Vascular Disorders

11

Vascular disorders usually are divided into disorders affecting the portal veins, the sinusoids, the hepatic veins, and the hepatic arteries, although these components rarely are affected in isolation. Portal and hepatic vein thrombosis usually is the result of elements of the Virchow triad, including hypercoagulative states, endothelial injury, and stasis. Signs of portal vein obliteration may be too patchy and subtle to be recognised, particularly on a liver biopsy. In more advanced cases, parenchymal signs of vein obliteration include atrophy, extinction, or hyperplasia. Vascular obliterative changes now are considered an essential step in the progression of fibrosis in chronic liver disease, and their resolution may have a role in the regression of fibrosis.

Injury to the sinusoids may be induced by several causes, with chemotherapeutic agents representing the commonest risk factor. The term *sinusoidal obstruction syndrome* is now preferred over *veno-occlusive disease*.

The liver parenchyma is relatively resistant to ischaemia, as it is protected by its dual portal and arterial blood supply. The biliary tree, however, is only arterialised and therefore more sensitive to alterations of the arterial blood flow.

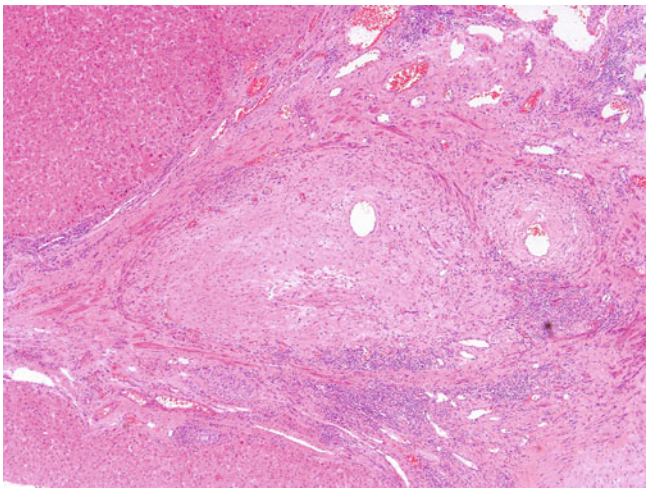

Fig. 11.1 Portal vein thrombosis. A thrombosed portal vein shows partial recanalisation with a small lumen. Thrombosis is the commonest disease of the large portal veins; its predisposing factors are those of classic Virchow's triad: hypercoagulative status, endothelial injury, and stasis. Thrombophilic conditions may be found in about 60% of cases, whereas local predisposing conditions may be identified in about 30% of cases. Cirrhosis and malignancy are the most frequent local predisposing factors in adults. Portal vein thrombosis may present acutely with a sudden onset of severe abdominal pain, or chronically with clinical features of portal hypertension (varices, ascites, and splenomegaly) and/or portal biliopathy (jaundice, biliary colic, cholangitis, and pancreatitis).

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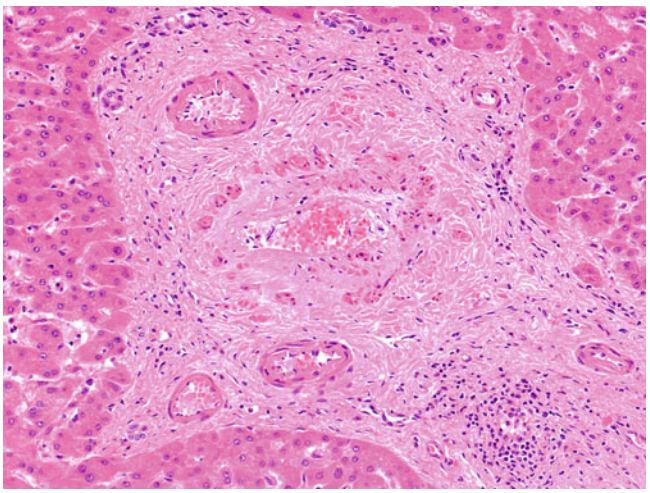

Fig. 11.2 Portal vein thrombosis. A small portal vein radicle is involved by extension of thrombosis from a larger vein. An organizing thrombus is present, with incorporation of a fibrous scar into the muscular wall of the involved vein. Portal vein thrombosis typically is found in portal veins larger than 200 μm, which rarely are found in liver biopsy specimens. Complete fibrous obliteration, organisation with subtle intimal fibrosis or mural calcification, or recanalisation with complex fibrous webs may be found. Recurrent thrombosis is evidenced by multiple layers of mural fibrosis. Portal vein thrombi may extend into smaller portal veins, which may be obstructed by thrombi or replaced by a fibrous scar. Uninvolved small portal veins may be dilated and even herniate into the periportal hepatic parenchyma.

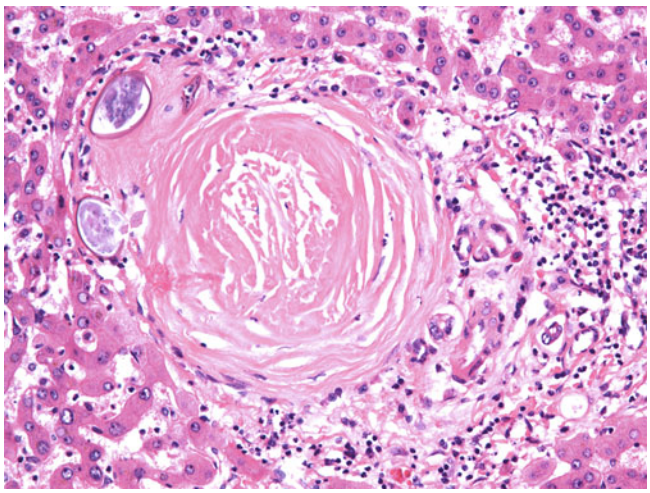

Fig. 11.4 Obliterative portal venopathy in schistosomiasis. This portal tract contains a fibrous obliterated portal vein and *Schistosoma* ova. Obliterative portal venopathy is a rare cause of portal hypertension secondary to the obstruction of small portal veins. It is associated with portal-based inflammation (e.g., primary biliary cirrhosis, primary sclerosing cholangitis, sarcoidosis, schistosomiasis, and congenital hepatic fibrosis), vasculitis (e.g., polyarteritis nodosa, rheumatic arthritis, and systemic lupus erythematosus), thrombosis (e.g., extension from large portal vein thrombosis, local stasis in cirrhosis), congestive portal venopathy (e.g., Budd-Chiari syndrome, cirrhosis), and drug-induced vascular injury (e.g., from azathioprine, arsenic compounds, mercaptopurine, methotrexate, oral contraceptives, oxaliplatin, and vinyl chloride).

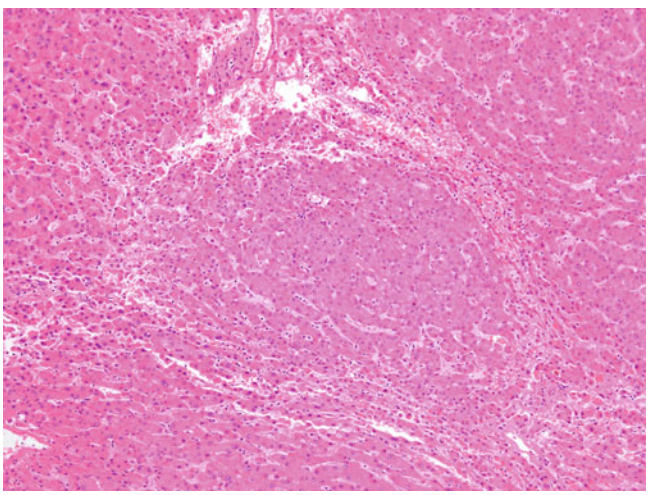

Fig. 11.3 Nodular regenerative hyperplasia in portal vein thrombosis. Parenchymal nodular change is present without any fibrosis. Nodular regenerative hyperplasia is characterised by diffuse benign transformation of the hepatic parenchyma into small regenerative nodules with minimal or no fibrosis. It sometimes is associated with thrombotic or nonthrombotic obliteration of small portal veins and, occasionally, small hepatic veins. Gordon-Sweets reticulin stain highlights the characteristic peripheral condensation of reticulin fibres in nodular regenerative hyperplasia. Drugs and toxins are major causes of nodular regenerative hyperplasia; others include autoimmune diseases, inflammatory diseases, haematologic diseases, congenital or acquired immunodeficiency, primary biliary cirrhosis, and cystinosis.

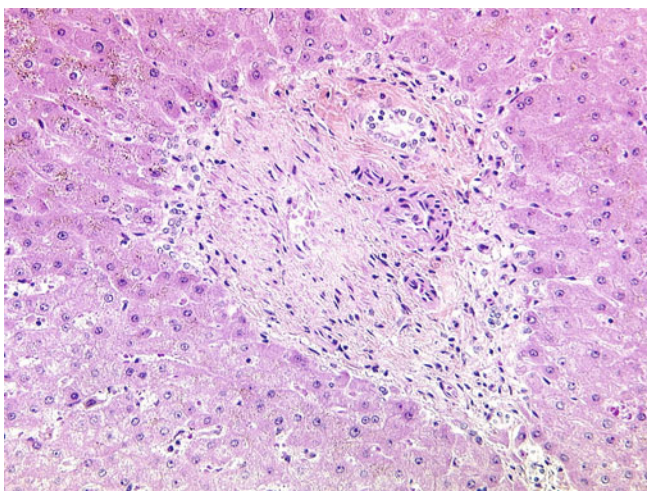

Fig. 11.5 Hepatoportal sclerosis. This portal tract contains a largely obliterated portal vein and is accompanied by mild portal fibrosis. Hepatoportal sclerosis may be regarded as an idiopathic form of obliterative portal venopathy. Many synonyms exist in the literature, including noncirrhotic portal hypertension, idiopathic portal hypertension, (benign) intrahepatic portal hypertension, noncirrhotic portal fibrosis, and Banti disease. Clinically, patients present with features of portal hypertension in the absence of chronic liver disease, cirrhosis, or obstructed extrahepatic portal vein obstruction.

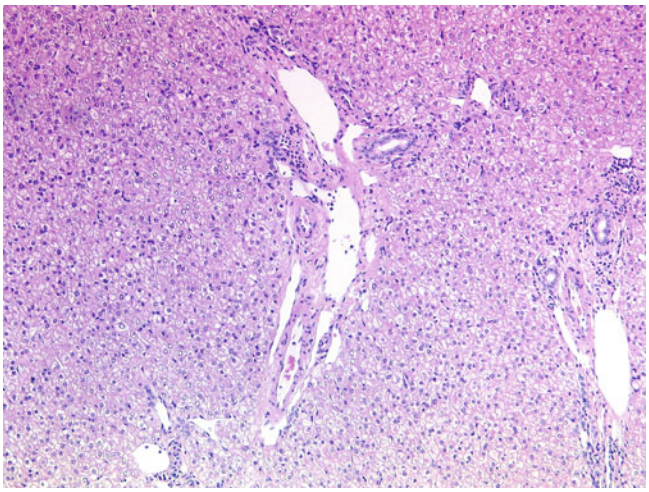

Fig. 11.6 Hepatoportal sclerosis. Multiple dilated portal venous channels are present. In obliterative portal venopathy and hepatoportal sclerosis, occluded small portal veins largely are replaced by fibrous tissues and may disappear. The involved portal tracts usually are expanded by fibrosis. Uninvolved small portal veins may be dilated and may increase in number, with herniation into the periportal hepatic parenchyma. Sinusoidal dilatation, a variable degree of parenchymal atrophy, and occasional bridging fibrosis may be found.

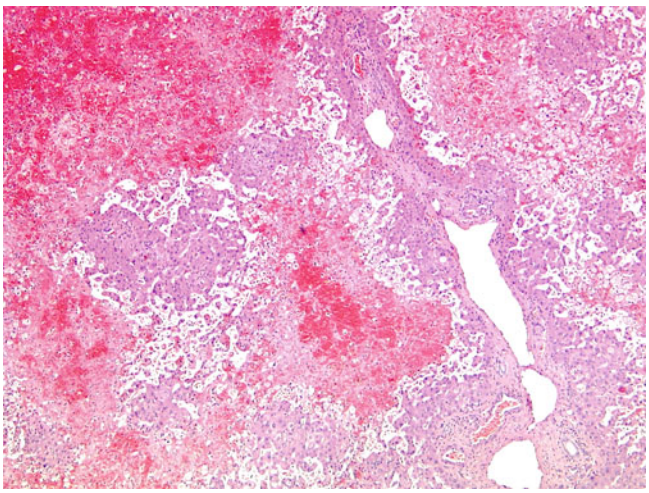

Fig. 11.8 Liver in Budd-Chiari syndrome. This thrombosed hepatic vein is associated with perivenular haemorrhagic necrosis and sinusoidal dilatation. Budd-Chiari syndrome currently is defined as a broad spectrum of diseases associated with hepatic venous outflow tract obstruction, irrespective of the level or aetiology of obstruction. Cardiac and pericardial diseases and sinusoidal obstruction syndrome are excluded from this definition. Budd-Chiari syndrome is classified as primary (intramural obstruction by thrombosis or phlebitis) or secondary (extramural obstruction by space-occupying lesion). Thrombosis is the commonest cause of large hepatic vein obstruction and is associated with hypercoagulative status, endothelial injury, and stasis. The classical clinical triad of acute Budd-Chiari syndrome is painful hepatomegaly, ascites, and liver dysfunction. However, up to 20% of patients are asymptomatic.

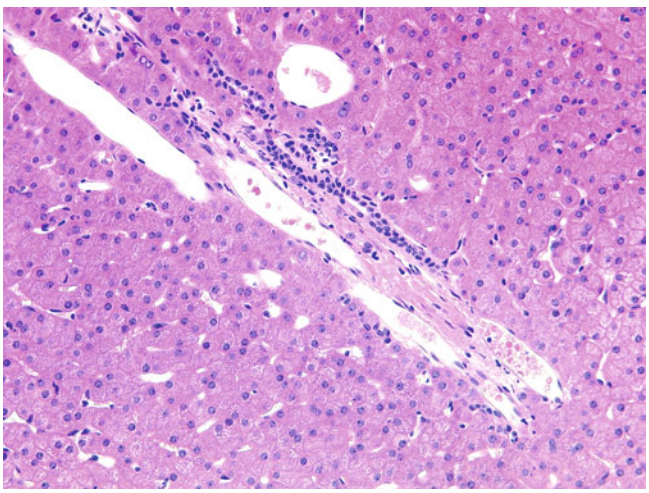

Fig. 11.7 Hepatoportal sclerosis. Dilated portal venous channels herniate into the periportal hepatic parenchyma. Hepatoportal sclerosis essentially is a diagnosis of exclusion. Clinical, serologic, radiologic, and histologic correlations are required to eliminate other aetiologies of small portal vein obliteration. Careful histologic examination should be performed to rule out primary biliary cirrhosis (florid duct lesions, portal granulomas), primary sclerosing cholangitis (fibro-obliterative bile duct lesions), sarcoidosis (noncaseating granulomas), schistosomiasis (ova and haemozoin pigments), congenital hepatic fibrosis (ductal plate malformation), and polyarteritis nodosa (active or healed vasculitis). Exclusion of cirrhosis also is crucial to establish the diagnosis of hepatoportal sclerosis.

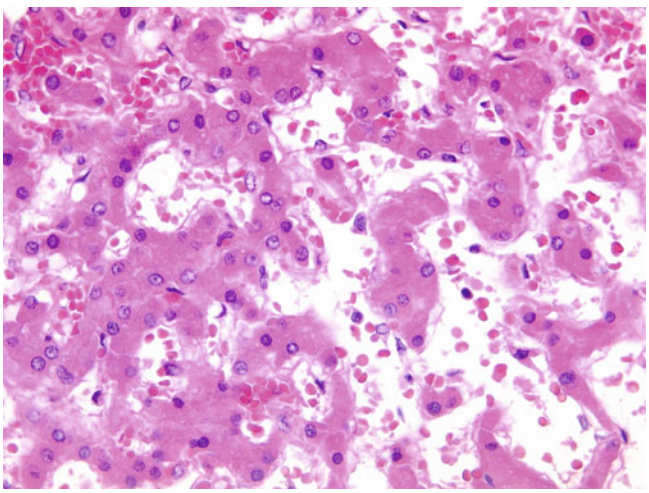

Fig. 11.9 Liver in Budd-Chiari syndrome. Dilated sinusoids and extravasation of red cells into the space of Disse may be seen. Acute hepatic vein thrombosis is associated with perivenular congestion, necrosis, sinusoidal dilatation, and extravasation of red cells into the space of Disse. Thrombosed hepatic veins later may become completely obliterated, organised with subtle intimal fibrosis, or recanalised with multiple venous lumina. Recurrent thrombosis is characterised by multiple layers of mural fibrosis. Pericellular/perisinusoidal fibrosis and atrophy of hepatocytes may be found. Fibrous septa bridging occluded hepatic veins may produce a venocentric cirrhosis or so-called reversed lobulation cirrhosis. Secondary portal vein thrombosis frequently is found. Nodular regenerative hyperplasia and focal nodular hyperplasia-like large regenerative nodules also may be observed.

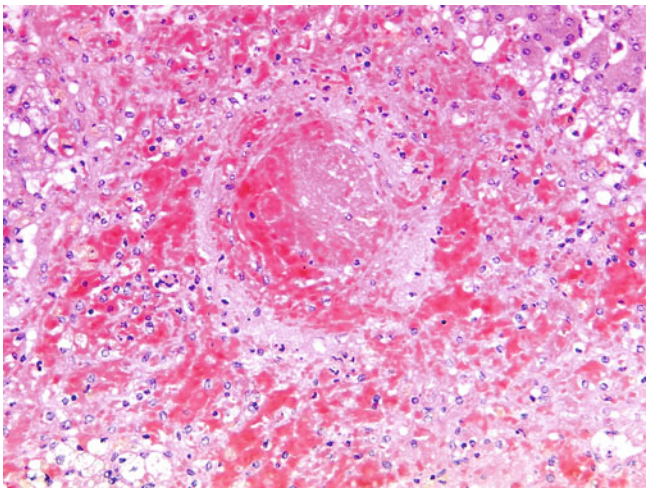

Fig. 11.10 Liver in Budd-Chiari syndrome. A thrombosed hepatic vein may be seen, associated with prominent perivenular haemorrhagic necrosis. Pathologically, Budd-Chiari syndrome may be indistinguishable from sinusoidal obstruction syndrome, obliterative hepatic venopathy, and congestive hepatopathy secondary to heart failure or constrictive pericarditis. Demonstration of thrombosis in large hepatic veins is difficult on liver biopsy, as sampling of large hepatic veins is uncommon in needle biopsy specimens.

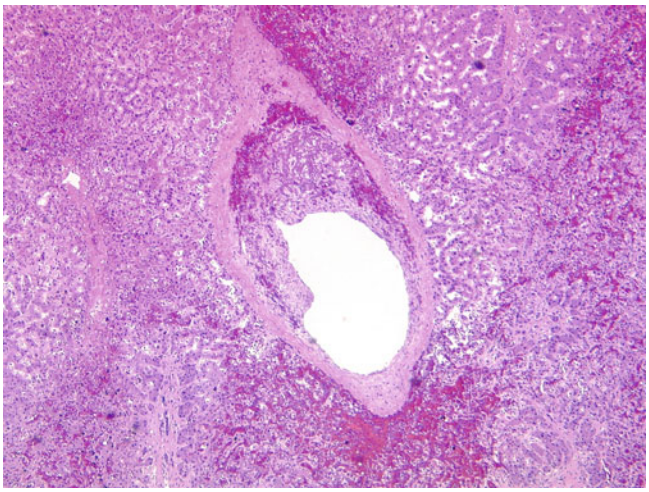

Fig. 11.12 Liver in Budd-Chiari syndrome. A large hepatic vein is partially occluded by a fibrin clot containing basophilic immune complex material in a patient with antiphospholipid syndrome. Clinical, serologic, radiologic, and histologic correlations are required to establish the underlying aetiology of Budd-Chiari syndrome. Liver biopsy is useful in confirming the diagnosis, excluding other aetiologies of liver dysfunction, assessing disease severity in terms of necrosis and fibrosis, and determining the underlying cause (e.g., vasculitis, sarcoid noncaseating granuloma, pyogenic abscess, mycetoma, or neoplasm). To minimize the problems associated with sampling, biopsy cores from two or more sites are recommended.

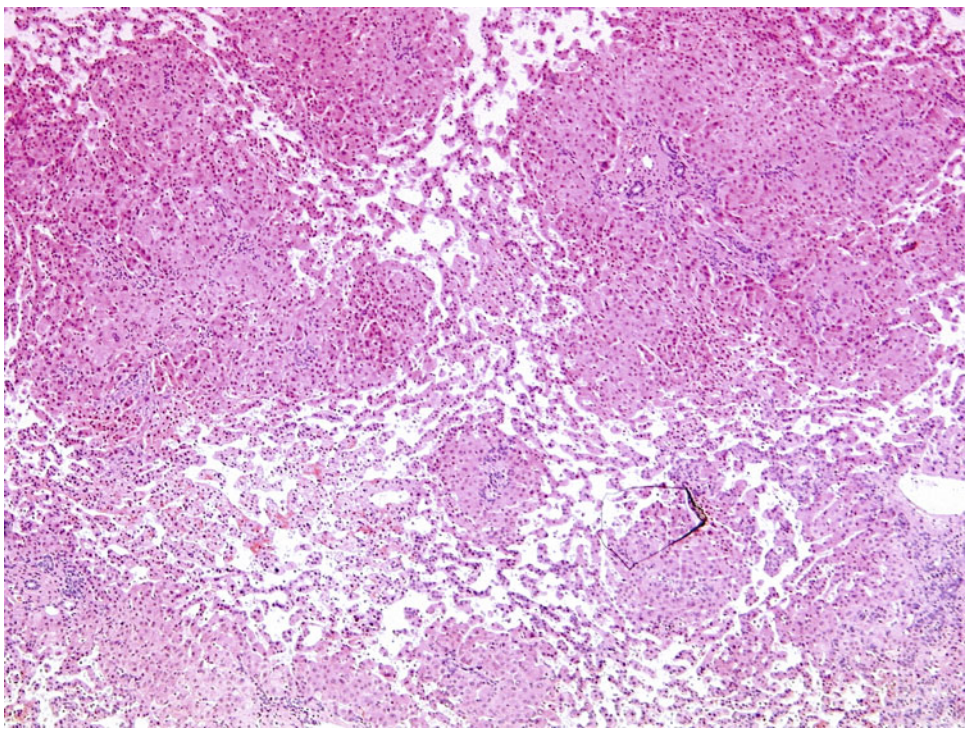

Fig. 11.11 Liver in Budd-Chiari syndrome. Prominent sinusoidal dilatation of zones 3 and 2 is associated with atrophied hepatocytes. Sinusoidal dilatation usually is accompanied by atrophy of hepatocytes and may be caused by hepatic venous outflow tract obstruction, portal vein obstruction, or increased arterial flow. Oral contraception, pregnancy, sickle cell anaemia, and various chronic wasting illnesses (e.g., tuberculosis, HIV, Hodgkin lymphoma, renal cell carcinoma) also may be associated with sinusoidal dilatation.

Fig. 11.13 Acute hepatic artery thrombosis. There are wedge-shaped infarcts in the subcapsular region, associated with extravasation of bile. Hepatic artery thrombosis is uncommon but important in two situations, namely liver transplantation and transarterial chemoembolization for hepatic tumour. Hepatic artery thrombosis is the commonest vascular complication in liver allograft and affects 2.5% to 11% of patients post transplantation, particularly children and patients receiving reduced-size grafts. Transarterial chemoembolisation is a regional treatment for primary hepatocellular carcinoma and, occasionally, metastases. Pathologically, hepatic artery thrombosis is characterised by ischaemic hepatic necrosis of varying sizes and ischaemic cholangitis.

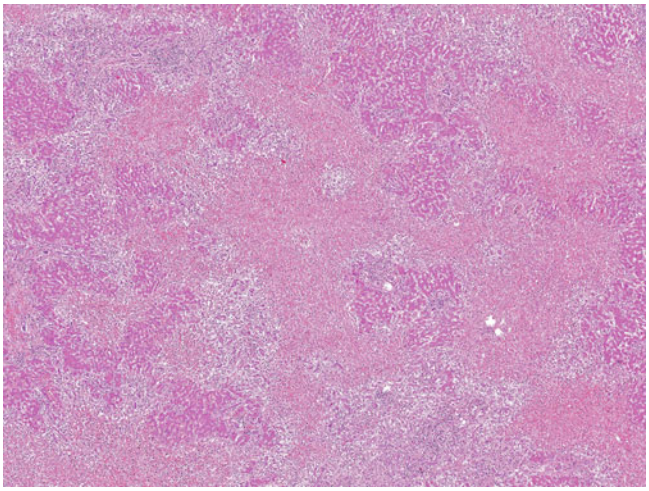

Fig. 11.14 Acute hepatic ischaemia in a patient with shock secondary to ruptured hepatocellular carcinoma. Ischaemic necrosis is present in zones 3 and 2 and is accompanied by marked congestion. Hepatic infarction is defined as ischaemic necrosis of at least two contiguous acini. The dual blood supply from the hepatic artery and portal vein generally protects the liver from ischaemic injury. However, generalised hepatic infarction may occur in shock, disseminated intravascular coagulation, toxaemia of pregnancy, and combined thrombosis of the hepatic artery/portal vein, hepatic artery/hepatic vein, and hepatic vein/portal vein.

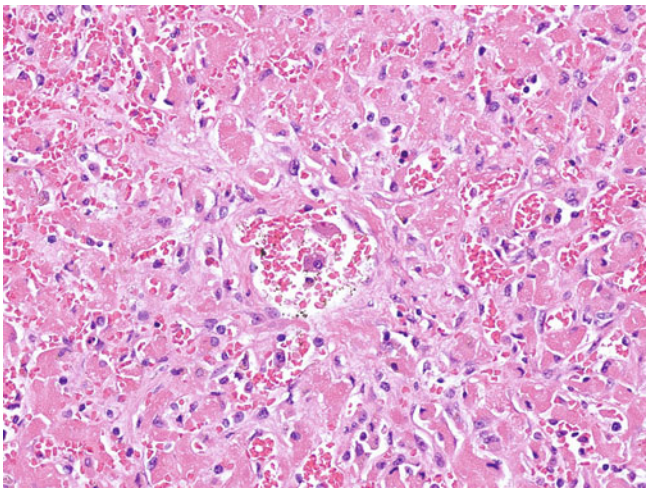

Fig. 11.15 Acute hepatic ischaemia in a patient with shock secondary to ruptured hepatocellular carcinoma. Coagulative necrosis may be seen in the perivenular region and accompanied by sinusoidal congestion. The differential diagnosis of the histologic picture of acute hepatic ischaemia includes other vascular disorders (e.g., Budd-Chiari syndrome, sinusoidal obstructive syndrome), drug/toxin-induced acute hepatic necrosis (e.g., acetaminophen), and necrosis associated with nonhepatotropic viral infections (e.g., herpes simplex virus and adenovirus).

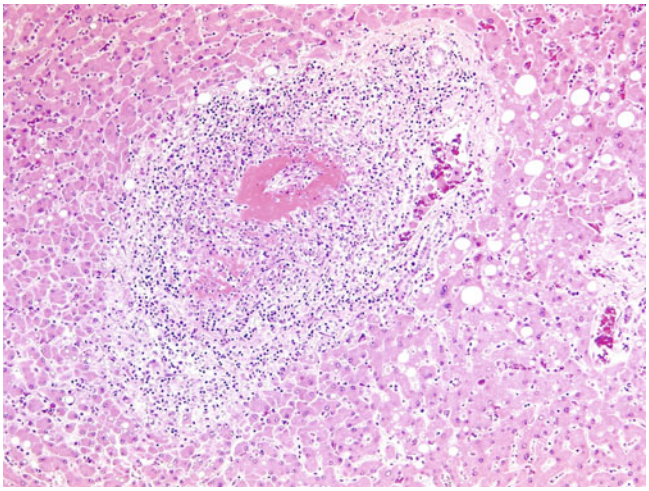

Fig. 11.16 Arteritis in polyarteritis nodosa. Fibrinoid necrosis of the hepatic arterial wall is seen, associated with a dense inflammatory infiltrate. The hepatic arteries may be involved by a vasculitic process in polyarteritis nodosa, Churg-Strauss syndrome, Wegener granulomatosis, systemic lupus erythematosus and rheumatoid arthritis. Certain drugs, including allopurinol, chlorothiazide, chlorpropamide, penicillin, phenylbutazone, phenytoin, and sulphonamide, also may cause arteritis in the liver. Most cases are asymptomatic, but a few cases may be complicated by hepatic artery aneurysm, hepatic rupture, and infarction. Obliteration of small portal veins secondary to small hepatic artery vasculitis may lead to nodular regenerative hyperplasia and portal hypertension.

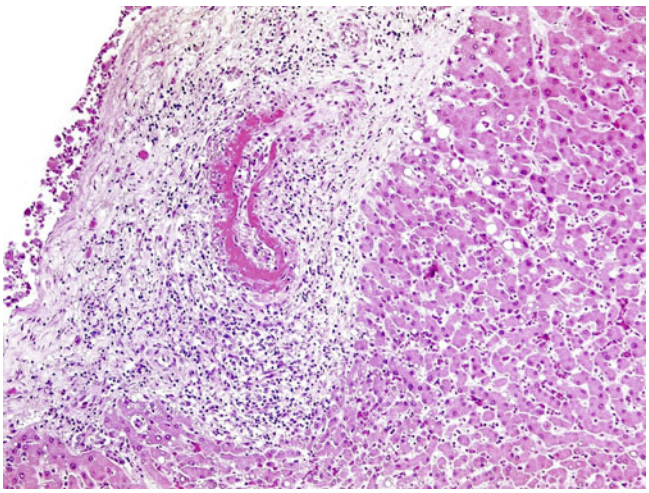

Fig. 11.17 Arteritis in polyarteritis nodosa. Fibrinoid necrosis of the hepatic arterial wall. The features of arteritis in the liver are the same as those in other organs.

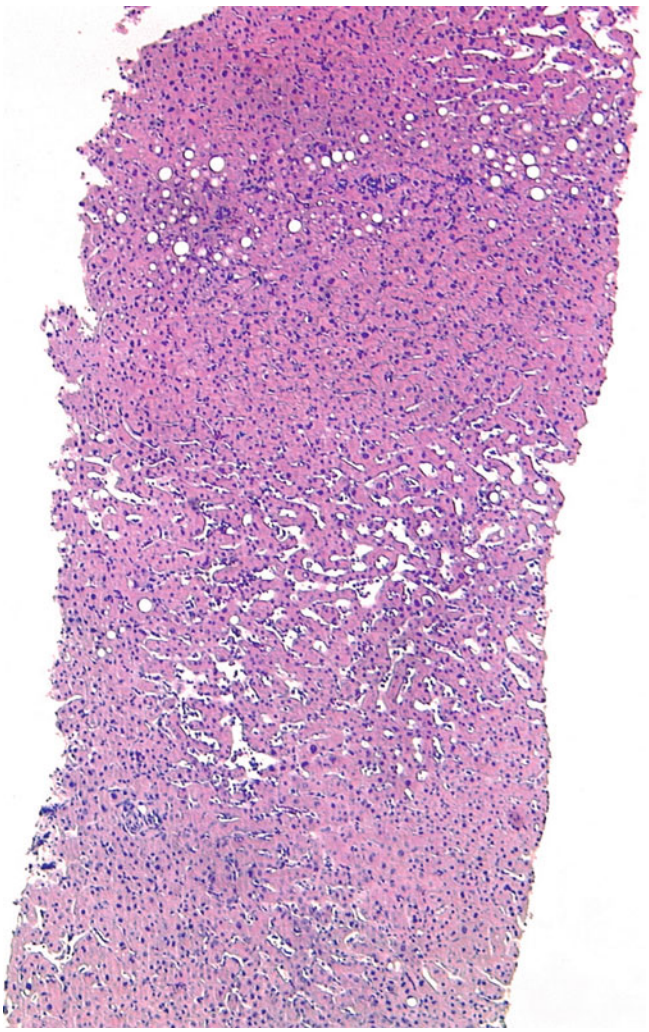

Fig. 11.18 Sinusoidal dilatation induced by oral contraceptive use. There is marked midzonal sinusoidal dilatation. Sinusoidal dilatation may be caused by hepatic venous outflow tract obstruction, portal vein obstruction, or increased arterial flow. Oral contraceptive treatment, pregnancy, sickle cell anaemia, and various chronic wasting illnesses (e.g., tuberculosis, HIV, Hodgkin lymphoma, renal cell carcinoma) also may be associated with sinusoidal dilatation. Sinusoidal dilatation may be accompanied by atrophy of the hepatocytes, focal apoptosis, and pericellular/perisinusoidal fibrosis. *Infarct of Zahn* is the term often used for localized sinusoidal dilatation and hepatocytic atrophy associated with regional portal vein obstruction. Sinusoidal dilatation is also seen in the inflammatory type of hepatocellular adenoma commonly associated with oral contraceptive use.

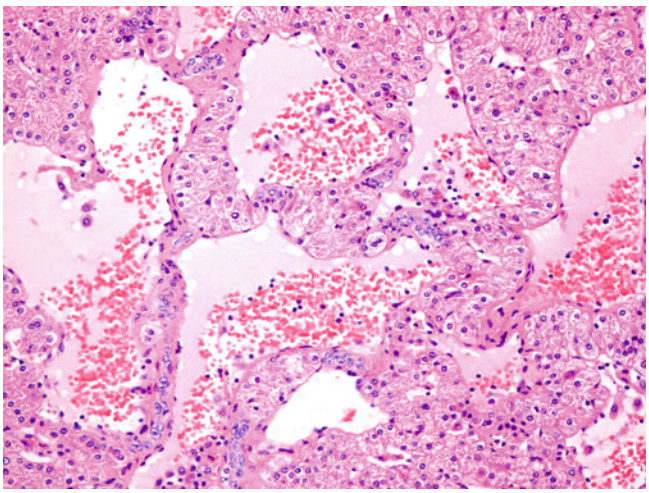

Fig. 11.19 Peliosis hepatis. Dilated sinusoidal spaces are separated by benign hepatocyte plates and partially lined by bland endothelial cells. Peliosis hepatis is the presence of cystic blood-filled spaces due to loss of integrity of the sinusoidal wall. Most cases represent incidental findings, but rarely, it may present with haemoperitoneum secondary to rupture. It is associated with certain drugs (e.g., anabolic steroids, oestrogenic steroids, corticosteroids, azathioprine, methotrexate, and 6-mercaptopurine), infection (e.g., bartonellosis, tuberculosis, and leprosy), and hairy cell leukaemia. Peliosis hepatis associated with *Bartonella* species also is referred to as bacillary peliosis and is restricted to patients with AIDS and other immunocompromised states. Bacillary peliosis is manifest by peliosis of the spleen and lymph nodes, in addition to the liver, and commonly is associated with bacillary angiomatosis of the skin and other organs.

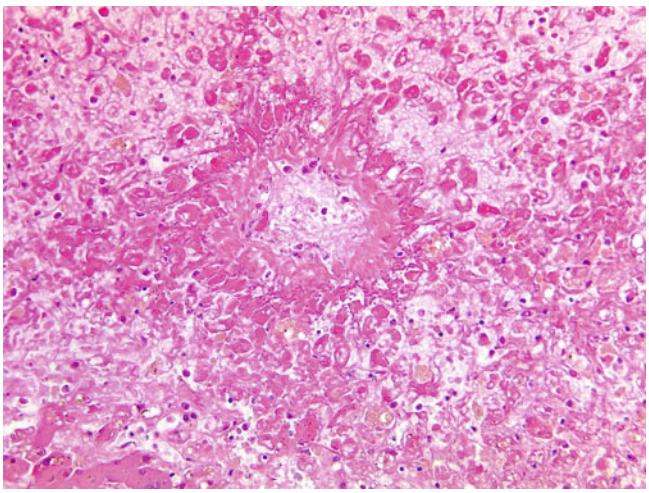

Fig. 11.21 Acute sinusoidal obstruction syndrome. Hepatic vein obstruction with subintimal fibrin deposition is associated with extensive zone 3 haemorrhagic necrosis. Sinusoidal obstruction syndrome, previously referred to as veno-occlusive disease or toxic sinusoidal injury, is strongly associated with the use of chemotherapeutic agents and radiation. A similar and somewhat confusing term, *veno-occlusive lesion*, sometimes is used to describe obliteration of small hepatic veins by injuries other than those associated with drugs or radiation; *obliterative hepatic venopathy* perhaps is a better term. Sinusoidal obstruction syndrome may present clinically in acute, subacute, or chronic form. Mortality is up to 20% to 50% with acute sinusoidal obstruction syndrome.

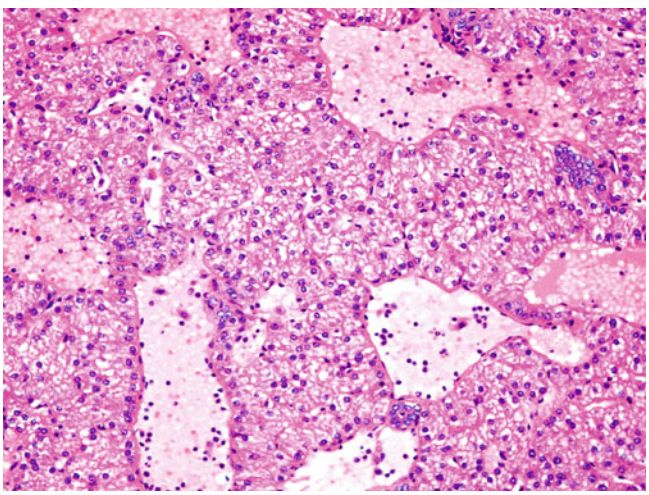

Fig. 11.20 Peliosis hepatis. Peliosis hepatis is composed of cystic blood-filled spaces from millimetres to a few centimetres. The endothelial lining may be absent initially but reappears after reendothelialisation. Rupture of the sinusoidal wall is evident by disruption of reticulin fibres, demonstrated by Gordon-Sweets reticulin stain. Warthin-Starry stain and immunostains for *Bartonella* may be helpful in ruling out bacillary peliosis.

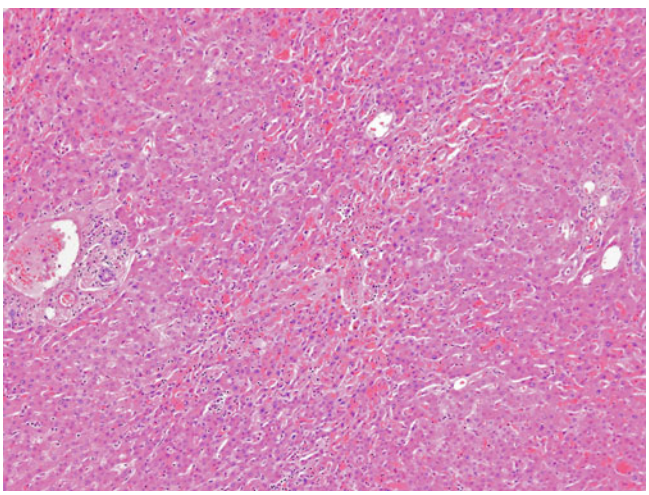

Fig. 11.22 Acute sinusoidal obstruction syndrome. Sinusoidal congestion and fibrin deposition are accompanied by hepatocyte drop-out. Sinusoidal obstruction syndrome is characterised pathologically by subintimal oedema, haemorrhage, and fibrin deposition in sinusoids and small hepatic veins less than 300 μm. Sinusoidal congestion and haemorrhagic necrosis usually are found. As the disease advances, involved hepatic veins may become completely obliterated, organised with subtle intimal fibrosis, or recanalised with multiple venous lumina. Pericellular/perisinusoidal fibrosis and atrophy of hepatocytes may be found.

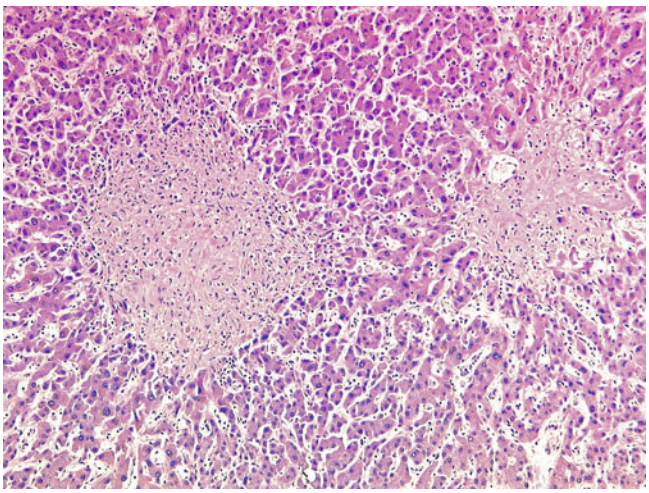

Fig. 11.23 Chronic sinusoidal obstruction syndrome. Fibrous obliteration of small hepatic veins is associated with perivenular fibrosis and hepatocellular atrophy. Acute sinusoidal obstructive syndrome may be mimicked by acute Budd-Chiari syndrome with retrograde extension of thrombi into smaller venules. Absence of thrombi in large hepatic veins on imaging excludes acute Budd-Chiari syndrome. The histologic differential diagnoses of chronic sinusoidal obstruction are the conditions associated with perivenular fibrosis, including alcoholic and nonalcoholic steatohepatitis, congestive heart failure, chronic Budd-Chiari syndrome, and sickle cell disease.