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Pathophysiology of ascites in cirrhosis

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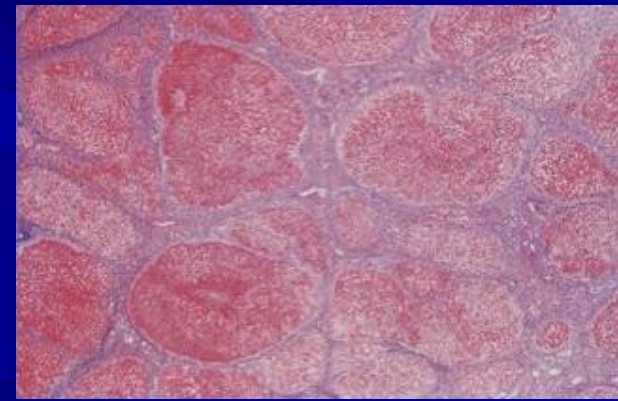
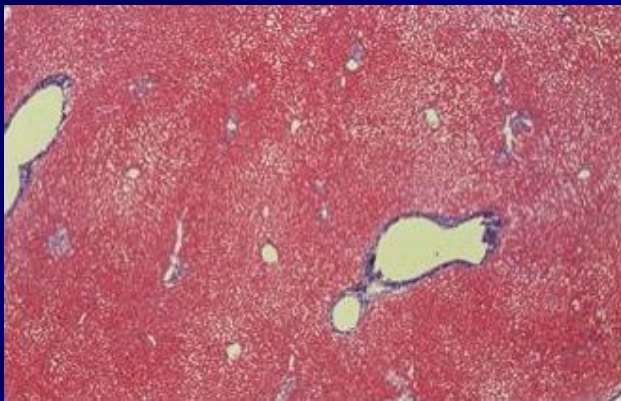
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Objectives

- To understand basic pathophysiologic steps in the development of ascites secondary to cirrhosis.
- To correlate the anatomic and pathophysiologic changes with clinical manifestations.
- To understand the basic steps in evaluation of patients with ascites

Cirrhosis: Late stage of chronic liver inflammation and fibrosis, in which liver parenchyma is distorted and replaced by fibrous tissue and regenerating nodules.



NORMAL LIVER

CIRRHOTIC LIVER

Causes of Cirrhosis

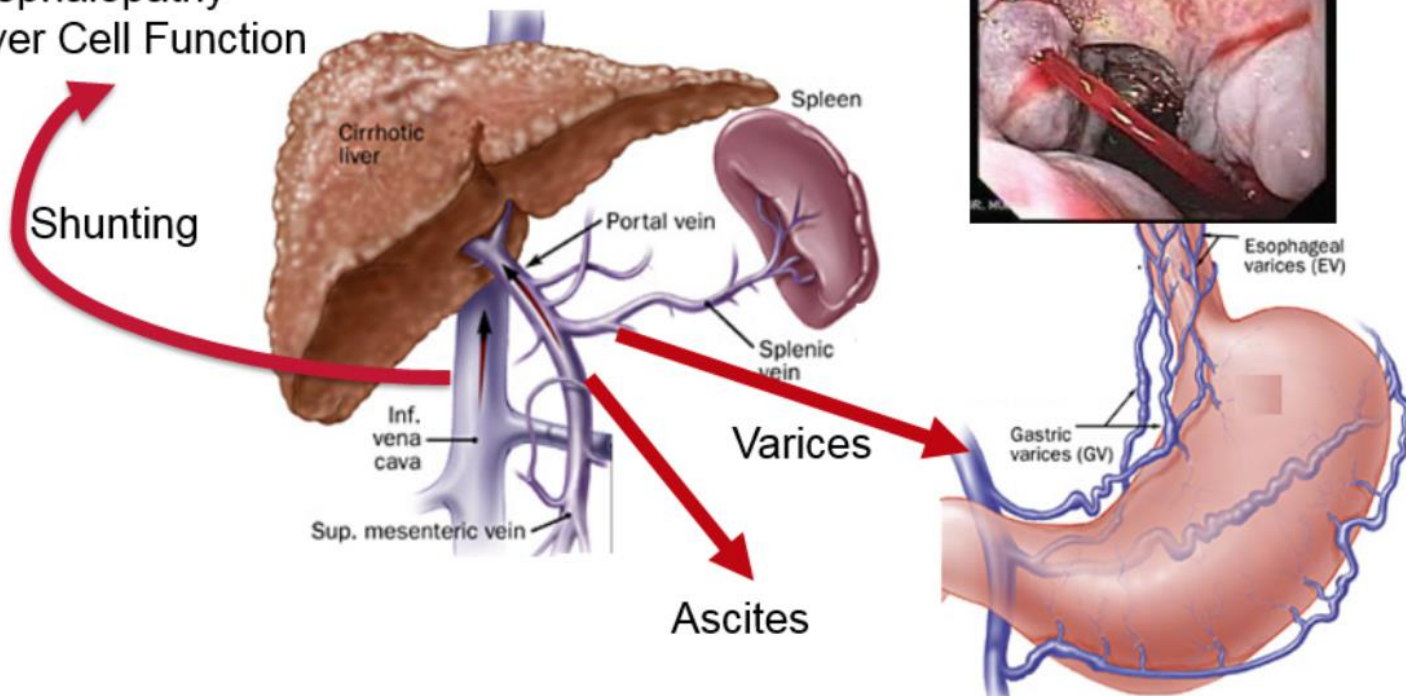
Commonest

- Viral (HBV+- HDV, HCV)
- NASH
- ASH

Other causes

- Autoimmune (AIH, PBC, PSC)
- Metabolic & Hereditary WD, A1AT, HH
- Vascular BCS, HF
- Biliary SC
- Drugs

Encephalopathy
↓ Liver Cell Function



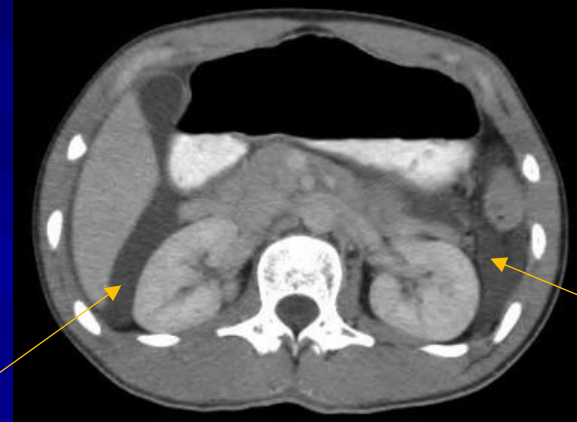
Definition

The pathologic accumulation of fluid in the peritoneal cavity

- It is the most common complication of cirrhosis

Ascites:

- Cirrhosis 85%
- Other causes 15 %



- The development of ascites is the final consequence of a series of anatomic, pathophysiologic, and biochemical abnormalities occurring in patients with cirrhosis.
- The formation of ascites is governed by the same principles as edema formation at other sites: net capillary permeability and the hydraulic and oncotic pressure gradients.

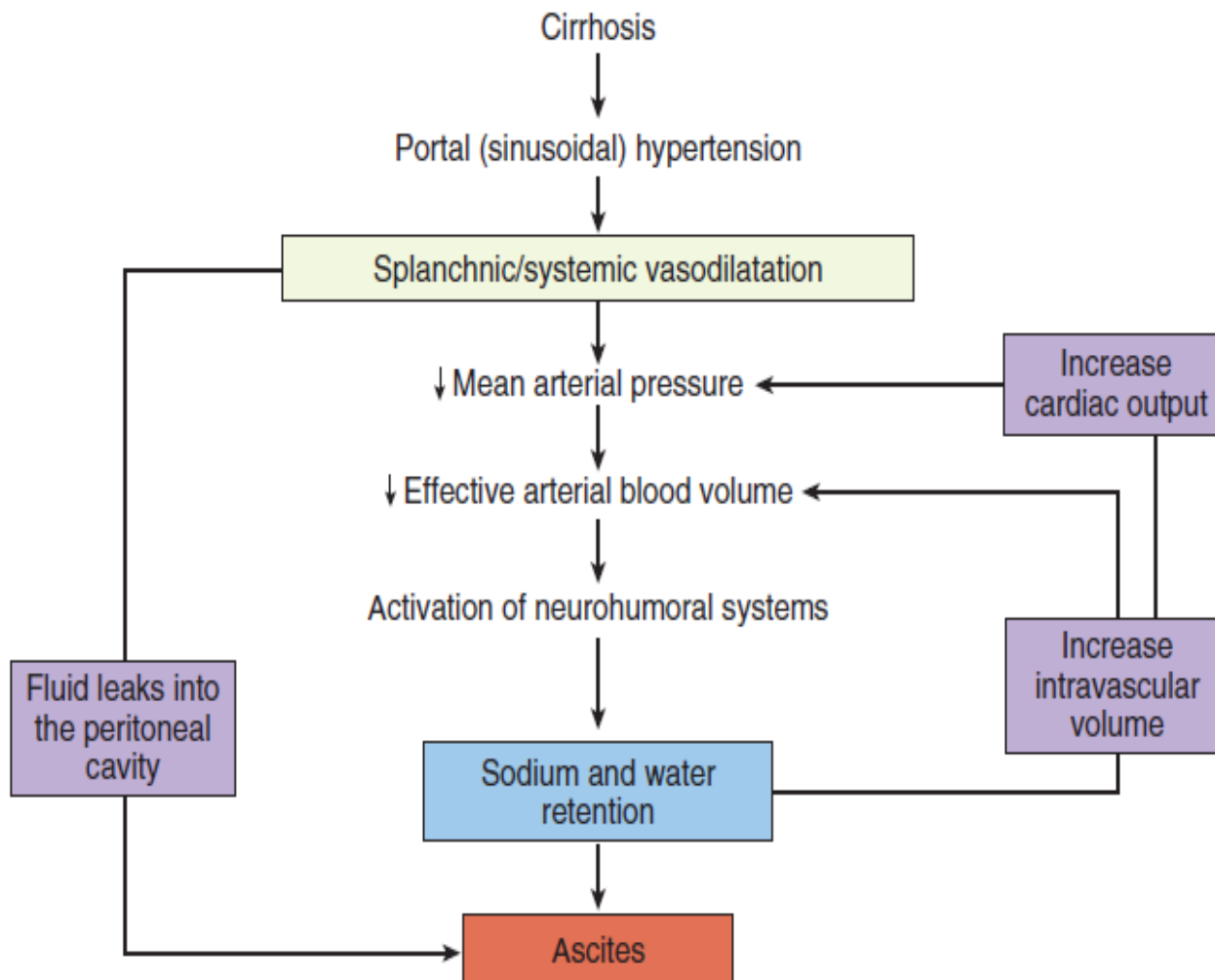
PORTAL HYPERTENSION

- The development of portal hypertension (PHT) is the first step toward fluid retention in the setting of cirrhosis.
- Patients with cirrhosis but without PHT do not develop ascites or edema
- A portal pressure >12 mmHg appears to be required for fluid retention

PORTAL HYPERTENSION

2 main mechanisms involved in portal hypertension:

- 1-Mechanical (due to structural changes in the liver with fibrosis and regenerative nodules)
- 2-Hemodynamic (circulatory, vascular, functional, and biochemical abnormalities)



Vasodilation(VD)

- Portal hypertension leads to VD

Mechanisms of vasodilation

- Increase production of nitric oxide (NO), which is the primary mediator of VD in cirrhosis (for splanchnic and peripheral vasodilation).
- Increased levels of other circulating VDs. (Glucagon , vasoactive intestinal peptide(VIP), prostacyclin.

production of these VDs may be stimulated by endotoxins or other bacterial products

VD

- VD initially develops in the arterial splanchnic circulation (i.e., the mesenteric arteries).
- Subsequently, vasodilation develops in the arterial systemic circulation.

Hyperdynamic circulation

- Systemic consequences to VD
 - reduction in systemic vascular resistance (SVR)
 - reduction in mean arterial pressure (MAP)
 - increase in cardiac output
 - hyperdynamic circulation

Usually patients with cirrhosis and ascites have hyperdynamic circulation.

CONSEQUENCES OF VASODILATION

- Activation of endogenous vasoconstrictors
- Sodium and water retention
- Increase renal vasoconstriction.

Pathogenic mechanisms responsible for the activation of vasoactive systems and hyperdynamic circulation in cirrhosis



Activation of endogenous vasoconstrictor agents

- VD → The reduction in pressure (or stretch) at the carotid and renal baroreceptors → activation of the sodium-retaining neurohumoral mechanisms (in an attempt to restore perfusion pressure to normal
 - *renin-angiotensin-aldosterone system*
 - *sympathetic nervous system*
 - *antidiuretic hormone (vasopressin)*.
- The net effect is avid sodium and water retention

Sodium retention

- impaired sodium excretion

Water retention

- Initially water excretion is normal in patients with cirrhosis before the development of ascites and then becomes increasingly impaired as the liver disease progresses. (Increase ADH)
- Thus, patients with cirrhosis and ascites usually demonstrate urinary sodium retention, increased total body sodium, and dilutional hyponatremia.

Renal vasoconstriction —

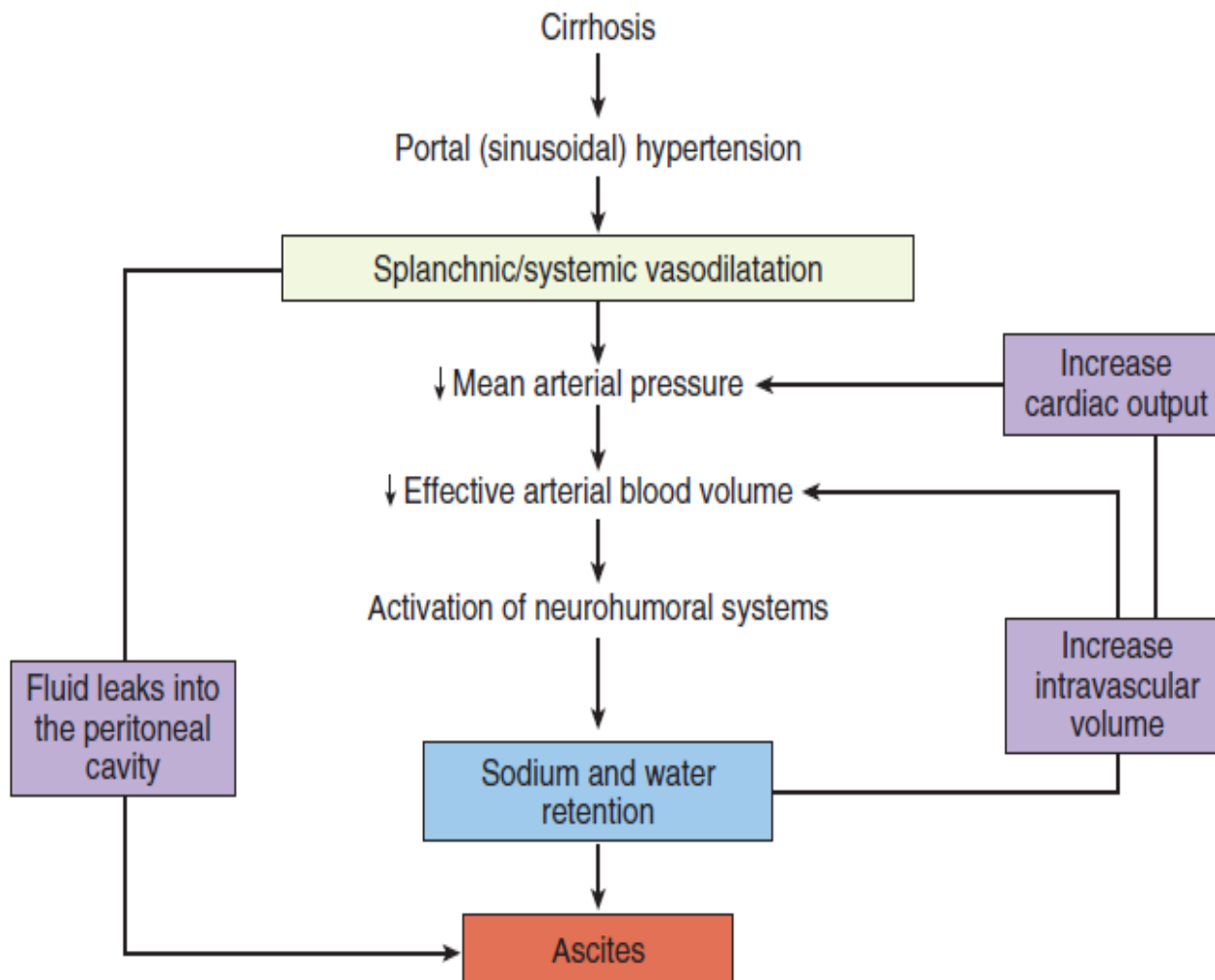
- VC → renal hypoperfusion → decrease GFR → (in some patient hepatorenal syndrome)

So ultimately

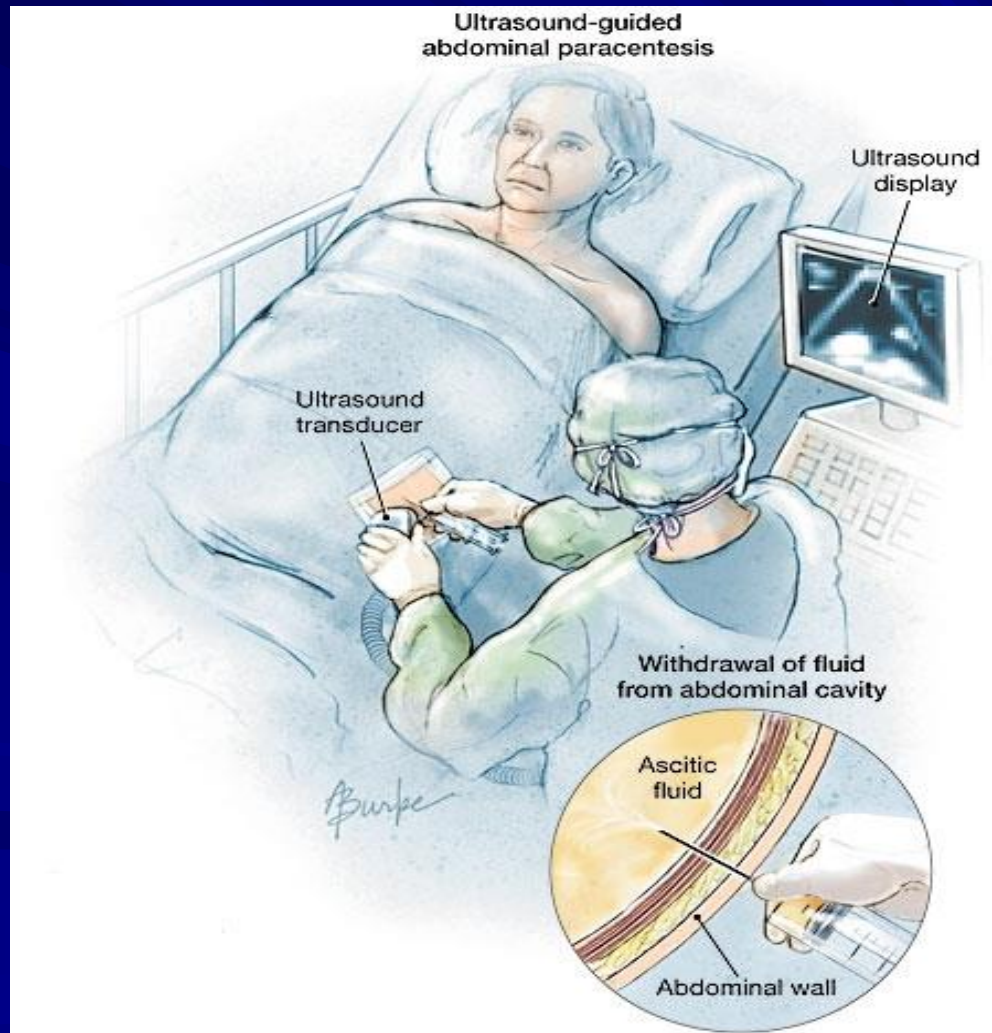
- This excess retained blood volume is thought to leak-out (filtered) (extravasate) directly from both the liver surface, and the mesenteric vessels.
- due to:
 - increased hydrostatics pressure
 - Increase vascular wall permeability
 - **concurrently decreased oncotic (osmotic) pressure (hypoalbuminemia)**

Abnormalities in patients with cirrhosis and ascites

Circulatory	Vascular	Functional	Biochemical
Reduced systemic vascular resistance	Splanchnic vasodilation	Activation of systemic vasodilator factors	Sodium retention
Reduced arterial pressure	Renal artery vasoconstriction	Activation of systemic vasoconstrictor factors	Water retention
Increased heart rate	Pulmonary vasodilation	Activation of renal vasodilator factors	Increased systemic nitric oxide
Increased cardiac index		Reduced glomerular filtration rate	Increased systemic prostaglandins
Increased plasma volume			Increased renal nitric oxide and prostaglandins
Reduced renal blood flow			
Increased portal blood flow			



Any new ascites should be tapped and analyzed!



Ascitic Fluid Analysis

ROUTINE	OPTIONAL (WHEN THERE IS SUSPICION OF INFECTION)	UNUSUAL	UNHELPFUL
Cell count and differential	Culture in blood culture bottles	AFB smear and culture	pH
Albumin	Glucose	Cytology	Lactate
Total protein	Lactate dehydrogenase	Triglyceride	Cholesterol
	Amylase	Bilirubin	Fibronectin
	Gram's stain		Glycosaminoglycans

Abbreviation: AFB, acid-fast bacteria. *Adapted from Runyon.¹⁷ Reprinted with permission from Saunders Elsevier.



Measure **SAAG**

Serum-to-Ascites Albumin Gradient (SAAG)

High SAAG ≥ 1.1 g/dL

- Cirrhosis
- Heart failure/constrictive pericarditis
- Alcoholic hepatitis
- Budd chiari
- Massive hepatic metastases

Low SAAG < 1.1 g/dL

- Peritoneal carcinomatosis
- Peritoneal tuberculosis
- Secondary peritonitis
- Pancreatitis
- Serositis
- Nephrotic syndrome

Initial treatment of ascites

- 1-Dietary sodium restriction
 - Limiting sodium intake to 88 meq (2000 mg) per day
- 2-Diuretics (most successful therapeutic regimen is the *combination* of Spironolactone and Furosemide)
 - Monitor electrolytes and kidney function
- Discontinue non-steroidal anti-inflammatory drugs
- Rx of underlying cause
- Evaluation for liver transplantation

Take home message-1

- Ascites is the most common liver cirrhosis complication.
- Development of ascites indicates advanced stage of liver disease and poorer prognosis.
- Development of ascites is complex process.
- Portal hypertension is first step in ascites development in patient with cirrhosis.
- Portal hypertension and possible bacterial toxin trigger VDs.

Take home message-2

- VD with activation of secondary mechanisms;
 - *renin-angiotensin-aldosterone system*
 - *sympathetic nervous system*
 - *antidiuretic hormone (vasopressin).*

*LEADS TO SALT AND WATER RESTENTION and
Increase plasma volume*

All these with hypoalbuminemia and increase vascular permeability lead to fluid extravasation.

Thank you