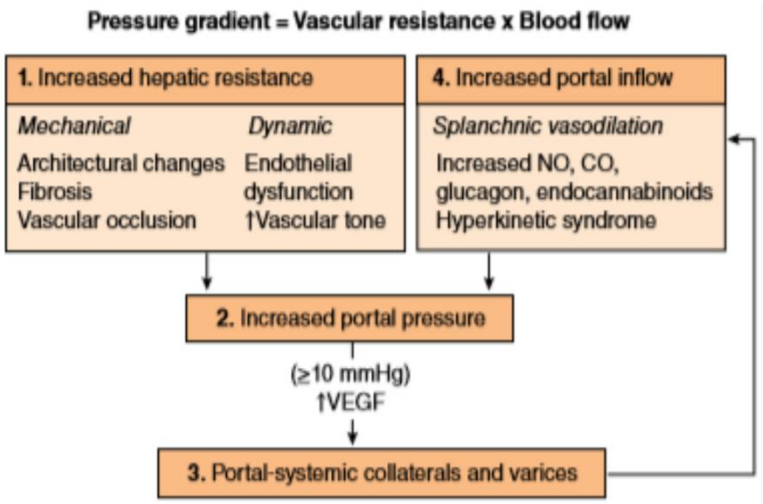
Lecture 6[2hrs]
Portal Hypertension [PHT

*Cirrhosis interferes with liver blood flow and function. This derangement produces the clinical features of portal hypertension and its complication's
*PHT characterized by increase in hepatic venous pressure gradient > 5 mm Hg
*The normal hepatic venous pressure gradient HVPG (the difference between the wedged hepatic venous pressure [sinusoidal pressure]and free hepatic venous pressure) is 5–6 mmHg.
*Clinically significant portal hypertension is present when the HVPG > 10 mm Hg.
*Patients developing clinical features or complications of PHT usually have portal venous pressure >12 mmHg.
*Portal pressure is the product of portal blood flow and intrahepatic resistance so any condition causing an increase in flow or resistance will increase portal pressure
P (pressure) =Q (blood flow) ×R (resistance).

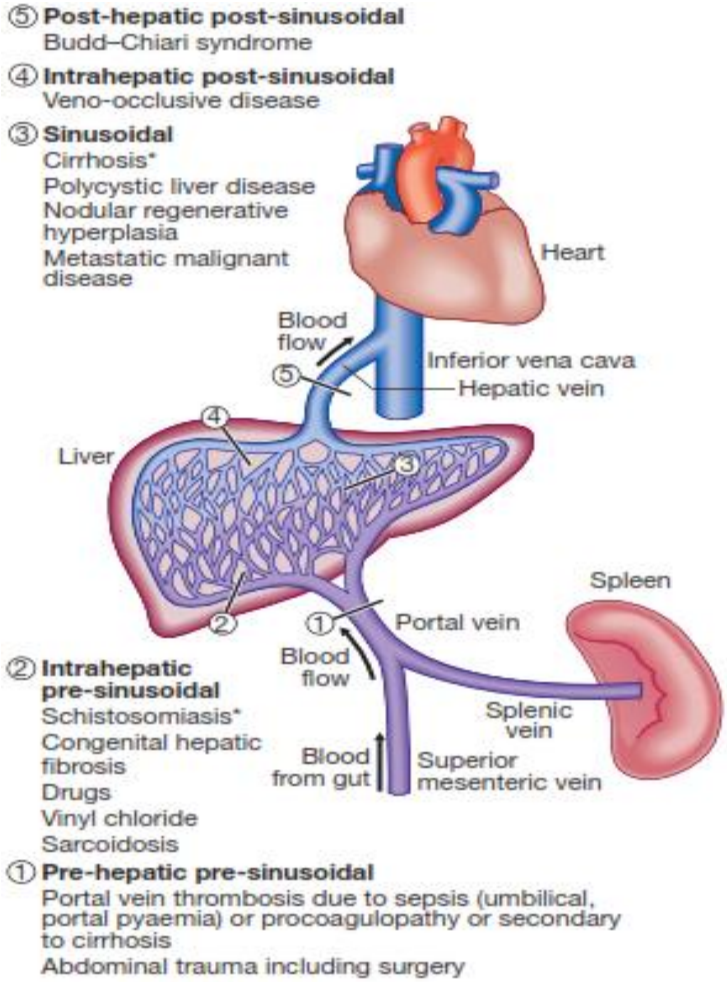
Pathophysiology

*The initial factor in the development of PHT is venous compression and/or obstruction leading to an increase in vascular resistance. This can occur at the pre-hepatic, sinusoidal, or post-hepatic levels.
*PHT secondary to Pre hepatic or posthepatic obstructive, stenotic, or constrictive vascular lesions develop because of increased resistance to flow in the vessels.
*In Cirrhosis obstruction occurs at the level of the sinusoid and affects the hepatic microcirculation.
*In a cirrhotic liver on-going fibro genesis result in the fibrosis, architectural and vascular occlusion causing [mechanical component] **and** release of many endogenous factors such as endothelin-1, α-adrenergic stimulus, and angiotensin II causing vasoconstriction [dynamic component] both factors cause vasoconstriction and increased vascular resistance. Causing increased portal pressure with the development of collaterals and varices.
*Another major component in the etiology of increased PHT is the increased portal venous inflow,
which occurs as a result of concomitant splanchnic arteriolar vasodilatation due to increasing nitric oxide and another mediator



Pathophysiology of PHT in cirrhosis.

Causes of PHT. Anatomically can be classified as
• Pre hepatic – a blockage of the portal vein.
• Hepatic – a disruption or change of liver architecture.
• Post hepatic – a blockage in the venous system after the liver
Another classification based the site of involvement relating to sinusoid: presinusoid, sinusoidal and post-sinusoidal



*Presinusoidal conditions generally have a well-preserved hepatocellular function and thus respond well to surgical shunting procedures.
*Whereas sinusoidal and post-sinusoidal conditions usually associated with hepatic insufficiency. *Ascites occurs only with sinusoidal and post sinusoidal hypertension.
*Increase portal vascular resistance leads to the development of portosystemic collateral vascular channels that link the portal venous and systemic venous circulation.
*Collateral vessel formation occurs in Esophagus, Stomach, Rectum, anterior abdominal wall, Renal, Lumbar, ovarian and testicular.
*Normally all the portal blood flows through the liver.
After the development of collateral vessels, about 1/2 or more and occasionally all of the portal blood flow can be shunted directly to the systemic circulation.

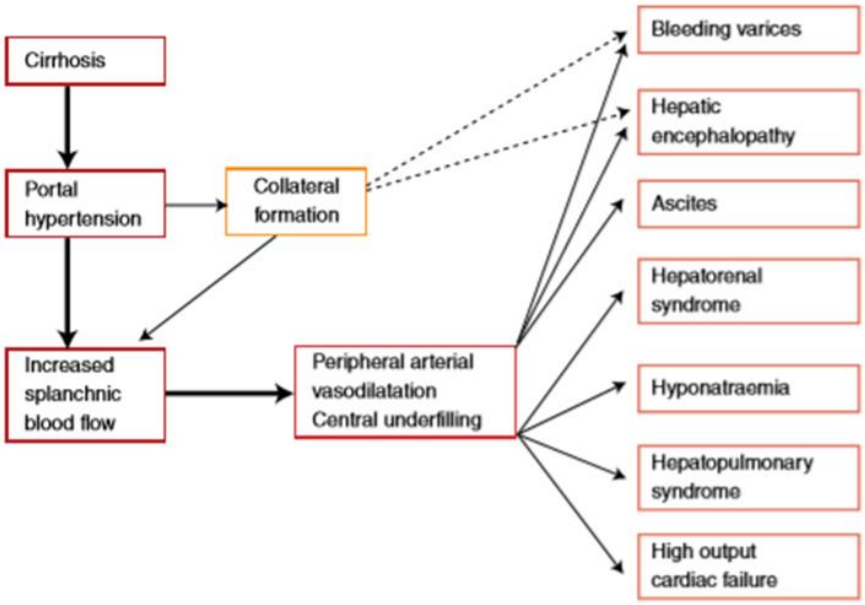
Clinical Features

*Splenomegaly is a cardinal finding and a diagnosis of portal hypertension.
*PHT is unusual when splenomegaly cannot be detected clinically or by ultrasonography.
*Collateral vessels may be visible on the anterior abdominal wall and occasionally radiate from the umbilicus to form a 'caput-medusae.
*Rarely a large umbilical collateral vessel has a blood flow sufficient to give a venous hum on auscultation (Cruveilhier–Baumgarten syndrome).

*The most important collateral vessel formation occurs in the esophagus and stomach, and this can be a source of severe bleeding. Rectal varices also cause bleeding and are often mistaken for hemorrhoids.
*Fetor hepaticus results from portosystemic shunting of blood, which allows mercaptans to pass directly to the lungs.
*Ascites occurs as a result of renal sodium retention and portal hypertension.

Complications of portal hypertension include

• Esophageal, gastric and rectal varices • Congestive gastropathy• Splenomegaly and hypersplenism • Ascites• Hepatic hydrothorax•Hepatorenal syndrome (type I and type II). •Hepatopulmonary syndrome • Hepatic encephalopathy.



Many of the complications of cirrhosis are due to arterial dilation and the hyperdynamic circulations

Esophageal Variceal Bleeding

*The lower end of the esophagus, between the left gastric vein (portal) and the azygos vein (systemic): when dilated, they are called esophageal varices
*Portal hypertension results in the formation of portosystemic collaterals and dilation of pre-existing collaterals.
*Varices are dilated and tortuous veins that develop to decompress the elevated hepatic sinusoidal pressure.
*Portal pressure must be at least 10 mmHg for gastroesophageal varices to develop and at least
12 mmHg for varices to bleed.
*Varices within 3–5 cm of the gastroesophageal junction are more likely to bleed because of less soft-tissue support.
*Gastroesophageal variceal bleeding produces large volume, brisk bleeding [Hematemesis and melena or hematochezia].

Risk factors for an initial bleeding episode include.

1-Severity of liver disease (Child-Pugh).**2**-Continuing alcohol consumption.

3-Endoscopic predictors of bleeding. The size of the varices. Presence of red spots and stripes corresponding to areas of thinning of the varix wall due to high wall tension.
4-Haemodynamic factors include. Portal pressure> 12 mmHg, Blood volume, Collateral blood flow. Intra-abdominal pressure.
5- Use of salicylates and NSAIDs. **6**-Bacterial infection**.**

1-Treatment of acute variceal bleeding includes.

General Resuscitation Measures.

*Securing the airway and stabilization of the circulation with blood, plasma because of shock decrease liver blood flow and leads to deterioration of liver function.
*Bleeding EV should be confirmed by OGD because Approximately 20% of upper GI bleeding episodes in patients with portal hypertension originate from non-variceal sources especially acute gastric erosions or peptic ulcer disease.

***Pharmacotherapy**

Vasoconstrictive drugs include

1- Octreotide synthetic form of somatostatin. these drugs suppress the release of vasodilatory hormones such as glucagon, causing splanchnic vasoconstriction and decreased portal inflow. *Dose 50 micrograms IV followed by infusion of 50 micrograms/hr. for 3-5 days.

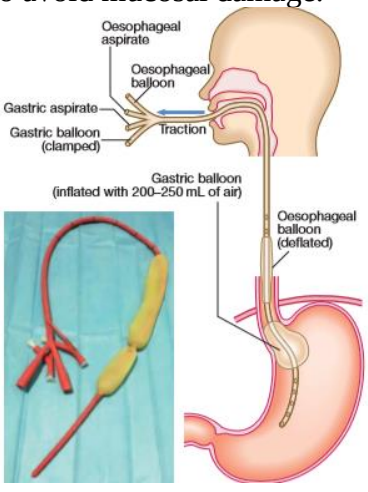
2-Vasopressin-infusions induce generalized arteriolar and venous constriction with resultant decrease PV flow and thus pressure.

***** Dose 0.4 U/min iv infusions until bleeding stops or for 24 hrs and then 0.2 U/min for further 24 hrs. Side effects of vasopressin include angina, Arrhythmia, myocardial infarction, and renal tubular damage to prevent these side effects nitroglycerin should be given Trans dermally or intravenous.
*Vasopressin should not be used in-patient with IHD [ischemic heart disease].

3-Terlipressin is an alternative to Vasopressin with certain advantages since vasopressin is released from it over several hrs in amounts sufficient to decrease portal pressure without producing systemic effects. *Dose 2 mg IV/6 hourly until bleeding stop and then 1 mg/6hr for 24 hr.

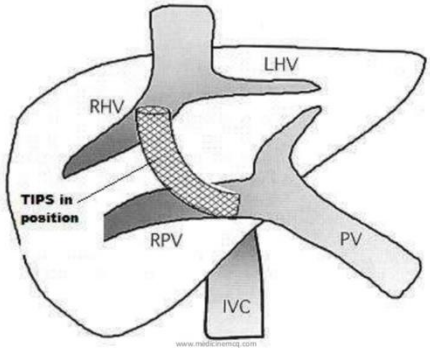
Mechanical modes of therapy

include inflatable balloons. Sengstaken- blakemor tube and Minnesota tube.
The disadvantage of a mechanical model of therapy includes- the risk of rebleeding following deflation, risk of aspiration, and esophageal perforation. It should be deflated for about 10 min every 3 hrs to avoid mucosal damage.



Sengstaken- blakemor tube for esophageal tamponed.

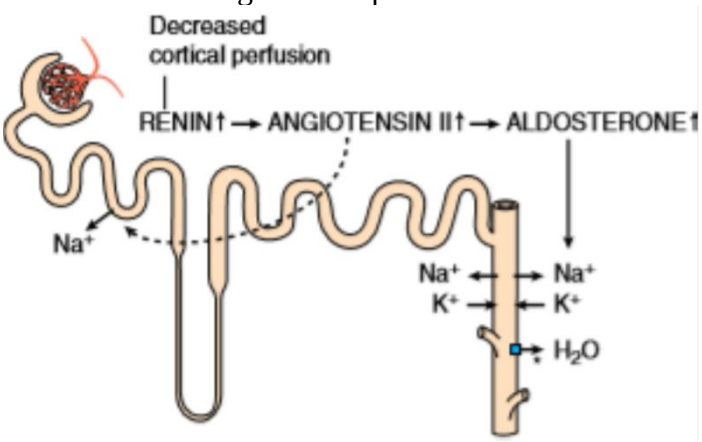
Endoscopical Therapy includes.
*Endoscopic variceal sclerotherapy and band ligation. For sclerotherapy, highly irritant solutions such as ethanolamine or polidocanol are injected through endoscopic direct vision into and around bleeding varix. The subsequent inflammation leads to thrombosis and fibrosis of the varix lumen.
Complications include *chest pain, *dysphagia * esophageal ulcerating *stricturing*perforation, and fever.
*Endoscopic band ligation -The varices are sucked into an endoscope accessory allowing them to be occluded with a tight rubber band. More effective and have fewer side effect than Sclerotherapy
Surgical Therapy. Include *Esophageal transaction. *Porto systemic shunts which include:
Porto-caval shunt, distal Spleno-renal shunt and transjugular intrahepatic Portosystemic stent-shunt [TIPSS]
Prevention of a first Variceal bleeding [Primary Prophylaxis].
Pharmacotherapy
Therapy aims to reduce HVPG <12 mmHg to prevent bleeding EV.
*Non- cardioselective beta-blocker [NSBB] reduces cardiac output, splanchnic arterial vasoconstriction this reduction leads to decrease flow and pressure within the portal vein, and this lead to decrease pressure and flow within the varices. NSBB are Propranolol, Nadolol, and Carvedilol starting in low dose and increasing dose step by step until reaching a reduction of resting heart rate by 25%, but not lower than 55/min. NSBB should be discontinued at the time of spontaneous bacterial peritonitis, Renal impairment and Hypotension
*Banding- is indicated in a patient who does not tolerate or have a contraindication to beta-blockers.
*Combining isosorbide 5-mononitrate [NO donor] with nonselective beta-blocker.
Prevention of Re-bleeding after an initial bleeding episode [secondary prophylaxis]
1-Non-Selective B Blocker. [NSBB]
2-Sclerotherapy*:* for preventing recurrent EV bleeding. injection repeated every 1-2 w.
3-Banding: -.
4-Porto systemic shunt include*Porto-caval*Spleno-renal shunt.
5-TIPSS: - Stent is placed between P.V and H.V in the liver to provide a Portosystemic shunt to decrease portal pressure. Carried out under radiological control throw the internal jugular vein. Hepatic encephalopathy may be aggravated and require the shunt to be reduced.



Portal Hypertensive Gastropathy [PHGP]
Long-standing portal hypertension causes chronic gastric congestion recognizable at endoscopy as multiple areas of punctate erythema ('snakeskin gastropathy'). These areas may become eroded, causing bleeding from multiple sites. Acute bleeding can occur but repeated minor bleeding causing iron-deficiency anemia is more common. Treatment - Anemia by oral iron supplements or repeated blood transfusions and Reduction of the portal pressure using propranolol 80-160 mg/day. If this is ineffective a TIPSS procedure can be undertaken**.**

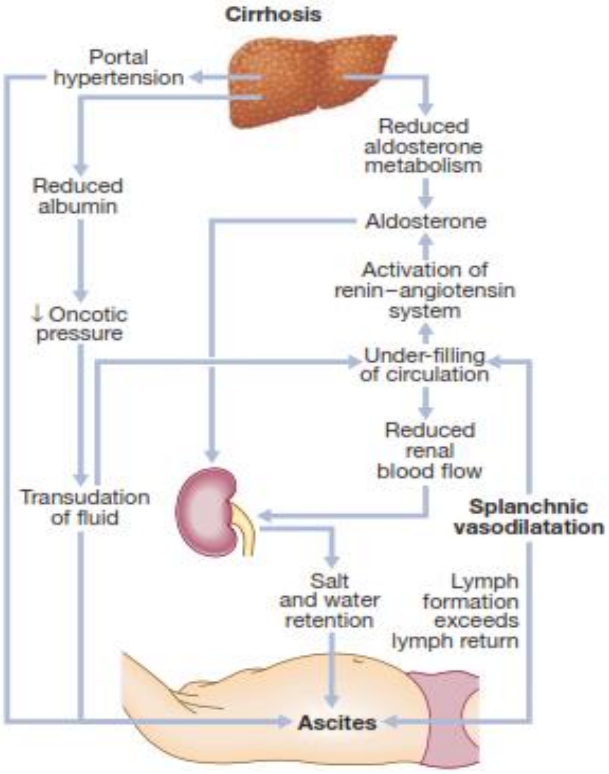
Ascites

*Ascites is a pathological accumulation of fluid within the peritoneal cavity.
Causes of ascites are *Malignant disease [liver or peritoneal] * Liver cirrhosis or heart failure *Peritoneal infections like [TB and SBP] *hepatic Veno-occlusive disease [budd-chiari syndrome] *hypoproteinemia *Pancreatic disease* lymphatic obstruction* Hypothyroidism
*Meigs syndrome [ovarian tumor with ascites and pleural effusion that resolves after resection of tumor] *Peritoneal dialysis.
Pathogenesis of Cirrhotic Ascites - 2 Theory that may explain ascites
1-The underfill theory [Sodium retention] - When ascites formation begins there is a contraction of the intravascular fluid compartment with an increase in the plasma oncotic pressure this results in a secondary increase in renal sodium retention in an attempt to compensate**.**
2-The peripheral vasodilatation Theory.
Splanchnic vasodilatation is mediated by vasodilators nitric oxide results in an increase in vascular capacitance and a decrease in effective plasma volume. In response to the reduction in pressure at the carotid and renal baroreceptors, there is a compensatory activation of the Renin-angiotensin-aldosterone system, Sympathetic nervous system, and Antidiuretic hormone. These neurohormonal mechanisms causing an increase in sodium and water retention resulting in the expansion of the extracellular fluid.



Mechanisms of increased Na and water reabsorption in cirrhosis, increased ADH stimulated water in the collecting system.
*A local hydrostatic pressure increases due to portal hypertension, resulting in an increased production of lymph in the hepatic and splanchnic regions, and Transudation of the fluid into the peritoneal cavity causes ascites.
• Low serum albumin levels (hypoalbuminemia), due to decreased liver synthesis, causing a low plasma oncotic pressure lead to the excess extracellular fluid accumulates in the peritoneal cavity.

• Secondary hyperaldosteronism with reduced catabolism of this salt-retaining hormone in the liver



Pathogenesis of cirrhotic ascites

Pathogenesis of Non-Cirrhotic Ascites

1-Malignant Ascites. The mechanism of fluid retention in patients with malignancy-related ascites depends on the location of the tumor

a-Peritoneal carcinomatosis produces proteinaceous fluid by tumor cells lining the peritoneum. extracellular fluid enters the peritoneal cavity to reestablish oncotic balance.

b-Fluid accumulates in patients with massive liver metastases because of portal hypertension caused by or occlusion of portal veins by tumor nodules or tumor emboli.

c-In hepatocellular carcinoma. Ascites arises because of the underlying cirrhosis related portal hypertension, tumor-induced portal vein thrombosis, or both.

d-Chylous ascites in patients with malignant lymphoma caused by lymphatic obstruction by tumor and rupture of chyle -containing lymphatics.

2-Cardiac Ascites and Nephrotic Syndrome. both conditions causing decrease Effective arterial blood volume. Decreased effective blood volume leads to activations of the vasopressin, renin-aldosterone, and sympathetic nervous systems causing renal vasoconstriction, sodium, and water retention .fluid then sweeps from the congested lymphatic sinusoids.

3-TB, Chlamydia, and Coccidioidomycosis cause ascites by the production of proteinaceous fluid. extracellular fluid enters the peritoneal cavity to reestablish oncotic balance.

4-Pancreatic or Biliary Ascites. Fluid accumulates by leaking pancreatic juice or bile into the peritoneal cavity or forms secondary to chemical burns of the peritoneum.

Evaluation of the Patient with Ascites

History

History of alcohol, risk factors for chronic viral hepatitis, injecting drugs use, blood transfusion, tattoos, acupuncture, and ear piercing

*****Acute onset of uncontrollable ascites can be associated with Budd-Chiari syndrome

*Ascites associated with fever and or abdominal pain may indicate ascitic fluid infection or malignancy.

*Cirrhotic ascites usually painless unless bacterial peritonitis or alcoholic hepatitis is superimposed.

*Abdominal pain and weight loss in the absence of stigmata of CLD suggest malignant ascites

*Symptoms and signs of heart failure indicate- cardiac ascites,

*Hx of diabetic patients and anasarca indicate- Nephrotic syndrome

*Hx of acute or chronic pancreatitis.

*Hx of biliary surgery may indicate bile leak.

Physical Examination

Physical Signs Suggestive of Portal Hypertension and Cirrhosis

*Spider telangiectasia and palmar erythema.

*Abdominal wall collaterals.

*Splenomegaly.

*Asterixis due to hepatic encephalopathy.

The physical finding of ascites-

Abdominal examinations reveal

* Fullness in the flanks* dilated abdominal vein [caput medusa*Shifting dullness on percussion become evident when peritoneal fluid >1500 mL

*Ttransmitted thrill occurs intense ascites*Hernia * divarication of the abdominal recti

*Distortion or eversion of umbilicus *Abdominal striae, Meralgia paresthetica., Scrotal and leg edema is found with severe fluid retention.

*A pleural effusion can accompany ascites and it is usually on the right side. This is due to the presence of a diaphragmatic defect which allows ascitic fluid to pass into the pleural cavity.

*Occasionally only a pleural effusion is present without any ascites[hepatic hydrothorax**].**

*Hepatomegaly and elevated jugular venous pressure occurs in severe heart failure, constrictive pericarditis, and hepatic venous outflow obstruction.

*Umbilical Sister Mary Joseph nodule indicates peritoneal carcinomatosis.

Investigation: -

* US is the investigation of choice for detecting ascites as little as 100mL, may valuable in differentiating obesity from ascites and detecting ovarian or mesenteric masses. And of the presence of splenomegaly.

*Abdominal radiographs can show ascites but they are insensitive and non-specific.
*Chest X-ray may show hydrothorax.

Ascitic Fluid Analysis

Diagnostic Paracentesis. (if necessary under ultrasonic guidance) can be used to obtain ascitic fluid for analysis. Indications of diagnostic paracentesis include
1-Sudden increase in the amount of ascitic fluid 2-worsening of encephalopathy.
3-Abdominal pain and fever to rule out SBP, hepatocellular carcinoma, or other non-cirrhotic causes of ascites.

Procedure

A 22 gauge needle can be inserted in a Z tract technique below the level of percussed dullness [to minimize leakage of fluid after the paracentesis] in the midline between the umbilicus and the pubic symphysis to avoid collateral vessels .in the presence of a midline scar a position 1.5 inches above and medial to the anterior superior iliac spine can be used safely.

***Examination of ascitic fluid include**

1-Color

*Pale straw indicates [Cirrhosis, nephrotic and cardiac failure].
*Hemorrhagic fluid indicate[carcinomatosis, pancreatitis ,tuberculosis].
*Turbid fluid indicates infection and pancreatitis].
*Malignant disease [Bloody.]
*Biliary communication [bile staining dark-brown fluid]
*Lymphatic obstruction [Milky, white (chylous).

2-Protein

< 25 gr/L transudate occur in [cirrhosis or Hypoalbuminemia].
> 25gr/L exudates occur in [malignancy, inflammation or Budd-chiari syndrome].
Protein: <1.5 g% in ascitic fluid is associated with an increased risk of SBP.

A Serum-Ascitic Albumin Gradient (SAAG)= Serum albumin- ascitic fluid albumin obtained on the same day.
SAAG > 1.1g % has a > 97% accuracy in predicting PHT as a cause of ascites.
SAAG < 1.1g% confers a > 97% accuracy in excluding portal hypertension as a cause of the ascites.

Causes of SAAG < 1.1 g% include- Peritoneal carcinomatosis, TB,Pancreatic disease
Causes of SAAG > 1.1 g% include Cirrhosis, congestive heart failure, Budd-Chiari syndrome, constrictive pericarditis, *veno*-occlusive disease, Hypoalbuminemia, Massive liver metastases, and Myxedema.

3-Ascitic fluid cell count.

Ascitic fluid with >250 polymorphonuclear neutrophils [PMNs]/mm3 is indicative of spontaneous bacterial peritonitis (SBP).

4-Culture and sensitivities ± AFB (if TB likely).
5-Cytology: especially when malignancy is suspected.
6-Amylase: if pancreatic etiology likely.
7-Glucose and LDH: decreased glucose and increased LDH is suggestive of secondary bacterial peritonitis.
Urine protein-[24 hr collection].
Echocardiography-[to exclude cardiac cause].
Laparoscopy.