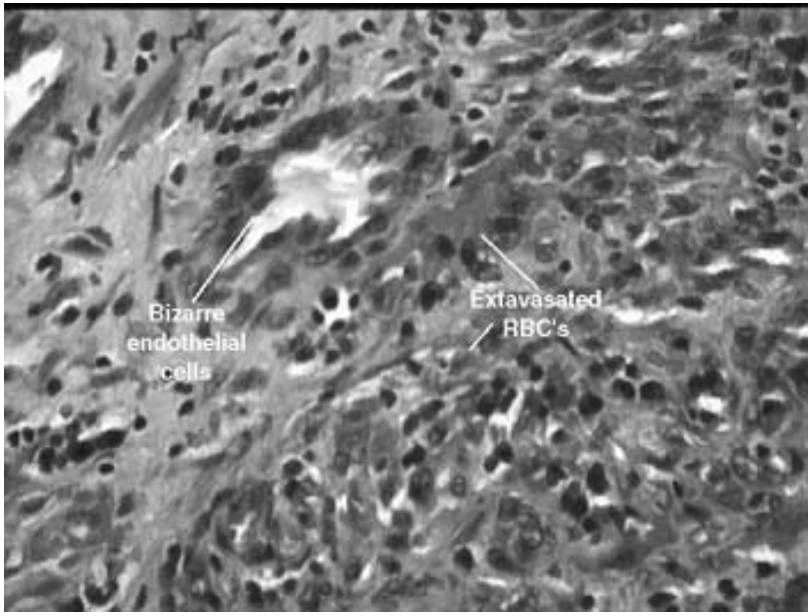
Your observations



This case shows a cup shaped lesion of the skin with many very odd looking cells containing blue or red granules. These inclusions are the little packages of viruses, ready to hop to someone else or somewhere else on the person. We use the term "kissing lesions" occasionally to apply to two verrucae on the same person. What do you suppose this applies to? No it has nothing to do with romantic activity.

Slide 190: Kaposi's Sarcoma of the Skin





Here we have multiple serial sections of the skin biopsy. Once you've scanned the entire slide, look in the dermis for the characteristic malignant endothelial cells.

Your observations

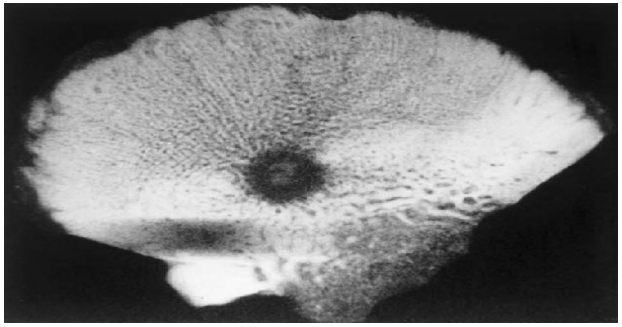
Yes, this biopsy is from an AIDS patient. Note the extravasated RBC's in the surrounding connective tissue and the bizarre and very disturbed looking endothelial cells that comprise this lesion. You will see many very abnormal "fibroblast" looking cells, but these are really bizarre endothelial cells. You will also see some dark brown or black pigment in the background and possibly in some of the histiocytes. This pigment is actually iron from the red blood cells that have previously broken down. An iron stain, such as a Prussian Blue, would really highlight this feature.

General and Systemic Histopathology
C601 and C602

Section 18 *Disorders of the Musculoskeletal System*

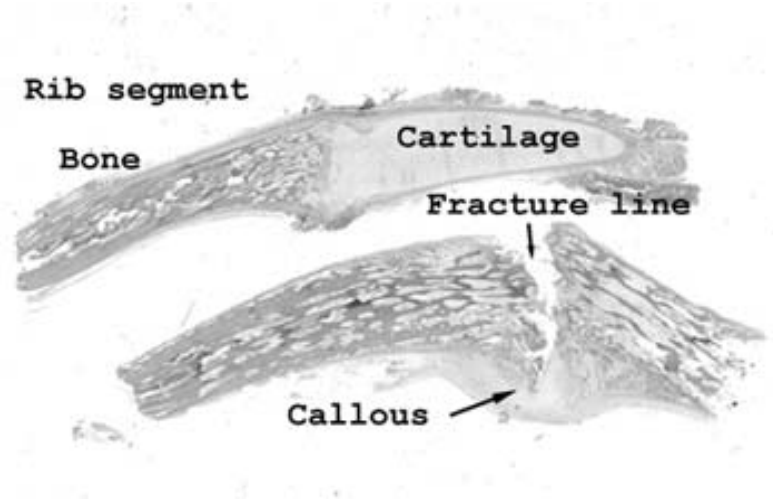
Disorders of the musculoskeletal system cut a wide path across all categories and types of injury. For example vascular and neurological conditions can directly affect muscular activity and strength. Moreover, it's often difficult, at least initially, to distinguish underlying causes of progressive muscular weakness, and occasionally a muscle or even peripheral nerve biopsy is called for. In other situations, serum antibody studies prove helpful in making a particular diagnosis. But always, the diagnostic process begins with the history and physical exam.

In this unit we will be looking at a number of categories of disease with either primary or significant secondary effects on the muscular system, bone and/or connective tissue. In some situations the causation may be straight forward, whereas in others the mechanism of injury and development of the disease will be baffling. A case in point is myositis ossificans. Here we will see an example of fully developed benign bone forming at a site of injury either in soft tissue or skeletal muscle. Very peculiar. We will also study examples of primary inflammatory states, as well as malignancies, of the skeletal muscle and soft tissues. Even though we may not review a case of every type of injury or disease, remember the musculoskeletal system can suffer from each of the major divisions of injury. Here are a few that are representative of all.

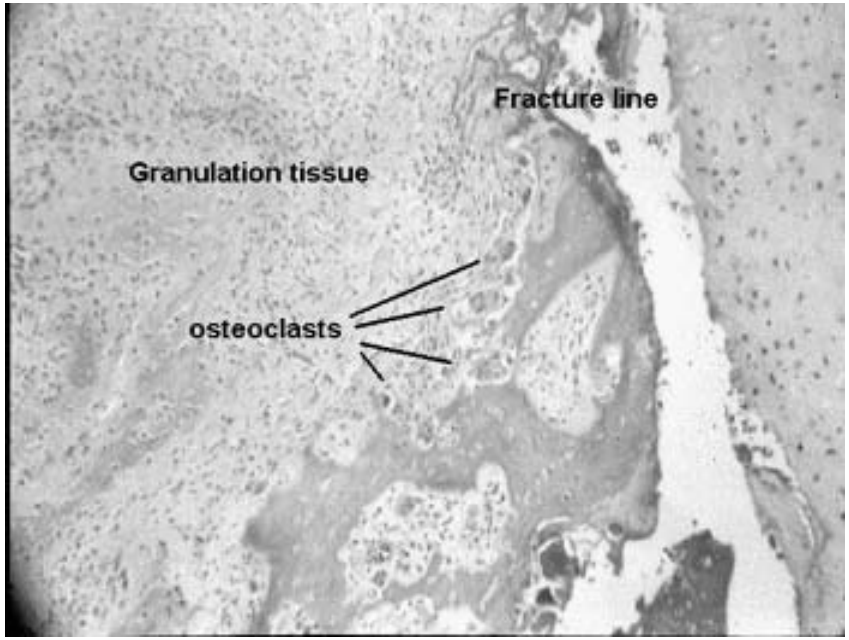


Slide 7: Healing fracture of bone

Your observations



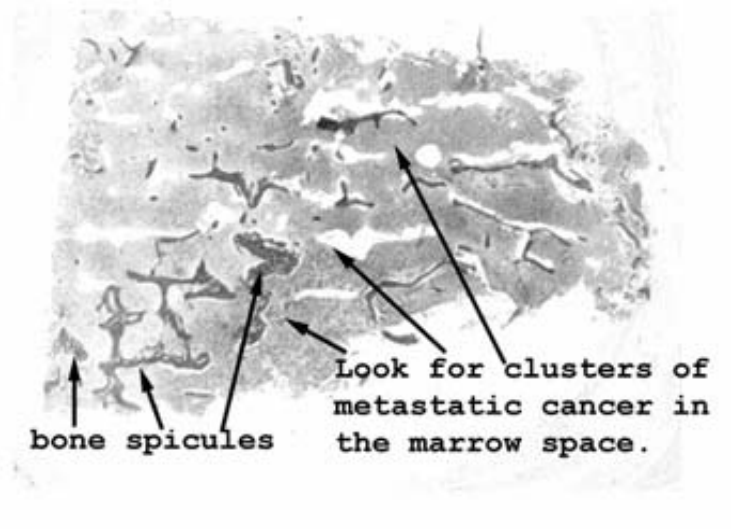
This slide obviously has two sections of tissue. Both are of a rib and the lower portion shows a partially healed fracture line. You can see the developing callous on one side and there is abundant granulation tissue in the fracture line itself. We split the fracture line open at the time the specimen was embedded so as to highlight where to look for the healing process. In life, the fracture was closed and the edges were knit together with the newly formed granulation tissue.



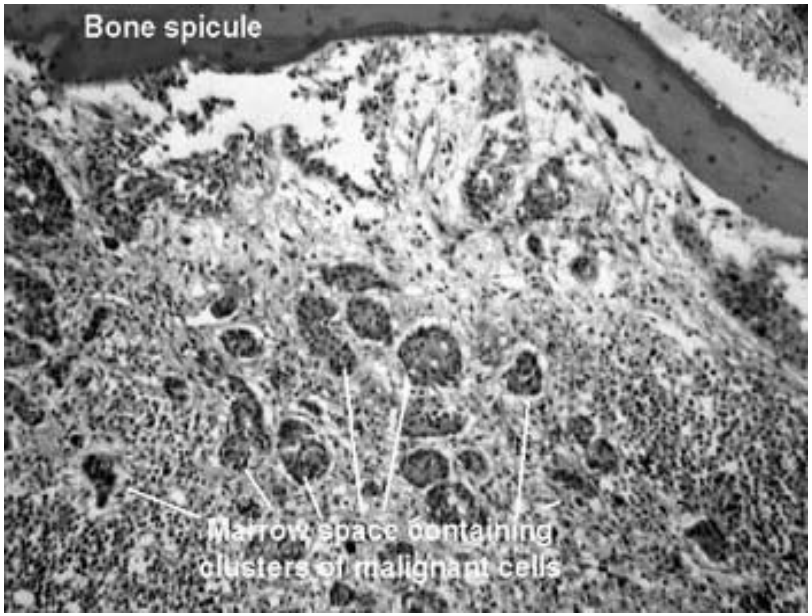
This healing "fracture" is approximately two weeks old, and shows early changes of the healing process. Note the remodeling taking place by the osteoclasts and the rather marked degree of fibrosis (scarring) that is taking place as the new bone is being formed. In your slide, you should be able to see many active fibroblasts and angioblasts as part of the initial healing "team." See if you can find the area just by looking at your slide.

Slide 23: Metastatic transitional cell carcinoma

Your observations

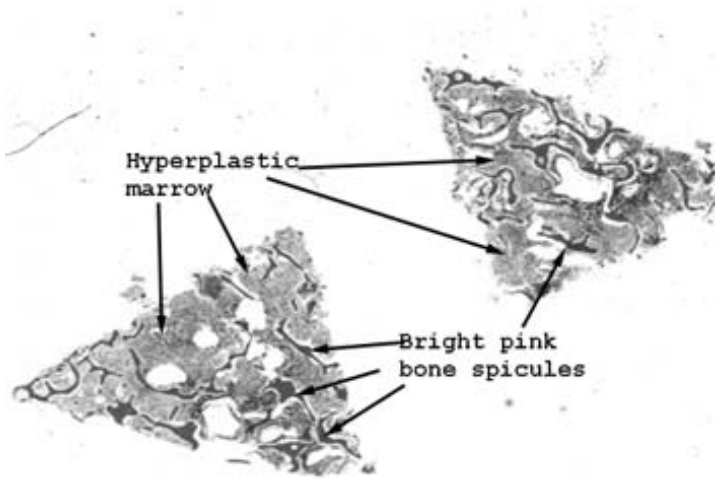


Note how "meaty" the bone marrow space is. Much of the hematopoietic space has been replaced by scar tissue and tumor.

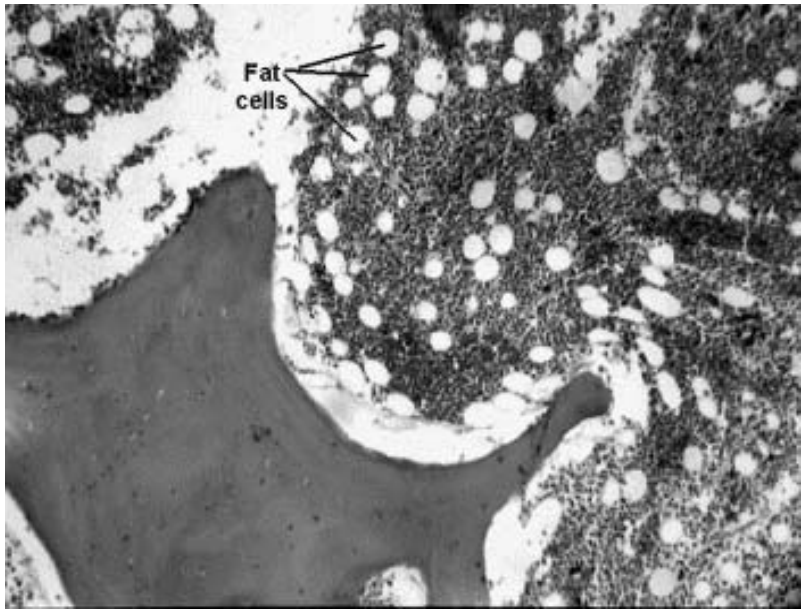


This slide shows metastatic "transitional cell carcinoma" in the bone marrow. What are the sources of "transitional cell carcinoma?" First, try to get oriented by finding some bone spicules and hematopoietic tissue. The malignant cells occur in clusters and closely resemble malignant squamous cells. Although these cells don't look too wild, they are not in the right place. Observe the "desmoplasia" (i.e. fibrosis) associated with the groups of tumor cells.

Slide 49: Bone Marrow Hyperplasia



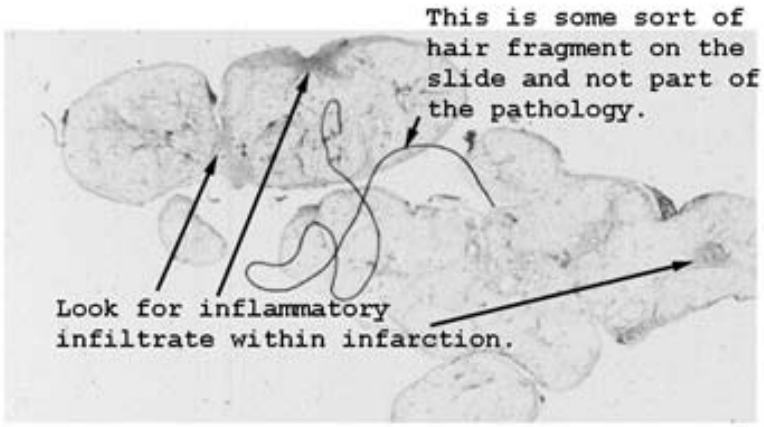
Normally one sees about 50% fat and 50% hematopoietic bone marrow. It's obvious just by looking at the scan to the left that this bone marrow is at least 80-90% cellular. That's definitely hyperplastic.

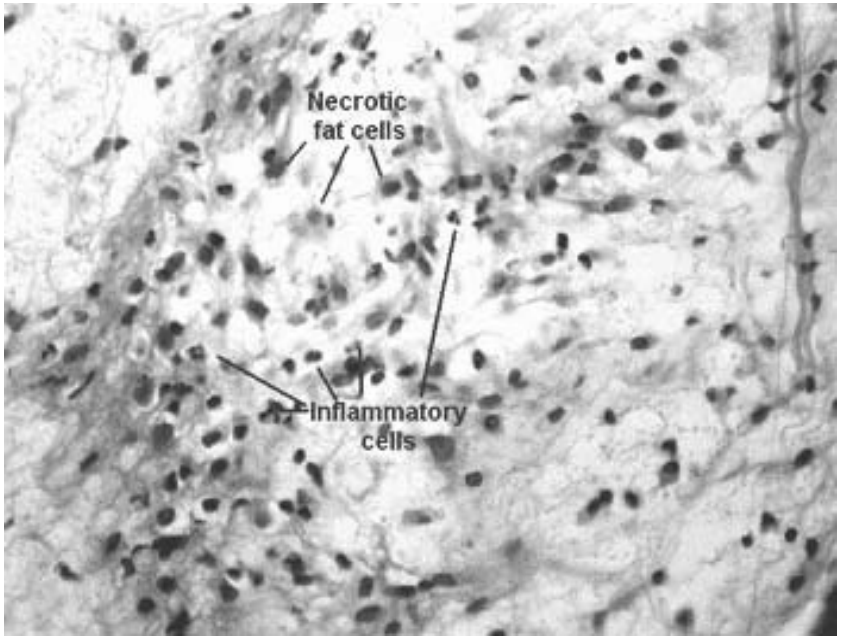


The changes here may seem subtle, and it would be wise to look at normal bone marrow first, but this slide does show generalized hyperplasia of all hematopoietic elements. The key to seeing this is knowing how much bone marrow fat there normally is. Generally fat represents about 50% of the marrow space, at least in bones that are normally involved in hematopoiesis. The fat cells are generally distributed evenly throughout the marrow tissue. See if you can identify the expected red and white cell precursors.

Your observations

Slide 88: Fat Necrosis of Omentum



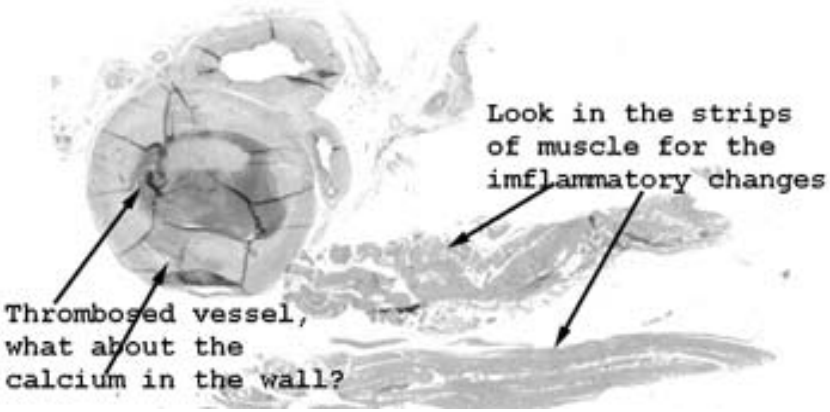


This is pretty much necrotic fat with inflammation. Look in the areas with a little more color to see the inflammatory action.

I'll agree, this slide is not too exciting. You should see the areas of fat necrosis and some liquifactive changes. There will be a scattering of acute inflammatory cells. That's pretty much it.

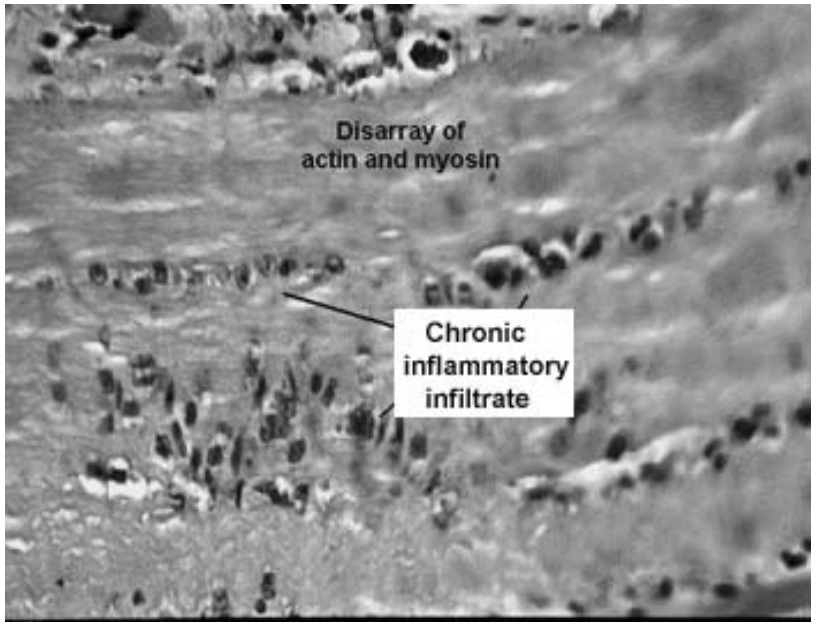
Your observations

Slide 121: Chronic Myositis



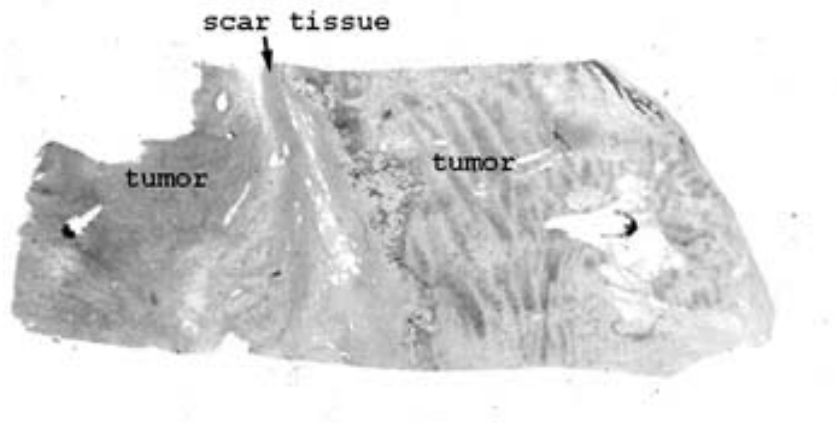
Obviously there are several pieces of tissue on this slide. Look in the strip of muscle. You are looking for inflammatory cells in between the individual muscle cells as well as disruption of the actin and myosin within the cells.

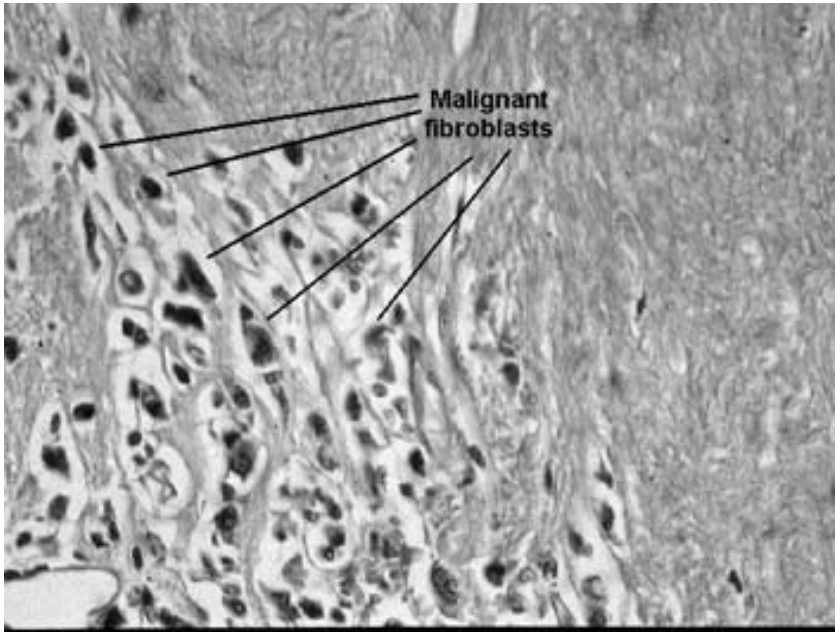
Your observations



You will see many "ratty" looking and fragmented bundles of muscle cells, as well as disrupted actin and myosin within a few of the individual myocytes. There should be no trouble finding the chronic inflammatory infiltrate located between the muscle cells. On low power you should be able to appreciate the great variation in muscle cell diameter. What types of conditions would bring about this change? What serum enzymes would you expect to be elevated in a patient with such a condition?

Slide 125: Fibrosarcoma of Bone



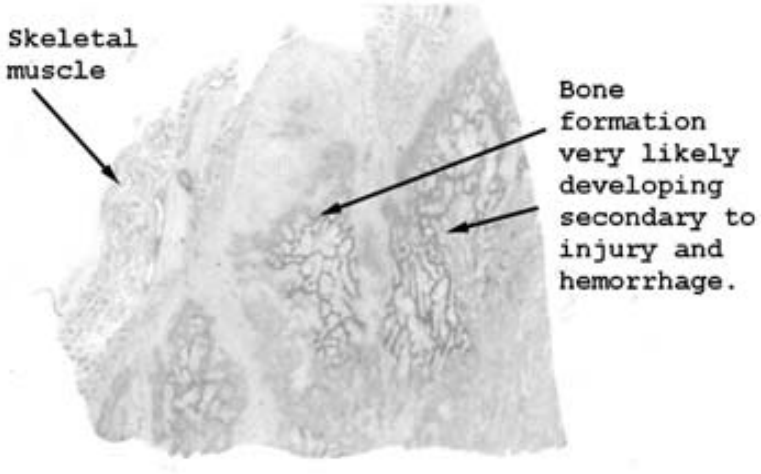


There are only a few small fragments of bone on this slide. It's mostly tumor. Look in the areas that are most cellular for the features characteristic of this tumor. Among other things, the degree of collagen production tells the nature of this malignancy.

This is a very anaplastic lesion, as is the case with many sarcomas. Yes it would very difficult to tell the origin of this lesion if it weren't on the list of diagnosis. Note how some cells are spindle shaped and have elongated nuclei, this is one of the diagnostic tips that this a malignancy of fibroblast origin. You should see many mitoses and some even with tripolar metaphases. This tumor can arise in practically any soft tissue and I cannot say for sure if this one is primary in the bone or metastatic.

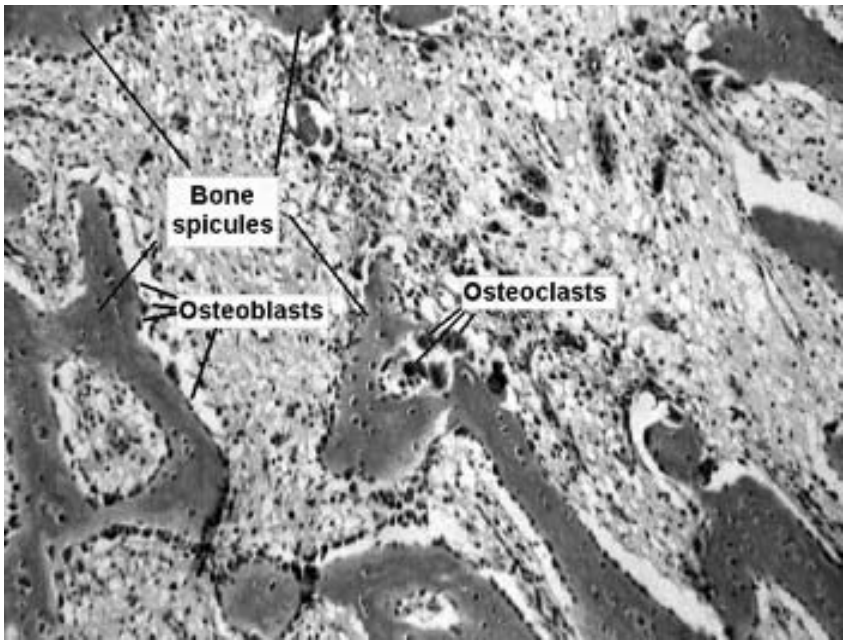
Your observations

Slide 134: Myositis Ossificans



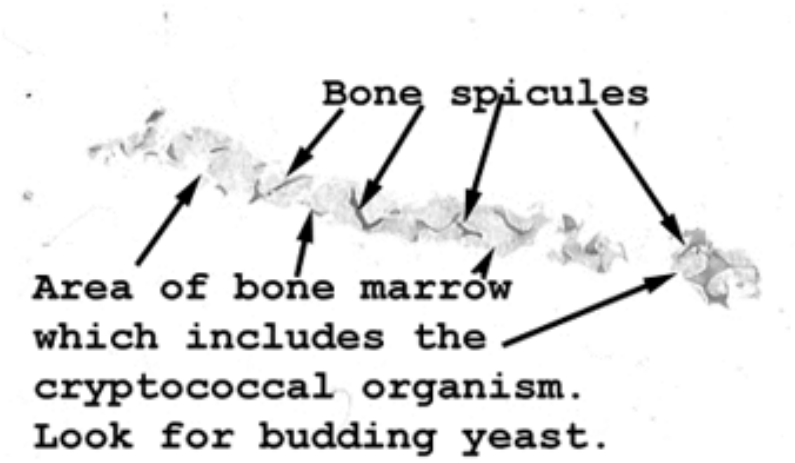
Believe it or not this is benign. If you look at the bone, it appears healthy with all cellular constituents present. I wouldn't be surprised if in some slides there is even active hematopoietic bone marrow present. Auto mechanics get these often in their hands at sites of recurrent injury.

Your observations



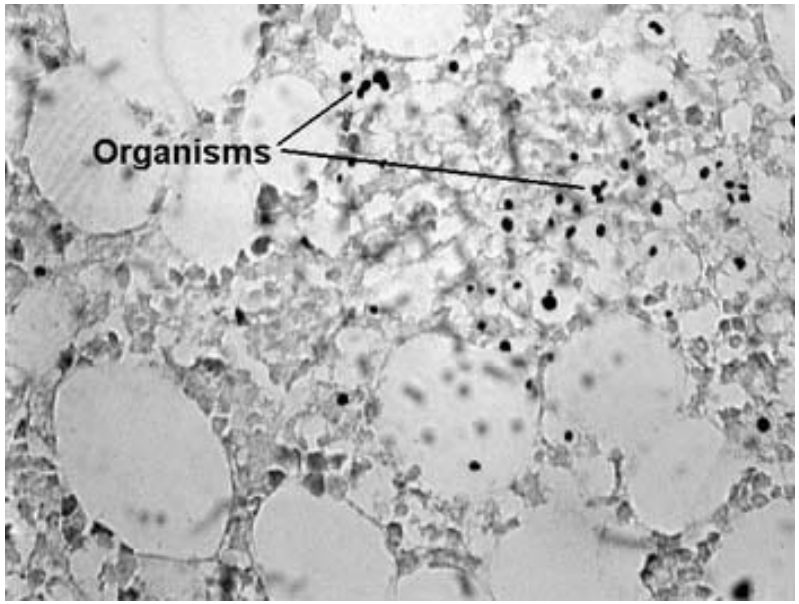
This is one of those odd lesions for which numerous explanations abound. Always benign, it looks just like its name sounds. It is a focus of bone formation on the fascia, within the muscle or subcutaneous fat. Sounds odd, but fascial tissue has a wide range of possible reactions to injury. This probably started as an area of hemorrhage, then became partially organized and finally developed bone. In some lesions like this, it is possible to even see bone marrow with active hematopoiesis develop.

Slide 166: Bone marrow with cryptococcal infection



This is a small core biopsy of bone which shows only minimal replacement of the bone marrow space with an inflammatory infiltrate. It takes the special stain to show the organisms. Obviously, the history was very important in knowing what to do to make the diagnosis in this case.

Your observations

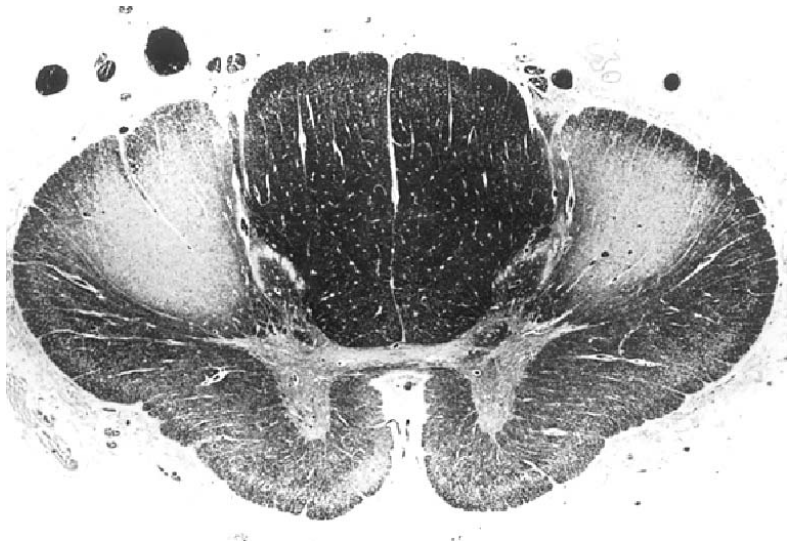


This is the counterpart to slide 165. It has been stained with a silver containing stain, Gomori's Methenamine Silver (GMS), which stains the organisms black. You will need to look a little to spot the definitive forms, as sometimes nuclear debris will also take up the stain. Generally the nuclear trash looks like small amorphous fragments, and with a little practice will not be mistaken for the budding yeast.

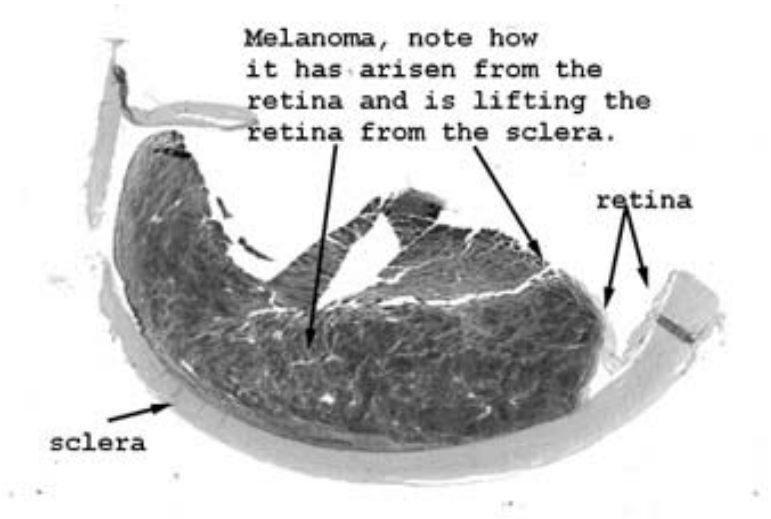
General and Systemic Histopathology
C601 and C602

Section 19 *Diseases of the Nervous System*

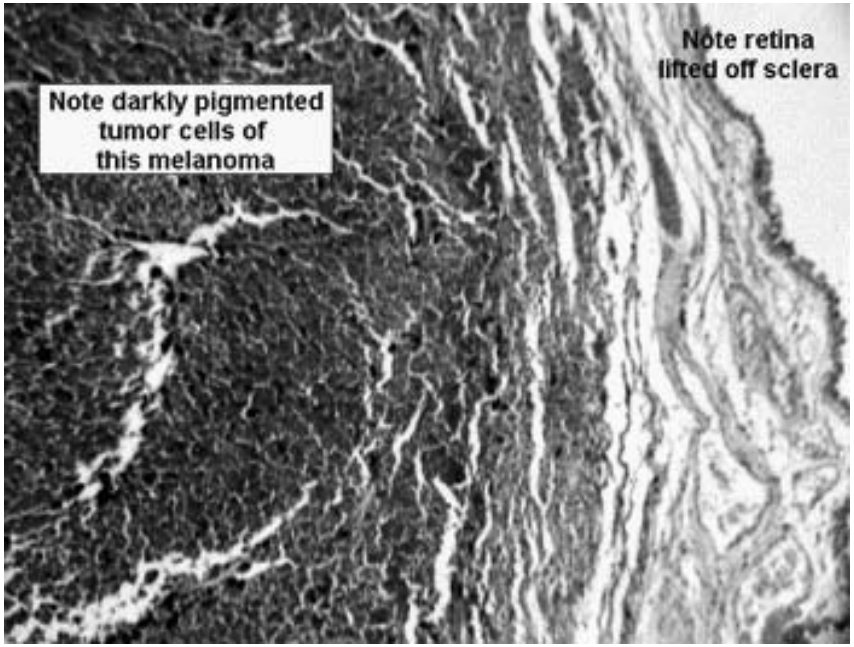
In this unit we will be studying disorders of the central and peripheral nervous systems. The most important feature of CNS pathology is the location of the lesion. Time and again we will see that a benign tumor, or seemingly inconsequential injury, can be devastating when it occurs in a strategic location. Just as it is said of real estate, the three most important facets of a property are its location, its location and finally its location. Another important element of pathology of the brain stems from the fact that it is a veritable prisoner within the fixed cranial vault. Edema and mass lesions have no where to go. Pressure on surrounding structures will prove most important.



Slide 35: Retinal Melanoma



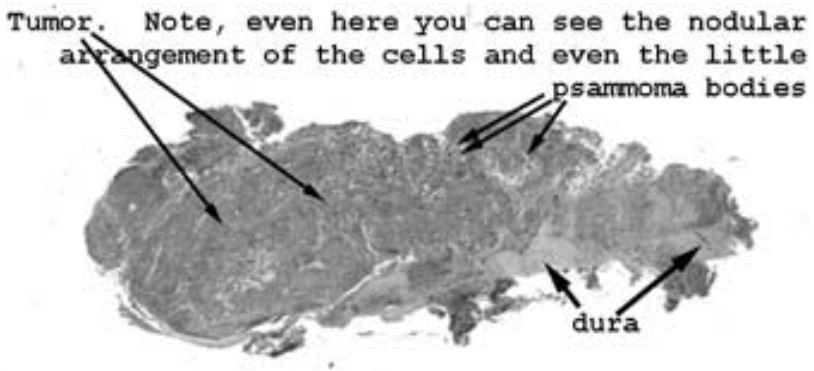
Again, there is probably no trouble seeing the tumor in this slide. It is obviously black because it is a melanoma. They can occur in various places in the eye but this is probably most common.

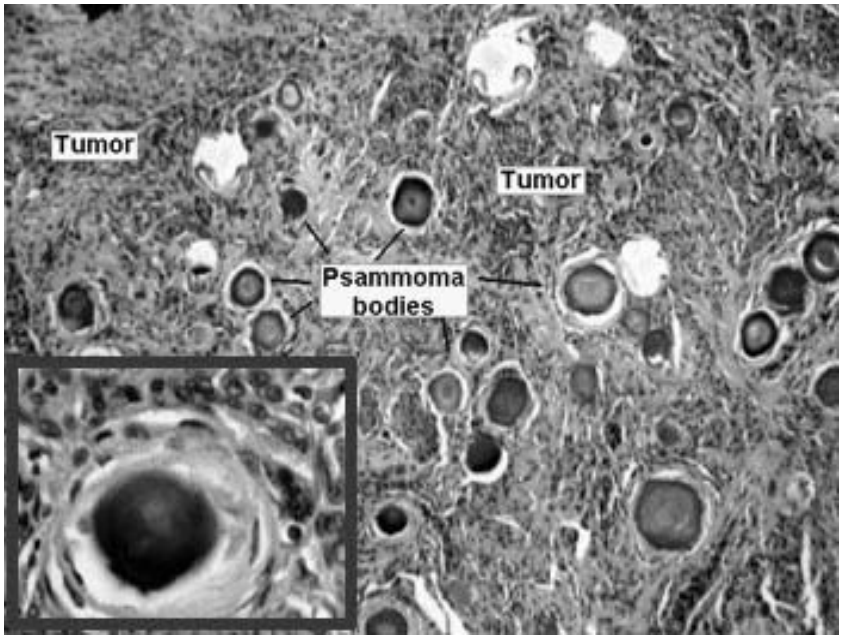


This slide shows a primary malignant melanoma of the retina. Most of the histological features of this tumor are just like those of cutaneous melanomas. You will note a lot of pigment, so much so, in fact, that in many instances you won't be able to see the nuclear morphology of the malignant cells. The one curious feature of this tumor is its propensity to metastasize to the liver. I have actually heard, jokingly so, the term "ocular-hepatic" shunt applied to this property of retinal melanomas. For what it's worth, there are actually three sites where primary ocular melanomas arise: the retina, the iris and the conjunctiva. It is the retinal variety that frequently metastasizes to the liver, and often very early in the course of the disease.

Your observations

Slide 38: Meningioma





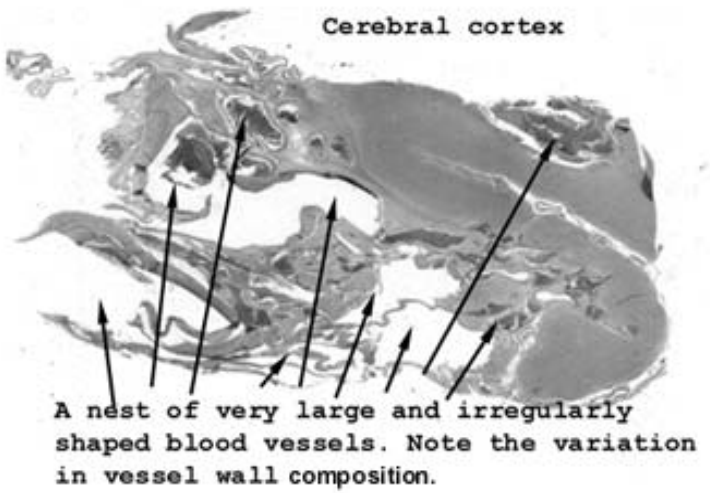
Be sure you identify the dura itself in this slide. Then look to the tumor. Even in this magnification we can see clusters of whirls of the tumor cells and if you have really good eyes you might be able to detect the pink "sand" of the psammoma bodies.

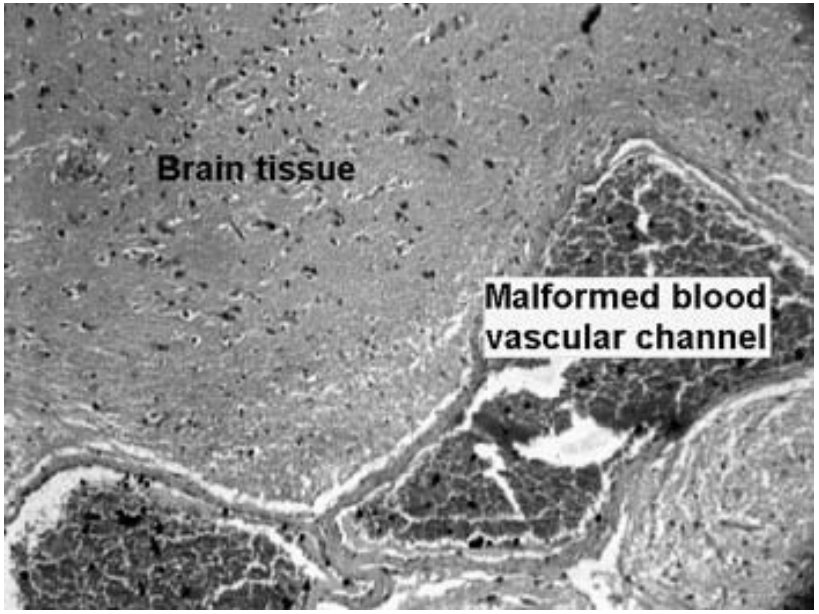
This lesion is benign and might be considered the "fibroma" of the coverings of the central nervous system. Note the long spindly cells grouped in whirl like clusters. On low and medium power, you may be able to appreciate an interdigitating pattern to these groups. You should see many curious little calcium concretions often associated with this type of tumor; the psammoma body. These are sometimes sufficiently numerous to be seen on X-Ray. Can you think of another tumor we have studied this year in which these little calcium concretions were seen? Hint: think endocrine.

The insert, lower left, shows detail of one of the psammoma bodies.

Your observations

Slide 83: Ateriovenous Malformation in the Brain





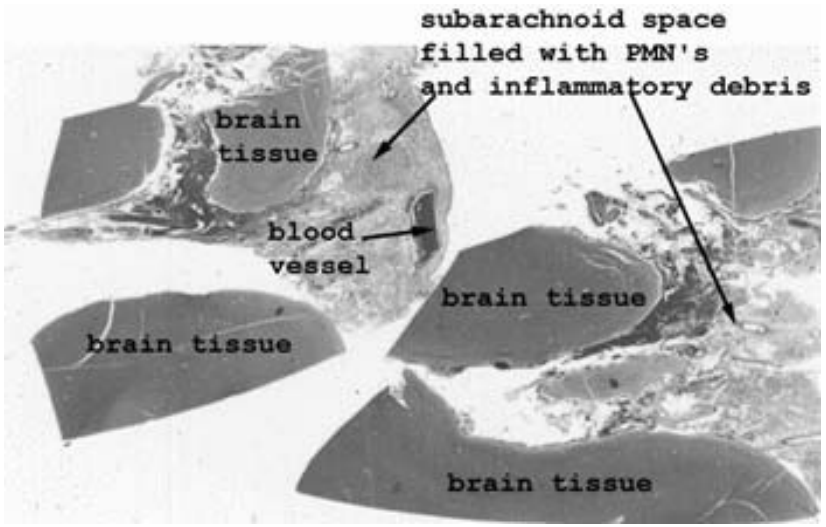
The many malformed vascular channels are quite evident in the picture to the left. These lesions are apt to bleed, as the presence of this specimen in our study attests to. No this is not a surgical specimen.

Here you will see many large and malformed blood vessels that have a "hybrid" wall structure. In some areas the wall resembles a vein and in others an artery. Look for an elastic interna. One would never expect to see vessels of this size with such peculiar wall structure within the brain. This represents a congenital deformity and can cause death at any age. The vessels are subject to leakage or rupture and this subject in fact died with an intracerebral hemorrhage.

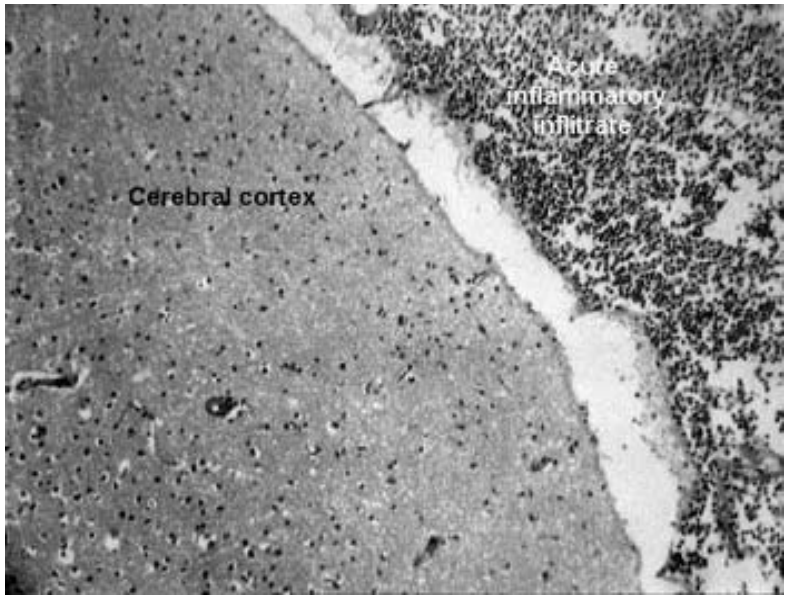
Your observations

Slide 90: Acute meningitis

Your observations

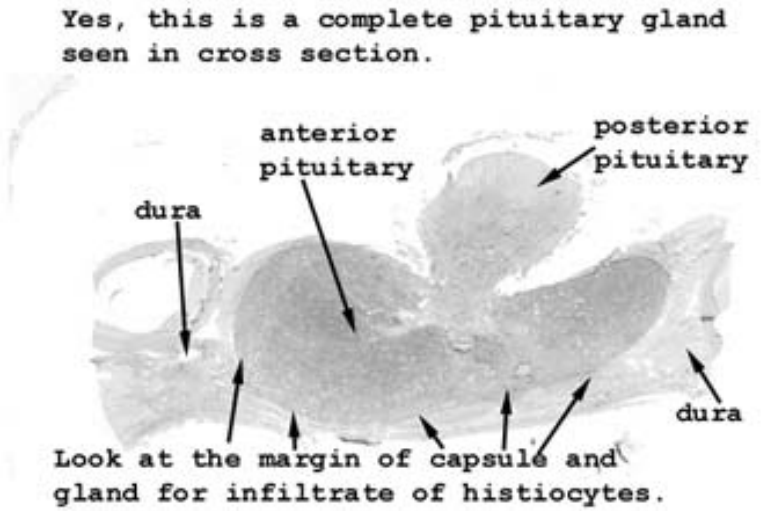


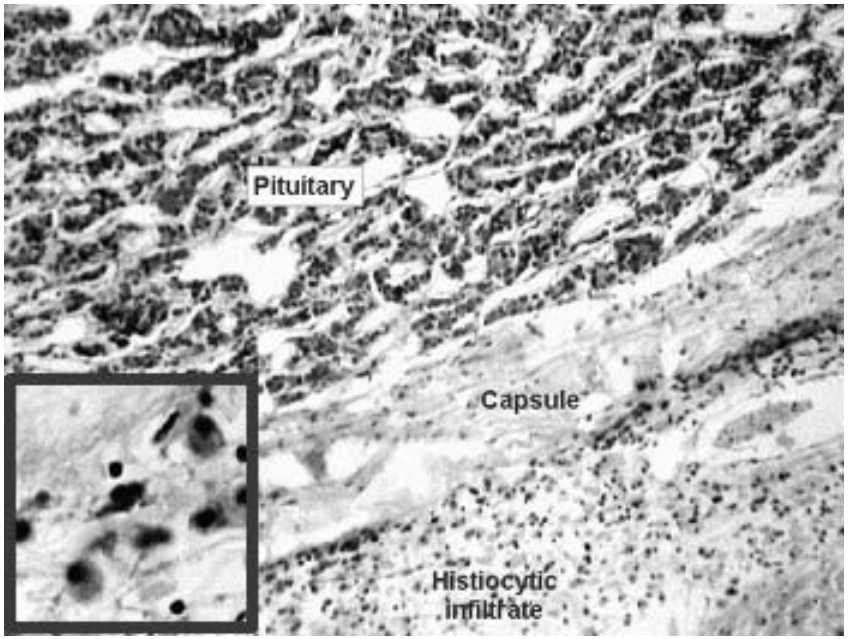
Here you see the unbelievably expanded subarachnoid space containing numerous polymorphonuclear leukocytes. What do you suspect the exudate looked like grossly?



This slide shows a profound acute inflammatory infiltrate associated with Hemophilus influenza meningitis. The organism most likely gained entrance into the subarachnoid space by way of the blood stream. The child with this condition died shortly after being admitted to the hospital, despite vigorous antibiotic therapy. Unfortunately, the child was not brought in until he was virtually moribund. You should have no trouble finding the polymorphonuclear leukocytes in this slide.

Slide 102: Pituitary with Histiocytosis





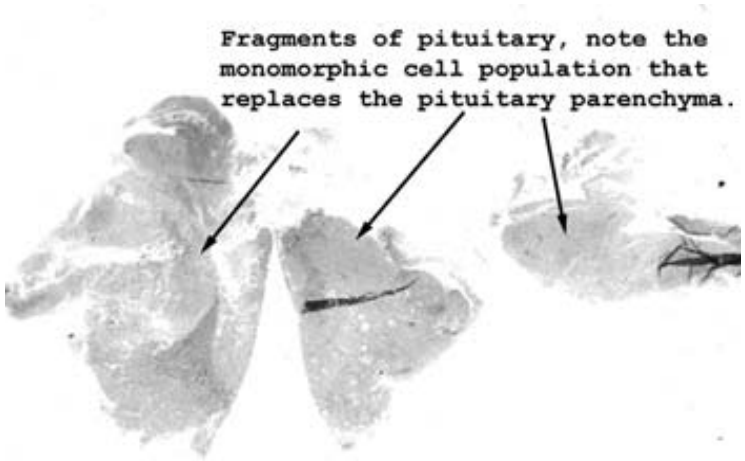
Look at this, a complete cross section of a pituitary gland! We want to concentrate on the area right at the edge of the gland for the infiltration of the histiocytes.

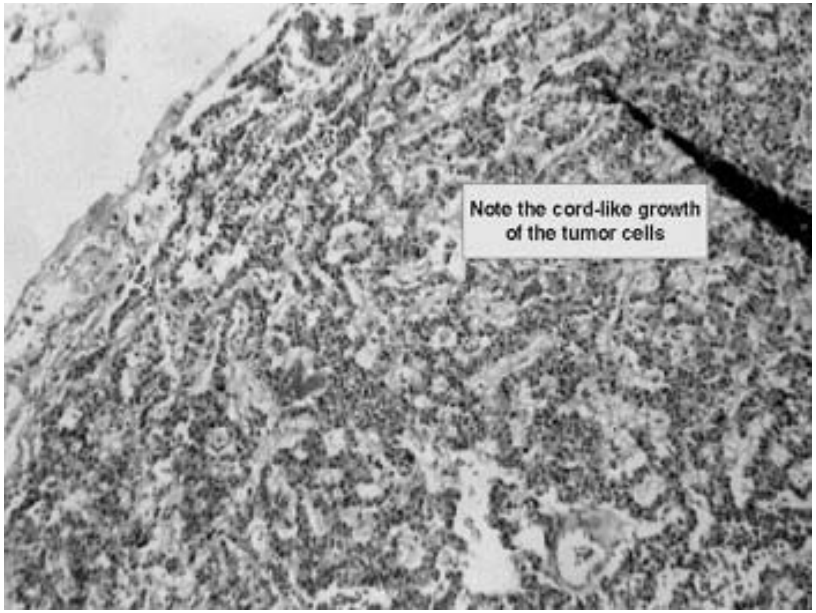
The histiocytic infiltrate in this case is around the capsule of the gland. It is kind of subtle, and you may want to check on the histology of the normal gland to appreciate the difference. The histiocytes do not look particularly aggressive, but they continue to slowly reproduce and cause organ failure.

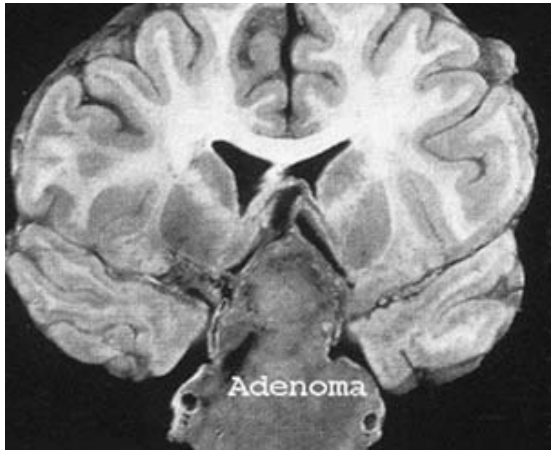
The insert, lower left, shows the detail of several of the histiocytes seen surrounding this pituitary.

Your observations

Slide 149: Pituitary adenoma





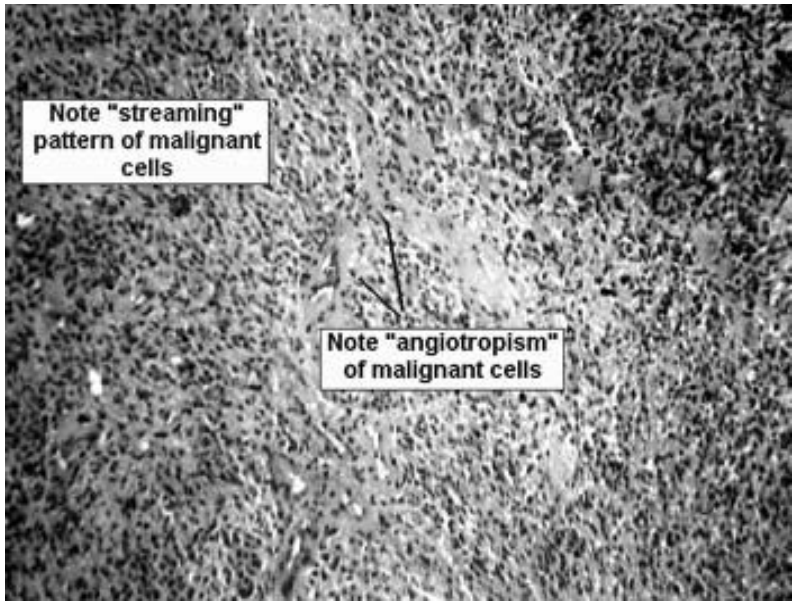


This gross photo of the brain with the adenoma was initially published in Laboratory Medicine, volume 29, number 10, page 612. It had been submitted as one of the photographs in the 1998 Art and Science of Medicine Photography contest. It was taken and submitted by Dr. James M. Gulizia of Brigham and Women's Hospital, Boston.

This picture is of a "benign" pituitary adenoma. Although biologically benign, it is sure in the wrong place and can be lethal just because of its location. You will see clusters and cords of the tumor cells, and it may be tricky to distinguish the tumor from the surrounding normal pituitary. Does the term "tumor" apply here? You should see no mitoses.

Your observations

Slide 184: Glioblastoma Multiforme



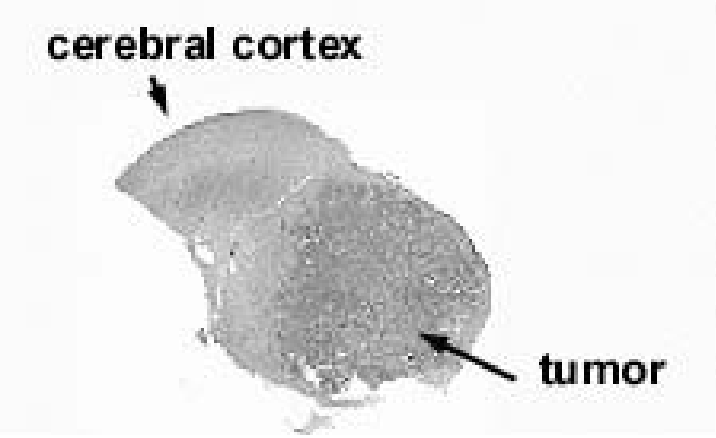
We see here just small fragments of brain and tumor. This is how these specimens come to us from surgery.

This is a high grade malignant astrocytic glial tumor. You will see areas of necrosis and marked nuclear atypia of the malignant cells. Pay special attention to the reactive, yet highly atypical looking, vascular changes in the capillary sized vessels. The endothelial cells become extremely agitated in the presence of this tumor. You should see some large pink staining cells at the periphery of this lesion; they are called gemistocytes, gem like cells. These are benign reactive glial cells, and similar changes are seen in many types of central nervous system injury. This tumor is highly aggressive and universally fatal, at least at the present time.

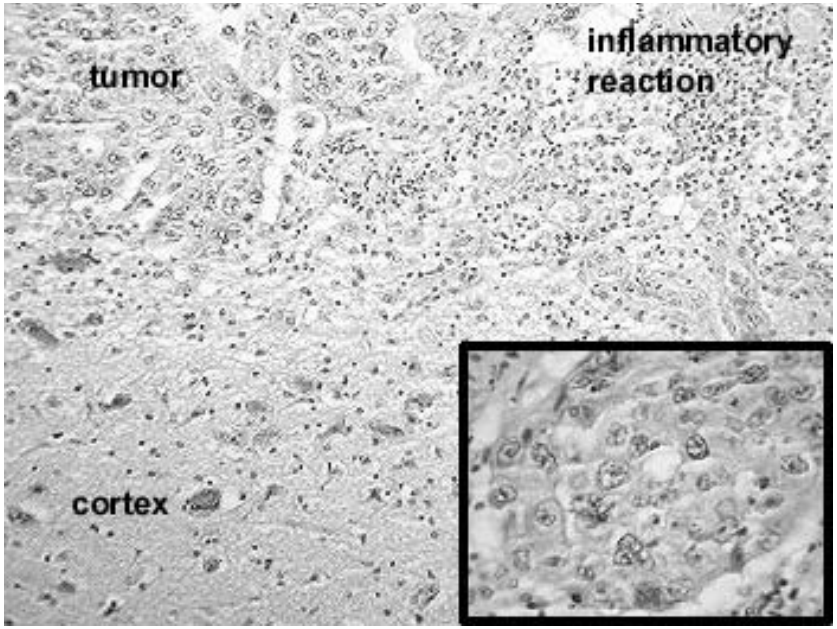
Your observations

Slide 218: metastatic carcinoma

Your observations



It shouldn't be difficult to find the tumor. Even so, look at all the tissue.



Note the inflammatory infiltrate at the margins of the tumor. As for the tumor, there are several possibilities for it's origin. There is kind of a squamous quality to the cells, raising the possibility of lung. On occasion breast can even look like this. It's likely not renal cell, melanoma or testicular.

APPENDIX A: Slide List by System

A. CARDIOVASCULAR SYSTEM

2. Artery – Monckeberg's sclerosis
3. Artery – arteriosclerosis with thrombosis
6. Heart – infarction
8. Heart – amyloidosis
14. Lung – embolus
19. Esophagus – esophagitis and varicosities
43. Heart – infarction
44. Heart – infarction with mural thrombus
48. Heart – fibrinous pericarditis
50. Heart – endocardial fibroelastosis (trichrome on 119)
53. Aorta– dissecting aneurysm
54. Heart – myocarditis
55. Heart – uremic pericarditis
56. Heart – metastatic carcinoma
68. Lung – bone marrow embolus and emphysema
78. Heart – tuberculosis in pericardium
83. Brain – arteriovenous malformation
100. Lung – arteriosclerosis and emboli
106. Aorta – syphilitic aneurysm
107. Lung – arteriosclerosis
110. Artery – arteriosclerosis and thrombosis: Heart-myocarditis
119. Heart – endocardial fibroelastosis (trichrome stain), see 50
129. Rectum – hemorrhoids
140. Veins – varicose veins
147. Artery – giant cell arteritis
190. Skin – Kaposi's sarcoma
208. Heart – acute viral myocarditis
209. Heart – mitral valvulitis with kidney showing accompanying glomerulonephritis
210. Heart – infectious pericarditis
213. Artery – berry aneurysm
214. Heart – acute rheumatic valvulitis
215. Heart – diphtherial myocarditis
217. Vein – thrombophlebitis
221. Heart – chronic rheumatic valve
224. Angiosarcoma of breast following treatment for breast cancer

B. RESPIRATORY SYSTEM

1. Lung – fungal pneumonia
14. Lung – embolus
16. Lung – caseous tuberculosis
26. Lung – bronchiectasis, purulent
36. Lung – pneumoconiosis
58. Lung – abscess
64. Lung – metaplasia
66. Lung – granuloma (asteroid)
68. Lung – bone marrow embolus and emphysema
70. Lung – bronchiectasis
72. Lung – healed pleuritis
74. Lung – acute congestion
76. Lung – tuberculosis
80. Lung – metastatic renal cell carcinoma
89. Lung – hyaline membrane disease
100. Lung – arteriosclerosis and emboli
101. Lung – squamous cell carcinoma
107. Lung – arteriosclerosis
108. Lung – embolus
120. Lung – lobar pneumonia
122. Lung – infarct: Artery-embolus
127. Lung – squamous cell carcinoma
135. Lung – disseminated intravascular coagulation
172. Lung – interstitial pneumonia
201. Lung – emphysema and bronchial obstruction
202. Lung – metastatic adenocarcinoma from colon
203. Lung – cartilage hamartoma
211. Lung – adenocarcinoma, alveolar cell type

C. LIVER and GALLBLADDER

4. Liver – fatty metamorphosis
5. Liver – cirrhosis (nutritional)
18. Liver – subacute fulminating hepatic necrosis
27. Gallbladder – acute and chronic cholecystitis
29. Liver – adenomatosis
40. Liver – acute yellow atrophy
41. Liver – acute and chronic cholangitis with sclerosis (status post roux and Y surgical procedure)
42. Liver – secondary biliary cirrhosis
45. Liver – post-necrotic cirrhosis (history of ulcerative colitis)
46. Liver – cirrhosis with necrosis
47. Liver – metastatic carcinoma
63. Liver – hepatocellular carcinoma
69. Liver – chronic lymphocytic leukemia
    Spleen – chronic lymphocytic leukemia
71. Liver – hemangioma
80. Liver – metastatic renal cell carcinoma
    Kidney – renal cell carcinoma
    Lung – metastatic renal cell carcinoma
92. Liver – cirrhosis (history of Crohn's disease)
    Pancreas – chronic pancreatitis
103. Gallbladder – adenocarcinoma
115. Liver – biliary obstruction, secondary to carcinoma
117. Liver – glycogenated nuclei
126. Gallbladder – acute and chronic cholecystitis
132. Liver – acute hepatitis
137. Gallbladder – cholesterolosis

D. SPLEEN and LYMPH NODES

30. Soft-tissue – plasmacytoma
57. Spleen – nodular sclerosing Hodgkin's disease
60. Lymph node – lymphoma
62. Lymph node – Hodgkin's disease
67. Spleen – sickle cell crisis
69. Spleen – chronic lymphocytic leukemia
    Liver – chronic lymphocytic leukemia
77. Lymph node – tuberculosis
84. Lymph node – reactive hyperplasia
102. Pituitary – histiocytosis X
111. Lymph node – metastatic duct cell carcinoma
114. Spleen - infarction
118. Lymph node – metastatic malignant melanoma
123. Spleen – infarct
124. Spleen – amyloidosis
130. Spleen – acute and chronic perisplenitis
142. Small intestine – lymphoma
146. Testis – lymphoma
160. Salivary gland – lymphoma
167. Intestine – lymphoma
176. Lymph node – metastatic anaplastic seminoma
191. Lymph node with Hodgkin's disease
197. Lymphn node – malignant lymphoma
206. Lymph node – follicular lymphoma

E. GASTROINTESTINAL TRACT, PANCREAS AND SALIVARY GLANDS

5. Stomach – penetrating ulcer: Small intestine peritonitis
9. Pylorus – ulcer
19. Esophagus – esophagitis and varicosities
20. Small intestine – infarction
21. Colon – familial polyposis
32. Rectum – adenocarcinoma
39. Esophagus – congenital esophageal cyst
59. Colon – ulcerative colitis
75. Pancreas – fatty infiltration
92. Pancreas – chronic pancreatitis
98. Cecum – Crohn's disease
104. Colon – endometriosis
105. Colon – adenocarcinoma
128. Stomach – hemorrhagic gastritis
129. Rectum – hemorrhoids
131. Colon – acute pseudomembranous colitis
138. Stomach – signet ring cell carcinoma
139. Appendix – acute appendicitis
141. Stomach – gastric ulcer

142. Small intestine – carcinoid
143. Ileum – lymphoma
144. Salivary gland – adenolymphoma (Warthin's tumor)
160. Salivary gland – lymphoma
161. Stomach – perforated gastric ulcer
167. Intestine – lymphoma
173. Colon – diverticulosis with diverticulitis
183. Colon – inflammatory polyp
188. Bowel – malignant lymphoma
189. Stomach – poorly differentiated carcinoma with ulceration
194. Bowel with radiation injury & inflammation & fibrosis
199. Parotid – Sjogren's syndrome
202. Lung – metastatic adenocarcinoma of colon
207. Stomach – gastric ulcer with cancer
212. Small intestine – sprue
216. Small intestine – intussusception
222. Appendix – with pin worm

F. RENAL SYSTEM

23. Bone – metastatic transitional cell carcinoma
79. Kidney – chronic pyelonephritis and arteriosclerosis
80. Kidney – renal cell carcinoma
    Liver – metastatic renal cell carcinoma
    Lung – metastatic renal cell carcinoma
91. Kidney – polycystic kidney disease
95. Kidney – diabetic nephropathy
112. Kidney – polycystic disease, juvenile form
113. Kidney – acute and chronic pyelonephritis
133. Kidney – diabetic glomerulosclerosis
135. Lung – disseminated intravascular coagulation
    Kidney – disseminated intravascular coagulation
145. Kidney – renal cell carcinoma
164. Kidney – rapidly progressive glomerulonephritis
175. Kidney – host graft rejection
219. Kidney – fetal, normal 31 week gestation
220. Kidney – papillary adenoma with chronic pyelonephritis with marked arteriosclerosis

G. REPRODUCTIVE SYSTEM

22. Uterus – adenomyosis
34. Uterus – leiomyoma
37. Ovary – Stein-Leventhal syndrome
61. Cervix – dysplasia
85. Prostate – hyperplasia
86. Fallopian tube – acute salpingitis
94. Uterine contents – chorionic villi
136. Fallopian tube – endometriosis
146. Testis – lymphoma
153. Cervix – squamous cell carcinoma with lymphatic invasion
155. Uterine contents – hydatidiform mole
159. Ovary – mature teratoma
162. Testis – seminoma
163. Ovary – cystic teratoma benign
174. Fallopian tube – acute salpingitis
176. Lymph node – metastatic seminoma
177. Testis – seminoma
178. Testis – teratoma with embryonal carcinoma
180. Ovary – multiloculated serous cyst
181. Umbilical cord and amniotic membranes – acute amnionitis and funisitis
182. Placenta – molar pregnancy
187. Cervix – scrapings with viral changes
192. Ovary – papillary adenocarcinoma
198. Fallopian tube – tubal pregnancy
200. Prostate – adenocarcinoma with capsular involvement
204. Placenta – erythroblastosis fetalis
223. Pap smear – dysplasia

H. ENDOCRINE SYSTEM: THYROID, ADRENAL, etc.

10. Thyroid – colloid goiter
11. Thyroid – adenoma
12. Thyroid – hyperthyroidism, treated
15. Thyroid – adenoma (microfollicular)
24. Thyroid – papillary carcinoma

25. Thyroid – Hashimoto's disease
28. Thyroid – thyroiditis with fibrosis
81. Adrenal – cortical hyperplasia
82. Adrenal – pheochromocytoma
97. Adrenal – tuberculosis
99. Thyroid – adenoma
102. Pituitary – histiocytosis X
109. Adrenal – adenoma
148. Parathyroid – hyperplasia
149. Pituitary – adenoma
170. Adrenal – amyloidosis
171. Adrenal – amyloidosis (Congo Red)
193. Thyroid – papillary carcinoma
196. Parathyroid – adenoma

I. SKIN

13. Skin – sinus tract with foreign body reaction
17. Skin – leishmaniasis (azure-eosin stain)
31. Breast – Paget's disease
33. Skin – metastatic breast cancer
52. Skin – intradermal nevus
65. Skin – ruptured epidermal inclusion cyst
87. Skin – squamous cell carcinoma
93. Skin – basal cell carcinoma
116. Skin – malignant melanoma
118. Lymph node – metastatic malignant melanoma
150. Skin – intradermal nevus
151. Skin – seborrheic keratosis
152. Skin – epidermal inclusion cyst
154. Skin – keratoacanthoma
156. Skin – dermatofibrosarcoma protuberans
157. Skin – recurrent squamous cell carcinoma
168. Skin – amyloidosis
169. Skin – amyloidosis (Congo Red)
185. Skin – molluscum contagiosum
186. Skin – verrucae vulgaris
190. Skin – Kaposi's sarcoma

J. BREAST

31. Breast – Paget's disease
33. Skin – metastatic breast cancer
51. Breast – infiltrating duct cell carcinoma (scirrhous)
73. Breast – fibrocystic disease
96. Breast – fibroadenoma
111. Lymph node – metastatic duct cell carcinoma
158. Breast – duct cell carcinoma
224. Angiosarcoma following therapy for breast cancer

K. CENTRAL NERVOUS SYSTEM, EYES, AND EARS

35. Eye – malignant melanoma
38. Meninges – meningioma
83. Brain – arteriovenous malformation
90. Meninges – acute meningitis
102. Pituitary – histiocytosis X
149. Pituitary – adenoma
179. Meninges – meningioma
184. Brain – glioblastoma multiforme-grade IV glioma
218. Brain – metastatic carcinoma

L. BONE and SOFT TISSUE

7. Bone – healing fracture
23. Bone – metastatic transitional cell carcinoma
34. Uterus – leiomyoma
49. Bone marrow – hyperplasia
88. Omentum – infarction
121. Muscle – myositis
Artery – Monckeberg's sclerosis
125. Bone – fibrosarcoma
134. Muscle – myositis ossificans
165. Bone marrow – AIDS (cryptococcus neoformans fungi)
166. Bone marrow – AIDS (cryptococcus neoformans fungi) (Gomori-methenamine silver nitrate)
190. Skin – Kaposi's sarcoma
195. Retroperitoneal fat – liposarcoma

205. Bone marrow – hyperplasia

M. INFECTIOUS DISEASES

1. Lung – fungal pneumonia (cryptococcosis)
16. Lung – caseous tuberculosis
17. Skin – leishmaniasis (azure-eosin stain)
76. Lung – tuberculosis
77. Lymph node – tuberculosis
78. Lymph node – tuberculosis
97. Adrenal – tuberculosis
131. Colon – acute pseudomembranous colitis
165. Bone marrow – AIDS (cryptococcus neoformans fungi)
166. Bone marrow – AIDS (cryptococcus neoformans fungi) (Gomori-methenamine silver nitrate)
173. Colon – diverticulosis with diverticulitis
B4. Peripheral blood – mononucleosis
185. Skin – molluscum contagiosum
186. Skin – verruca vulgaris
187. Cervix – scrapings with viral changes
210. Heart – infectious pericarditis
214. Heart – acute rheumatic valvulitis
215. Heart – diphtherial myocarditis
222. Appendix – pin worms

NORMAL SLIDES

There are five boxes of normal tissues available. They are kept in the new location and are as follows:

N1. Eyelid
N2. Heart
N3. Lung
N4. Trachea
N5. Liver
N6. Gastroesophageal junction
N7. Appendix
N8. Adrenal
N9. Kidney
N10. Uterus
N11. Fallopian tube
N12. Aorta
N13. Brain, cerebral cortex
N14. Brain, cerebellum
N15. Spinal cord
N16. Testis
N17. Prostate
N18. Ovary

Blood smears are in the third box of the teaching set:

Case 2. Peripheral blood - sickle cell anemia
Case 6. Peripheral blood - chronic lymphocytic leukemia
Case 8. Peripheral blood - chronic myelogenous leukemia
Case 9. Peripheral blood - acute myelomonocytic leukemia
Case 10. Peripheral blood - acute lymphoblastic leukemia
Case 12. Peripheral blood - leukoerythroblastosis
Case 13. Peripheral blood - mononucleosis

APPENDIX B: Pathology Slide List

1. Lung – fungal pneumonia (cryptococcosis)
2. Artery – Monckeberg's sclerosis
3. Artery – arteriosclerosis with thrombosis
4. Liver – fatty metamorphosis
5. Liver – cirrhosis (nutritional)
   Stomach – penetrating ulcer: Small intestine peritonitis
6. Heart – infarction
7. Bone – healing fracture
8. Heart – amyloidosis
9. Pylorus – ulcer
10. Thyroid – colloid goiter
11. Thyroid – adenoma
12. Thyroid – hyperthyroidism, treated
13. Skin – sinus tract with foreign body reaction
14. Lung – embolus
15. Thyroid – adenoma (microfollicular)
16. Lung – caseous tuberculosis
17. Skin – leishmaniasis (azure-eosin stain)
18. Liver – subacute fulminating hepatic necrosis
19. Esophagus – esophagitis and varicosities
20. Small intestine – infarction
21. Colon – familial polyposis
22. Uterus – adenomyosis
23. Bone – metastatic transitional cell carcinoma
24. Thyroid – papillary carcinoma
25. Thyroid – Hashimoto's disease
26. Lung – bronchiectasis, purulent
27. Gallbladder – acute and chronic cholecystitis
28. Thyroid – thyroiditis with fibrosis
29. Liver – adenomatosis
30. Soft-tissue – plasmacytoma
31. Breast – Paget's disease
32. Rectum – adenocarcinoma
33. Skin – metastatic breast cancer
34. Uterus – leiomyoma
35. Eye – malignant melanoma
36. Lung – pneumoconiosis
37. Ovary – Stein-Leventhal syndrome
38. Meninges – meningioma
39. Esophagus – congenital esophageal cyst
40. Liver – acute yellow atrophy
41. Liver – acute and chronic cholangitis with sclerosis (status post roux and Y surgical procedure)
42. Liver – secondary biliary cirrhosis
43. Heart – infarction
44. Heart – infarction with mural thrombus
45. Liver – post-necrotic cirrhosis (history of ulcerative colitis)
46. Liver – cirrhosis with necrosis
47. Liver – metastatic carcinoma
48. Heart – fibrinous pericarditis
49. Bone marrow – hyperplasia
50. Heart – endocardial fibroelastosis (trichrome on 119)
51. Breast – infiltrating duct cell carcinoma (scirrhous)
52. Skin – intradermal nevus
53. Aorta– dissecting aneurysm
54. Heart – myocarditis
55. Heart – uremic pericarditis
56. Heart – metastatic carcinoma
57. Spleen – nodular sclerosing Hodgkin's disease
58. Lung – abscess
59. Colon – ulcerative colitis
60. Lymph node – lymphoma
61. Cervix – dysplasia
62. Lymph node – Hodgkin's disease
63. Liver – hepatocellular carcinoma
64. Lung – metaplasia
65. Skin – ruptured epidermal inclusion cyst
66. Lung – granuloma (asteroid)
67. Spleen – sickle cell crisis
68. Lung – bone marrow embolus and emphysema
69. Liver – chronic lymphocytic leukemia
    Spleen – chronic lymphocytic leukemia
70. Lung – bronchiectasis
71. Liver – hemangioma
72. Lung – healed pleuritis
73. Breast – fibrocystic disease

74. Lung – acute congestion
75. Pancreas – fatty infiltration
76. Lung – tuberculosis
77. Lymph node – tuberculosis
78. Heart – tuberculosis in pericardium
79. Kidney – chronic pyelonephritis and arteriosclerosis
80. Kidney – renal cell carcinoma
    Liver – metastatic renal cell carcinoma
    Lung – metastatic renal cell carcinoma
81. Adrenal – cortical hyperplasia
82. Adrenal – pheochromocytoma
83. Brain – arteriovenous malformation
84. Lymph node – reactive hyperplasia
85. Prostate – hyperplasia
86. Fallopian tube – acute salpingitis
87. Skin – squamous cell carcinoma
88. Omentum – infarction
89. Lung – hyaline membrane disease
90. Meninges – acute meningitis
91. Kidney – polycystic kidney disease
92. Liver – cirrhosis (history of Crohn's disease)
    Pancreas – chronic pancreatitis
93. Skin – basal cell carcinoma
94. Uterine contents – chorionic villi
95. Kidney – diabetic nephropathy
96. Breast – fibroadenoma
97. Adrenal – tuberculosis
98. Cecum – Crohn's disease
99. Thyroid – adenoma
100. Lung – arteriosclerosis and emboli
101. Lung – squamous cell carcinoma
102. Pituitary – histiocytosis X
103. Gallbladder – adenocarcinoma
104. Colon – endometriosis
105. Colon – adenocarcinoma
106. Aorta – syphilitic aneurysm
107. Lung – arteriosclerosis
108. Lung – embolus
109. Adrenal – adenoma
110. Artery – arteriosclerosis and thrombosis: Heart-myocarditis
111. Lymph node – metastatic duct cell carcinoma
112. Kidney – polycystic reanl disease, juvenile form
113. Kidney – acute and chronic pyelonephritis
114. Spleen - infarction
115. Liver – biliary obstruction, secondary to carcinoma
116. Skin – malignant melanoma
117. Liver – glycogenated nuclei
118. Lymph node – metastatic malignant melanoma
119. Heart – endocardial fibroelastosis (trichrome stain), see 50
120. Lung – lobar pneumonia
121. Muscle – myositis
122. Lung – infarct: Artery-embolus
123. Spleen – infarct
124. Spleen – amyloidosis
125. Bone – fibrosarcoma
126. Gallbladder – acute and chronic cholecystitis
127. Lung – squamous cell carcinoma
128. Stomach – hemorrhagic gastritis
129. Rectum – hemorrhoids
130. Spleen – acute and chronic perisplenitis
131. Colon – acute pseudomembranous colitis
132. Liver – acute hepatitis
133. Kidney – diabetic glomerulosclerosis
134. Muscle – myositis ossificans
135. Kidney – disseminated intravascular coagulation
    Lung – disseminated intravascular coagulation
136. Fallopian tube – endometriosis
137. Gallbladder – cholesterolosis
138. Stomach – signet ring cell carcinoma
139. Appendix – acute appendicitis
140. Veins – varicose veins
141. Stomach – gastric ulcer
142. Small intestine – lymphoma

143. Ileum – carcinoid
144. Salivary gland – adenolymphoma (Warthin's tumor)
145. Kidney – renal cell carcinoma
146. Testis – lymphoma

147. Artery – giant cell arteritis
148. Parathyroid – hyperplasia
149. Pituitary – adenoma
150. Skin – intradermal nevus
151. Skin – seborrheic keratosis
152. Skin – epidermal inclusion cyst
153. Cervix – squamous cell carcinoma with lymphatic invasion
154. Skin – keratoacanthoma
155. Uterine contents – hydatidiform mole
156. Skin – dermatofibrosarcoma protuberans
157. Skin – recurrent squamous cell carcinoma
158. Breast – duct cell carcinoma
159. Ovary – mature teratoma
160. Salivary gland – lymphoma
161. Stomach – perforated gastric ulcer
162. Testis – seminoma
163. Ovary – cystic teratoma benign
164. Kidney – rapidly progressive glomerulonephritis
165. Bone marrow – AIDS (cryptococcus neoformans fungi)
166. Bone marrow – AIDS (cryptococcus neoformans fungi) (Gomori-methenamine silver nitrate)
167. Intestine – lymphoma
168. Skin – amyloidosis
169. Skin – amyloidosis (Congo Red)
170. Adrenal – amyloidosis
171. Adrenal – amyloidosis (Congo Red)
172. Lung – interstitial pneumonia
173. Colon – diverticulosis with diverticulitis
174. Fallopian tube – acute salpingitis
175. Kidney – host graft rejection
176. Lymph node – metastatic anaplastic seminoma
177. Testis – seminoma
178. Testis – teratoma with embryonal carcinoma
179. Meninges – meningioma
180. Ovary – multiloculated serous cyst
181. Umbilical cord and amniotic membranes – acute amnionitis and funisitis
182. Placenta – molar pregnancy
183. Colon – inflammatory polyp
184. Brain – glioblastoma multiforme-grade IV glioma
185. Skin – molluscum contagiosum
186. Skin – verruca vulgaris
187. Cervix – scrapings with viral changes
188. Bowel – malignant lymphoma
189. Stomach – poorly differentiated carcinoma with ulceration
190. Skin – Kaposi's sarcoma
191. Lymph node with Hodgkin's disease
192. Ovary – papillary adenocarcinoma
193. Thyroid – papillary carcinoma
194. Bowel – radiation injury with inflammation and fibrosis
195. Retroperitoneal fat – liposarcoma
196. Parathyroid – adenoma
197. Lymphn node – malignant lymphoma
198. Fallopian tube – tubal pregnancy
199. Parotid – Sjogren's syndrome
200. Prostate – adenocarcinoma with capsular involvement
201. Lung – emphysema and bronchial obstruction
202. Lung – metastatic adenocarcinoma from colon
203. Lung – cartilage hamartoma
204. Placenta – erythroblastosis fetalis
205. Bone marrow – hyperplasia
206. Lymph node – follicular lymphoma
207. Stomach – gastric ulcer with cancer
208. Heart – acute viral myocarditis
209. Heart – mitral valvulitis with kidney showing accompanying glomerulonephritis
210. Heart – infections pericarditis
211. Lung – adenocarcinoma, alveolar cell type
212. Small intestine – sprue
213. Artery – berry aneurysm
214. Heart – acute rheumatic valvulitis
215. Heart – diphtherial myocarditis
216. Small intestine – intussusception
217. Vein – thrombophlebitis
218. Brain – metastatic ?? Carcinoma
219. Kidney – fetal, normal 31 week gestation
220. Kidney – papillary adenoma with chronic pyelonephritis with marked arteriosclerosis

221. Heart – chronic rheumatic valve
222. Appendix with pin worm
223. Pap smear – dysplasia
224. Angiosarcoma of breast following treatment for breast cancer

APPENDIX A: Slide List by System

A. CARDIOVASCULAR SYSTEM

2. Artery – Monckeberg's sclerosis
3. Artery – arteriosclerosis with thrombosis
6. Heart – infarction
8. Heart – amyloidosis
14. Lung – embolus
19. Esophagus – esophagitis and varicosities
43. Heart – infarction
44. Heart – infarction with mural thrombus
48. Heart – fibrinous pericarditis
50. Heart – endocardial fibroelastosis (trichrome on 119)
53. Aorta– dissecting aneurysm
54. Heart – myocarditis
55. Heart – uremic pericarditis
56. Heart – metastatic carcinoma
68. Lung – bone marrow embolus and emphysema
78. Heart – tuberculosis in pericardium
83. Brain – arteriovenous malformation
100. Lung – arteriosclerosis and emboli
106. Aorta – syphilitic aneurysm
107. Lung – arteriosclerosis
110. Artery – arteriosclerosis and thrombosis: Heart-myocarditis
119. Heart – endocardial fibroelastosis (trichrome stain), see 50
129. Rectum – hemorrhoids
140. Veins – varicose veins
147. Artery – giant cell arteritis
190. Skin – Kaposi's sarcoma
208. Heart – acute viral myocarditis
209. Heart – mitral valvulitis with kidney showing accompanying glomerulonephritis
210. Heart – infectious pericarditis
213. Artery – berry aneurysm
214. Heart – acute rheumatic valvulitis
215. Heart – diphtherial myocarditis
217. Vein – thrombophlebitis
221. Heart – chronic rheumatic valve
224. Angiosarcoma of breast following treatment for breast cancer

B. RESPIRATORY SYSTEM

1. Lung – fungal pneumonia
14. Lung – embolus
16. Lung – caseous tuberculosis
26. Lung – bronchiectasis, purulent
36. Lung – pneumoconiosis
58. Lung – abscess
64. Lung – metaplasia
66. Lung – granuloma (asteroid)
68. Lung – bone marrow embolus and emphysema
70. Lung – bronchiectasis
72. Lung – healed pleuritis
74. Lung – acute congestion
76. Lung – tuberculosis
80. Lung – metastatic renal cell carcinoma
89. Lung – hyaline membrane disease
100. Lung – arteriosclerosis and emboli
101. Lung – squamous cell carcinoma
107. Lung – arteriosclerosis
108. Lung – embolus
120. Lung – lobar pneumonia
122. Lung – infarct: Artery-embolus
127. Lung – squamous cell carcinoma
135. Lung – disseminated intravascular coagulation
172. Lung – interstitial pneumonia
201. Lung – emphysema and bronchial obstruction
202. Lung – metastatic adenocarcinoma from colon
203. Lung – cartilage hamartoma
211. Lung – adenocarcinoma, alveolar cell type

C. LIVER and GALLBLADDER

4. Liver – fatty metamorphosis
5. Liver – cirrhosis (nutritional)
18. Liver – subacute fulminating hepatic necrosis
27. Gallbladder – acute and chronic cholecystitis
29. Liver – adenomatosis
40. Liver – acute yellow atrophy
41. Liver – acute and chronic cholangitis with sclerosis (status post roux and Y surgical procedure)
42. Liver – secondary biliary cirrhosis
45. Liver – post-necrotic cirrhosis (history of ulcerative colitis)
46. Liver – cirrhosis with necrosis
47. Liver – metastatic carcinoma
63. Liver – hepatocellular carcinoma
69. Liver – chronic lymphocytic leukemia
    Spleen – chronic lymphocytic leukemia
71. Liver – hemangioma
80. Liver – metastatic renal cell carcinoma
    Kidney – renal cell carcinoma
    Lung – metastatic renal cell carcinoma
92. Liver – cirrhosis (history of Crohn's disease)
    Pancreas – chronic pancreatitis
103. Gallbladder – adenocarcinoma
115. Liver – biliary obstruction, secondary to carcinoma
117. Liver – glycogenated nuclei
126. Gallbladder – acute and chronic cholecystitis
132. Liver – acute hepatitis
137. Gallbladder – cholesterolosis

D. SPLEEN and LYMPH NODES

30. Soft-tissue – plasmacytoma
57. Spleen – nodular sclerosing Hodgkin's disease
60. Lymph node – lymphoma
62. Lymph node – Hodgkin's disease
67. Spleen – sickle cell crisis
69. Spleen – chronic lymphocytic leukemia
    Liver – chronic lymphocytic leukemia
77. Lymph node – tuberculosis
84. Lymph node – reactive hyperplasia
102. Pituitary – histiocytosis X
111. Lymph node – metastatic duct cell carcinoma
114. Spleen - infarction
118. Lymph node – metastatic malignant melanoma
123. Spleen – infarct
124. Spleen – amyloidosis
130. Spleen – acute and chronic perisplenitis
142. Small intestine – lymphoma
146. Testis – lymphoma
160. Salivary gland – lymphoma
167. Intestine – lymphoma
176. Lymph node – metastatic anaplastic seminoma
191. Lymph node with Hodgkin's disease
197. Lymphn node – malignant lymphoma
206. Lymph node – follicular lymphoma

E. GASTROINTESTINAL TRACT, PANCREAS AND SALIVARY GLANDS

5. Stomach – penetrating ulcer: Small intestine peritonitis
9. Pylorus – ulcer
19. Esophagus – esophagitis and varicosities
20. Small intestine – infarction
21. Colon – familial polyposis
32. Rectum – adenocarcinoma
39. Esophagus – congenital esophageal cyst
59. Colon – ulcerative colitis
75. Pancreas – fatty infiltration
92. Pancreas – chronic pancreatitis
98. Cecum – Crohn's disease
104. Colon – endometriosis
105. Colon – adenocarcinoma
128. Stomach – hemorrhagic gastritis
129. Rectum – hemorrhoids
131. Colon – acute pseudomembranous colitis
138. Stomach – signet ring cell carcinoma
139. Appendix – acute appendicitis
141. Stomach – gastric ulcer

142. Small intestine – carcinoid
143. Ileum – lymphoma
144. Salivary gland – adenolymphoma (Warthin's tumor)
160. Salivary gland – lymphoma
161. Stomach – perforated gastric ulcer
167. Intestine – lymphoma
173. Colon – diverticulosis with diverticulitis
183. Colon – inflammatory polyp
188. Bowel – malignant lymphoma
189. Stomach – poorly differentiated carcinoma with ulceration
194. Bowel with radiation injury & inflammation & fibrosis
199. Parotid – Sjogren's syndrome
202. Lung – metastatic adenocarcinoma of colon
207. Stomach – gastric ulcer with cancer
212. Small intestine – sprue
216. Small intestine – intussusception
222. Appendix – with pin worm

F. RENAL SYSTEM

23. Bone – metastatic transitional cell carcinoma
79. Kidney – chronic pyelonephritis and arteriosclerosis
80. Kidney – renal cell carcinoma
    Liver – metastatic renal cell carcinoma
    Lung – metastatic renal cell carcinoma
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95. Kidney – diabetic nephropathy
112. Kidney – polycystic disease, juvenile form
113. Kidney – acute and chronic pyelonephritis
133. Kidney – diabetic glomerulosclerosis
135. Lung – disseminated intravascular coagulation
    Kidney – disseminated intravascular coagulation
145. Kidney – renal cell carcinoma
164. Kidney – rapidly progressive glomerulonephritis
175. Kidney – host graft rejection
219. Kidney – fetal, normal 31 week gestation
220. Kidney – papillary adenoma with chronic pyelonephritis with marked arteriosclerosis
225. Urinary bladder - invasive transition cell carcinoma

G. REPRODUCTIVE SYSTEM

22. Uterus – adenomyosis
34. Uterus – leiomyoma
37. Ovary – Stein-Leventhal syndrome
61. Cervix – dysplasia
85. Prostate – hyperplasia
86. Fallopian tube – acute salpingitis
94. Uterine contents – chorionic villi
136. Fallopian tube – endometriosis
146. Testis – lymphoma
153. Cervix – squamous cell carcinoma with lymphatic invasion
155. Uterine contents – hydatidiform mole
159. Ovary – mature teratoma
162. Testis – seminoma
163. Ovary – cystic teratoma benign
174. Fallopian tube – acute salpingitis
176. Lymph node – metastatic seminoma
177. Testis – seminoma
178. Testis – teratoma with embryonal carcinoma
180. Ovary – multiloculated serous cyst
181. Umbilical cord and amniotic membranes – acute amnionitis and funisitis
182. Placenta – molar pregnancy
187. Cervix – scrapings with viral changes
192. Ovary – papillary adenocarcinoma
198. Fallopian tube – tubal pregnancy
200. Prostate – adenocarcinoma with capsular involvement
204. Placenta – erythroblastosis fetalis
223. Pap smear – dysplasia

H. ENDOCRINE SYSTEM: THYROID, ADRENAL, etc.

10. Thyroid – colloid goiter
11. Thyroid – adenoma
12. Thyroid – hyperthyroidism, treated
15. Thyroid – adenoma (microfollicular)
24. Thyroid – papillary carcinoma

25. Thyroid – Hashimoto's disease
28. Thyroid – thyroiditis with fibrosis
81. Adrenal – cortical hyperplasia
82. Adrenal – pheochromocytoma
97. Adrenal – tuberculosis
99. Thyroid – adenoma
102. Pituitary – histiocytosis X
109. Adrenal – adenoma
148. Parathyroid – hyperplasia
149. Pituitary – adenoma
170. Adrenal – amyloidosis
171. Adrenal – amyloidosis (Congo Red)
193. Thyroid – papillary carcinoma
196. Parathyroid – adenoma
226. Thyroid - adenoma

I. SKIN

13. Skin – sinus tract with foreign body reaction
17. Skin – leishmaniasis (azure-eosin stain)
31. Breast – Paget's disease
33. Skin – metastatic breast cancer
52. Skin – intradermal nevus
65. Skin – ruptured epidermal inclusion cyst
87. Skin – squamous cell carcinoma
93. Skin – basal cell carcinoma
116. Skin – malignant melanoma
118. Lymph node – metastatic malignant melanoma
150. Skin – intradermal nevus
151. Skin – seborrheic keratosis
152. Skin – epidermal inclusion cyst
154. Skin – keratoacanthoma
156. Skin – dermatofibrosarcoma protuberans
157. Skin – recurrent squamous cell carcinoma
168. Skin – amyloidosis
169. Skin – amyloidosis (Congo Red)
185. Skin – molluscum contagiosum
186. Skin – verrucae vulgaris
190. Skin – Kaposi's sarcoma

J. BREAST

31. Breast – Paget's disease
33. Skin – metastatic breast cancer
51. Breast – infiltrating duct cell carcinoma (scirrhous)
73. Breast – fibrocystic disease
96. Breast – fibroadenoma
111. Lymph node – metastatic duct cell carcinoma
158. Breast – duct cell carcinoma
224. Angiosarcoma following therapy for breast cancer

K. CENTRAL NERVOUS SYSTEM, EYES, AND EARS

35. Eye – malignant melanoma
38. Meninges – meningioma
83. Brain – arteriovenous malformation
90. Meninges – acute meningitis
102. Pituitary – histiocytosis X
149. Pituitary – adenoma
179. Meninges – meningioma
184. Brain – glioblastoma multiforme-grade IV glioma
218. Brain – metastatic carcinoma

L. BONE and SOFT TISSUE

7. Bone – healing fracture
23. Bone – metastatic transitional cell carcinoma
34. Uterus – leiomyoma
49. Bone marrow – hyperplasia
88. Omentum – infarction
121. Muscle – myositis
Artery – Monckeberg's sclerosis
125. Bone – fibrosarcoma
134. Muscle – myositis ossificans
165. Bone marrow – AIDS (cryptococcus neoformans fungi)
166. Bone marrow – AIDS (cryptococcus neoformans fungi) (Gomori-methenamine silver nitrate)

190. Skin – Kaposi's sarcoma
195. Retroperitoneal fat – liposarcoma
205. Bone marrow – hyperplasia

M. INFECTIOUS DISEASES

1. Lung – fungal pneumonia (cryptococcosis)
16. Lung – caseous tuberculosis
17. Skin – leishmaniasis (azure-eosin stain)
76. Lung – tuberculosis
77. Lymph node – tuberculosis
78. Lymph node – tuberculosis
97. Adrenal – tuberculosis
131. Colon – acute pseudomembranous colitis
165. Bone marrow – AIDS (cryptococcus neoformans fungi)
166. Bone marrow – AIDS (cryptococcus neoformans fungi) (Gomori-methenamine silver nitrate)
173. Colon – diverticulosis with diverticulitis
B4. Peripheral blood – mononucleosis
185. Skin – molluscum contagiosum
186. Skin – verruca vulgaris
187. Cervix – scrapings with viral changes
210. Heart – infectious pericarditis
214. Heart – acute rheumatic valvulitis
215. Heart – diphtherial myocarditis
222. Appendix – pin worms

NORMAL SLIDES

There are five boxes of normal tissues available. They are kept in the new location and are as follows:

N1. Eyelid
N2. Heart
N3. Lung
N4. Trachea
N5. Liver
N6. Gastroesophageal junction
N7. Appendix
N8. Adrenal
N9. Kidney
N10. Uterus
N11. Fallopian tube
N12. Aorta
N13. Brain, cerebral cortex
N14. Brain, cerebellum
N15. Spinal cord
N16. Testis
N17. Prostate
N18. Ovary

Blood smears are in the third box of the teaching set:

Case 2. Peripheral blood - sickle cell anemia
Case 6. Peripheral blood - chronic lymphocytic leukemia
Case 8. Peripheral blood - chronic myelogenous leukemia
Case 9. Peripheral blood - acute myelomonocytic leukemia
Case 10. Peripheral blood - acute lymphoblastic leukemia
Case 12. Peripheral blood - leukoerythroblastosis
Case 13. Peripheral blood - mononucleosis

APPENDIX B: Pathology Slide List

1. Lung – fungal pneumonia (cryptococcosis)
2. Artery – Monckeberg's sclerosis
3. Artery – arteriosclerosis with thrombosis
4. Liver – fatty metamorphosis
5. Liver – cirrhosis (nutritional)
   Stomach – penetrating ulcer: Small intestine peritonitis
6. Heart – infarction
7. Bone – healing fracture
8. Heart – amyloidosis
9. Pylorus – ulcer
10. Thyroid – colloid goiter
11. Thyroid – adenoma
12. Thyroid – hyperthyroidism, treated
13. Skin – sinus tract with foreign body reaction
14. Lung – embolus
15. Thyroid – adenoma (microfollicular)
16. Lung – caseous tuberculosis
17. Skin – leishmaniasis (azure-eosin stain)
18. Liver – subacute fulminating hepatic necrosis
19. Esophagus – esophagitis and varicosities
20. Small intestine – infarction
21. Colon – familial polyposis
22. Uterus – adenomyosis
23. Bone – metastatic transitional cell carcinoma
24. Thyroid – papillary carcinoma
25. Thyroid – Hashimoto's disease
26. Lung – bronchiectasis, purulent
27. Gallbladder – acute and chronic cholecystitis
28. Thyroid – thyroiditis with fibrosis
29. Liver – adenomatosis
30. Soft-tissue – plasmacytoma
31. Breast – Paget's disease
32. Rectum – adenocarcinoma
33. Skin – metastatic breast cancer
34. Uterus – leiomyoma
35. Eye – malignant melanoma
36. Lung – pneumoconiosis
37. Ovary – Stein-Leventhal syndrome
38. Meninges – meningioma
39. Esophagus – congenital esophageal cyst
40. Liver – acute yellow atrophy
41. Liver – acute and chronic cholangitis with sclerosis (status post roux and Y surgical procedure)
42. Liver – secondary biliary cirrhosis
43. Heart – infarction
44. Heart – infarction with mural thrombus
45. Liver – post-necrotic cirrhosis (history of ulcerative colitis)
46. Liver – cirrhosis with necrosis
47. Liver – metastatic carcinoma
48. Heart – fibrinous pericarditis
49. Bone marrow – hyperplasia
50. Heart – endocardial fibroelastosis (trichrome on 119)
51. Breast – infiltrating duct cell carcinoma (scirrhous)
52. Skin – intradermal nevus
53. Aorta– dissecting aneurysm
54. Heart – myocarditis
55. Heart – uremic pericarditis
56. Heart – metastatic carcinoma
57. Spleen – nodular sclerosing Hodgkin's disease
58. Lung – abscess
59. Colon – ulcerative colitis
60. Lymph node – lymphoma
61. Cervix – dysplasia
62. Lymph node – Hodgkin's disease
63. Liver – hepatocellular carcinoma
64. Lung – metaplasia
65. Skin – ruptured epidermal inclusion cyst
66. Lung – granuloma (asteroid)
67. Spleen – sickle cell crisis
68. Lung – bone marrow embolus and emphysema
69. Liver – chronic lymphocytic leukemia
    Spleen – chronic lymphocytic leukemia
70. Lung – bronchiectasis
71. Liver – hemangioma
72. Lung – healed pleuritis
73. Breast – fibrocystic disease

74. Lung – acute congestion
75. Pancreas – fatty infiltration
76. Lung – tuberculosis
77. Lymph node – tuberculosis
78. Heart – tuberculosis in pericardium
79. Kidney – chronic pyelonephritis and arteriosclerosis
80. Kidney – renal cell carcinoma
    Liver – metastatic renal cell carcinoma
    Lung – metastatic renal cell carcinoma
81. Adrenal – cortical hyperplasia
82. Adrenal – pheochromocytoma
83. Brain – arteriovenous malformation
84. Lymph node – reactive hyperplasia
85. Prostate – hyperplasia
86. Fallopian tube – acute salpingitis
87. Skin – squamous cell carcinoma
88. Omentum – infarction
89. Lung – hyaline membrane disease
90. Meninges – acute meningitis
91. Kidney – polycystic kidney disease
92. Liver – cirrhosis (history of Crohn's disease)
    Pancreas – chronic pancreatitis
93. Skin – basal cell carcinoma
94. Uterine contents – chorionic villi
95. Kidney – diabetic nephropathy
96. Breast – fibroadenoma
97. Adrenal – tuberculosis
98. Cecum – Crohn's disease
99. Thyroid – adenoma
100. Lung – arteriosclerosis and emboli
101. Lung – squamous cell carcinoma
102. Pituitary – histiocytosis X
103. Gallbladder – adenocarcinoma
104. Colon – endometriosis
105. Colon – adenocarcinoma
106. Aorta – syphilitic aneurysm
107. Lung – arteriosclerosis
108. Lung – embolus
109. Adrenal – adenoma
110. Artery – arteriosclerosis and thrombosis: Heart-myocarditis
111. Lymph node – metastatic duct cell carcinoma
112. Kidney – polycystic reanl disease, juvenile form
113. Kidney – acute and chronic pyelonephritis
114. Spleen - infarction
115. Liver – biliary obstruction, secondary to carcinoma
116. Skin – malignant melanoma
117. Liver – glycogenated nuclei
118. Lymph node – metastatic malignant melanoma
119. Heart – endocardial fibroelastosis (trichrome stain), see 50
120. Lung – lobar pneumonia
121. Muscle – myositis
122. Lung – infarct: Artery-embolus
123. Spleen – infarct
124. Spleen – amyloidosis
125. Bone – fibrosarcoma
126. Gallbladder – acute and chronic cholecystitis
127. Lung – squamous cell carcinoma
128. Stomach – hemorrhagic gastritis
129. Rectum – hemorrhoids
130. Spleen – acute and chronic perisplenitis
131. Colon – acute pseudomembranous colitis
132. Liver – acute hepatitis
133. Kidney – diabetic glomerulosclerosis
134. Muscle – myositis ossificans
135. Kidney – disseminated intravascular coagulation
    Lung – disseminated intravascular coagulation
136. Fallopian tube – endometriosis
137. Gallbladder – cholesterolosis
138. Stomach – signet ring cell carcinoma
139. Appendix – acute appendicitis
140. Veins – varicose veins
141. Stomach – gastric ulcer
142. Small intestine – lymphoma

143. Ileum – carcinoid
144. Salivary gland – adenolymphoma (Warthin's tumor)
145. Kidney – renal cell carcinoma
146. Testis – lymphoma

147. Artery – giant cell arteritis
148. Parathyroid – hyperplasia
149. Pituitary – adenoma
150. Skin – intradermal nevus
151. Skin – seborrheic keratosis
152. Skin – epidermal inclusion cyst
153. Cervix – squamous cell carcinoma with lymphatic invasion
154. Skin – keratoacanthoma
155. Uterine contents – hydatidiform mole
156. Skin – dermatofibrosarcoma protuberans
157. Skin – recurrent squamous cell carcinoma
158. Breast – duct cell carcinoma
159. Ovary – mature teratoma
160. Salivary gland – lymphoma
161. Stomach – perforated gastric ulcer
162. Testis – seminoma
163. Ovary – cystic teratoma benign
164. Kidney – rapidly progressive glomerulonephritis
165. Bone marrow – AIDS (cryptococcus neoformans fungi)
166. Bone marrow – AIDS (cryptococcus neoformans fungi) (Gomori-methenamine silver nitrate)
167. Intestine – lymphoma
168. Skin – amyloidosis
169. Skin – amyloidosis (Congo Red)
170. Adrenal – amyloidosis
171. Adrenal – amyloidosis (Congo Red)
172. Lung – interstitial pneumonia
173. Colon – diverticulosis with diverticulitis
174. Fallopian tube – acute salpingitis
175. Kidney – host graft rejection
176. Lymph node – metastatic anaplastic seminoma
177. Testis – seminoma
178. Testis – teratoma with embryonal carcinoma
179. Meninges – meningioma
180. Ovary – multiloculated serous cyst
181. Umbilical cord and amniotic membranes – acute amnionitis and funisitis
182. Placenta – molar pregnancy
183. Colon – inflammatory polyp
184. Brain – glioblastoma multiforme-grade IV glioma
185. Skin – molluscum contagiosum
186. Skin – verruca vulgaris
187. Cervix – scrapings with viral changes
188. Bowel – malignant lymphoma
189. Stomach – poorly differentiated carcinoma with ulceration
190. Skin – Kaposi's sarcoma
191. Lymph node with Hodgkin's disease
192. Ovary – papillary adenocarcinoma
193. Thyroid – papillary carcinoma
194. Bowel – radiation injury with inflammation and fibrosis
195. Retroperitoneal fat – liposarcoma
196. Parathyroid – adenoma
197. Lymphn node – malignant lymphoma
198. Fallopian tube – tubal pregnancy
199. Parotid – Sjogren's syndrome
200. Prostate – adenocarcinoma with capsular involvement
201. Lung – emphysema and bronchial obstruction
202. Lung – metastatic adenocarcinoma from colon
203. Lung – cartilage hamartoma
204. Placenta – erythroblastosis fetalis
205. Bone marrow – hyperplasia
206. Lymph node – follicular lymphoma
207. Stomach – gastric ulcer with cancer
208. Heart – acute viral myocarditis
209. Heart – mitral valvulitis with kidney showing accompanying glomerulonephritis
210. Heart – infections pericarditis
211. Lung – adenocarcinoma, alveolar cell type
212. Small intestine – sprue
213. Artery – berry aneurysm
214. Heart – acute rheumatic valvulitis
215. Heart – diphtherial myocarditis
216. Small intestine – intussusception
217. Vein – thrombophlebitis
218. Brain – metastatic ?? Carcinoma
219. Kidney – fetal, normal 31 week gestation
220. Kidney – papillary adenoma with chronic pyelonephritis with marked arteriosclerosis

221. Heart – chronic rheumatic valve
222. Appendix with pin worm
223. Pap smear – dysplasia
224. Angiosarcoma of breast following treatment for breast cancer
225. Urinary bladder - invasive transition cell carcinoma
226. Thyroid - adenoma