Pathophysiology of Ascites in Cirrhosis

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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

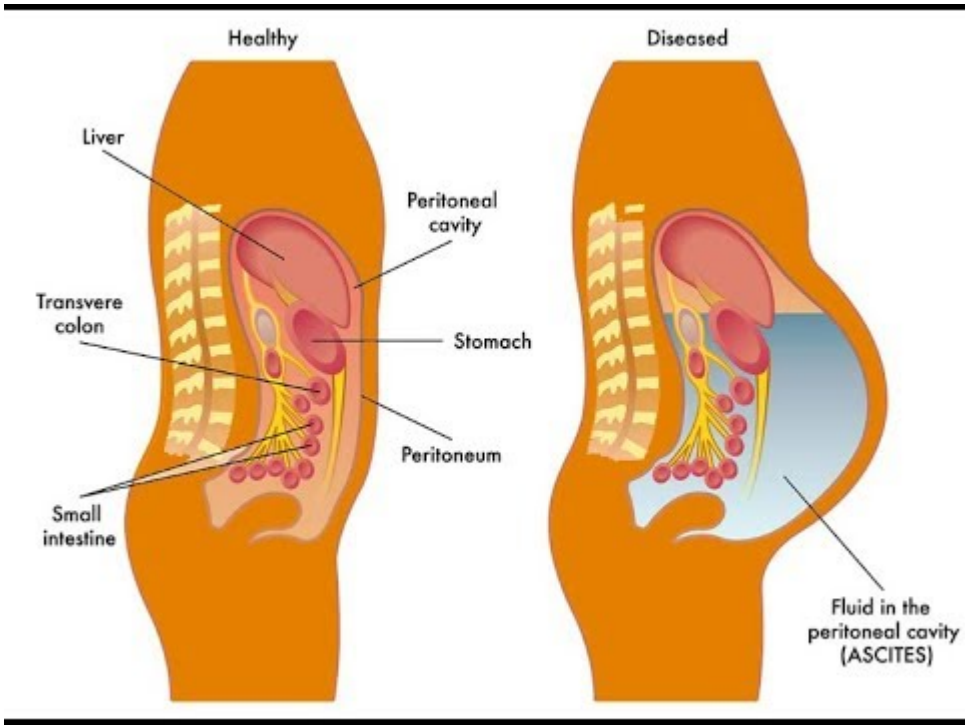
Definition

The pathologic accumulation of fluid in the peritoneal cavity

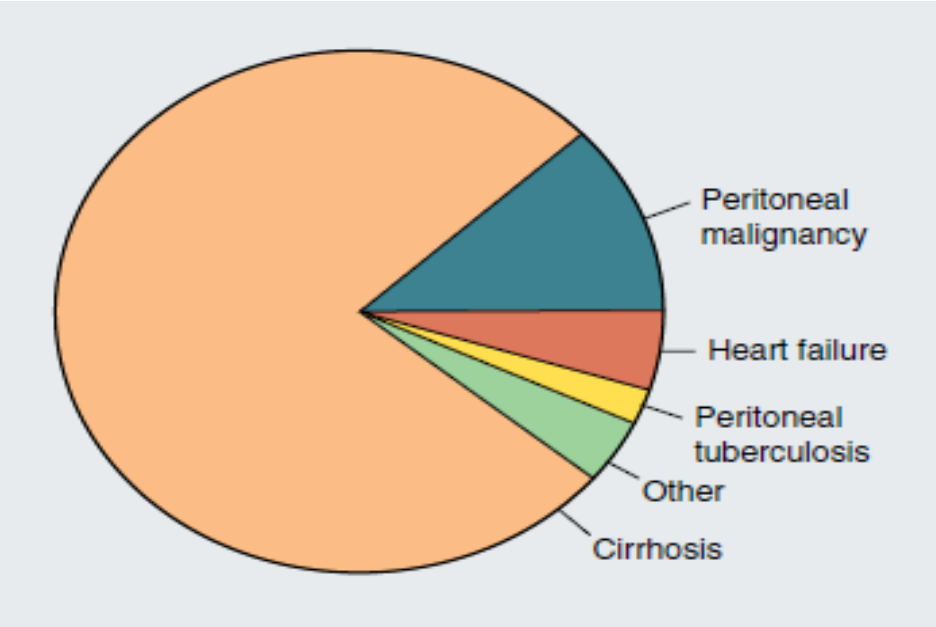
- It is the most common complication of cirrhosis

Ascites:

- Cirrhosis 85%
- Other causes 15 %

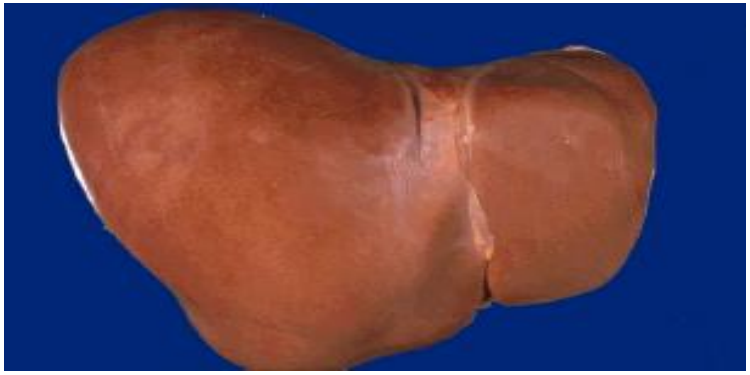


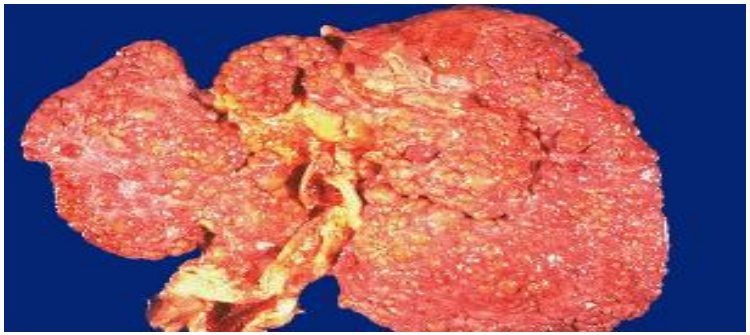
Causes of ascites

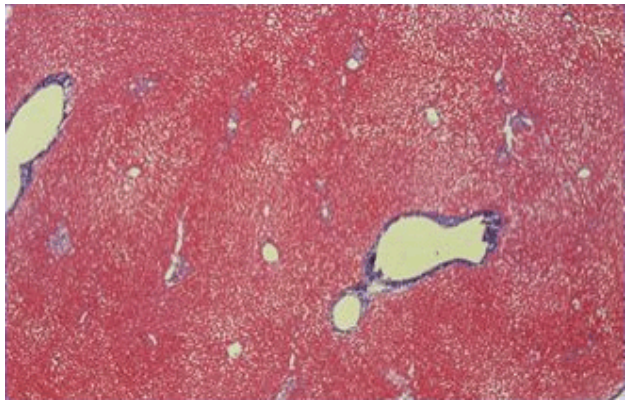


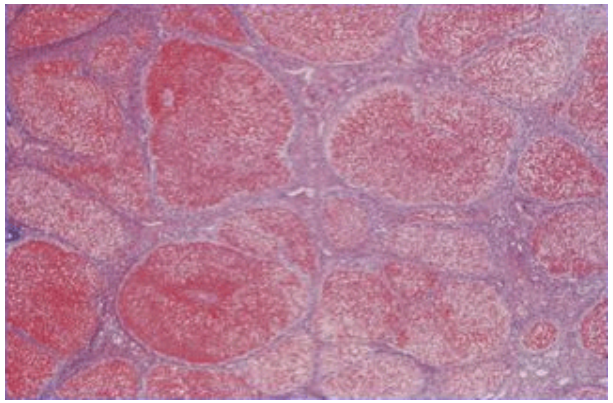
Sherlock's Diseases of the Liver and Biliary System

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



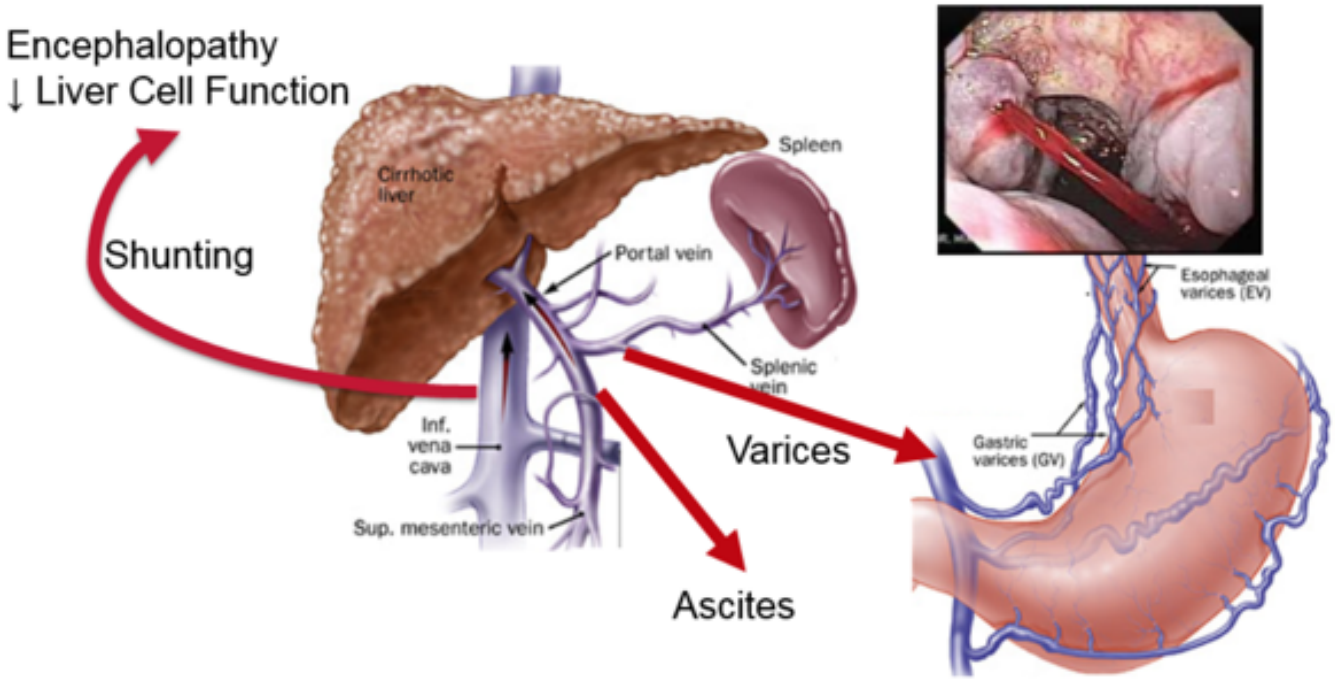






NORMAL LIVER

CIRRHOTIC LIVER


Encephalopathy
↓ Liver Cell Function
Shunting
Cirrhotic liver
Spleen
Portal vein
Splenic vein
Inf. vena cava
Sup. mesenteric vein
Varices
Ascites
Esophageal varices (EV)
Gastric varices (GV)

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

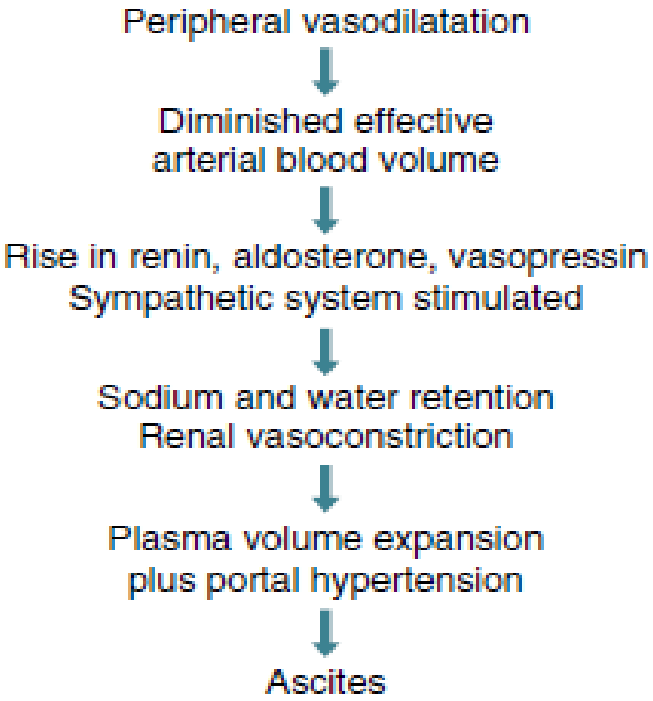
How portal hypertension develop?

2 main mechanisms involved in portal hypertension:

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

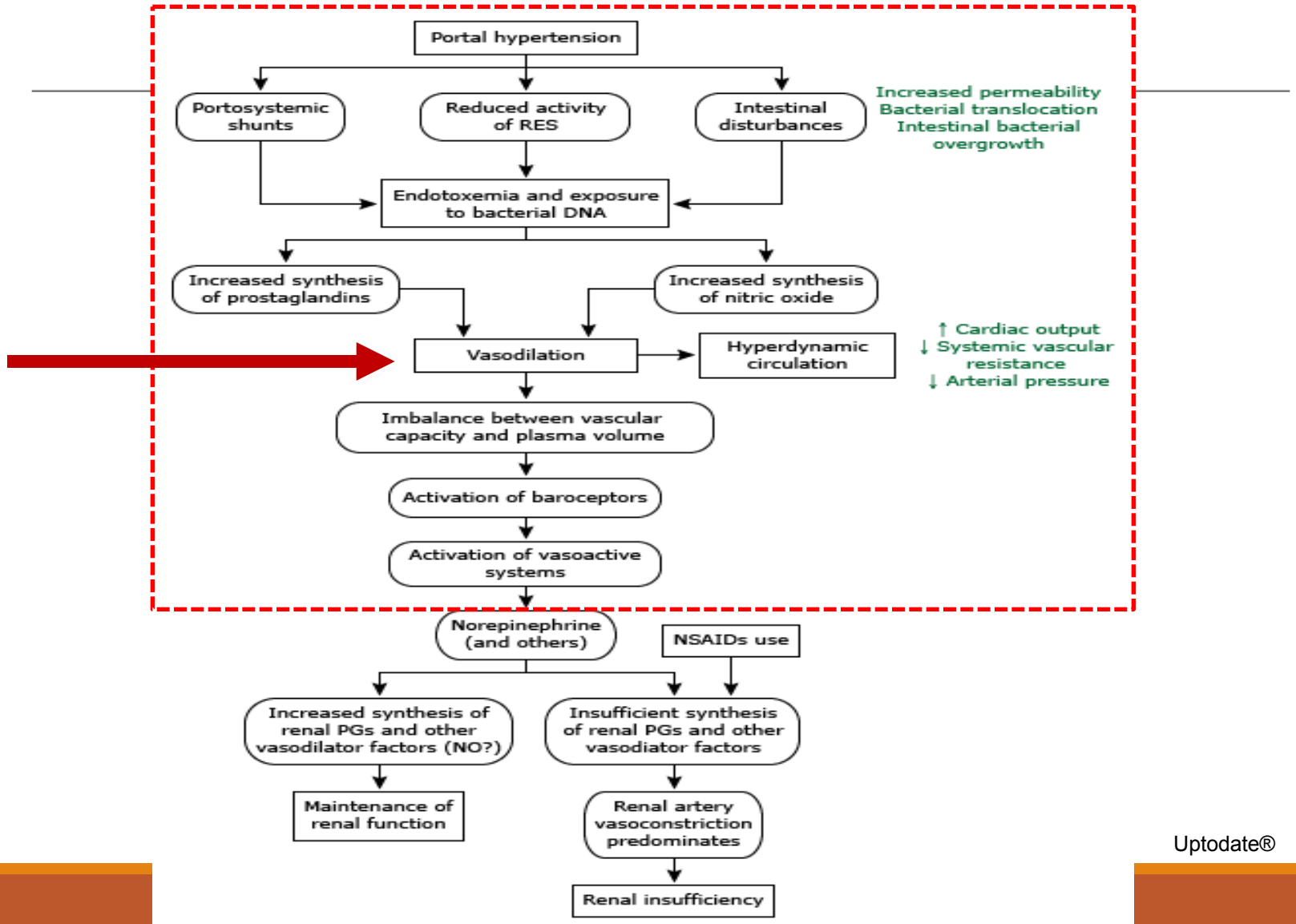
Pathophysiology of ascites in cirrhosis

How ascites develop?



Sherlock's Diseases of the Liver and Biliary System

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



Uptodate®

Vasodilation(VD)

Portal hypertension leads to VD (How?)

- VD initially in the splanchnic circulation, later in systemic systemic circulation. (arterial underfilling)

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. (Why?)
- *Production of these VDs may be stimulated by endotoxins or other bacterial products*

Consequences of vasodilation

1. Activation of endogenous vasoconstrictors.(compensatory)
   a) *renin-angiotensin-aldosterone system*
   b) *sympathetic nervous system*
   c) *antidiuretic hormone (vasopressin).*
2. Sodium and water retention.
3. Increase renal vasoconstriction.

1-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

2-Sodium and water retention

- In patients with cirrhosis and ascites, the normal regulation of sodium balance is lost. (Impaired sodium excretion)
- 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.

3-Renal vasoconstriction

- VC → renal hypoperfusion→ decrease GFR (Glomerular filtration rate)

- Renal perfusion may initially be maintained due to vasodilators such as prostaglandins and perhaps nitric oxide (local)

- However, progression renal hypoperfusion can lead to gradual decline in the glomerular filtration rate, and, in some patients, the hepatorenal syndrome

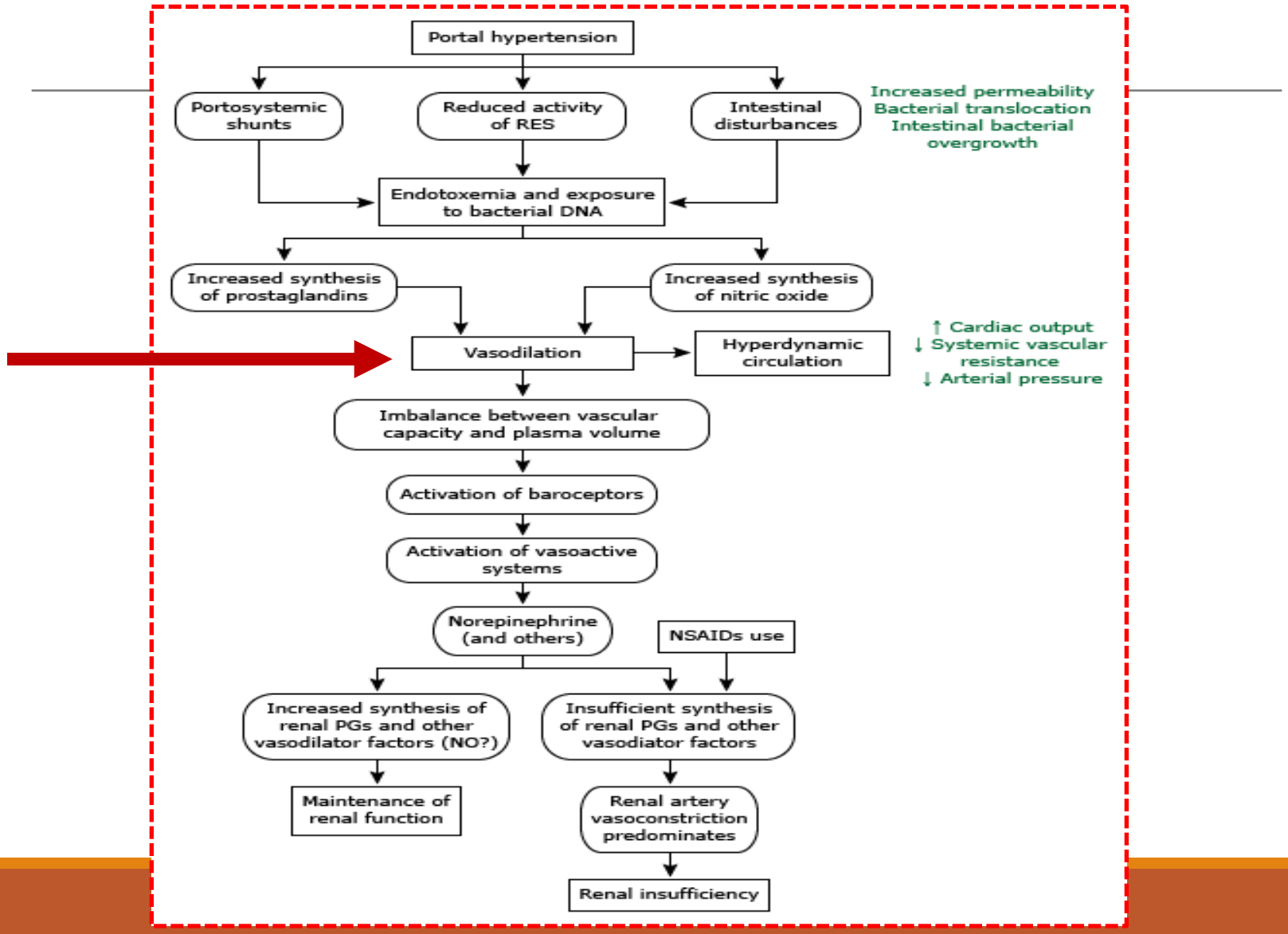
So ultimately

This excess retained blood volume leaks-out (filtered) (extravasate) directly from both the liver surface, and the mesenteric vessels.

Due to:

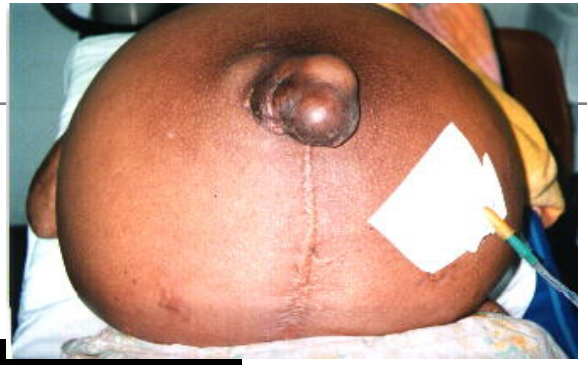
1. Increased hydrostatics pressure
2. Increase vascular wall permeability
3. Concurrently decreased oncotic (osmotic) pressure (hypoalbuminemia)

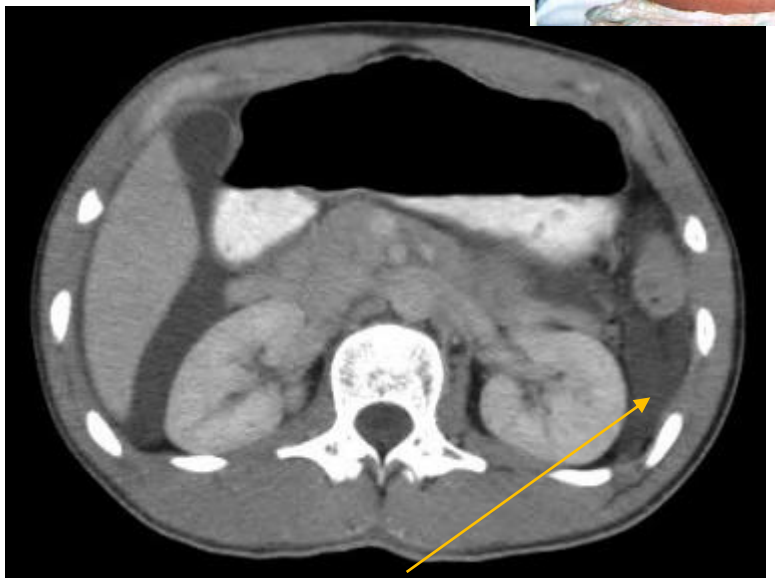
Pathogenic mechanisms responsible for the activation of vasoactive systems and hyperdynamic circulation in cirrhosis



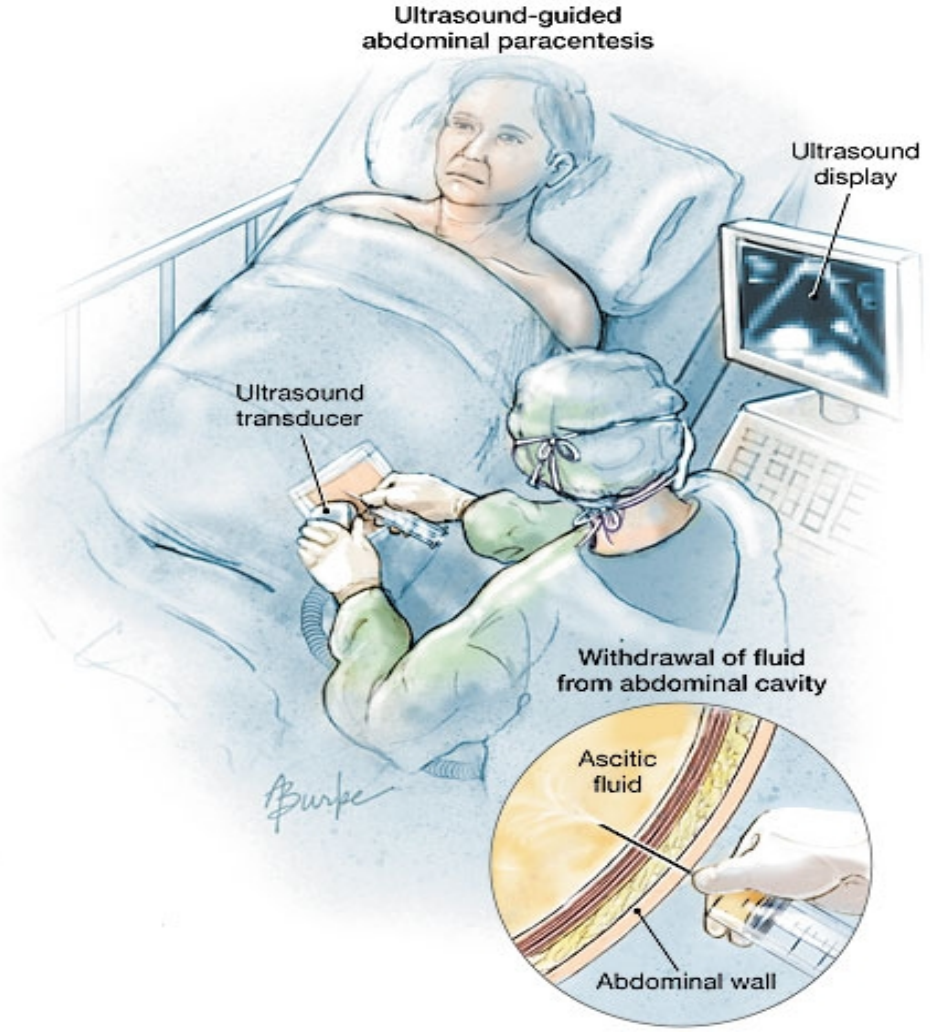
Evaluation of patient with ascites

- History: symptoms of chronic liver disease, abdominal distention
- Examination: Flank fullness, shifting dullness or fluid thrill
- Imaging : Ultrasound
- Ascitic fluid analysis





Any new ascites should be tapped and analyzed!



Summary -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.

Summary -2

Pathophysiology is mostly explained by portal

(sinusoidal) hypertension and sodium retention due

to vasodilation and consequent activation of sodium retaining systems.

Explained:

- Portal hypertension is first step in ascites development in patient with cirrhosis.
- Possible bacterial toxin trigger VDs.

Summary -3

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