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 its 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

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?

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.

Your observations
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.
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.

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?
Slide 42: Liver with cirrhosis

As with the other slides of liver, the mottled quality of the tissue tells you there is a diffuse process.

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

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.
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

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
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

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.

Your observations

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

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.

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?)
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.

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.
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.

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.

Normal liver for comparison

This is it. You know, normal liver.
Slide 137: Gallbladder with cholesterolosis

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.