Noncirrhotic portal hypertension

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Literature review current through: **Sep 2023.**
This topic last updated: **Dec 30, 2022.**

INTRODUCTION

Portal hypertension is defined by a pathologic increase in the pressure of the portal venous system. Cirrhosis is the most common cause of portal hypertension, but it can also be present in the absence of cirrhosis, a condition referred to as "noncirrhotic portal hypertension."

This topic will discuss the etiology of noncirrhotic portal hypertension and two disorders associated with noncirrhotic portal hypertension: schistosomiasis and idiopathic noncirrhotic portal hypertension (INCPH). Other causes of noncirrhotic portal hypertension are discussed elsewhere.

- (See "Acute portal vein thrombosis in adults: Clinical manifestations, diagnosis, and management".)
- (See "Chronic portal vein thrombosis in adults: Clinical manifestations, diagnosis, and management".)
- (See "Clinical manifestations, diagnosis, and prognosis of primary biliary cholangitis".)
- (See "Primary sclerosing cholangitis in adults: Clinical manifestations and diagnosis".)
- (See "Budd-Chiari syndrome: Epidemiology, clinical manifestations, and diagnosis".)
- (See "Hepatic sinusoidal obstruction syndrome (veno-occlusive disease) in adults".)
- (See "Autosomal dominant polycystic kidney disease (ADPKD): Extrarenal manifestations", section on 'Hepatic cysts' and "Diagnosis and management of cystic lesions of the liver", section on 'Polycystic liver disease'.)
- (See "Acute fatty liver of pregnancy".)

- (See "Hepatotoxicity associated with chronic low-dose methotrexate for nonmalignant disease".)
- (See "Drug-induced liver injury".)
- (See "Amiodarone: Adverse effects, potential toxicities, and approach to monitoring", section on 'Adverse hepatic effects'.)
- (See "Evaluation of the adult patient with hepatic granuloma".)
- (See "Constrictive pericarditis: Diagnostic evaluation".)
- (See "Definition and classification of the cardiomyopathies", section on 'Restrictive cardiomyopathy'.)

ETIOLOGY

Disorders associated with noncirrhotic portal hypertension can be categorized based on their site of involvement into prehepatic, intrahepatic or posthepatic causes. Intrahepatic causes can be further subcategorized as presinusoidal, sinusoidal, and postsinusoidal (table 1). In some cases, a given disorder may affect multiple sites (eg, vinyl chloride toxicity, Gaucher disease).

Prehepatic and posthepatic causes — Prehepatic causes include disruption of the vascular system proximal to the liver, such as portal or splenic vein thrombosis and splanchnic arteriovenous fistulas.

Posthepatic causes include disruption of the vascular system distal to the liver, such as obstruction of the hepatic veins or the inferior vena cava (eg, Budd-Chiari syndrome) and cardiac diseases (eg, constrictive pericarditis and restrictive cardiomyopathy).

Intrahepatic causes — The intrahepatic causes of noncirrhotic portal hypertension may be presinusoidal, sinusoidal, or postsinusoidal.

Presinusoidal causes — Presinusoidal causes of noncirrhotic portal hypertension include [1]:

- Developmental abnormalities (eg, adult polycystic liver disease, congenital hepatic fibrosis, arteriovenous fistulas).
- Biliary diseases (eg, biliary cholangitis, autoimmune cholangiopathy, primary sclerosing cholangitis, toxic biliary injury from vinyl chloride).
- Neoplastic occlusion of the intrahepatic portal vein (eg, due to lymphoma, epithelioid hemangioendothelioma, epithelial malignancies, chronic lymphocytic leukemia).
- Granulomatous liver lesions (eg, schistosomiasis, mineral oil granuloma, sarcoidosis).
- Idiopathic noncirrhotic portal hypertension (INCPH). The term porto-sinusoidal vascular disease (PSVD) has been proposed to encompass a broader group of vascular liver

diseases [2]. (See 'Porto-sinusoidal vascular disease' below.)

Sinusoidal causes — Sinusoidal causes of noncirrhotic portal hypertension include [1]:

- Fibrosis of the space of Disse, which may be metabolic (eg, nonalcohol-associated fatty liver disease, Zellweger syndrome), inflammatory (viral hepatitis, chronic Q fever, prior cytomegalovirus, schistosomiasis), or induced by drugs or toxins (eg, amiodarone, methotrexate, alcohol, vinyl chloride, copper) [3-6].
- Amyloid or light-chain deposition in the space of Disse.
- Defenestration of the sinusoidal lining in early alcohol-associated liver disease.
- Sinusoidal destruction or collapse in the setting of acute hepatic injury.
- Infiltrative diseases such as mastocytosis, Gaucher disease, and idiopathic myeloid metaplasia.
- Compression of sinusoids by markedly hypertrophied hepatocytes, which may be seen with microvesicular steatosis.

Postsinusoidal causes — Postsinusoidal causes of noncirrhotic portal hypertension include [1]:

- Sinusoidal obstruction syndrome (previously called veno-occlusive disease)
- Budd-Chiari syndrome
- Phlebosclerosis of hepatic veins (eg, due to alcohol-associated liver disease, chronic radiation injury, hypervitaminosis A)
- Primary vascular malignancies (eg, epithelioid hemangioendothelioma, angiosarcoma)
- Granulomatous phlebitis (eg, from sarcoidosis, *Mycobacterium avium* or *M. intracellulare* infection)
- Lipogranulomas (eg, mineral oil granuloma)

SCHISTOSOMIASIS

Schistosomiasis is one of the most common causes of noncirrhotic portal hypertension worldwide [7]. Of the three main Schistosoma species, *S. japonicum* and *S. mansoni* are known to cause liver disease. *S. hematobium* affects mainly the urinary tract, although at advanced stages the liver can develop portal fibrosis. The acute stage of schistosomiasis mimics acute bacterial infection and is accompanied by marked eosinophilia. Chronic hepatic schistosomiasis is

characterized by features of portal hypertension: esophageal varices, hepatomegaly, and splenomegaly with hypersplenism. The diagnosis of schistosomiasis can be made by the detection of schistosomal ova in the stool. Management includes treating underlying parasitic infection and preventing or treating the consequences of portal hypertension. (See "Schistosomiasis: Epidemiology and clinical manifestations" and "Schistosomiasis: Diagnosis" and "Schistosomiasis: Treatment and prevention".)

S. japonicum is distributed widely throughout the world, predominantly in Asia. *S. mansoni* is endemic in Egypt, Africa, the Middle East, and South America. Two other species (*S. mekongi* and *S. intercalatum*) also cause hepatic infections in endemic areas in Southeast Asia and Western Africa, respectively.

Pathophysiology — The infection occurs when the schistosomal cercariae enter the body through the skin. Adult worms eventually find their way to inhabit tributaries of the inferior (*S. mansoni*) or superior (*S. japonicum*) mesenteric veins, where they produce hundreds to thousands eggs per day for several years before the end of their lifespan (figure 1). Some of these eggs pass through the intestinal mucosa and are excreted in the urine or feces to continue their life cycle. Others flow into the portal vein tributaries and become trapped in the terminal portal venules, where they induce chronic inflammation that is subsequently followed by marked fibrosis. *S. japonicum* is capable of producing far more eggs than *S. mansoni* and thus causes more severe liver disease [8,9]. (See "Schistosomiasis: Epidemiology and clinical manifestations".)

In the early stages of infection, the portal resistance is mainly presinusoidal. However, as the fibrotic changes in the portal tracts progress, lobular distortion at the sinusoidal level occurs. This results in an increase in resistance to portal venous flow, as evidenced by an increased wedged hepatic venous pressure (WHVP) in advanced cases [10]. Hemodynamic studies in patients with hepatic schistosomiasis have demonstrated a hyperdynamic systemic and splanchnic circulation with normal hepatic venous pressure gradient (HVPG) and total hepatic blood flow [8,11,12]. (See "Portal hypertension in adults", section on 'Hepatic venous pressure gradient'.)

Clinical features — Chronic hepatic schistosomiasis is characterized by features of portal hypertension: esophageal varices, hepatomegaly, and splenomegaly with hypersplenism. In children, chronic infection is associated with growth delay. Many patients with mild fibrosis are asymptomatic during the earlier phases of their disease. (See "Schistosomiasis: Epidemiology and clinical manifestations", section on 'Hepatosplenic schistosomiasis'.)

Underlying hepatic function remains preserved in hepatic schistosomiasis, and hepatic encephalopathy, ascites, and liver failure are uncommon. Patients with hepatic schistosomiasis usually tolerate episodes of acute variceal bleeding better than patients with cirrhosis because of their preserved liver function. In advanced cases, hepatic decompensation may develop, with hypoalbuminemia and chronic ascites. However, this tends to occur in patients with coexisting liver disease such as chronic viral hepatitis B or C virus infection. These coexisting liver diseases have been found to aggravate the course of hepatic schistosomiasis, changing its natural history [13-15]. Extrahepatic manifestations, such as pneumonia and pulmonary hypertension, have been described in *S. mansoni* infection [16]. (See "Schistosomiasis: Epidemiology and clinical manifestations", section on 'Hepatosplenic schistosomiasis'.)

Diagnosis — The diagnosis of schistosomiasis can be made by the detection of schistosomal eggs in the stool (picture 1). As an alternative, it can be demonstrated in biopsies of the rectal mucosa (picture 2) or the liver. Because the worms concentrate more densely in the distal colon, the rectal mucosa has a heavy load of schistosomal eggs. The diagnosis can also be made using various immunologic assays [17]. (See "Schistosomiasis: Diagnosis".)

The diagnosis of esophageal and/or gastric varices in schistosomiasis is established with endoscopy. However, access to endoscopy can be challenging in the areas of the world where schistosomiasis is endemic. Several studies have examined the role of non-invasive tests for the diagnosis of portal hypertensive complications of schistosomiasis [18]. Most studies focus on the role of ultrasound and hematologic parameters. Sonographic features such as portal vein diameter, spleen size, and periportal fibrosis were predictive of large varices and variceal bleeding [19]. A sonographic score assessing the degree of echogenic periportal thickening and portal vein dilation was shown to correlate with the presence and grade of varices and risk of variceal bleeding [20]. The platelet count/spleen diameter ratio demonstrated high sensitivity (85 to 100 percent) and specificity (83 to 92 percent) for predicting esophageal varices in patients with schistosomiasis [21,22].

Management — Antihelminthic treatment (eg, praziquantel, oxamniquine) is active against all forms of human schistosomiasis and is effective for eradicating the worms in the acute stage of the disease. Cure rates vary from 60 to 90 percent for *S. mansoni* and 60 to 80 percent for *S. japonicum* [23,24]. Even if treatment does not eradicate all the worms, it will result in a sharp reduction in egg laying. In patients with chronic schistosomiasis, the worms no longer lay eggs and the patient may not require any specific antihelminthic treatment. (See "Schistosomiasis: Treatment and prevention", section on 'Treatment'.)

In addition to treating the underlying parasitic infection, management should be aimed at preventing or treating the consequences of portal hypertension (predominantly variceal

bleeding). Only a few studies have described treatment options in these patients. As a result, patients are typically managed similarly to patients with varices in the setting of cirrhosis [25]. (See "Cirrhosis in adults: Overview of complications, general management, and prognosis", section on 'Complications of portal hypertension'.)

Treatment for acute variceal bleeding includes early pharmacologic treatment with vasoactive drugs, early endoscopic control of bleeding, careful blood product replacement, and prophylactic antibiotics. (See "Overview of the management of patients with variceal bleeding".)

Primary and secondary prevention of variceal bleeding includes the use of nonselective beta blockers and endoscopic variceal ligation. (See "Primary prevention of bleeding from esophageal varices in patients with cirrhosis" and "Prevention of recurrent bleeding from esophageal varices in patients with cirrhosis".)

Data on treatment for hepatic schistosomiasis complicated by portal hypertension and variceal bleeding are limited, and the optimal approach is uncertain [18,26,27]. In a study including 82 patients with schistosomiasis and portal hypertension-related bleeding, beta blocker therapy was associated a longer median time to rebleeding compared with placebo (589 versus 252 days) [18,26]. In a review of 16 studies involving endoscopic therapy for variceal bleeding related to schistosomiasis, sclerotherapy was used in most studies, while some studies evaluated band ligation [18]. Overall, endoscopic therapy was associated with lower mortality rates. However, sclerotherapy was associated with recurrent bleeding rates of approximately 30 percent, which was partially attributed to limited adherence to follow up endoscopy sessions.

Surgery has been used for patients with noncirrhotic portal hypertension from schistosomiasis who have recurrent variceal bleeding despite medical and endoscopic treatment [28]. Surgical options included splenectomy with esophagogastric devascularization or selective shunts (eg, distal splenorenal shunts) [29,30]. In a trial of 47 patients with schistosomiasis and a history of variceal bleeding, patients treated with splenectomy and esophageal devascularization had a lower rate of recurrent bleeding compared with patients treated with endoscopic sclerotherapy (9 versus 36 percent) [30]. Nonselective shunts (eg, proximal splenorenal shunts) are not recommended because they are associated with high rates of hepatic encephalopathy, hemolysis, and death [31].

Transjugular intrahepatic portosystemic shunt (TIPS) placement may be an alternative to surgery, but data are limited [18,29,32]. (See "Overview of transjugular intrahepatic portosystemic shunts (TIPS)".)

Studies have suggested that TIPS was associated with reduced variceal size and lower risk of recurrent bleeding but may be complicated by hepatic encephalopathy. In a cohort of 20

patients with schistosomiasis who had TIPS placement, hepatic encephalopathy was reported in 25 percent of patients, variceal rebleeding in 15 percent of patients, and mortality in 15 percent of patients [32]. Additional studies are required to establish the role of TIPS for patients with noncirrhotic portal hypertension due to schistosomiasis.

IDIOPATHIC NONCIRRHOTIC PORTAL HYPERTENSION/PORTO-SINUSOIDAL VASCULAR DISEASE

Terminology and diagnostic criteria

Idiopathic noncirrhotic portal hypertension — Idiopathic noncirrhotic portal hypertension (INCPH) is characterized by the presence of portal hypertension in the absence of cirrhosis on liver histology, the exclusion of obstruction of the extrahepatic portal vein or hepatic venous outflow tract and exclusion of conditions that may cause cirrhosis or noncirrhotic portal hypertension (e.g. congenital hepatic fibrosis, sarcoidosis, schistosomiasis) [1].

The diagnosis of INCPH requires that the following criteria are met [1]:

- Clinical signs of portal hypertension (at least one of the following) must be present:
  - Splenomegaly/hypersplenism in conjunction with another sign of portal hypertension.
  - Esophageal and/or gastric varices.
  - Ascites (nonmalignant).
  - Portovenous collaterals.
- Exclusion of cirrhosis on liver biopsy.
- Exclusion of chronic liver disease that may cause either cirrhosis or noncirrhotic portal hypertension:
  - Chronic hepatitis B or C virus infection (see "Hepatitis B virus: Screening and diagnosis in adults" and "Screening and diagnosis of chronic hepatitis C virus infection", section on 'Diagnostic techniques').
  - Nonalcohol-associated steatohepatitis (see "Epidemiology, clinical features, and diagnosis of nonalcoholic fatty liver disease in adults", section on 'Diagnosis').
  - Alcohol-associated steatohepatitis (see "Clinical manifestations and diagnosis of alcohol-associated fatty liver disease and cirrhosis", section on 'Diagnosis').
  - Autoimmune hepatitis (see "Overview of autoimmune hepatitis").

- Hereditary hemochromatosis (see "Approach to the patient with suspected iron overload", section on 'Diagnosis').
- Wilson disease (see "Wilson disease: Clinical manifestations, diagnosis, and natural history", section on 'Diagnostic evaluation').
- Primary biliary cholangitis (see "Clinical manifestations, diagnosis, and prognosis of primary biliary cholangitis", section on 'Diagnosis').

- Exclusion of other conditions that may cause noncirrhotic portal hypertension (eg, congenital liver fibrosis, sarcoidosis (see "Clinical manifestations and diagnosis of sarcoidosis"), schistosomiasis (see 'Schistosomiasis' above), myeloproliferative disease, hepatic arterioportal shunts).

- Imaging showing patent portal and hepatic veins.

Porto-sinusoidal vascular disease — To recognize that histologic findings of INCPH are not unique to patients with portal hypertension, the clinical entity of porto-sinusoidal vascular disease (PSVD) was described to include the following groups [2,33-35] (see 'Terminology and diagnostic criteria' above and 'Liver pathology' below):

- Patients with histologic features of INCPH on liver biopsy (eg, obliterative venopathy, nodular regenerative hyperplasia, incomplete septal cirrhosis) but without clinical manifestations of portal hypertension (eg, esophageal or gastric varices).

- Patients with histologic features of INCPH on liver biopsy who also have coexisting liver disease (eg, alcohol-related, metabolic syndrome, viral hepatitis) or extrahepatic portal vein thrombosis.

The liver biopsy specimen must be adequate (ie, greater than 8 to 10 portal tracts) to assess for these histologic features.

PSVD without portal hypertension is frequently seen in the setting of autoimmune, hematologic, thrombotic, or drug-induced diseases [2].

In addition to histologic features, the diagnosis of INCPH relies on excluding coexisting liver disease and demonstrating patent hepatic vessels on imaging. However, several limitations to the definition of INCPH have been recognized (see 'Idiopathic noncirrhotic portal hypertension' above). INCPH cannot be diagnosed if portal vein thrombosis is present on imaging. However, it has been recognized that the portal vein thrombosis is a frequent complication of INCPH during its course. Secondly, these criteria require the exclusion of other causes of liver disease (eg, alcohol, viral hepatitis). However, it has been recognized that other conditions may coexist in

patients with INCPH but are clearly not responsible for portal hypertension. Thirdly, the criteria require clinical signs of portal hypertension. However, early stages of the disease have been recognized in which histologic features (eg, obliterative venopathy, nodular regenerative hyperplasia, incomplete septal cirrhosis) are found on liver biopsy in the absence of clinical signs of portal hypertension. These limitations for diagnosing INCPH led a group of experts in vascular liver disease (The Vascular Liver Disease Interest Group [VALDIG]) to propose the term porto-sinusoidal vascular disease (PSVD) to describe a broader spectrum of disease and include these groups of patients [2,35].

Epidemiology — The incidence of INCPH (or PSVD with portal hypertension) varies worldwide. Older studies suggested that it accounts for approximately 23 percent of cases of portal hypertension in India In other countries (eg, Japan, Netherlands), it was thought to account for 14 to 27 percent of cases of noncirrhotic portal hypertension [36-38]. However, over time, fewer cases have been reported, suggesting that the incidence may be much lower [1,39].

In Eastern countries, the disease is often encountered in patients who are socioeconomically disadvantaged [40]. Slight differences in the sex and age distribution have been reported from different countries [41,42]. The reason for this is not clear, but differences in socioeconomic status, living conditions, pathogen exposure, average life span, and ethnicity may play a role. In Japan, the incidence of INCPH has declined over time, possibly because of improvements in hygiene and living standards [42]. The incidence of PSVD without PH is uncertain.

Pathophysiology — The etiology of INCPH (PSVD with portal hypertension) is unknown. However, several pathophysiologic mechanisms are believed to be involved, including chronic or recurrent infections, exposures to drugs or toxins, immunologic disorders, genetic disorders, and hypercoagulability. A large number of disorders, medications, and toxins have been associated with INCPH (table 2).

- Chronic or recurrent infections – Repeated episodes of umbilical sepsis, bacterial infections, and diarrhea in early childhood (all relatively common in socioeconomically disadvantaged populations) are believed to lead to portal pyemia and pylephlebitis, which may subsequently cause vascular endothelial injury, microthrombosis, sclerosis, and obstruction of small- and medium-sized portal vein radicals. This may subsequently lead to the development of INCPH in early adulthood [43]. Supporting this hypothesis, animal studies involving repeated injections of *Escherichia coli* into the portal system of rabbits resulted in the development of noncirrhotic portal fibrosis [44].

- Drugs and toxins – Drugs and toxins may induce fibrosis in the space of Disse, leading to INCPH [1]. Drugs associated with INCPH include azathioprine and several cytotoxic drugs.

- Human immunodeficiency virus (HIV) infection – There have been reports of patients with HIV infection who develop variceal bleeding due to underlying noncirrhotic portal hypertension [45-50]. The pathogenesis is thought to be related to the effect of highly active antiretroviral treatment (particularly long-term exposure to didanosine) on the microvasculature of the liver or the direct effect of the HIV itself [47,51]. The discontinuation of didanosine has been reported in some studies to reduce the progression of INCPH [52,53].

- Altered immune response – Several alterations in the immunologic response have been described in patients with INCPH [54,55]. In addition, different autoimmune diseases are frequently associated with INCPH (table 2) [56-58]. Anti-DNA antibodies are demonstrable in more than 65 percent of Japanese women with INCPH [56]. Studies have also reported the presence of INCPH and portal systemic collaterals in some patients with severe primary antibody deficiencies [59].

- Genetic predisposition – Few studies have shown potential genetic mechanisms involved in the development of INCPH. In a study of eight patients with early onset noncirrhotic portal hypertension, a shared mutation in DGUOK, a deoxyguanosine kinase required for mitochondrial DNA replication, was identified [60]. Familial aggregation of INCPH and a high frequency of HLA-DR3 have been observed, suggesting a potential genetic pathogenesis [61].

- Hypercoagulability – Some studies have suggested an association of INCPH with a hypercoagulable state. A study of INCPH in 28 Western patients found evidence of various prothrombotic disorders in 50 percent of patients [62]. Over the course of follow-up, 13 patients developed portal vein thrombosis within a median of 7.6 years (range 1 to 21 years). The authors advocated anticoagulant therapy in patients with INCPH found to have a prothrombotic disorder. Similarly, a report from Turkey described extrahepatic portal vein thrombosis in 7 of 34 (20 percent) patients with INCPH over a five-year follow-up period [63].

- Miscellaneous – Preliminary observations have described a role for endothelin-1, nitric oxide, and connective tissue growth factor in development of INCPH [64-68].

These risk factors have been also found in patients with PSVD without portal hypertension.

It has been proposed that a central event in the development of INCPH/PSVD is a portal venopathy caused by thrombosis or obliteration due to hypercoagulability, endothelial injury, or autoimmune injury (from immune complex deposition, autoantibodies, or activated T cells) [36,69-73].

A vascular cause of INCPH is supported by experimental studies in animals and histologic findings in humans. Blockage of the portal veins decreases blood flow to the liver, resulting in ischemia of the supplied hepatic parenchyma [74]. Ischemia leads to atrophy of the more vulnerable regions of the liver around the central vein and compensatory hypertrophy of the less vulnerable periportal areas [75]. Studies of human livers from patients with acute or chronic portal vein thrombosis have demonstrated apoptosis, atrophy, and the development of nodules [74]. In some cases, the primary insult to the liver was arterial rather than venous. The resulting periportal inflammation eventually leads to portal venopathy [69-71,74-77].

T cell-induced autoimmune mechanisms have also been implicated in the development of the portal vein injury [78]. In one report, sinusoidal infiltration with CD 8+ cytotoxic T cells was observed in 14 of 44 patients (32 percent) [72]. The T cells were located mainly in the atrophic areas and were adjacent to endothelial cells exhibiting evidence of apoptosis. The authors speculated that transient T cell-induced endothelial injury may be the trigger for the development of INCPH. Another study found that 77 percent of patients with INCPH had antiphospholipid antibodies, possibly indicating an antibody-dependent autoimmune mechanism [79].

A study involving transcriptomic analysis in liver tissue samples from 20 patients with PSVD has shown that such patients have a unique transcriptomic profile with deregulation of pathways involved in vascular homeostasis suggesting that this may be a main pathogenic event of disease development [80].

Clinical manifestations — The most common clinical presentation is variceal bleeding, which (in contrast to variceal bleeding in cirrhosis) is often relatively well tolerated due to the preserved liver function. In the late stages of the disease or following an episode of gastrointestinal bleeding, patients will occasionally develop jaundice, ascites, or hepatic encephalopathy. Hepatopulmonary syndrome has been described and reverses after liver transplantation [81-83]. Development of portal vein thrombosis is a frequent event during the natural course of the disease, particularly in patients with associated HIV infection or who have previously bled [84].

On examination, splenomegaly (>10 cm below the left subcostal margin) is present in more than 95 percent of patients. Dilated superficial abdominal veins can be seen in 15 percent of patients, and mild hepatomegaly (<4 cm below the right subcostal margin) can be found in 50 percent of patients [85]. Other stigmata of chronic liver disease are usually absent.

Liver biochemical tests are usually normal or nearly normal [38,71,74]. Anemia, leukopenia, and thrombocytopenia are common because of hypersplenism. (See "Splenomegaly and other

splenic disorders in adults", section on 'Hypersplenism'.) In some patients, hematologic alterations may also be caused by a hematologic-associated condition.

On imaging, the appearance of the liver may be normal or show changes similar to those found in patients with cirrhosis. (See "Cirrhosis in adults: Etiologies, clinical manifestations, and diagnosis", section on 'Radiologic findings'.)

Liver imaging may also show benign regenerative nodules that typically appear isoechoic on ultrasound. However, some nodules may be hypoechoic, often with a hypoechoic rim, and these features are also seen with hepatic metastases [36,86]. On computed tomography (CT) scan, nodules may be hypodense [36,86], while on MRI, nodules appear isointense on T2-weighted images and they contain foci of high intensity on T1-weighted images [36,87-89].

Diagnosis — The diagnosis of INCPH (PSVD with portal hypertension) is made by the presence of portal hypertension (manifested by esophageal and/or gastric varices, portal hypertensive bleeding and/or portosystemic shunting on imaging), while excluding cirrhosis and other causes noncirrhotic portal hypertension with liver biopsy [1,35,90]. (See 'Etiology' above.)

Liver biopsy may show obliterative portal venopathy, nodular regenerative hyperplasia, and/or incomplete septal cirrhosis.

The diagnosis of PSVD without portal hypertension is also based on histologic findings on liver biopsy, however, these patients do not have portal hypertension. In a series of 2500 autopsies, histologic findings consistent with INCPH were found in 3 percent. However, of that 3 percent, only 5 percent had evidence of PH [91].

Diagnostic approach — The diagnostic approach in a patient suspected of having INCPH includes the following: laboratory tests to rule out other causes of liver disease/noncirrhotic portal hypertension, history of drug or toxin exposure, hepatic imaging to rule out portal or hepatic vein occlusion, liver stiffness measurement and liver biopsy to rule out cirrhosis and to identify histological features associated with PSVD/INCPH.

Patients should be evaluated for the disorders associated with INCPH (table 2) if they have signs or symptoms of any of the conditions, hematologic manifestations of a myeloproliferative disease on the complete blood count and differential, prior thrombotic events that might reflect an underlying hypercoagulable state, or manifestations suggestive of a systemic disease associated with vascular injury (eg, vasculitis, lupus). (See "Overview of the myeloproliferative neoplasms", section on 'Diagnosis' and "Evaluating adult patients with established venous thromboembolism for acquired and inherited risk factors" and 'Etiology' above.)

Laboratory tests — We obtain laboratory studies to evaluate for risk factors for cirrhosis and portal hypertension; the etiology of cirrhosis is discussed separately. (See "Cirrhosis in adults: Etiologies, clinical manifestations, and diagnosis", section on 'Etiologies and classification'.)

A report has suggested that serum vitamin B12 levels are significantly lower in patients with INCPH than in patients with cirrhosis and may be useful in distinguishing between the two entities [92]. However, the potential diagnostic role of serum vitamin B12 levels has not been validated. Similarly, it has been suggested, but not yet validated, that a group of serum metabolites detected by metabolomics may aid with diagnosing INCPH [93] or the presence of antiendothelial cells antibodies may aid with diagnosing INCPH/PSVD [94].

Imaging — An imaging test is required to evaluate the liver parenchyma and circulation. The portal and hepatic veins in INCPH should be patent on imaging (eg, Doppler ultrasound, CT angiography, or MRI angiography). Patients with advanced disease may have secondary portal vein thrombosis, which may be misdiagnosed as primary extrahepatic portal vein thrombosis or thrombosis secondary to underlying cirrhosis. The clinical history, liver stiffness values, and liver biopsy findings may help to differentiate between these entities.

Liver stiffness — A patient with INCPH should have a liver stiffness value on transient elastography that is usually below the expected value for a patient with cirrhosis and portal hypertension (ie, <13 kPa) [95]. This can be helpful in differentiating patients with portal vein thrombosis due to cirrhosis from those with portal vein thrombosis in the setting of INCPH [50]. A multicenter study has shown that a liver stiffness value of <10 kPa strongly correlated with PSVD in patients with signs of portal hypertension. Conversely, when liver stiffness is >20 kPa, a diagnosis of PSVD is highly unlikely [96]. (See "Noninvasive assessment of hepatic fibrosis: Ultrasound-based elastography", section on 'Transient elastography'.)

Liver pathology — A liver biopsy is required for the diagnosis of INCPH. From a clinical perspective, the most important reason to obtain a liver biopsy in the evaluation of INCPH is to exclude the presence of cirrhosis and other specific disease entities that could account for the development of portal hypertension. Diagnosis requires a pathologist with expertise in liver disease and a sufficient tissue sample for histologic analysis, which can usually be obtained with a percutaneous or transjugular liver biopsy [97]. (See "Approach to liver biopsy".)

Gross pathology of the liver surface in patients with INCPH is normal in most patients, but it is markedly nodular in 10 to 15 percent of patients, with nodularity confined to the liver's surface [41]. The portal vein and its branches are prominent with sclerosed walls. Autopsy specimens often demonstrate the presence of thrombi in the small and medium portal vein branches [98].

The histologic findings associated with INCPH can be classified into three subtypes of INCPH:

- Obliterative portal venopathy is defined by the presence of phlebosclerosis of the small and medium branches of the portal vein. This is characterized by increased portal connective tissue around the vessels with irregular wall thickening and eccentric narrowing of the vessel lumen [2,99].

- Nodular regenerative hyperplasia is defined by micronodular transformation of the liver parenchyma, with central hyperplasia, an atrophic rim, and no fibrosis [2].

- Incomplete septal cirrhosis is defined by slender, incomplete septal fibrosis that demarcates the liver parenchyma into nodules. The portal tracts are hypoplastic and hepatocytes are hyperplastic [2].

Some patients may have features of more than one subtype. Some of the variability in histologic findings among patients may be the result of heterogeneity in the disease and its severity and because of sampling variability on liver biopsy specimens (table 3) [37,41,62,100].

Other histologic findings include aberrant thin-walled vessels radiating from the portal tract into the periportal space (and sometimes into the lobules where they may have pseudoangiomatous appearance [13]), dilatation of sinusoids due to increased portal pressure, and emergence of new aberrant portal channels (picture 3A-B) [99]. In advanced cases, parenchymal atrophy in the subcapsular regions may lead to collapse [37,100-102]. Uncommon histologic features include pseudonodules, piecemeal necrosis, and regenerative activity [98]. Regenerative nodules may develop near the hilum of atrophic livers in advanced cases. Electron microscopy has revealed widening of the space of Disse with fibrogenesis in the perisinusoidal space leading to capillarization of the sinusoids in some patients [44].

Hemodynamics — Measurement of the hepatic venous pressure gradient (HVPG) is useful in the evaluation of patients with suspected INCPH. Although the intrasplenic and portal vein pressures are markedly elevated in patients with INCPH [103,104], the wedged hepatic vein pressure (WHVP) is normal or only slightly elevated in many patients. As a result, the HVPG is often normal or only mildly elevated despite the clinical severity of portal hypertension. This is due to the presence of hepatic vein-to-vein communications, which are frequently seen during venography, but also because of the presinusoidal component of portal hypertension in INCPH. In both situations, the WHVP almost always underestimates the true portal pressure [105,106]. Demonstration of hepatic vein-to-vein communication during hepatic venography is also supportive of the diagnosis. (See "Portal hypertension in adults", section on 'Hepatic venous pressure gradient'.) Hence, the presence of unequivocal signs of portal hypertension (such as large esophageal varices and splenomegaly combined with HVPG values that are much lower

than the cutoff for clinically significant portal hypertension in cirrhosis [ie, HVPG <10 mmHg]) is strongly suggestive of the diagnosis of INCPH [107].

Differential diagnosis — The differential diagnosis includes portal hypertension due to cirrhosis of any etiology and a variety of pre-, intra-, or postsinusoidal disorders associated with portal hypertension (table 1). (See 'Etiology' above and 'Diagnostic approach' above.)

Management — The focus of management for patients with INCPH is preventing and treating variceal hemorrhage. While data are limited in this population regarding the best approach [84,108-112], patients are typically managed in the same manner as those with portal hypertension due to cirrhosis. A cohort study of patients with INCPH reported good long-term outcomes using a management strategy based on guidelines for varices in the setting of cirrhosis [84]. (See "Primary prevention of bleeding from esophageal varices in patients with cirrhosis" and "Prevention of recurrent bleeding from esophageal varices in patients with cirrhosis".)

Other elements of management include withdrawing drugs associated with INCPH and treating associated medical conditions (table 2). As an example, biochemical and histologic improvement or reversibility has been reported after stopping azathioprine in organ transplantation recipients [87,113]. In addition, patients with INCPH should be screened for portal vein thrombosis (eg, with Doppler ultrasonography every six months [25]). (See 'Etiology' above.)

Management of patients with acute variceal bleeding is discussed in more detail separately. (See "Overview of the management of patients with variceal bleeding".)

Nonselective beta blockers and endoscopic variceal ligation — Primary and secondary prevention of variceal bleeding include the use of nonselective beta blockers and endoscopic variceal ligation. Data from cohort studies suggest that strategies based on the recommendations for management of cirrhotic portal hypertension can be applied to patients with noncirrhotic portal hypertension, and that this approach results in similar outcomes [84,114].

Transjugular intrahepatic portosystemic shunt (TIPS) — TIPS is an option for treatment of complications of INCPH, but should be avoided in patients with poor renal function, ascites, and significant extrahepatic comorbidities (eg, prothrombotic condition, hematologic malignancy, solid organ transplantation). In a study of 41 patients with INCPH who underwent TIPS with a mean follow-up of 27 months, 7 of 25 patients with a history of variceal bleeding had recurrent bleeding (28 percent). The risk of mortality was higher in patients with extrahepatic comorbidities and elevated creatinine [115].

Other interventions — Several other interventions for INCPH have been reported [41,112,116]. Portosystemic shunt surgery has been shown to be an effective alternative for patients who fail endoscopic therapy [117-119]. However, shunt surgery has largely been replaced by TIPS. Splenectomy has been described in patients with symptomatic hypersplenism (spontaneous bleeding episodes, severe transfusion-dependent anemia, or repeated splenic infarcts) [41]. Case reports of patients with INCPH have also described splenic embolization and percutaneous transhepatic obliteration [112,116]. However, whether the benefit of these invasive interventions outweighs the risk is uncertain, and they are not routinely performed.

Liver transplantation — The indications for liver transplantation in patients with INCPH are similar to those for patients with cirrhosis and end-stage liver disease. Outcome data on liver transplantation in this setting are limited; small case series suggest that survival rates are favorable [69]. The risk of recurrence of INCPH after liver transplantation is not well-defined, but some cases of recurrent INCPH have been reported [120].

Anticoagulation — The role of anticoagulation in the management of INCPH remains unclear because of a lack of high-quality data demonstrating a benefit. INCPH is often associated with an underlying prothrombotic condition, and portal vein thrombosis frequently develops in patients with INCPH. Anticoagulation is not used for preventing portal vein thrombosis, but may be an option for patients with a hypercoagulable disorder [97].

The management of portal vein thrombosis in patients with INCPH is similar to the approach for patients with cirrhosis [84], and this is discussed separately. (See "Acute portal vein thrombosis in adults: Clinical manifestations, diagnosis, and management".)

Prognosis — Because of preserved liver function, the prognosis of patients with INCPH is better than that of patients with cirrhosis who have a similar degree of portal hypertension. Ten-year survival rates ranging from 56 to 82 percent have been reported for patients with INCPH [84,121]. However, a subgroup of patients progresses to develop advanced hepatic insufficiency, eventually requiring liver transplantation [122,123]. These patients generally have nodular transformation of the liver with extensive hepatic and portal fibrosis. A few case reports have suggested an association between INCPH and hepatocellular carcinoma, but whether other risk factors may have accounted for the observation is unclear [124,125]. Screening for hepatocellular carcinoma is not recommended for these patients. However, hypervascular benign lesions similar to focal nodular hyperplasia have been reported in 14 percent of patients with INCPH, and may be difficult to distinguish from HCC [126].

There are very few studies evaluating the long-term prognosis of patients with INCPH:

- One cohort study of Western patients suggested that overall survival was poorer compared with that of the general population, with a transplant-free survival of only 40 percent at 10 years [121]. However, the increased mortality in this study was related to non-liver related conditions and not to complications of portal hypertension or liver failure. Only 4 of 62 patients (6.5 percent) died from liver-related conditions.

- By contrast, another study reported good long-term outcomes in patients with biopsy-proven INCPH, with a 10-year transplant-free survival rate of 82 percent [84].

In both studies, the development of ascites was identified as a poor prognostic factor in patients with INCPH. In the latter study, the presence of a severe associated disorder (immunological disease or malignancy) was also identified as a poor prognostic factor [84].

Limited data have suggested that rates of sarcopenia in patients with INCPH were not significantly different compared with patients with compensated cirrhosis [127].

The prognosis for patients with PSVD without portal hypertension appears more favorable than INCPH (ie, PSVD with portal hypertension). In a study including 91 patients with PSVD without or with portal hypertension, PSVD alone was associated with lower rates of liver decompensation after three years compared with PSVD with clinical signs of portal hypertension (0 versus 11 percent) [128]. In addition, liver-related mortality rates were lower in patients with PSVD alone compared with PSVD with portal hypertension (0 percent versus 7 percent).

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Portal hypertension and ascites".)

SUMMARY AND RECOMMENDATIONS

- Cirrhosis is the most common cause of portal hypertension, but portal hypertension can also occur in the absence of cirrhosis, a condition referred to as "noncirrhotic portal hypertension." The causes of noncirrhotic portal hypertension can be divided into prehepatic, intrahepatic (presinusoidal, sinusoidal, and postsinusoidal), and posthepatic causes (table 1). (See 'Etiology' above.)

- Schistosomiasis is one of the most common causes of noncirrhotic portal hypertension worldwide [7].
  - Chronic hepatic schistosomiasis is characterized by features of portal hypertension: esophageal varices, hepatomegaly, and splenomegaly with hypersplenism. (See 'Clinical features' above.)
  - The diagnosis of schistosomiasis can be made by the detection of schistosomal eggs in the stool. (See 'Diagnosis' above.)
  - In addition to treating the underlying parasitic infection, management is aimed at preventing or treating the consequences of portal hypertension (predominantly variceal bleeding). (See 'Management' above and "Schistosomiasis: Treatment and prevention", section on 'Treatment' and "Overview of the management of patients with variceal bleeding" and "Methods to achieve hemostasis in patients with acute variceal hemorrhage" and "Primary prevention of bleeding from esophageal varices in patients with cirrhosis".)
- Idiopathic noncirrhotic portal hypertension (INCPH) is a clinical entity characterized by portal hypertension in the absence of all of the following: biopsy-proven cirrhosis, obstruction of extrahepatic portal vein or hepatic venous outflow tract, and other causes of noncirrhotic portal hypertension. The term porto-sinusoidal vascular disease (PSVD) includes patients with histologic features of INCPH but who do not have portal hypertension; in addition, PSVD does not exclude patients with portal vein thrombosis or with other chronic liver diseases. (See 'Idiopathic noncirrhotic portal hypertension/Porto-sinusoidal vascular disease' above.)
- The most common clinical presentation of INCPH is variceal bleeding, which is often relatively well tolerated due to preserved liver function. Development of portal vein thrombosis is a frequent event during the course of the disease. (See 'Clinical manifestations' above.)
- The diagnostic approach in a patient suspected of having INCPH includes the following: laboratory tests to rule out other causes of liver disease/noncirrhotic portal hypertension, hepatic imaging to rule out portal or hepatic vein occlusion, and liver biopsy to rule out cirrhosis. The differential diagnosis includes portal hypertension due to cirrhosis of any etiology and a variety of pre-, intra-, or postsinusoidal disorders associated with portal hypertension (table 1). (See 'Etiology' above and 'Diagnosis' above.)

- Management of INCPH is aimed at preventing or treating the consequences of portal hypertension (predominantly variceal bleeding). While data are limited in this population regarding the best approach to management, patients are typically managed in the same manner as those with portal hypertension due to cirrhosis. Patients also undergo screening for portal vein thrombosis (eg, with Doppler ultrasonography every six months). (See 'Management' above and "Schistosomiasis: Treatment and prevention", section on 'Treatment' and "Overview of the management of patients with variceal bleeding" and "Methods to achieve hemostasis in patients with acute variceal hemorrhage" and "Primary prevention of bleeding from esophageal varices in patients with cirrhosis".)

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Topic 3580 Version 32.0

GRAPHICS

Classification of noncirrhotic portal hypertension

Prehepatic
Portal vein thrombosis
Splenic vein thrombosis
Splanchnic arteriovenous fistula
Splenomegaly (eg, from lymphoma, Gaucher's disease*)
Intrahepatic
Presinusoidal
Schistosomiasis*
Idiopathic noncirrhotic portal hypertension (including nodular regenerative hyperplasia)
Primary biliary cholangitis
Sarcoidosis*
Congenital hepatic fibrosis
Primary sclerosing cholangitis
Hepatic arteriopetal fistula
Adult polycystic liver disease
Arteriovenous fistulas
Autoimmune cholangiopathy
Vinyl chloride toxicity*
Neoplastic occlusion of the intrahepatic portal vein
Mineral oil granuloma*
Sinusoidal
Arsenic poisoning
Vinyl chloride toxicity*
Drugs (eg, amiodarone, methotrexate)
Alcoholic liver disease*
Nonalcoholic fatty liver disease
Gaucher's disease*
Zellweger syndrome

Viral hepatitis
Chronic Q fever
Schistosomiasis*
Amyloid or light-chain deposition in the space of Disse
Acute hepatic injury
Mastocytosis
Agnogenic myeloid metaplasia
Acute fatty liver of pregnancy
Postsinusoidal
Sinusoidal obstruction syndrome (venoocclusive disease)
Budd-Chiari syndrome*
Alcoholic liver disease*
Chronic radiation injury
Vitamin A toxicity
Epithelioid hemangioendothelioma
Angiosarcoma
Sarcoidosis*
Mycobacterium avium or *M. intracellulare* infection
Mineral oil granuloma*
Posthepatic
IVC obstruction (eg, Budd-Chiari syndrome*)
Cardiac disease (constrictive pericarditis, restrictive cardiomyopathy)

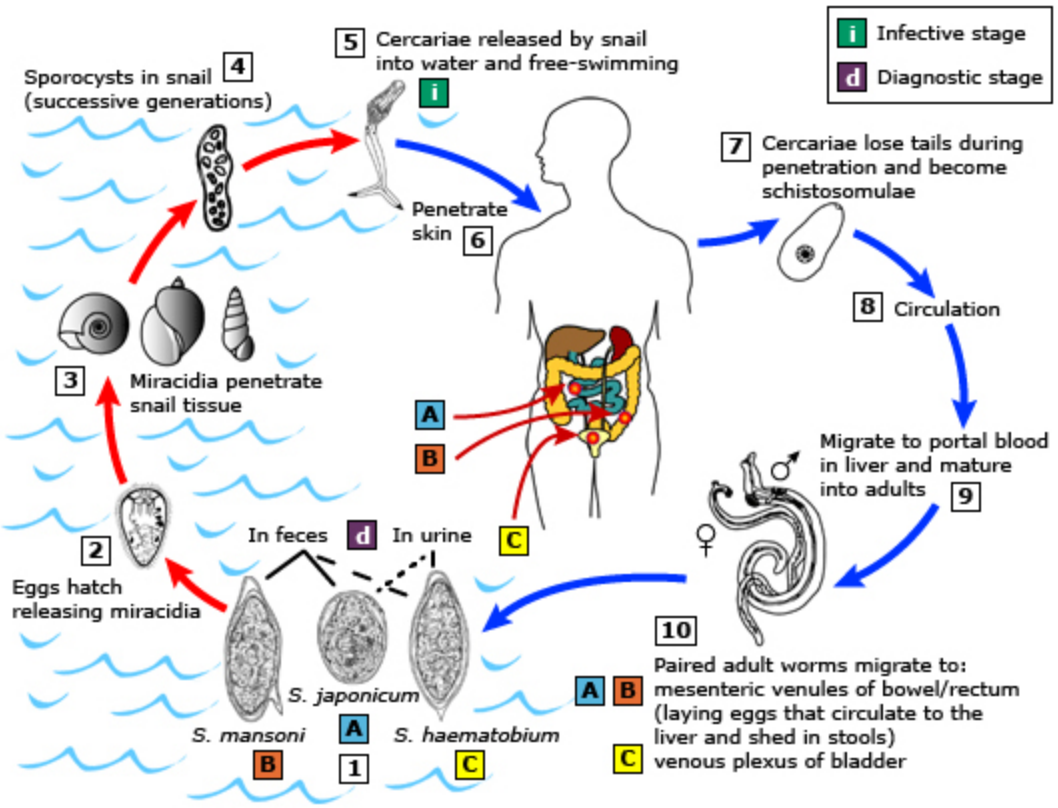
IVC: inferior vena cava.

* May cause noncirrhotic portal hypertension via several mechanisms.

Schouten JN, Garcia-Pagan JC, Valla DC, Janssen HL. Idiopathic noncirrhotic portal hypertension. Hepatology 2011; 54:1071.

Graphic 76516 Version 4.0

Life cycle of schistosomiasis



Life cycle: Eggs are eliminated with feces or urine **(1)**. Under optimal conditions, the eggs hatch and release miracidia **(2)**, which swim and penetrate specific snail intermediate hosts **(3)**. The stages in the snail include two generations of sporocysts **(4)** and the production of cercariae **(5)**. Upon release from the snail, the infective cercariae swim, penetrate the skin of the human host **(6)**, and shed their forked tail, becoming schistosomulae **(7)**. The schistosomulae migrate through several tissues and stages to their residence in the veins **(8,9)**. Adult worms in humans reside in the mesenteric venules in various locations, which at times seem to be specific for each species **(10)**. For instance, *S. japonicum* is more frequently found in the superior mesenteric veins draining the small intestine **(A)**, and *S. mansoni* occurs more often in the inferior mesenteric veins draining the large intestine **(B)**. However, both species can occupy either location, and they are capable of moving between sites, so it is not possible to state unequivocally that one species only occurs in one location. *S. haematobium* most often occurs in the venous plexus of bladder **(C)**, but it can also be found in the rectal venules. The females (size 7 to 20 mm; males slightly smaller) deposit eggs in the small venules of the portal and perivesical systems. The eggs are moved progressively toward the lumen of the intestine (*S. mansoni* and *S. japonicum*) and of the bladder and ureters (*S. haematobium*), and are eliminated with feces or urine, respectively **(1)**. Pathology of *S. mansoni* and *S. japonicum* schistosomiasis includes: Katayama fever, hepatic perisinusoidal egg granulomas, Symmers' pipe stem periportal fibrosis, portal hypertension, and occasional embolic egg granulomas in brain or spinal

cord. Pathology of *S. haematobium* schistosomiasis includes: hematuria, scarring, calcification, squamous cell carcinoma, and occasional embolic egg granulomas in brain or spinal cord.

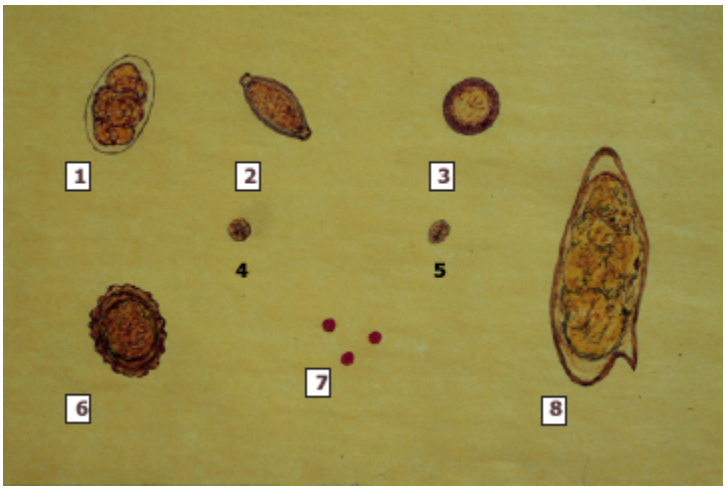
Human contact with water is thus necessary for infection by schistosomes. Various animals, such as dogs, cats, rodents, pigs, horses, and goats, serve as reservoirs for *S. japonicum*, and dogs for *S. mekongi*.

Geographic distribution: *Schistosoma mansoni* is found in parts of South America and the Caribbean, Africa, and the Middle East; *S. haematobium* in Africa and the Middle East; and *S. japonicum* in the Far East. *Schistosoma mekongi* and *S. intercalatum* are found focally in Southeast Asia and central West Africa, respectively.

Reproduced from: Centers for Disease Control and Prevention. DPDx: Schistosomiasis. Available at: http://www.cdc.gov/dpdx/schistosomiasis/.

Graphic 90007 Version 3.0

Appearance and relative sizes of stool ova and parasites

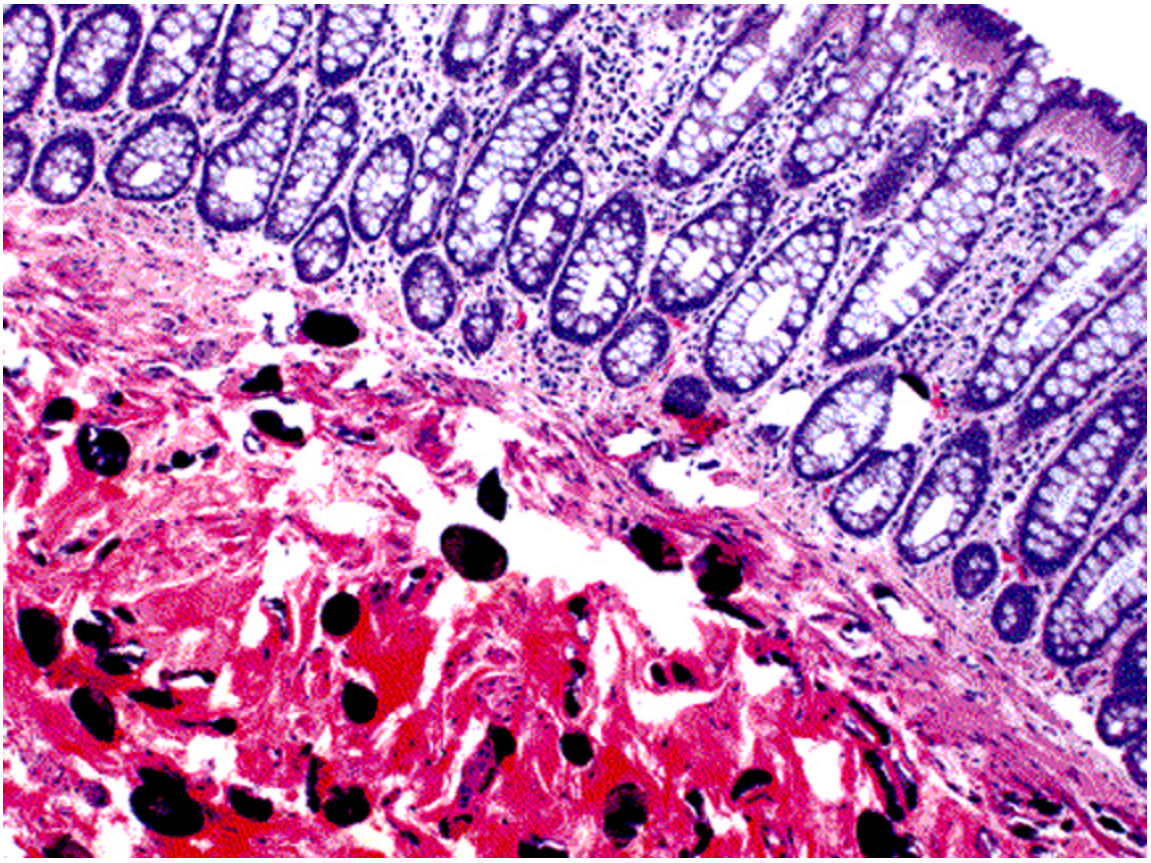


(1) Hookworm egg; (2) whipworm egg (*Trichuris trichura*); (3) *Taenia* egg; (4) *Entamoeba histolytica* cyst; (5) *Giardia lamblia* cyst; (6) infertile *Ascaris lumbricoides* egg; (7) red blood cells; (8) *Schistosoma mansoni* egg.

Courtesy of Harriet Provine.

Graphic 58729 Version 2.0

Calcified schistosomal ova in a rectal biopsy



Normal mucosa overlying a submucosal layer containing numerous calcified *Schistosoma japonicum* eggs.

Graphic 88449 Version 3.0

Disorders and medications associated with idiopathic noncirrhotic portal hypertension

Hematologic/neoplastic
Liver cancers
Sacrococcygeal teratoma
Essential thrombocytosis
Polycythemia vera
Myeloproliferative disorders
Lymphoproliferative disorders
Multiple myeloma
Spherocytosis
Sickle cell disease
Protein S deficiency
Factor V Leiden mutation
Hyperhomocysteinemia
Antiphospholipid syndrome
Immune
Primary biliary cholangitis
Polymyositis
Sjögren's syndrome
Scleroderma
CREST syndrome
Still's syndrome
Polyarteritis nodosa
Rheumatoid arthritis
Polymyalgia rheumatica
Systemic lupus erythematosus
Behçet's syndrome
Cryoglobulinemia
Idiopathic hypereosinophilic syndrome
Idiopathic thrombocytopenic purpura

Medications
Azathioprine
Thioguanine
Cyclophosphamide
Chlorambucil
Busulfan
Doxorubicin
Cytosine
Arabinoside
Bleomycin
Carmustine
Trastuzumab
Interleukin-2
Oxaliplatin
Miscellaneous
Liver transplantation
Renal transplantation
Atrial septal defect
Ventricular septal defect
Pulmonary vein anomalies
Congenital portal venous anomalies
VATER syndrome
Hereditary hemorrhagic telangiectasia
Cystinosis
Turner's syndrome

Celiac disease
Myasthenia gravis
HIV infection
Common variable immunodeficiency

CREST: calcinosis cutis, Raynaud phenomenon, esophageal dysmotility, sclerodactyly, telangiectasia; HIV: human immunodeficiency virus; VATER: Vertebral anomalies, anal atresia, TE fistula (tracheoesophageal fistula), renal defects.

Graphic 50663 Version 7.0

Histologic findings in patients with idiopathic noncirrhotic portal hypertension

Histologic feature*	Frequency (percent)
Irregular intimal thickening of portal veins	75-100¶
Organizing thrombus and/or recanalization of portal veins	20-100¶
Intralobular fibrous septa	95
Abnormal blood vessels in the lobules	75
Subcapsular atrophy	70
Dense portal fibrosis and portal venous obliteration	32-52
Periductal fibrosis of interlobular bile ducts	50
Portal inflammation	47
Nodular hyperplasia of parenchyma	25-40

* Needle biopsies from patients with idiopathic noncirrhotic portal hypertension are typically normal or show only nonspecific morphologic changes. Specific abnormalities are more commonly seen in larger wedge biopsies or autopsy specimens.

¶ Studies showing findings in 100 percent of patients were based upon autopsy specimens.

Data from:

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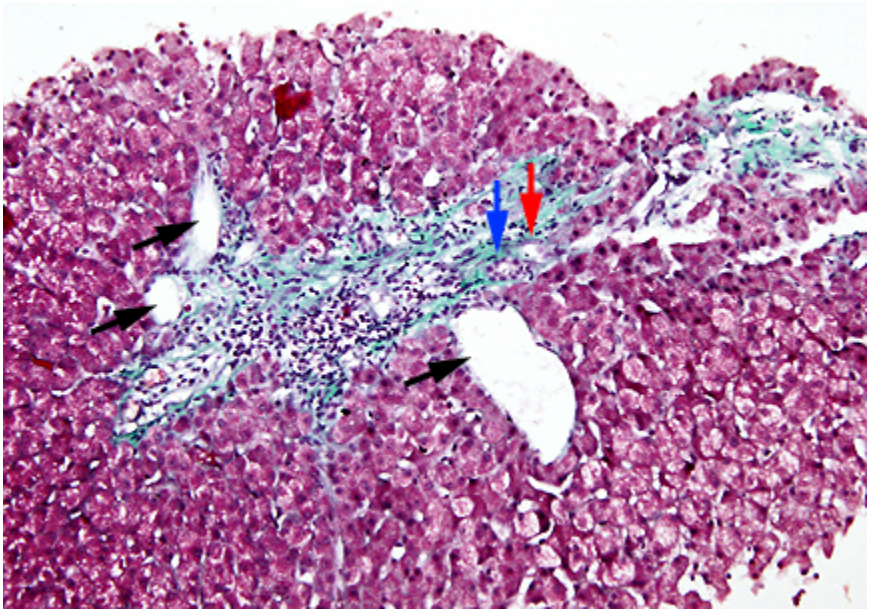
Graphic 80624 Version 5.0

Idiopathic portal hypertension (IPH)

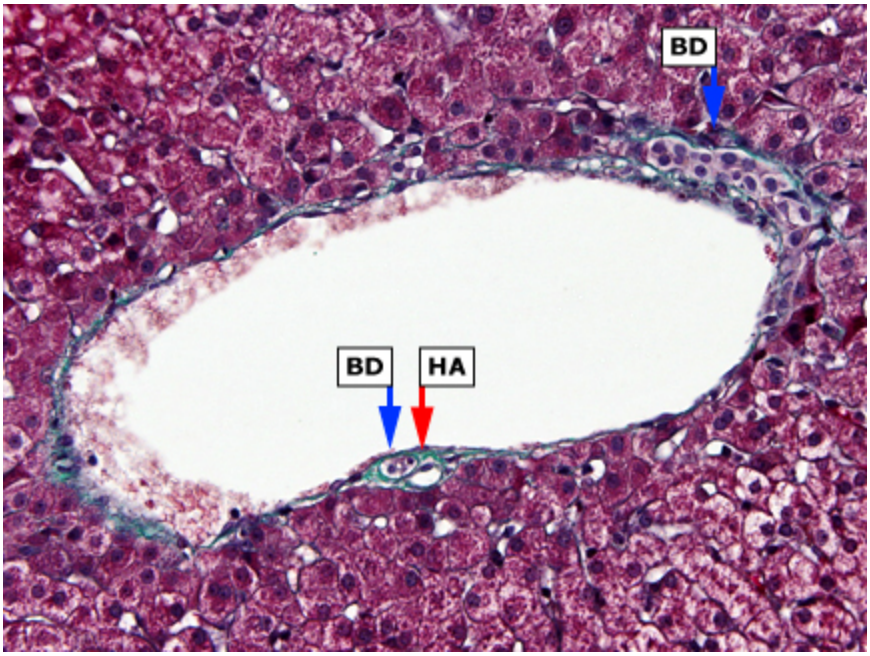


Masson's trichrome stain of a liver biopsy specimen in a patient with IPH showing portal tract fibrosis and mild chronic inflammation. There is no visible portal vein radicle. Some dilated aberrant vascular structures can be seen (black arrows) at the periphery of the portal tract. A relatively small bile duct (BD: blue arrow) and hepatic artery (HA: red arrow) are visible in the portal triad.

Courtesy of Rosa Miquel, MD.

Graphic 63404 Version 2.0

Idiopathic portal hypertension (IPH)



Masson's trichrome stain of a liver biopsy specimen in a patient with IPH showing marked abnormal dilatation of a portal vein radicle. The dilation is evident when comparing the portal vein radicle to the relatively small bile duct (BD) and hepatic artery (HA) in the portal triad.

Courtesy of Rosa Miquel, MD.

Graphic 51618 Version 2.0

Contributor Disclosures

Juan Carlos Garcia-Pagán, MD, PhD Grant/Research/Clinical Trial Support: Mallinckrodt [Portal hypertension in cirrhosis]; Novartis [Cirrhosis-Virus C]. Consultant/Advisory Boards: Cook Medical [Devices for hepatic vascular pressure measurements]; Shionogi [Chronic liver disease]; Vifor Pharma [Gastrointestinal bleeding]; WL Gore y Asociados [Portal hypertension and complications; TIPS]. All of the relevant financial relationships listed have been mitigated. **Jason Chang Pik Eu, MBBS, MRCP** No relevant financial relationship(s) with ineligible companies to disclose. **Sanjiv Chopra, MD, MACP** No relevant financial relationship(s) with ineligible companies to disclose. **Kristen M Robson, MD, MBA, FACG** No relevant financial relationship(s) with ineligible companies to disclose.

Contributor disclosures are reviewed for conflicts of interest by the editorial group. When found, these are addressed by vetting through a multi-level review process, and through requirements for references to be provided to support the content. Appropriately referenced content is required of all authors and must conform to UpToDate standards of evidence.

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