Pathophysiology Of Ascites In Cirrhosis

To acquire knowledge, one must; study
but to acquire wisdom, one must observe.
Marilyn Vos Savant

Color code
- Important
- doctor notes
- Notes/extra explanation

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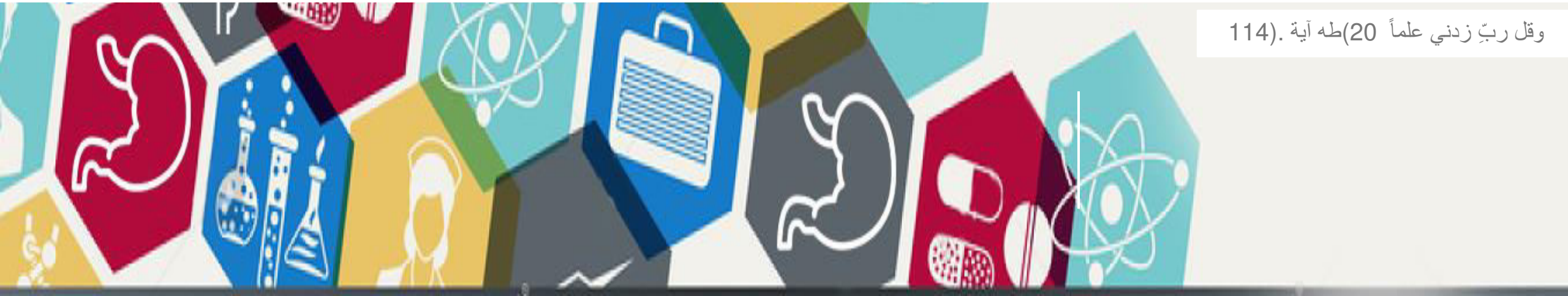

تقدير وشكر

الى كافة أعضاء فريق MEDICINE نشكر لكم جهدكم وتميزكم

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الاء العقيل
شهد العنزان

قادة فريق Medicine: جواهر الخيال &نايف الزيادي

OBJECTIVES:

By the end of the lecture you should able to:

- Understand mechanism of portal hypertension
- Understand basic pathophysiologic steps in the development of ascites secondary to cirrhosis.
- Causes of PHT
- Approach of ascites
- Correlate the anatomic and pathophysiologic changes with clinical manifestations.

- Understand the basic steps in evaluation of patients with ascites

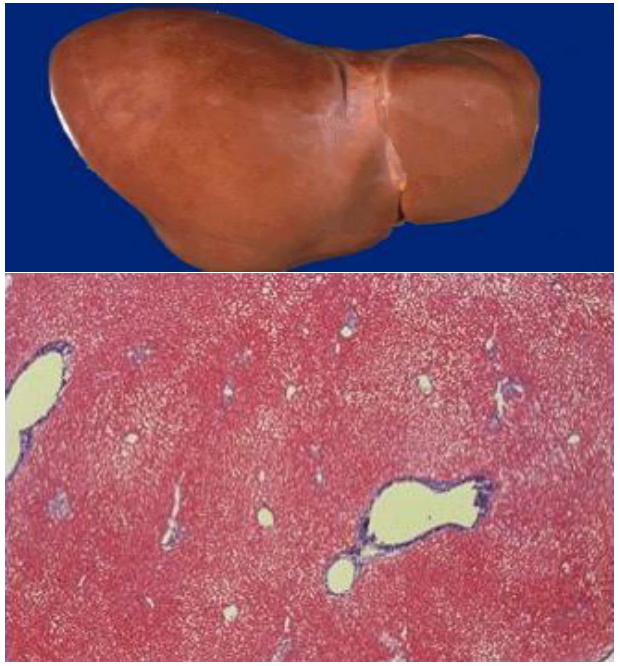
Cirrhosis

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

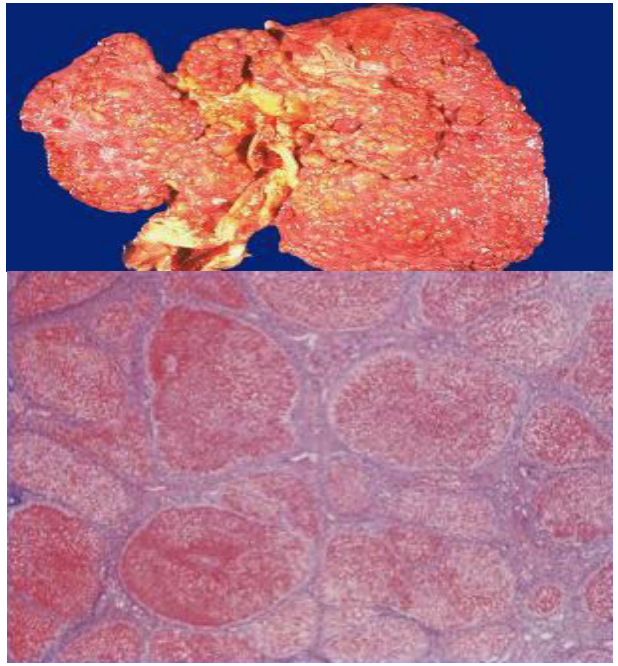
Causes of Cirrhosis

Commmonest	Other causes
Viral (HBV+-HDV,HCV)	Autoimmune (AIH, PBC, PSC)
NASH non alcoholic steatoHepatitis	Metabolic & Hereditary WD, A1AT, HH
ASH Alcoholic steatoHepatitis	Vascular BCS, HF
Obesity	Biliary SC
	Drugs

We should look for the color and surface if its smooth or nodular also normal hepatocyte and the appetance of hepatocyte fibrosis



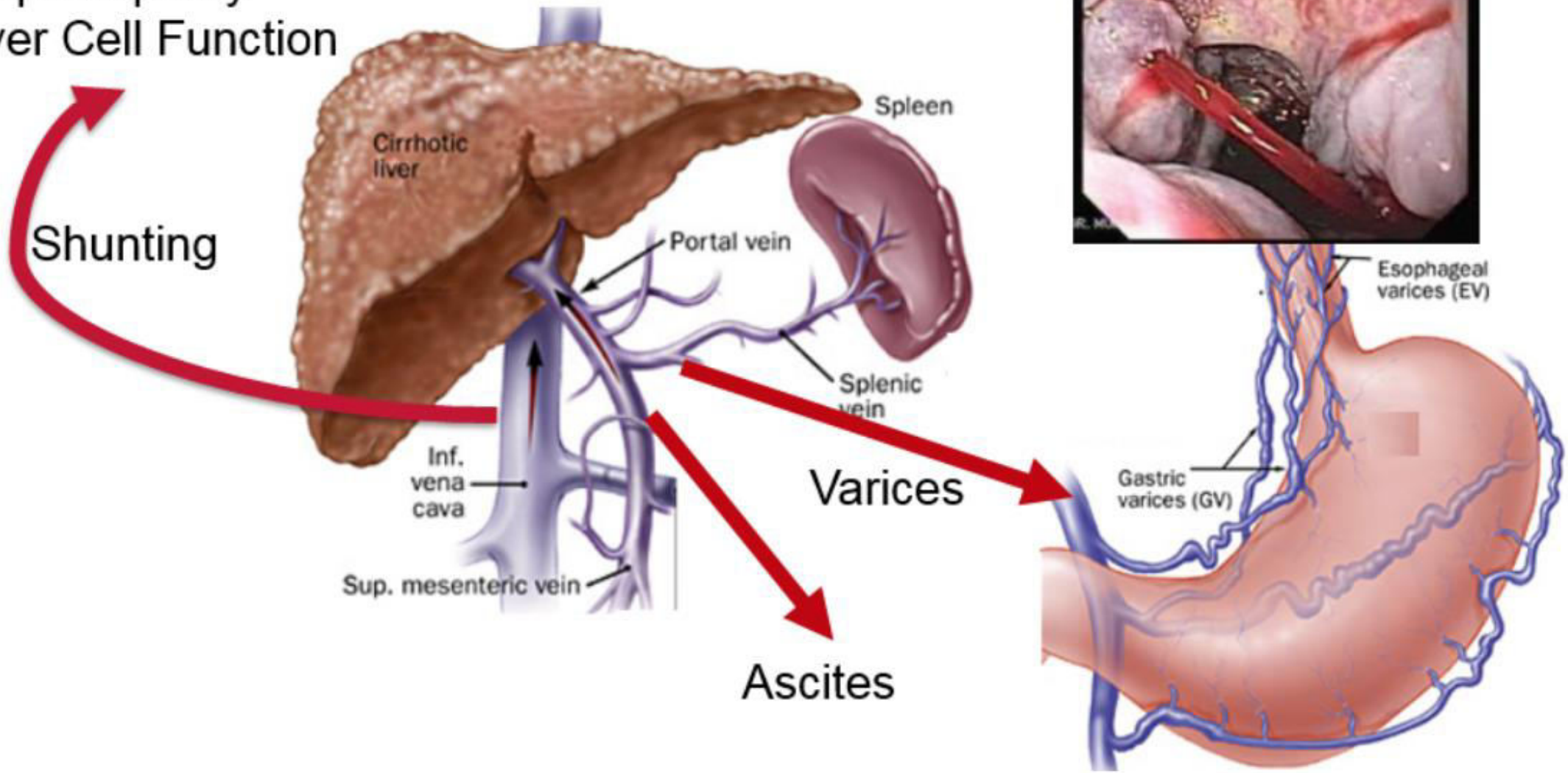
NORMAL LIVER



CIRRHOTIC LIVER

Encephalopathy

↓ Liver Cell Function



Ascites

The pathologic accumulation of fluid in the peritoneal cavity.

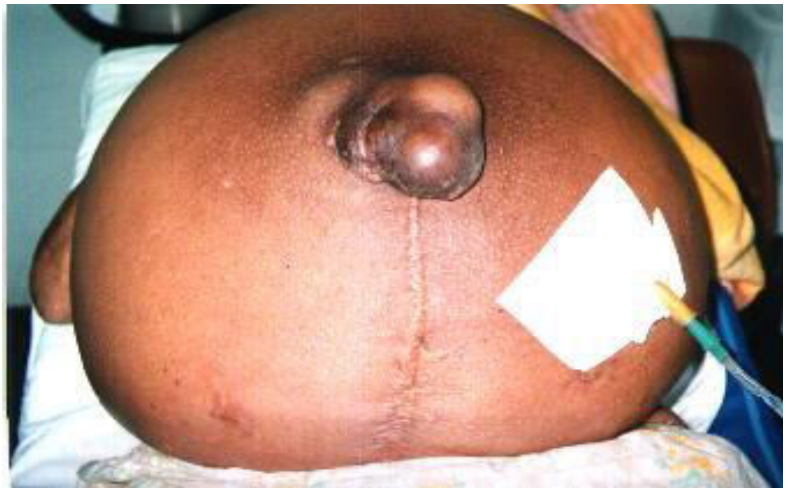
It is the most common complication of cirrhosis. " Normally there is no fluid in the peritoneal cavity in men but it might be liitle amount in women"

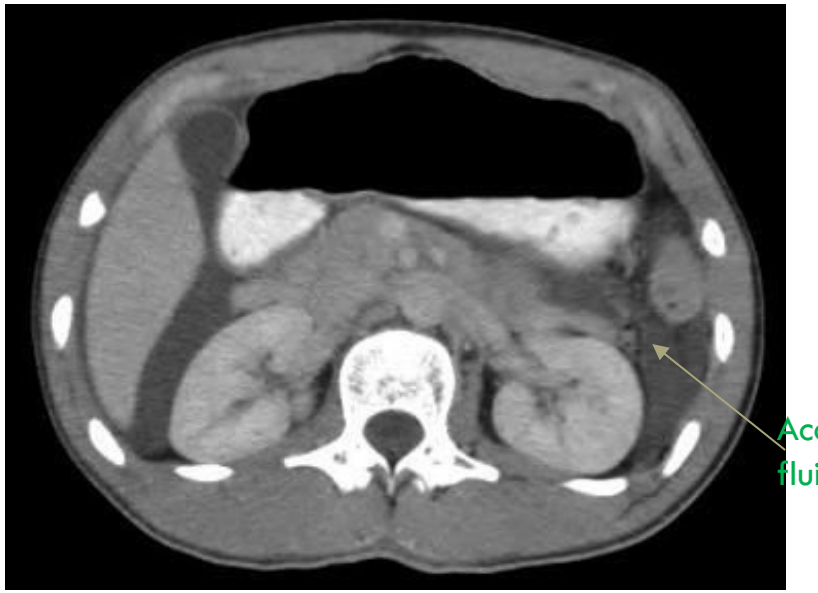
Ascites:

- Cirrhosis 85% the most common cause is cirrhosis
- 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.





Important slide**

PORTAL HYPERTENSION

The development of portal hypertension (PHT) is the first step toward fluid retention in the setting of cirrhosis.

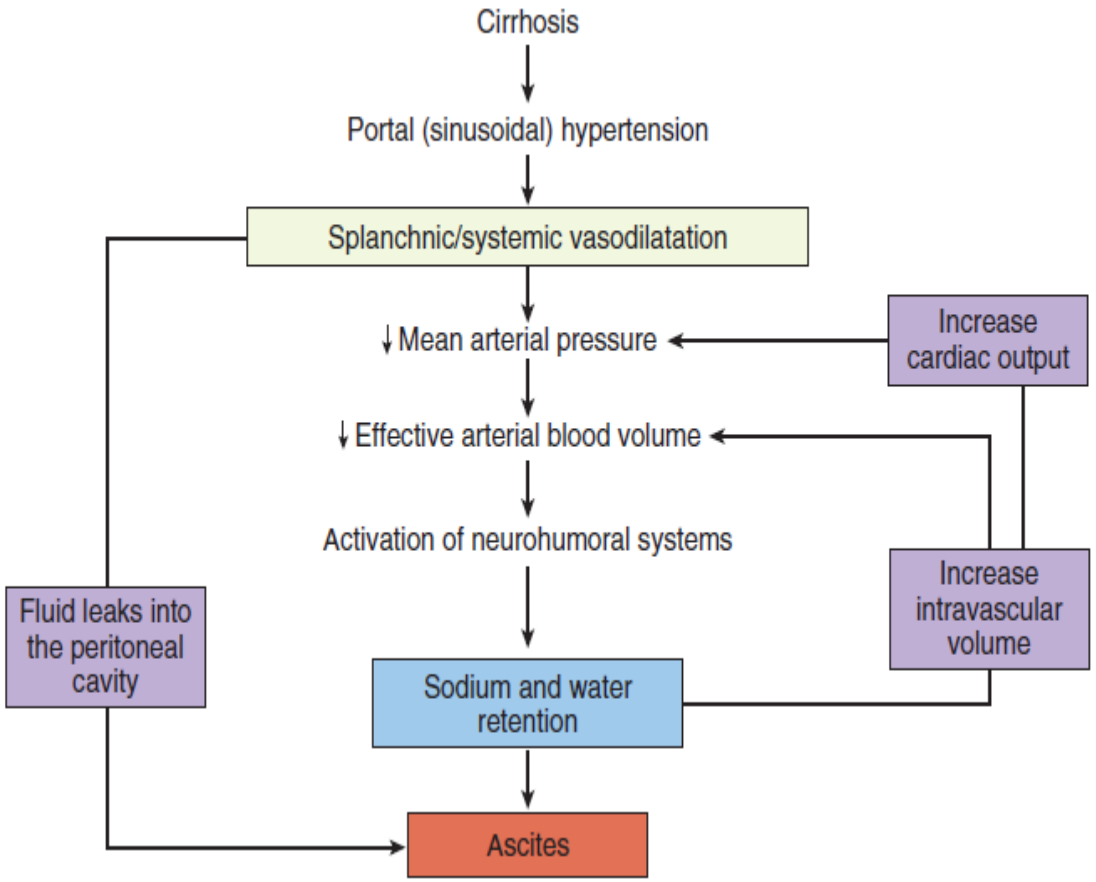
Patients with cirrhosis but without PHT do not develop ascites or edema.

A portal pressure >12 mmHg appears to be required for fluid retention

2 main mechanisms involved in portal hypertension:Portal hypertension usually 8 to 10 mmHg

1- Mechanical (due to structural changes in the liver with fibrosis and regenerative nodules)

2- Hemdynamic (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 initially develops in the arterial splanchnic circulation (i.e., the mesenteric arteries).

in systemic vessels, the NO is increased, as results of splanchnic vasodilation.

Subsequently, vasodilation develops in the arterial systemic circulation.

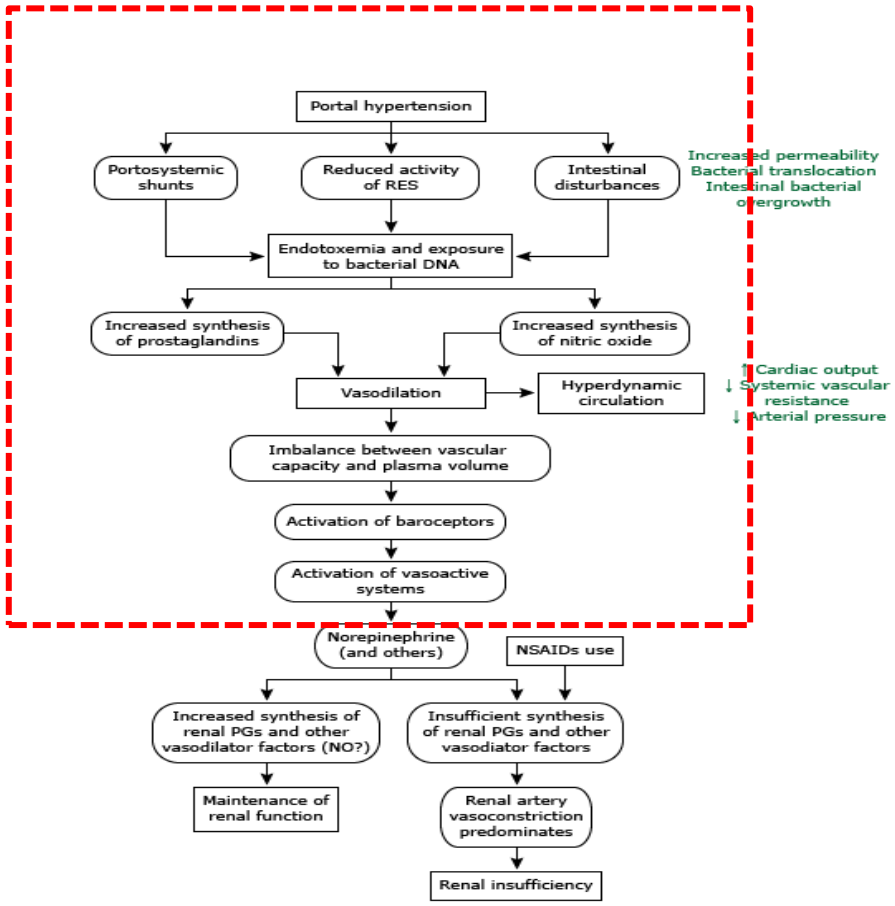
Hyperdynamic circulation

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 Increase intravascular volume
- Sodium and water retention
- Increase renal vasoconstriction. Increase in renin

Activation of endogenous vasoconstrictor agents

VD→ The reduction in pressure (or stretch) at the carotid and renal baroreceptors production of VDs may be stimulated bu endotoxins or other bacterial products" important

→ 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 avoid 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)

Important slide**

- 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)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)**
- hypoalbuminemia cause decrease in omcotic pressure
- always in ascites look for the underlying cause first before treatment"

Important slide**

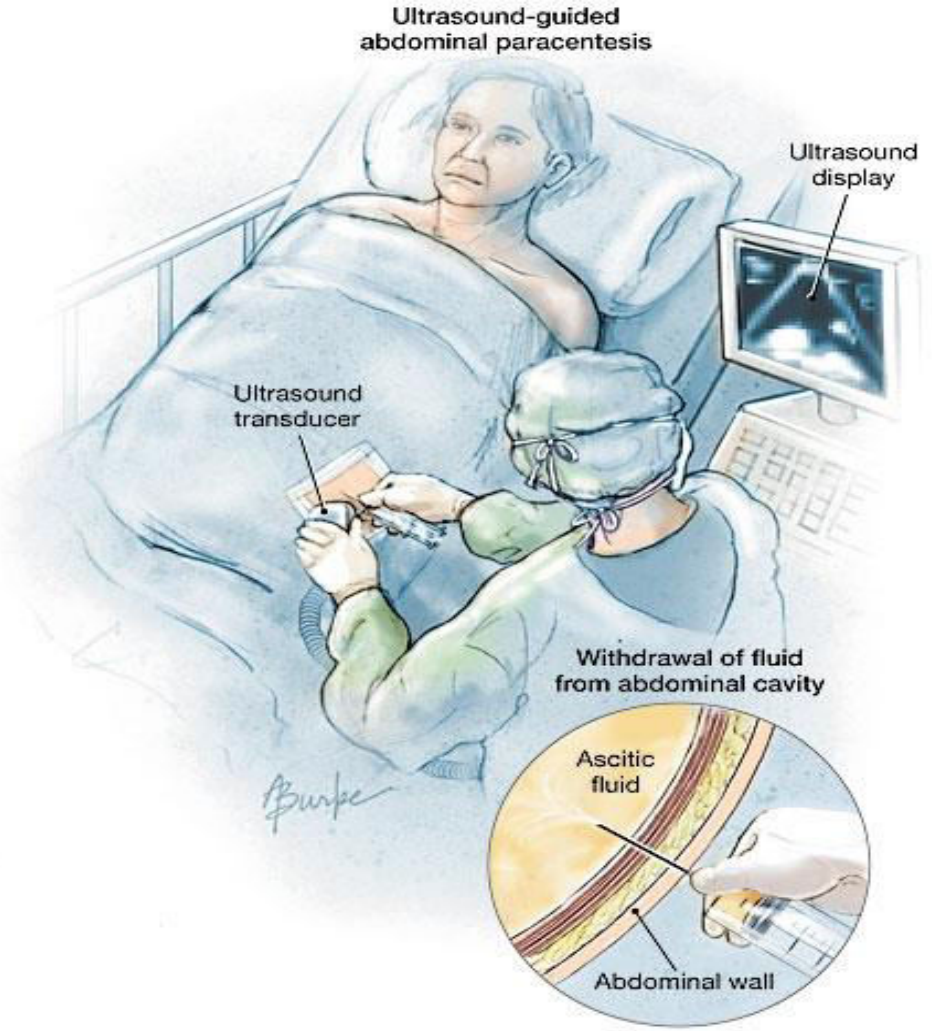
Abnormalities in patients with cirrhosis and ascites

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!

history: check if he has progressive abdomenal distention, jaundice, lower limb adema.

Clinically there will be extention and shifting.



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." Reprinted with permission from Saunders Elsevier.

Measure **SAAG**

From serum, if its high=portal hyper tension , High SAAG (mainly liver
if decresed=malegnancy Low SAAG (other cause

SAAG is more sensitive to fluid the idea is measure the serum & ascitic albumin

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
3. Discontinue non-steroidal anti-inflammatory drugs . avoid all hepatotoxic drugs.
4. Rx of underlying cause
5. Evaluation for liver transplantation. if the patient didnt respond to the treatment, he should have liver transplantation.

Take home message

- 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.
- 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.

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Causes of Cirrhosis

Commonest

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

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MCQs

Q1 - What's the main cause for ascites?

A.Live cirrhosis
B.Hepatitis
C.Heart failure
D.Viral hepatitis B

Q2 - The first step toward fluid retention in the setting of cirrhosis is:

A.Vasodilation
B.Activation of endogenous vasoconstrictor agents
C.Portal hypertension
D.Hyperdynamic circulation

Q3 - The primary mediator of vasodilatation in cirrhosis is :

A.VIP
B.nitric oxide (NO)
C.Prostaglandin
D.ADH

Q4 – Which one of the following is a systemic consequences to vasodilatation

A.Hyperdynamic circulation
B.Vomiting
C.Headach
D.Sodium and water retention

Q5 - Which of the following is a consequence of vasodilatation?

A.Activation of endogenous vasoconstrictors
B.Sodium and water retention
C.Increase renal vasoconstriction.
D.A,B&C

Q6 – Which one of the following isn't biochemical change in ascites:

A.Increased systemic nitric oxide
B.Increased systemic prostaglandin
C.Reduced glomerular filtration rate
D.Sodium water retention

Answers:
1-A
2-C
3-B
4-A
5-D
6-C

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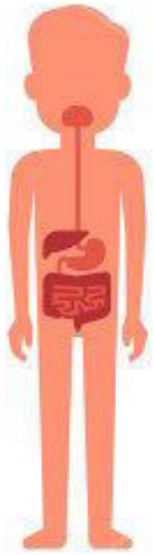
TEAM MEMBERS:



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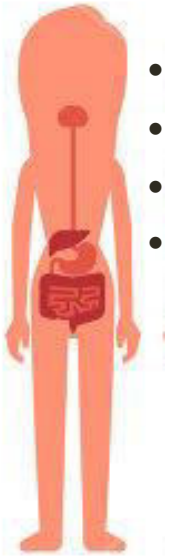

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Feedback

References : boys and girls slides.

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