Effects of Systemic Vascular Problems on the Liver

- Right heart failure
- Left heart failure
- Chronic passive congestion
- Shock liver
- Hepatic infarction
- Pylephlebitis

Diseases Affecting the Vasculature of the Liver

- Hepatic venous outflow obstruction
  - Budd-Chiari syndrome
  - Veno-occlusive disease
- Extrahepatic portal vein obstruction
- Sinusoidal dilatation
  - Peliosis hepatis
  - Hodgkin's disease
  - Pregnancy related
  - Miscellaneous
- Systemic vascular disease
  - Vasculitis
  - Atherosclerosis
  - Miscellaneous
- Idiopathic Portal Hypertension (noncirrhotic portal fibrosis)

Effects of Systemic Vascular Problems on the Liver

Frank A. Mitros, M.D.
Peer Review Status: Internally Peer Reviewed

There is a striking effect on the liver in situations where significant cardiac dysfunction occurs. These effects will vary greatly depending on how acutely the hemodynamic changes occur and whether or not they are predominantly affecting the right or left side of the circulation (Figure 3-1). In most instances there will be a combination of events affecting the entire circulation occurring over a variable period of time, perhaps modified by pre-existing conditions in the host liver. For purposes of clarity, classic examples of nearly "pure" conditions will be considered separately, although one must be cognizant that these circumstances are much less common than combined lesions.

Acute Right Heart Failure

The cardinal hepatic manifestations of significant right sided heart failure are sinusoidal dilatation and congestion with subsequent atrophy of hepatocyte cords (Figures 3-2 and 3-3). These changes are clearly zonal, with the centrilobular area (zone 3) being most severely affected; with time and increasing severity there may also be involvement of zone 2 and finally zone 1. This condition has been referred to as chronic passive congestion and is closely related to elevated pressures in the right atrium or with other conditions leading to an increase in systemic venous pressure. The space of Disse may become more prominent (Figure 3-4) and may contain red blood cells in the more severe lesions. The appearance of the sinusoids can be dramatically altered due to the process of biopsy, particularly with
needle biopsies. Blood may drain out of the specimen collapsing the sinusoids, but attention to detail such as atrophic cords and the widened space of Disse provide helpful clues. There is minimal if any necrosis, correlating with the observation that such patients may have normal transaminases or, less commonly, minor elevations (less than 2-fold).

**Acute Left Heart Failure**

Significant failure of the left side of the circulation is characterized by necrosis of hepatocytes in the centrilobular area (Figures 3-7 and 3-8). This necrosis is coagulative rather than lytic. It may appear to be asymmetric in zone 3, owing to the variability of blood flow through the various acini (Figure 3-9). It is clear that the presence of centrilobular necrosis correlates closely with the severity of hypotension, whether sustained or episodic. Overt clinical shock need not be present for severe necrosis to develop. When such necrosis is present, there may be dramatic increases in serum transaminases, sometimes leading to a mistaken clinical impression of a viral hepatitis (Figure 3-10); this has been referred to by some as ischemic hepatitis. In most cases with significant necrosis there will also be seen evidence of co-existing right sided failure with prominent congestive changes. As necrosis progresses, there may be replacement of hepatocytes within the cords by red blood cells. Associated with this zone 3 necrosis the adjoining intact hepatocytes have been known to contain PAS positive spherical inclusions (Figure 3-11 and 3-12). While these resemble alpha-1-antitrypsin deficiency inclusions they differ in their location (zone 3 rather than zone 1); they represent damaged enlarged lysosomes.

**Chronic Passive Congestion (Cardiac Sclerosis)**

Active deposition of perisinusoidal collagen has been noted with right sided failure, and both passive collapse of the reticulin framework as well as active deposition of stromal connective tissue are seen in left sided failure. With long-standing circulatory failure some degree of fibrosis will develop. This is most pronounced in zone 3. This phenomenon of centrilobular fibrosis with sparing of periportal hepatocytes leads to an appearance referred to as "reverse lobulation" (Figure 3-13). The central congestion and fibrosis with pale periportal areas (and perhaps some degree of fatty change in the zone 2 hepatocytes) combine to give an appearance which has commonly been referred to as "nutmeg liver" (Figures 3-14, 3-15, and 3-16). If the scarring is allowed to progress, the centrilobular collagen will eventually link with the portal connective tissue. At this stage the condition has been referred to as cardiac cirrhosis (Figure 3-17), but the term cardiac sclerosis is more accurate in that overall architectural integrity is maintained (see Chapter 9). Even at such a late stage clinical manifestations are usually minor with regards to signs of liver disease, there being minor elevations of serum bilirubin and even less impressive elevations of alkaline phosphatase and transaminases. The clinical picture is dominated by the signs of the underlying cardiovascular disease. In fact, with modern pharmacologic agents, valve replacement technology, and availability of cardiac transplantation, it is quite unusual to see significant hepatic sclerosis based on purely cardiovascular problems.

**Shock Liver**

The liver can be significantly damaged in shock from a variety of causes. With severe hemorrhage, burns, etc. the type of centrilobular necrosis described in left sided failure is seen. Such lesions are uncommon if shock is transitory (less than 10 hours) but are almost invariable if shock persists for 24 hours or more. Similar centrilobular necrosis occurs with severe hyperpyrexia or with heat stroke; in such circumstances the hepatocytes may contain small vacuoles. With septic shock, there may be striking cholestasis and even a prominent cholangitis (see Chapter 8).
Hepatic Infarction

Because of the dual blood supply of the liver (hepatic artery and portal vein) true infarction of the liver has been considered to be rare. This may not be true; there is considerable variation in the incidence of infarction as reported in several autopsy series. In at least one careful series, hepatic infarction, as defined by coagulation necrosis occupying more than one hepatic lobule, was seen in 14 of 700 autopsies. Most other investigators encounter hepatic infarction much less frequently. The underlying defect is usually hepatic arterial occlusion (usually thrombotic). Portal vein occlusion, or combined hepatic and portal vein occlusion, are occasionally found. Even less commonly, no vascular occlusion is identified. Recent abdominal surgery, particularly cholecystectomy, is frequently present historically in patients with arterial or combined arterial and venous thrombosis. Pure venous thrombosis is commonly related to tumor emboli. Patients without demonstrable vascular occlusion frequently have significant cardiovascular disease and have had significant recent hypotensive episodes. Arteritis has been the underlying mechanism in some cases. Recently a number of reports have documented hepatic infarction in liver transplant recipients secondary to the arteriopathy of chronic rejection (see Chapter 12).

Most hepatic infarcts are discovered incidentally at the time of autopsy. Clinical and laboratory findings are poorly defined, probably because they are masked by the overwhelming manifestations of the underlying disease. Sharp elevations of transaminases and mild hyperbilirubinemia and a mild increase in the alkaline phosphatase have been attributed to sublethal infarcts.

Grossly the infarcts are sharply demarcated and a uniform dark red; there is a mottled peripheral zone of congestion (Figure 3-18). With time the central area becomes pale. The size ranges from 1 to 15 cm in greatest diameter. Typical coagulative necrosis affects the parenchyma, but mesenchymal elements such as triads and central veins appear relatively viable (Figure 3-19).

True hepatic infarction must be distinguished from the atrophic red "infarct' of Zahn. These are areas of severe acute passive congestion with minimal parenchymal necrosis and atrophy (zone 3) resulting from focal thrombotic obstruction of portal vein branches. They present as sharply delimited areas of hyperemia grossly (Figure 3-20).

Pylephlebitis

Suppurative thrombophlebitis involving the portal vein and its intrahepatic branches was formerly much more common. It was most commonly seen complicating delayed treatment of appendicitis in the pre-antibiotic era. Multiple hepatic abscesses resulting from this seeding of the liver was frequently lethal (Figure 3-21). Abdominal sepsis still remains the most likely underlying mechanism for pylephlebitis, but the spectrum of disease has shifted. Clinically silent diverticulitis is the most common mechanism; complicated inflammatory bowel disease can also lead to pylephlebitis. The involved portal triad may have its architecture obscured by the suppurative process, but earlier lesions will show clear evidence of a fibrin neutrophil coagulum in the intrahepatic branches of the portal vein (Figures 3-22 and 23 A&B).

Diseases Affecting the Vasculature of the Liver

Frank A. Mitros, M.D.
Peer Review Status: Internally Peer Reviewed
The vasculature of the liver is frequently affected in systemic processes. Thromboses of the major vessels may affect either outflow (hepatic vein) or inflow (portal vein, hepatic artery). The exact location and mechanism of thrombosis will lead to vastly different outcomes. The most important of these diseases is the group which results in hepatic venous outflow obstruction.

In addition, the hepatic vessels can be affected directly by such systemic diseases as vasculitis, or indirectly as a result of an adverse effect of drugs or the remote effects of neoplasia.

**Hepatic Venous Outflow Obstruction**

There are a number of clinical situations in which the outflow of blood from the liver is impeded by an obstructive process which may be thrombotic or nonthrombotic, and affect either extrahepatic or intrahepatic vessels or both. The two classic clinical syndromes defining the ends of this spectrum are Budd-Chiari syndrome and veno-occlusive disease, but many areas of overlap or variations on this theme exist.

### Budd-Chiari Syndrome

In the most classic form of the syndrome patients present with striking hepatomegaly, abdominal pain and ascites. There may also be mild jaundice. This follows the development of obstruction of either the larger branches of the hepatic vein as they leave the liver or of the vena cava into which they empty before it enters the right atrium. Thus patients with severe right sided failure, such as might be seen in tricuspid insufficiency, are not considered to have Budd-Chiari syndrome, although their clinical appearance may be identical to that just described. Patients with chronic obstructive lesions may have developed sufficient collateral circulation so that ascites may not be present.

In a large portion of the world, including South Africa, Japan and India, the most common underlying lesion is a membranous obstruction in the inferior vena cava. The nature of the fibrous web within the cava is very poorly understood. It may represent organization of a prior thrombus. In the United States, such webs are not commonly seen and more obvious thrombotic events are the usual underlying event. There are a number of reasons for thrombosis to occur. The more commonly reported clinical situations include hematologic diseases (particularly polycythemia rubra vera, paroxysmal nocturnal hemoglobinuria, and myelofibrosis), trauma, infection (ameba, hydatid disease), and coagulopathies (protein C deficiency). Another cause encountered with some frequency is tumor invasion of the hepatic vein, particularly hepatocellular or renal cell carcinoma (Figure 3-24 and 3-25). In about 25% of cases no cause can be identified. Of paramount importance, severe cardiac failure must be excluded, since the gross and microscopic appearance of severe failure may be indistinguishable from that of Budd-Chiari syndrome.

Grossly the liver is enlarged and congested Figure 3-26. With thrombosis of large intrahepatic veins Zahn's infarcts may develop. The distribution within the liver may be quite irregular (Figure 3-27); the caudate lobe is particularly likely to be spared since it has some venous branches that empty directly into the cava.

The changes histologically are those seen with acute congestion, and are almost purely those of severe right sided failure. Significant coagulative necrosis is not regularly seen, although the massive congestion may lead to significant loss of zone 3 hepatocytes. While one cannot make a definitive diagnosis of Budd-Chiari syndrome from the histology alone, several features do favor the diagnosis. The centrilobular congestion is particularly severe and
uniform in the affected areas of liver (Figure 3-28). There may be significant loss of centrilobular hepatocytes (Figure 3-29). Although the terminal hepatic venules are usually patent, organizing thrombi may be seen on occasion in the large sublobular veins (Figure 3-30). Significant extravasation of blood into the space of Disse and the hepatocyte cords is very common (Figure 3-31). If the underlying cause is not corrected, fibrosis occurs and the picture of cardiac sclerosis appears.

**Veno-occlusive Disease (VOD)**

The other major cause of hepatic venous outflow obstruction is veno-occlusive disease; it differs from Budd-Chiari syndrome in that it is the smaller intrahepatic venules within the liver that are primarily involved usually in a non-thrombotic manner. There is usually a defined exposure to a toxic agent or physical injury. In some parts of the world naturally occurring toxins (pyrrolizidine alkaloids - Jamaican bush tea) remains a significant cause of hepatic disease, particularly in children. Presently in the United States bone marrow transplantation is the most frequent setting for the development of VOD. This is related to the radiation and chemotherapeutic agents used in these patients. Renal transplant patients receiving immunosuppressive agents are also at risk for VOD.

The clinical presentation resembles that of Budd-Chiari syndrome with the sudden onset of ascites and hepatomegaly, although the clinical background is usually quite different. While it was originally thought to be a complication limited to the early period after bone marrow transplantation (the first month) it is clear that VOD can appear many months after the transplant.

The histology of VOD is again that seen in severe right sided failure. It differs from both Budd-Chiari syndrome and failure by the fact that it is characteristically erratically distributed throughout the liver (Figure 3-32). More importantly, the terminal hepatic venules show a characteristic histologic lesion. Not all venules are involved, and the erratic distribution of the involved vessels matches that of the areas of congestive type change. While the histology of the venous lesion is characteristic, it can be easily overlooked. Trichrome or reticulin stains are a must in these circumstances (Figures 3-33, 3-34, and 3-35). There is a narrowing of the lumen, with eventual complete obliteration of the lumen. In the earliest stages the intima appears to be strikingly edematous with red blood cells trapped amongst wisps of loose connective tissue (Figure 3-36). As the lesion progresses, the edema is replaced by more dense fibrous tissue and macrophages with hemosiderin may be present (Figure 3-37). Eventually the lumen can become completely obliterated (Figure 3-38), and the individual lesion cannot be distinguished from chronic Budd-Chiari syndrome or from cardiac sclerosis.

**Extrahepatic Portal Vein Obstruction**

Obstruction of the portal vein outside the liver does not usually cause significant parenchymal damage, but may mimic or complicate hepatic disease. The obstruction is likely thrombotic in origin in the majority of cases, although the thrombus may not be recognizable as such at the time of diagnosis. The usual finding is an area of obliteration in the portal vein surrounded by a large number of collateral vessels. The liver is usually histologically normal. The portal vein may be involved alone, or in combination with the splenic or splenic and mesenteric veins. Patients present with clinical features of portal hypertension. Ascites may be present early on, but often resolves. Hematemesis from varices is the most common problem, but portal encephalopathy or features of hypersplenism may also occur.
Extrahepatic portal venous obstruction is seen most commonly in children, where it was once believed to be a complication of umbilical sepsis. This view has been questioned since a history of omphalitis and intra-abdominal sepsis has been documented in relatively few patients, and there is a seemingly higher than expected incidence of a variety of congenital abnormalities. The process can also be seen in adults, where it may complicate sepsis or pylephlebitis. Infection remains the overall most commonly identified precipitating factor at all ages. Abdominal trauma or surgical injury are documented causes of such obstruction, as is invasion of the portal venous system in neoplastic processes. The thrombotic and gynecologic disorders associated with Budd-Chiari syndrome have also been seen in the setting of portal venous obstruction, although the portal venous system is much less frequently involved than the hepatic venous system. Pancreatitis can give rise to splenic vein thrombosis, which can then propagate and involve the portal vein; this may present a particularly difficult diagnostic dilemma in patients who are alcoholics. A very high percentage of cases remain idiopathic; of interest is the fact that a large number of such cases are seen in parts of the world such as India where idiopathic portal hypertension is frequent (see below). The main clinical problem is to clearly distinguish patients with this condition from those whose portal hypertension is related to parenchymal liver disease. Unfortunately, cirrhosis of many etiologies may itself be complicated by a secondary extrahepatic portal vein thrombosis. The relationship amongst these diseases affecting the hepatic vessels is depicted diagrammatically (Figure 3-39).

### Sinusoidal Dilatation

Most commonly significant dilatation of the sinusoids is due to hemodynamic failure or to venous outflow obstruction. There are a number of situations where the sinusoids themselves appear to be affected.

**Peliosis hepatitis** is characterized by blood filled spaces in the liver which are almost always multiple (Figure 3-40). The size range is from several millimeters to several centimeters in diameter; in the latter instance they may cause confusion with vascular tumors (see Chapter 11). Although peliosis may be associated with hepatomegaly and even hepatic failure, it is more commonly a lesion found incidentally. Two types have been described. In one, the parenchymal variant, there are cystic spaces filled with blood and without an endothelial lining (Figure 3-41). In the other, the phlebectatic variant, the prominent vascular spaces are in continuity with what appears to be dilated sinusoids (Figure 3-42). The types may coexist; both may result in thrombosis. Presumably the precipitating condition weakens or damages the sinusoidal lining in some fashion. Tuberculosis was formerly the most common underlying disease, but it is now seen most frequently as a complication of the use of androgenic-anabolic steroids. It has also been seen complicating a variety of tumors, and occasionally in hypervitaminosis A or complicating hemodialysis for renal failure. Peliosis-like changes can be seen in hepatic adenomas (see Chapter 11).

**Hodgkin's disease** frequently shows a peculiar unexplained sinusoidal dilatation, and may even show overt peliosis. The reasons for this phenomenon are not understood.

**Pregnant patients** or patients on oral contraceptives may show a peculiar sinusoidal dilatation showing selective involvement of zone 2 (Figure 3-43).

Miscellaneous causes of sinusoidal dilatation also include AIDS, **chenodeoxycholic acid therapy** for gallstones, and the presence of nearby **space occupying lesions**.

### Systemic Vascular Disease
The liver is affected in a variety of systemic diseases involving the vessels; usually the manifestation in other organs are more important than those in the liver.

Vasculitis involves the liver not infrequently. Known causes include polyarteritis nodosa, systemic lupus erythematosus, rheumatoid arthritis, and temporal (giant cell) arteritis. The intrahepatic vessels may show fibrinoid necrosis (Figure 3-44), and aneurysms and hemorrhage may be found. Polyarteritis is of particular interest because it may be related to hepatitis B infection. The liver in such patients typically show an active vasculitis in the setting of a liver showing minimal histologic evidence of damage by the chronic hepatitis (Figure 3-45).

Atherosclerotic cardiovascular disease may affect the intrahepatic vessels. Cholesterol emboli may be seen in patients will severe atherosclerosis (Figure 3-46). Such lesions are usually of no clinical significance. Systemic hypertension may cause hyaline arteriosclerosis in portal triad vessels. Likewise the vascular changes of diabetes mellitus may be identified in vessels within the triads.

Patients with hairy cell leukemia may have cystic spaces lined by the leukemic cells in the portal areas or in the lobules. These spaces are filled with red blood cells and may be mistaken for peliosis.

Patients with Osler-Weber-Rendu Disease (hemorrhagic hereditary telangiectasia) may have large thin walled portal vessels that may extend into the parenchyma and become associated with fibrosis (Figure 3-47). The resulting appearance has been referred to as pseudo-cirrhosis; nodular regenerative hyperplasia may occur.

Patients with sickle cell anemia may have a variety of liver problems. In crisis there may be sequestration of large numbers of sickled red blood cells in the sinuses (Figure 3-48) with subsequent mild hepatocyte necrosis. More typical liver diseases, such as obstructive processes from complicating gallstones, or intercurrent viral hepatitis are more common and must be excluded before attributing the liver dysfunction to the vascular phenomenon.

Disseminated intravascular coagulation may manifest in the liver with sinusoidal microthrombi which may extend into central veins on occasion.

**Idiopathic Portal Hypertension**

When such causes of portal hypertension as cirrhosis, extrahepatic portal vein obstruction, and infections such as Schistosomiasis have been excluded there remains an enigmatic group of patients who present with clear-cut evidence of portal hypertension of uncertain etiology. Most of these patients would fit under the previously used rubric of Banti's syndrome. As our understanding of the clinical and pathologic aspects of this process have progressed, a number of synonyms have appeared in the world's literature. These include idiopathic portal hypertension (IPH), noncirrhotic portal hypertension or fibrosis (NCPF), and hepatoporal sclerosis.

There is a striking geographic variability in incidence. There are also some relatively subtle differences in the way the disease manifests itself in different parts of the world. In Japan, where it is usually known as IPH, the patients are typically middle aged women; 75% of patients are female, and the mean age of presentation is 36, although patients in their 50's are not uncommon. In these patients gastrointestinal bleeding, splenomegaly, or anemia are equally frequent modes of presentation. In India, where the process is usually referred to as NCPF, the usual patient is a young man; 80% of the patients are male, and the mean age of presentation is 30 years of age. Presentation with gastrointestinal bleeding is the rule in the
vast majority and anemia or symptomatic splenomegaly are uncommon. Careful physical exam will show splenomegaly in both groups, and hepatomegaly is present about half the time. Not infrequently the liver is smaller than normal. In the United States, the sex incidence is nearly equal and the patients are slightly older, with gastrointestinal bleeding being the usual presentation. Liver function tests are normal or near normal; anemia and leukopenia are frequent.

Parallel similarities and differences exist with regards to the pathology of these two groups of patients. The liver may look nodular from the surface, but the nodularity is usually relatively superficial; the nodularity is more pronounced in the cases from India. Cirrhosis by definition is not present; the nodules are similar in appearance and pathogenesis to those seen in nodular regenerative hyperplasia or partial nodular transformation. In fact, many believe that the latter term has been incorrectly used to describe patients who actually have IPH or NCRF. There is usually significant fibrosis along the portal vein and its branches particularly near the hilus (Figure 3-49 A&B). Portal vein thrombosis can occur, but this is thought to be a complication rather than a cause of IPH since it usually occurs later in the course of well-established disease.

Microscopically there is no evidence of cirrhosis, although a number of histological clues may be present. The portal vein itself will usually have a thick sclerotic wall rich in elastic fibers (Figure 3-50). There may be stellate or concentric fibrosis in the portal areas in the advanced cases; the connective tissue in these areas may have a peculiar wrinkled appearance and stain strongly for elastic fibers (Figure 3-51). There may be diminution or obliteration of portal vein branches within the triads. Frequently abnormal large dilated veins may be seen juxtaposed to the portal triads; these have been mistaken on occasion for terminal hepatic venules (Figure 3-52 A&B). Inflammation and necrosis are not prominent features.

The etiology of this condition is not known. Exposure to such environmental toxins such as arsenic has been suspected but not clearly proven. Infection has also been suspected, perhaps associated with a peculiar immunologic response to subclinical infection. It is of interest that the incidence of NCPF is high in countries like India, where the incidence of extrahepatic portal vein obstruction (more closely linked to episodes of infection) is also high.

Patients with non-cirrhotic portal hypertension have excellent parenchymal reserve. They tolerate the condition well, having much better survival than patients with similar degrees of portal hypertension caused by cirrhosis.
Figure 3-2: Pure, right sided congestive failure; note the dilated sinusoids in zone 3 with some degree of atrophy of the hepatocyte cords. Most of the blood has drained from the biopsy (Klatskin, x25).

Figure 3-3: The central vein is intact but there is striking zone 3 sinusoidal dilatation and atrophy (PAS, x40).

Figure 3-4: Edema fluid has expanded the space of Disse; most of the red cells are still contained within the sinusoids (x100).
Figure 3-5: In a more severe, long-standing case of predominant right sided heart failure the congestion is greater and some red cells are replacing hepatocyte cords (Klatskin, x50).

Figure 3-6: In a patient with severe cardiomyopathy and long-standing failure the red cells are currently present within the space of Disse; the sinusoids remain dilated (Klatskin, x250).

Figure 3-7: The result of almost pure left sided heart failure; there is substantial loss of zone 3 hepatocytes around the central vein (x40).
Figure 3-8: At higher power the loss of cellular detail in zone 3 is more evident; the sinuses are not dilated but there is hemorrhage into the stroma. The pigment within the macrophages is largely residual lipofuscin; hemosiderin is minimal in the early stages (x80).

Figure 3-9: Ischemic necrosis due to left heart failure; the zone 3 of the Rappaport acinus is affected while other acini contributing to the hepatic lobule are spared (Masson, x40).

Figure 3-10: This patient with severe cardiac valvular disease was denied cardiac surgery because the surgical team feared viral hepatitis based on a transaminase of 1800; this is a percutaneous needle biopsy obtained post-mortem (Masson trichrome, x40).
Figure 3-11: There is marked coagulative necrosis in the centrilobular area of this child dying from intractable congestive heart failure secondary to congenital heart disease (PAS diastase, x50).

Figure 3-12: A higher power of the junction of zones 2 and 3 in the same child; note the spherical PAS positive inclusions representing giant lysosomes in the hepatocytes adjacent to the area of necrosis (PAS with diastase, x132).

Figure 3-13: A normal portal triad sits in the center of what resembles a classical lobule; the periphery is composed of sclerotic central veins in this patient with long-standing cardiac failure (Klatskin, x10).
Figure 3-14: The liver in this patient dying of failure was firm and diffusely mottled.

Figure 3-15: The surface showed a slight degree of irregularity; some degree of fatty change was present. A transected nutmeg is present for comparison.

Figure 3-16: A close-up reveals the alternating areas of sclerosis and retained hepatic parenchyma in this nutmeg liver.
Figure 3-17: Full fledged cardiac sclerosis characterized by irregular skeins of mature collagen linking adjacent central veins and occasionally extending to portal areas (Klatskin, x5).

Figure 3-18: Multiple pale infarcts with a surrounding slightly hyperemic rim are noted in this patient dying from sepsis complicated by shock.
Figure 3-19: (A) A hyperemic rim marks the boundary between the area of coagulative necrosis and intact liver (x10). (B) There is loss of cellular and nuclear detail typical of coagulative necrosis (x40).

Figure 3-20: This infarct of Zahn was secondary to intrahepatic portal vein thrombosis; although hyperemic, significant necrosis was not present (photograph courtesy of Dr. X).

Figure 3-21: Multiple hepatic abscesses were the immediate cause of death in this patient with untreated diverticulitis and complicating pylephlebitis.
Figure 3-22: Suppurative necrosis within the triad is evident; while centered on the dilated portal vein branch, the infectious process has spread into the substance of the triad and adjacent liver (Masson, x40).

Figure 3-23: (A) The inflammatory change within this triad was slight; the patient was thought to have "pericholangitis" complicating Crohn's disease (x40). (B) At a higher power, the coagulum of neutrophils and fibrin represent the suppurative thrombophlebitis of the portal vein complicating this man's Crohn's disease (x100).
Figure 3-24: The entire inferior vena cava is filled with a tumor thrombus which has entered through the renal veins from an adjacent renal carcinoma; note the enlarged hyperemic liver.

Figure 3-25: Cut surface of this liver reveals marked irregularly distributed congestion; note the tumor thrombi present within several of the larger branches of the hepatic vein.

Figure 3-26: This patient has the typical appearance of Budd-Chiari syndrome; the liver is diffusely enlarged, hyperemic, and has a tense capsule. The enlarged spleen also resulted from the outflow obstruction.
**Figure 3-27:** The changes of Budd-Chiari syndrome spared a significant portion of the liver in this patient with an underlying renal carcinoma.

**Figure 3-28:** This wedge biopsy showed uniform, severe, acute hemorrhage and congestion in all centrilobular areas; the patient was a young woman on oral contraceptives (x5).

**Figure 3-29:** At a higher power in the same patient there is loss of virtually all zone 3 hepatocytes; a poorly formed mesh of fibrin is present in the terminal hepatic venule (x25).
Figure 3-30: A large sublobular vein is filled with organizing thrombotic material in this patient with chronic Budd-Chiari syndrome (Masson, x25).

Figure 3-31: There is a striking dissection of red blood cells into the space of Disse with subsequent loss of hepatocytes; many of the cords contained nothing but red cells and macrophages with breakdown pigment (Klatskin, x80).

Figure 3-32: This patient with a history of bone marrow transplantation developed VOD; about one-half of the central veins were involved (Klatskin, x4).
Figure 3-33: Even at high power the central vein is not readily demonstrable in this patient with VOD (x100).

Figure 3-34: The trichrome stain brings out the mature collagen in the wall of the central vein allowing for ready demonstration of the characteristic lesion of the terminal hepatic venule in VOD (Klatskin, x100).

Figure 3-35: The reticulin stain is also helpful in identifying VOD; the fine meshwork of protein fibers in the occluded terminal hepatic venule are apparent (Reticulin, x100).
Figure 3-36: An early lesion in VOD; the lumen is still visible and the expanded intima is largely edematous; it contains scattered red cells. Note the dilated sinusoid vainly trying to enter the central vein (Klatskin, x80).

Figure 3-37: The intimal fibrosis becomes more dense as VOD progresses; several hemosiderin laden macrophages are present (Klatskin, x100).

Figure 3-38: In well established VOD there may be complete lumenal obliteration of the venules (Klatskin, x50).
Figure 3-40: Peliosis hepatis discovered incidentally at autopsy; multiple blood filled spaces are evident on the cut surface of liver.

Figure 3-41: The parenchymal variant of peliosis showed multiple blood filled spaces with a distinct border; no endothelial lining was identified (x50).

Figure 3-42: The phlebectatic variant of peliosis associated with areas of the parenchymal variant. Note the multiple areas of dilated sinusoids giving way to blood filled spaces and large areas of fibrin deposition (x25).
Figure 3-43: Mid-zonal sinusoidal dilatation is most frequently a complication of steroid therapy (Klatskin, x25).

Figure 3-44: Fibrinoid necrosis was present within the portal triad in this patient with rheumatoid arthritis (x40).

Figure 3-45: Fibrinoid necrosis within the arteriole was a marker for vasculitis secondary to hepatitis B; little damage was seen in the triads without affected vessels (x40).
Figure 3-46: Multiple cholesterol emboli were an incidental finding in this individual with severe atherosclerotic cardiovascular disease (Klatskin, x40).

Figure 3-47: There are numerous dilated vascular channels adjacent to an otherwise unremarkable triad; the associated fibrosis extends into and distorts the parenchyma (Klatskin, x16).

Figure 3-48: Numerous sickled red blood cells can be seen bulging the sinusoids (x100).
Figure 3-49: (A) The firm, white triad near the hilus was indicative of the fibrosis and increased elastic tissue in this patient with idiopathic portal hypertension. (B) Longitudinal sections of portal vein branches showed firm, white tissue consistent with the increased elastic fibers.

Figure 3-50: Note the thick fibrotic wall with an increase in elastic fibers in this branch of the portal vein at the hilus in a patient with IPH (Elastichrome, x25).
Figure 3-51: Several triads have abundant elastic fibers; adjacent triads have a near normal appearance in this young woman with IPH (Elastichrome, x16).

Figure 3-52: (A) The striking large vein branches arrayed around this portal triad present a confusing appearance (H&E, x13). (B) At a higher power, the presence of an interlobular bile duct identifies the structure as an abnormal triad (x66).