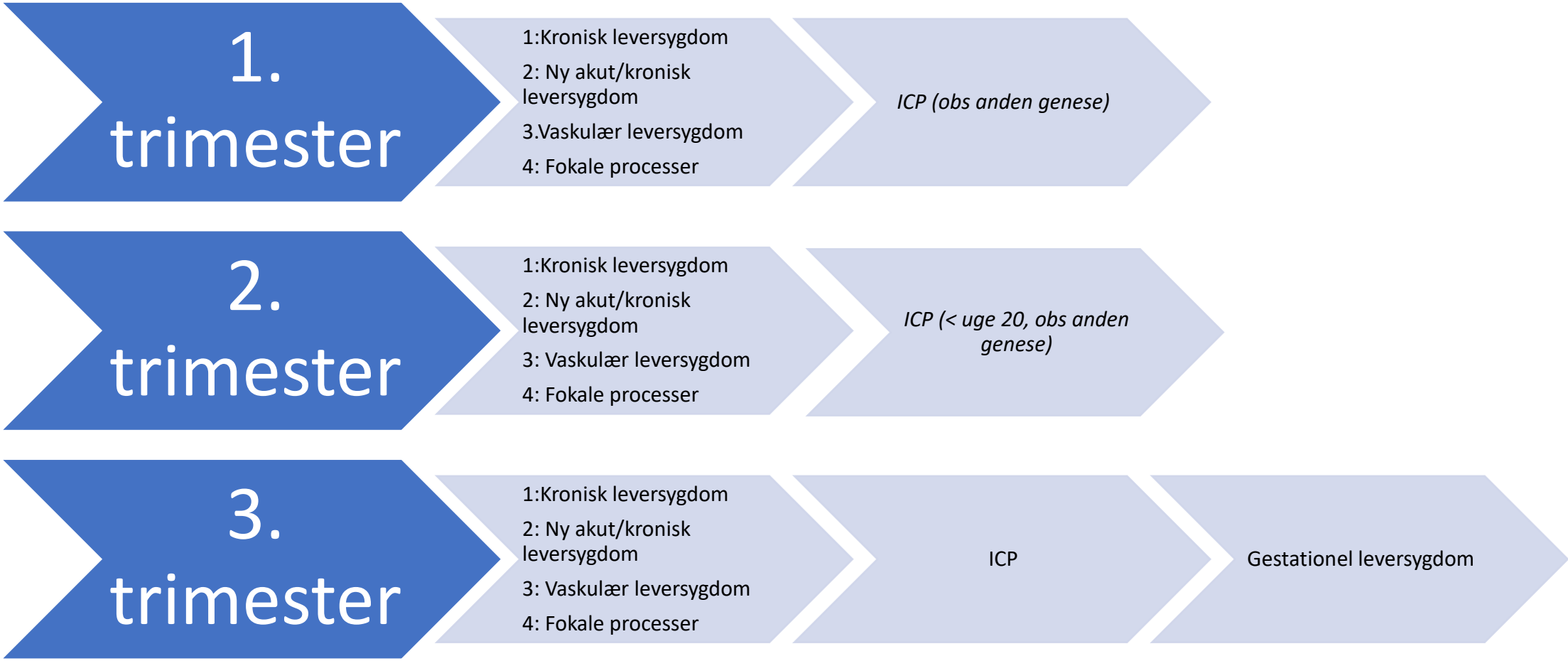
# Graviditet og leversygdom

Annette Dam Fialla

Overlæge, ph.d, klinisk lektor

Odense Universitetshospital

# HITLISTEN


1. trimester
1:Kronisk leversygdom
2: Ny akut/kronisk leversygdom
3.Vaskulær leversygdom
4: Fokale processer
ICP (obs anden genese)
2. trimester
1:Kronisk leversygdom
2: Ny akut/kronisk leversygdom
3: Vaskulær leversygdom
4: Fokale processer
ICP (< uge 20, obs anden genese)
3. trimester
1:Kronisk leversygdom
2: Ny akut/kronisk leversygdom
3: Vaskulær leversygdom
4: Fokale processer
ICP
Gestationel leversygdom

# Påvirkede leverenzymer

## Medikamentel toksisk

- Antibiotika (Bioclavid, Nitrofurantoin)
- Simvastatin
- Psykofarmaka
- Immundæmpende (MTX, Imurel)
- Anabolske steorider
- Check point hæmmere
- Kemoterapeutika
- **Livertox.com (ca 1600 forskellige lægemidler)**

## Toxisk

- Svampe
- Herbals

## Alkohol/steatose

## Viral

- Hepatitis A + E
- CMV + EBV virus

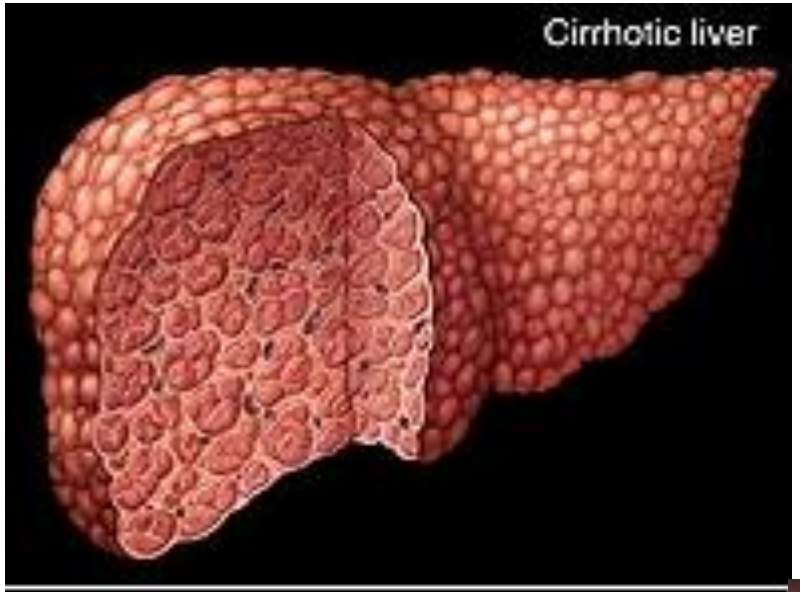
## Akut debut af kronisk leversygdom

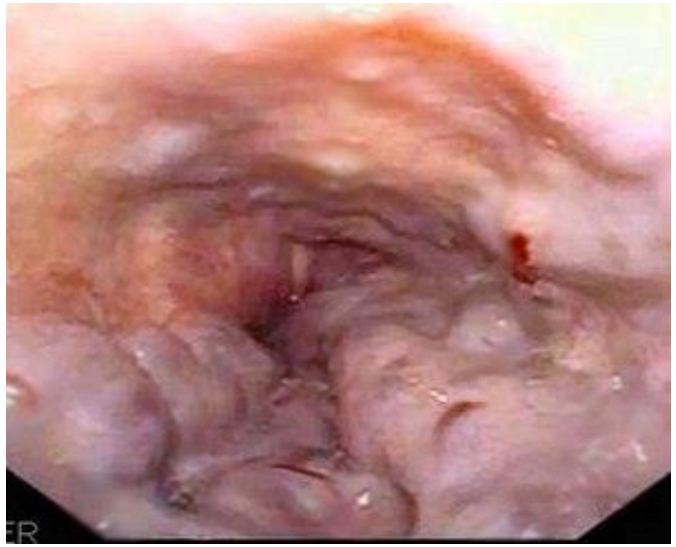
- Autoimmun hepatitis

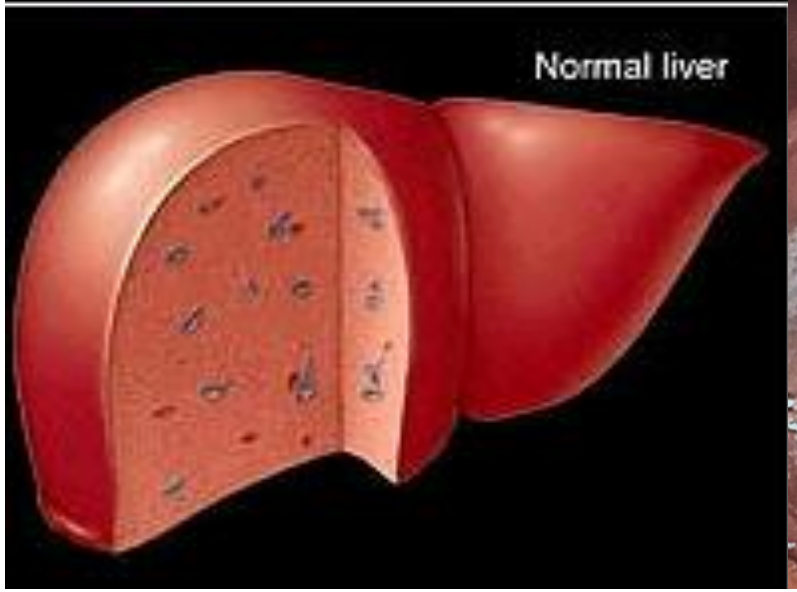
## Cancer

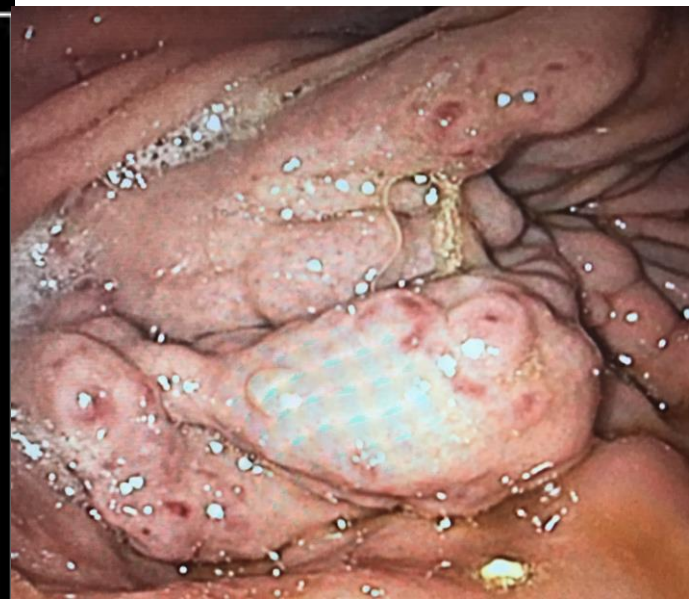
## Sekundær

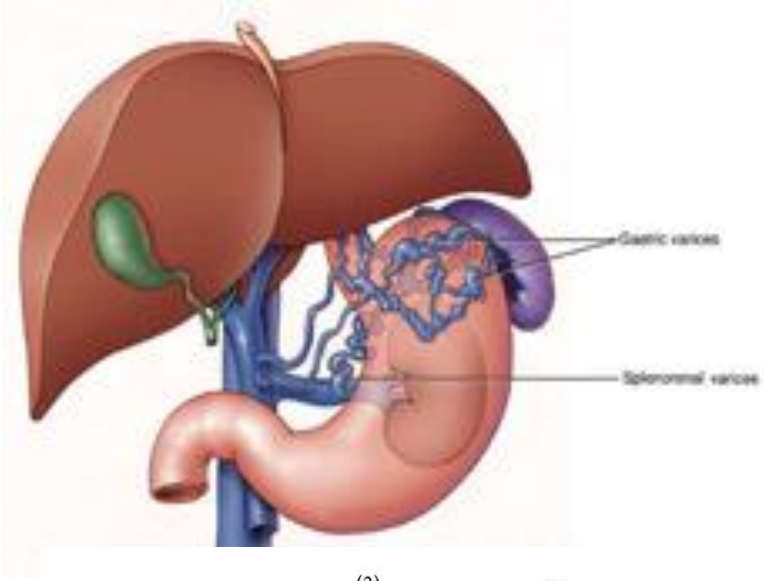
# Kronisk leversygdom og graviditet

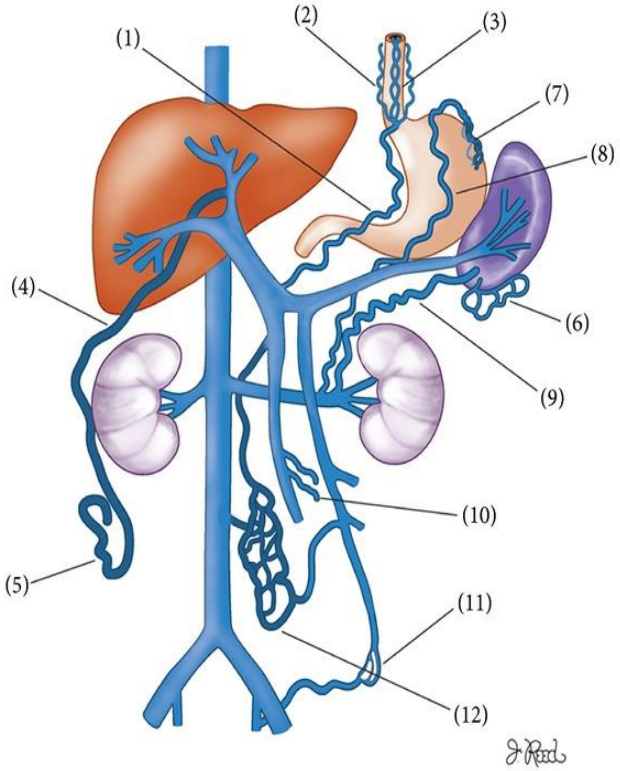






Ikke cirrose
Ikke portal hypertension

# Autoimmun hepatitis

## Forhøjet IgG

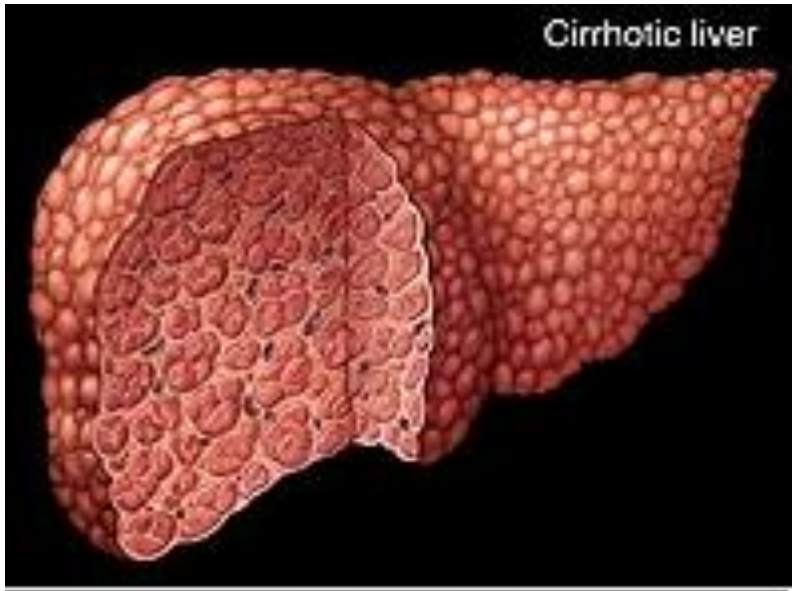
## Positiv actin antistof

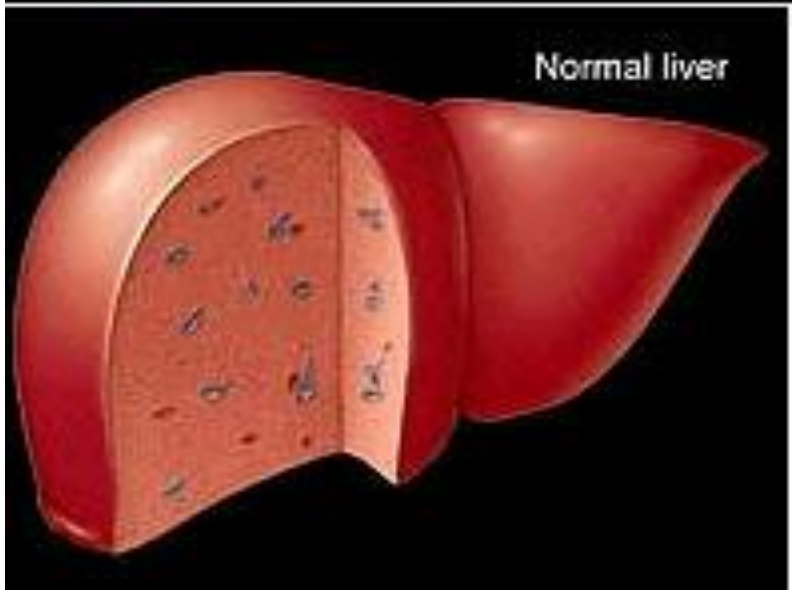
**Autoimmun hepatitis**


- Forværring/forbedring
- Debut under graviditet
- Gestationel diabetes
- Hypertensive komplikationer


- Intrauterin væksthæmning
- Præterm fødsel

- Prednisolon
- Azathioprin



# Kronisk cholestatisk leversygdom
## *uden cirrose, uden portal hypertension*

### Primær billiær cirrose
”små galdeveje”
Højet IgG, pos AMA


Forværring/forbedring
Øget hudkløe hos 50 %


Øget fosterdødelighed
Præterm fødsel

Ursochol
Hudkløe: Rifampicin (300-600 mg dagligt, cholestagel/colestyramin (5-10 g dagligt)

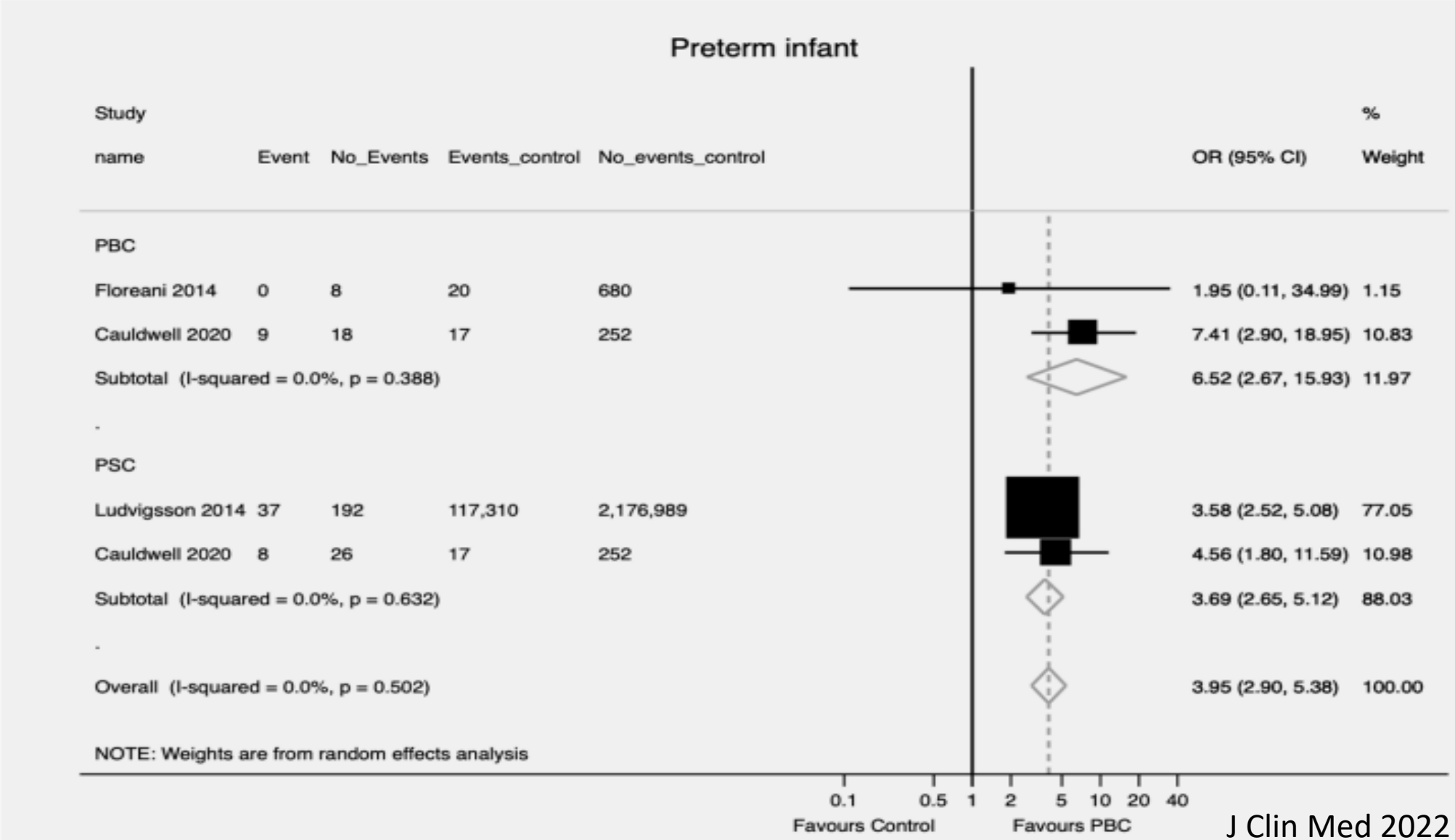
### Primær scleroserende cholangitis
”store og små galdeveje”
MRCP


Risiko for galdevejsstenoser
Øget hudkløe


Øget fosterdødlighed
Præterm fødsel

Ursochol
Hudkløe: Rifampicin (300-600 mg dagligt, cholestagel/colestyramin (5-10 g dagligt)
ERCP +/- ballon dilatation

# Kronisk cholestatisk leversygdom
## *uden cirrose, uden portal hypertension*




J Clin Med 2022

# Kronisk cholestatisk leversygdom
## *uden cirrose, uden portal hypertension*

| Primær billiær cirrose<br>”små galdeveje” | Primær scleroserende cholangitis<br>…e og små galdeveje” |
|---|---|
|  <br>Pregnancy | Forværring/forbedring<br>Øget hudkløe hos 50 %<br>Øget fosterdødlig… |
|  <br>Delivery | Øget fostedødlighed<br>Præterm fødsel |
|  | Ursochol<br>Hudkløe: Rifampicin (300-600 mg dagligt, cholestagel/colestyramin (5-10 g dagligt) |

OBS GALDESALTE

| | |
|---|---|
|  <br>Pregnancy | Risiko for galdevejsstenoser<br>Øget hudkløe<br>Øgt fosterdødlighed |
|  <br>Delivery | Øget fosterdødlighed<br>Præterm fødsel |
|  | Ursochol<br>Hudkløe: Rifampicin (300-600 mg dagligt, cholestagel/colestyramin (5-10 g dagligt)<br>ERCP +/- ballon dilatation |

**BILLEDDIAGNOSTIK**

**Table 3. Data relating to safety of radiological investigations used to assess pregnant women with liver disorders.**

| | |
|---|---|
| **Radiological investigations** | |
| Ultrasound | Safe at any gestation in pregnancy |
| Liver elastography | Safe at any gestation in pregnancy<br>It should be noted that there may be a small increase in liver stiffness and controlled attenuation parameter in the third trimester which reflects the physiology of normal pregnancy[3] |
| MRCP | Safe at any gestation in pregnancy |
| ERCP | Fetal radiation estimated between <0.1-0.5 mGy[4] (threshold for malformation = 50 mGy)<br>Can be performed in pregnancy, ideally in the 2nd/ 3rd trimester |
| **Other** | |
| OGD | Safe in pregnancy, ideally performed in 2nd trimester in left lateral position<br>Midazolam may be used judiciously |
| Liver biopsy | Can be performed where clinical need/diagnostic uncertainty dictates, and delay in diagnosis would be more dangerous for the pregnant woman<br>Ensure coagulopathy corrected |

ERCP, endoscopic retrograde cholangiopancreaticography; MRCP, magnetic resonance cholangiopancreatography; OGD, oesophago-gastroduodenoscopy.

EASL guideline

# 22 år. GA 7+
# Mavesmerter

ALAT: 305

BASP: 208

BILI: 63

# Samme kvinde, 2 grav GA 30 + 4
# ICP

| | Dag 0 + ursochol | Dag 5 | Dag 15 | Fødsel | 1 mdr post partum |
|---|---|---|---|---|---|
| ALAT | 753 | 286 | 142 | 134 | 12 |
| BASP | 165 | 126 | 127 | 225 | 110 |
| Galdesalte | 22 | 14 | | 26 | |

Gentest negativ

# ICP: intrahepatisk cholestasis of pregnancy (incidens op til 1,5 %)

**Behandling:**

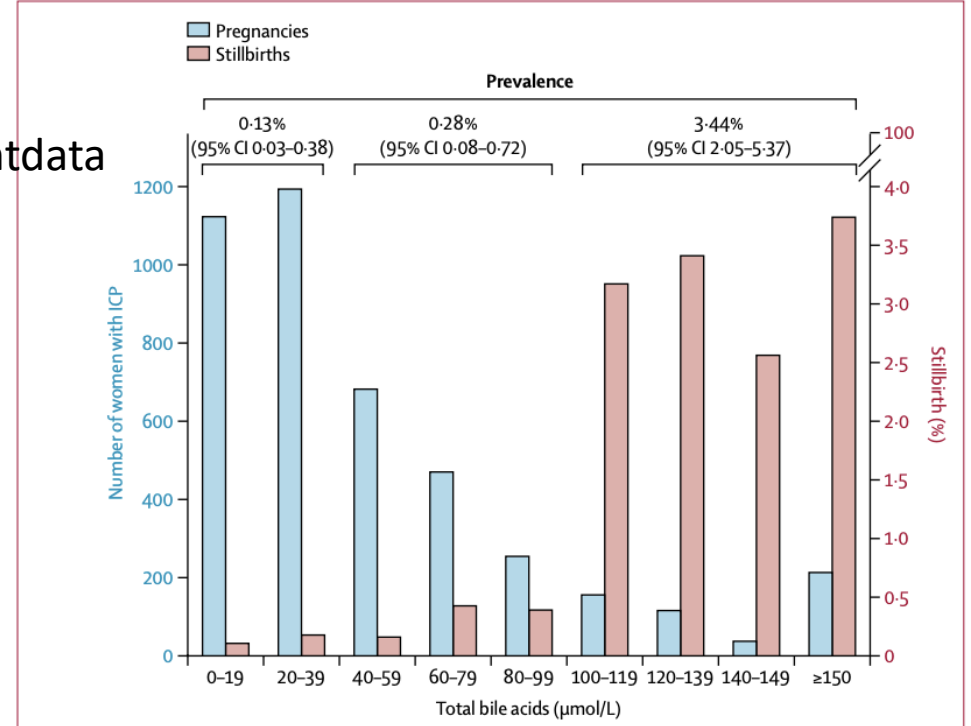
| | |
|---|---|
| Ursodeoxycholsyre 12,5 mg/kg/dag ~ 250mg x 3, eventuelt stigende til 500 mg x 3 til fødslen anbefales som førstevalgspræparat. | A |
| Questran (Cholestyramin) og Rifampicin kan anvendes, såfremt Ursodeoxycholsyre ikke giver sufficient effekt. | B |

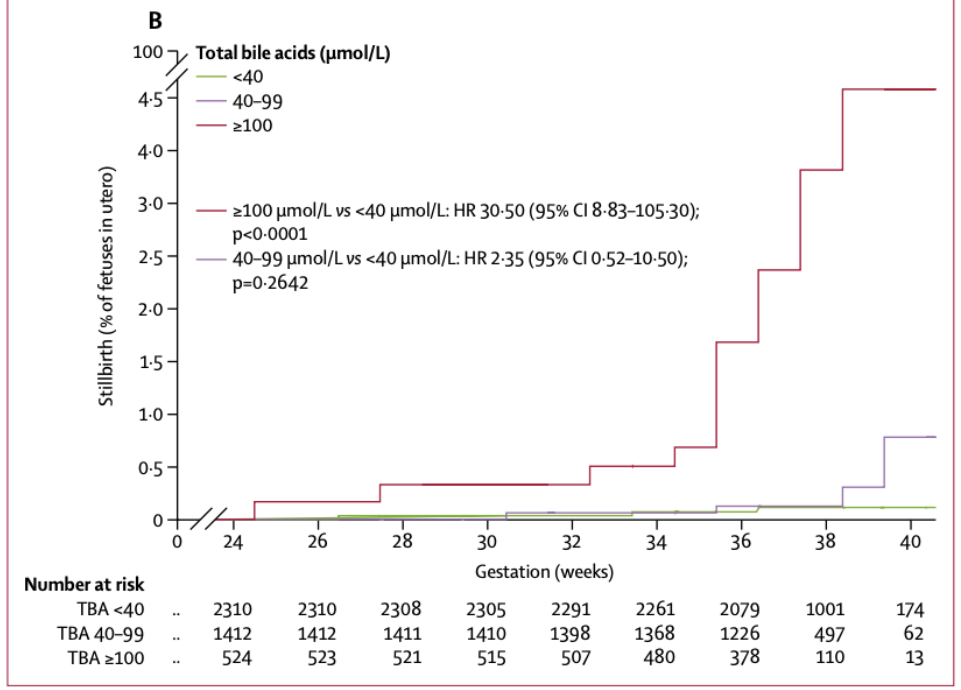
**Forløsningstidspunkt:**

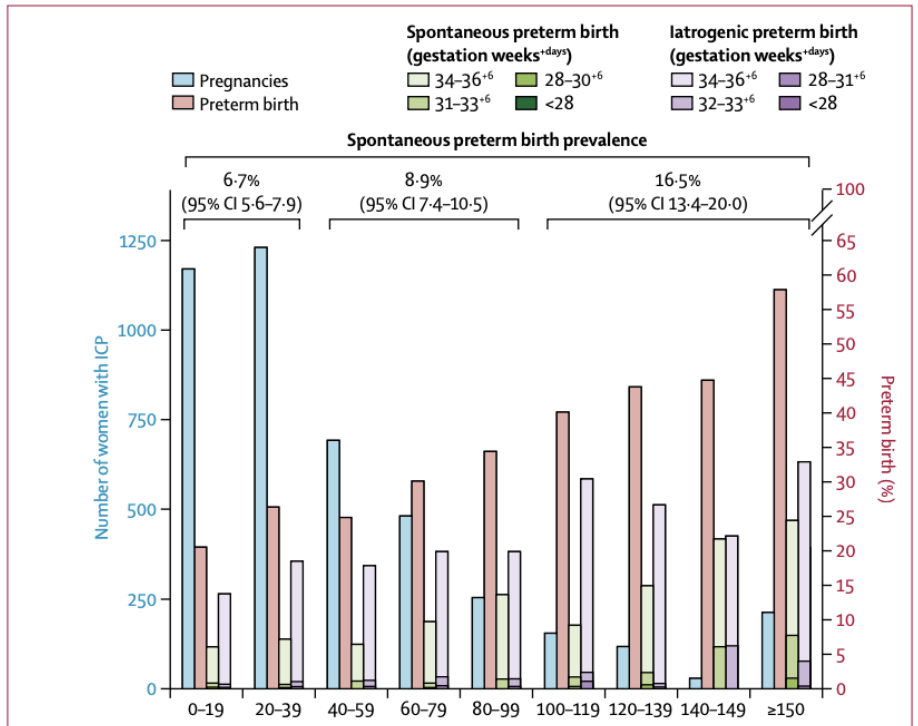
| | |
|---|---|
| Ved galdesalte < 40 µmol/l er risiko for barnet lille og individuelt forløsningstidspunkt kan afventes indtil terminen. Igangsættelse i uge 40+0 anbefales. | B |
| Ved galdesalte mellem 40 og 100 µmol/L anbefales igangsættelse uge 38+0. | B |
| Ved galdesalte ≥ 100 µmol/L må igangsættelse overvejes fra uge 34+0. | B |

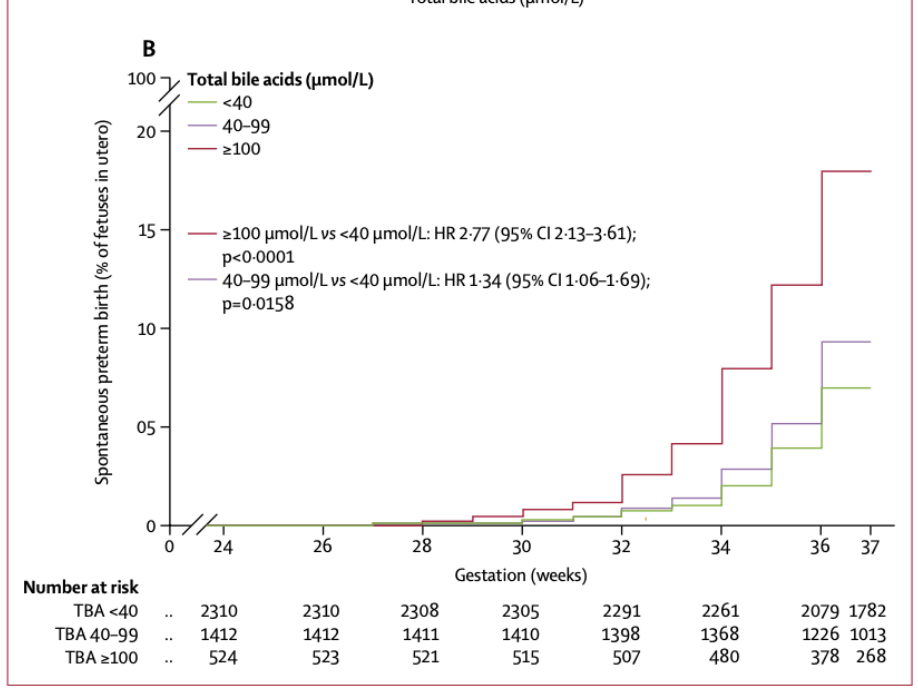
DSOG guideline

Metaanalyse
5500 graviditeter
Individuelle patientdata

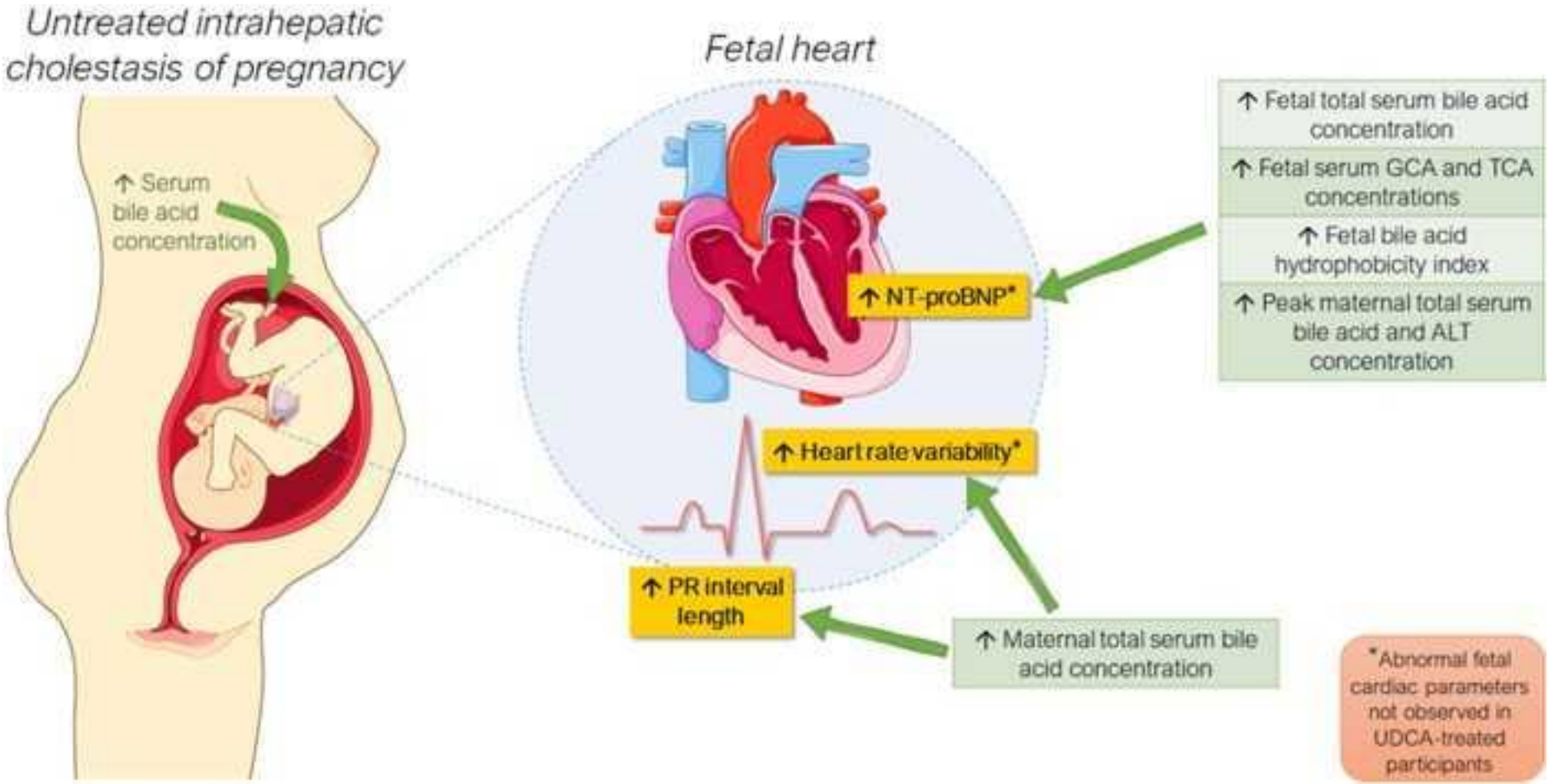


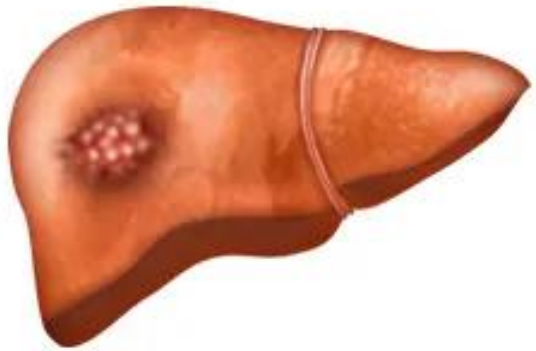



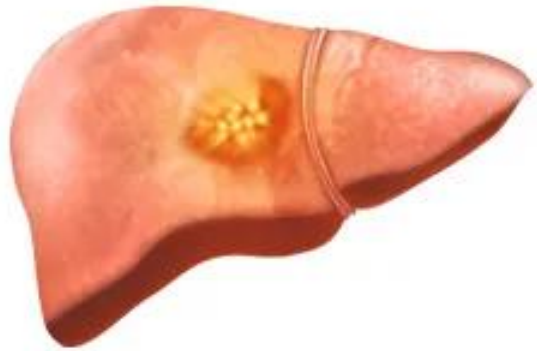

Lancet 2019


Untreated intrahepatic cholestasis of pregnancy
↑ Serum bile acid concentration
Fetal heart
↑ NT-proBNP*
↑ Heart rate variability*
↑ PR interval length
↑ Fetal total serum bile acid concentration
↑ Fetal serum GCA and TCA concentrations
↑ Fetal bile acid hydrophobicity index
↑ Peak maternal total serum bile acid and ALT concentration
↑ Maternal total serum bile acid concentration
*Abnormal fetal cardiac parameters not observed in UDCA-treated participants

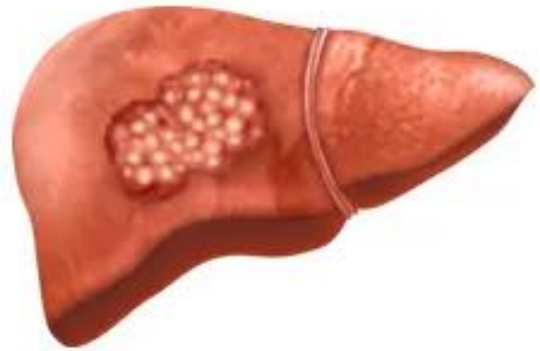
# Types of Liver Tumour



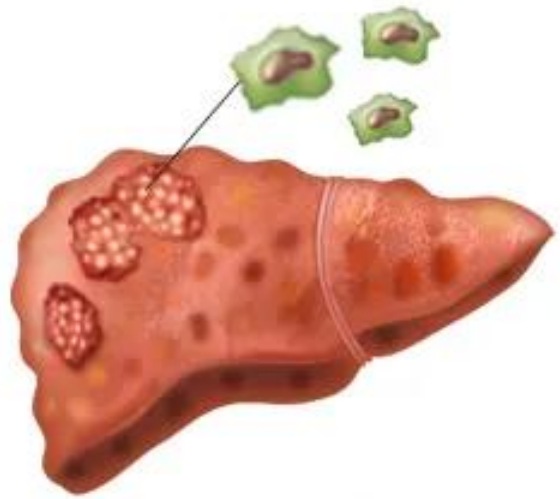
- Hemangioma



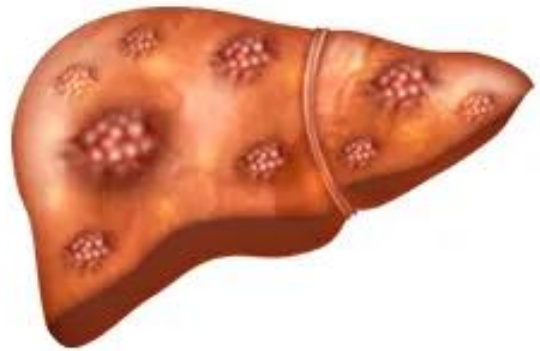
- Adenoma



- FNH



- HCC



- Metastasis

## Benign hepatic tumours: management in pregnancy

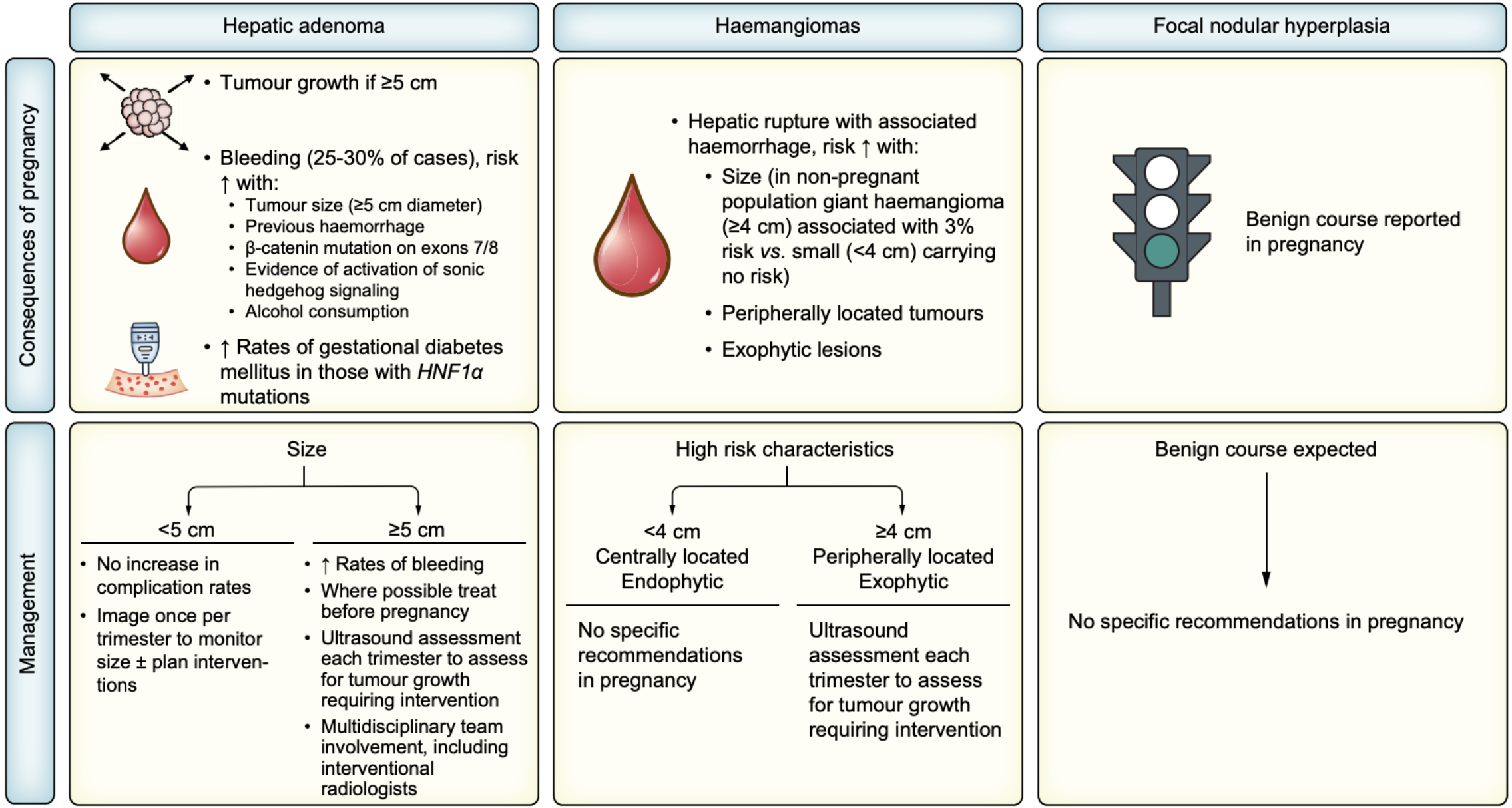
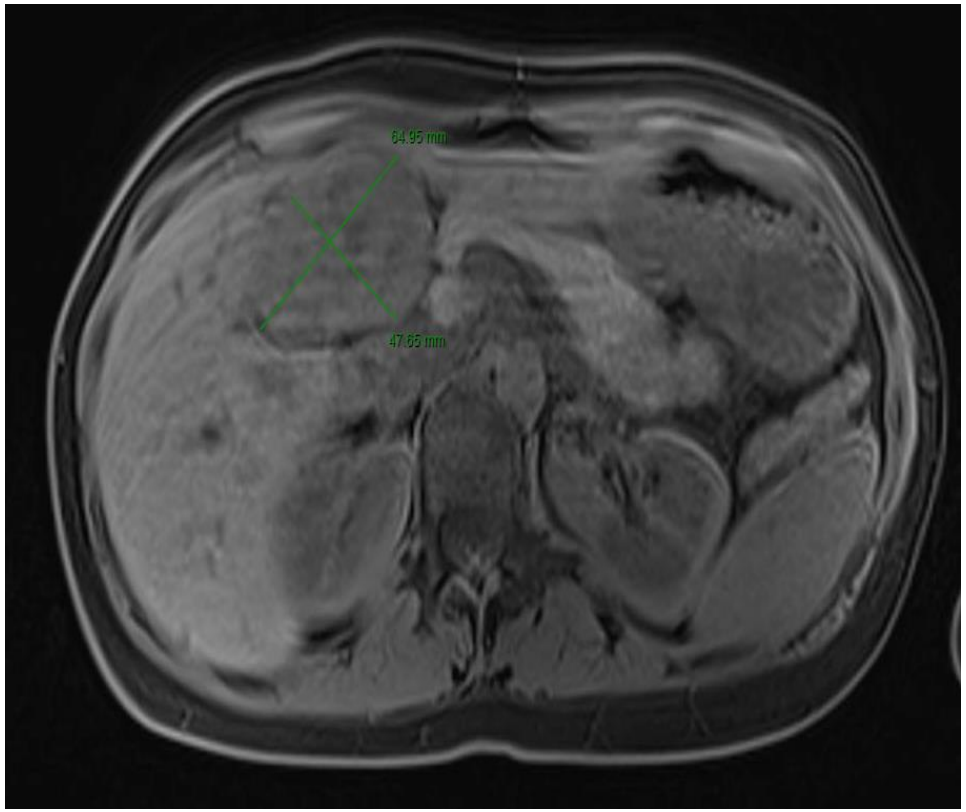
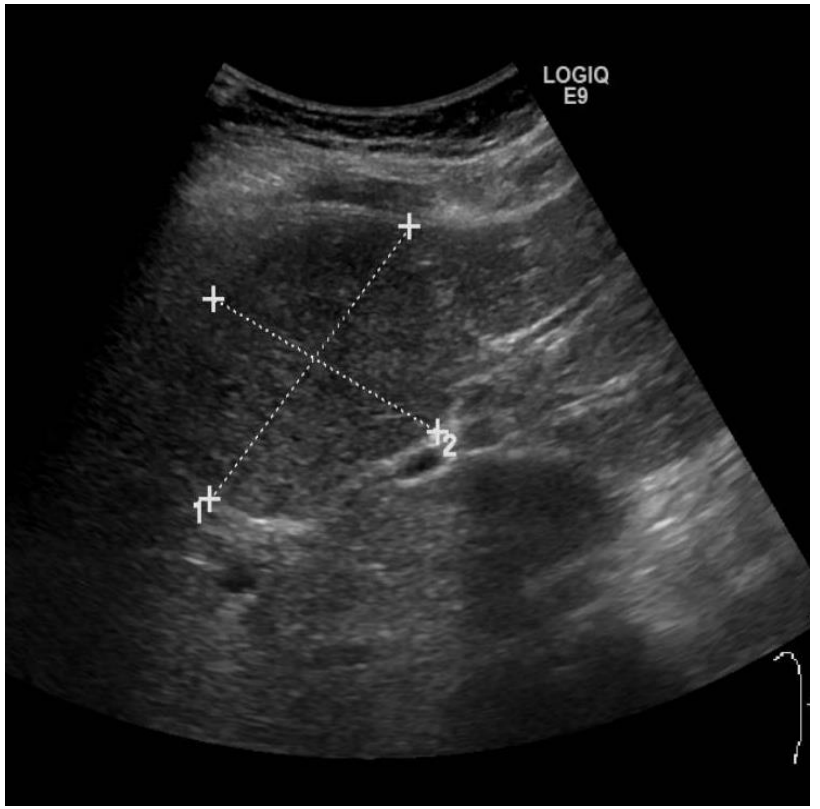


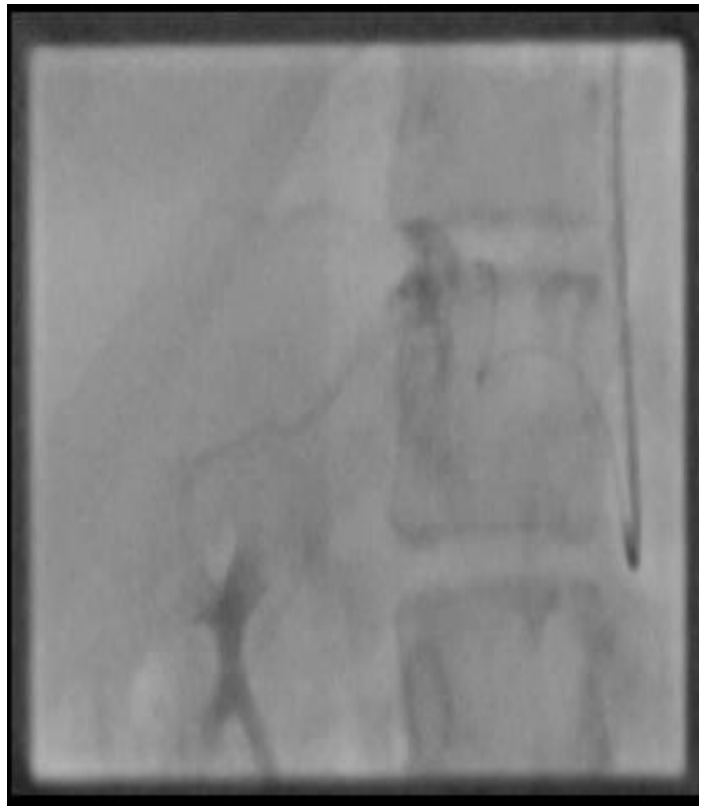

**Fig. 2. Management of benign hepatic tumours in pregnancy.**

EASL guideline

# 35 år. Grav uge 24-25



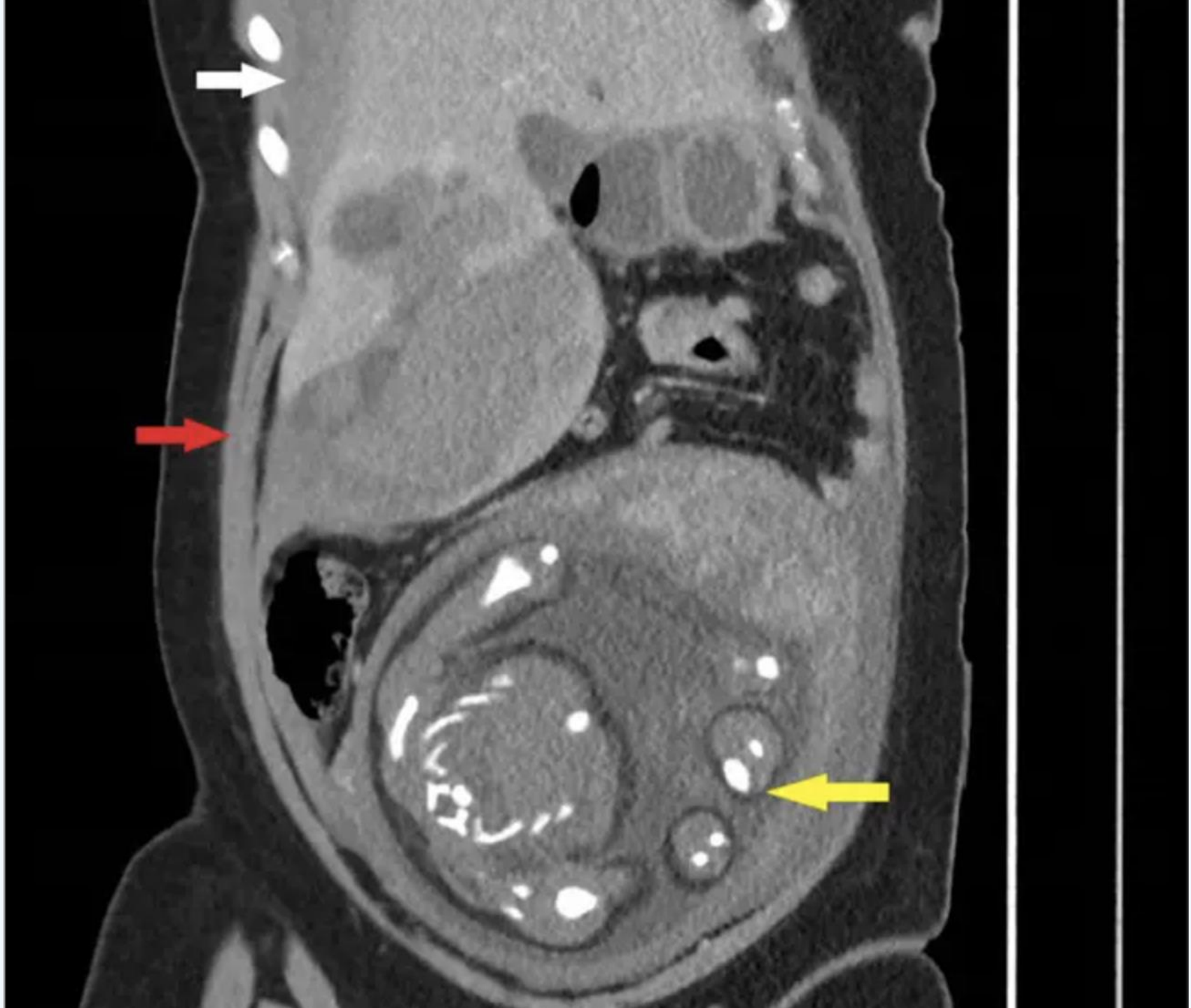



**=> Operation post partum**

Ugeskrift for Læger 2021

# DET KAN GÅ RIGTIG GALT



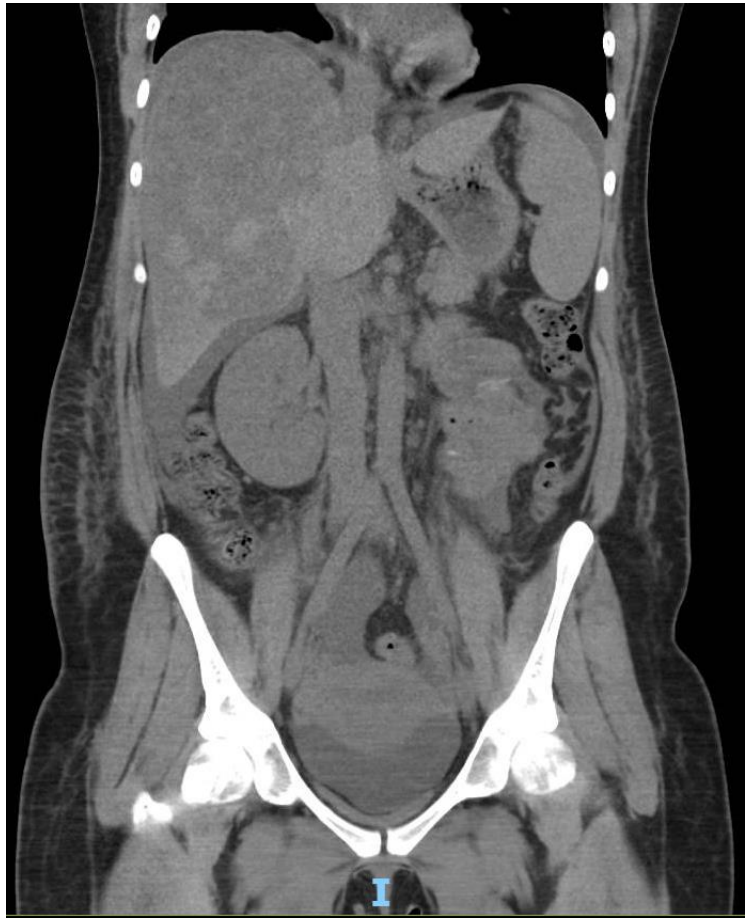
# Gestationel leversygdom

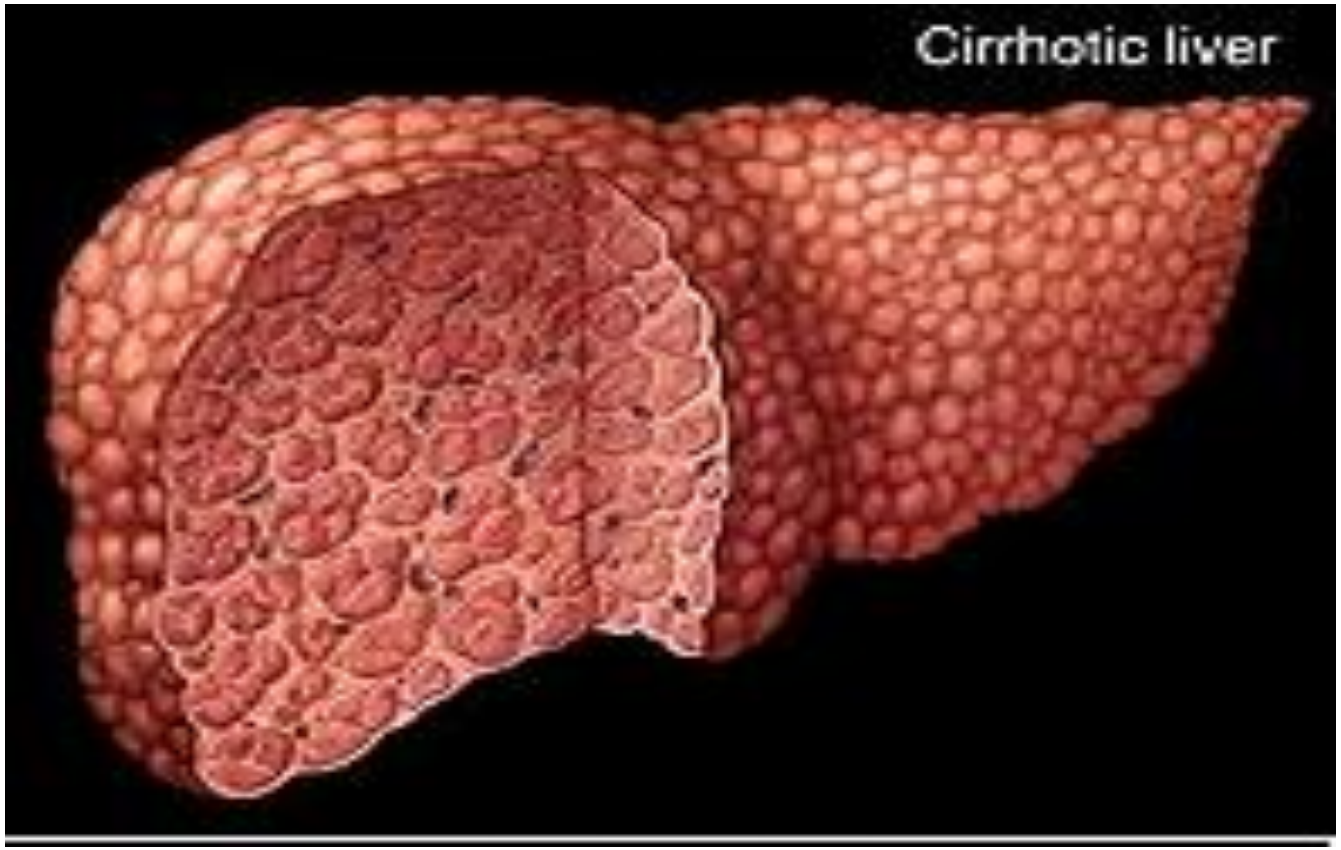
Uge 32
Hypertension, ødemer
Smerter i epigastriet
Stigende leverenzymer
Stigende bilirubin
Sløret sensorium
Akut forløsning
Nyrepåvirkning

**Table 6. Clinical and laboratory features of HELLP *vs.* AFLP.**

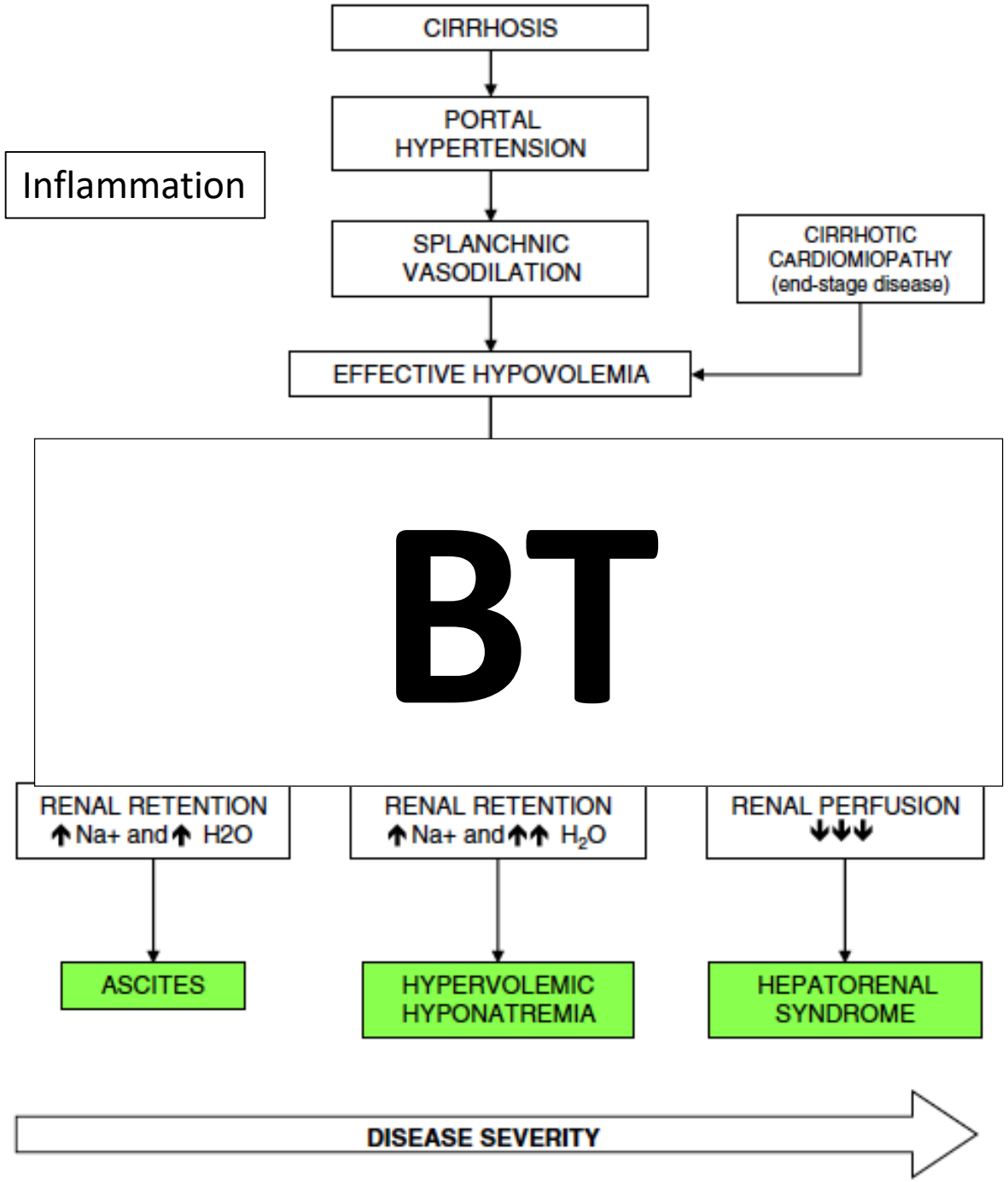
| Clinical/laboratory feature | HELLP | AFLP |
|---|---|---|
| **Clinical** | | |
| Altered sensorium | Late feature | + |
| Hypertension | ++ | +/- |
| Polyuria and polydipsia | – | + |
| **Laboratory** | | |
| Thrombocytopenia | Early feature | Late feature |
| Coagulopathy | Late feature | + |
| Acidosis | – | + |
| Acute kidney injury | +/- | ++ |
| Abnormal serum liver tests<br>Low fibrinogen<br>Prolonged aPTT (disproportionate to platelet fall) | + | ++ |
| Hyperbilirubinemia | +/- | ++ |
| Hypoglycaemia | – | ++ |

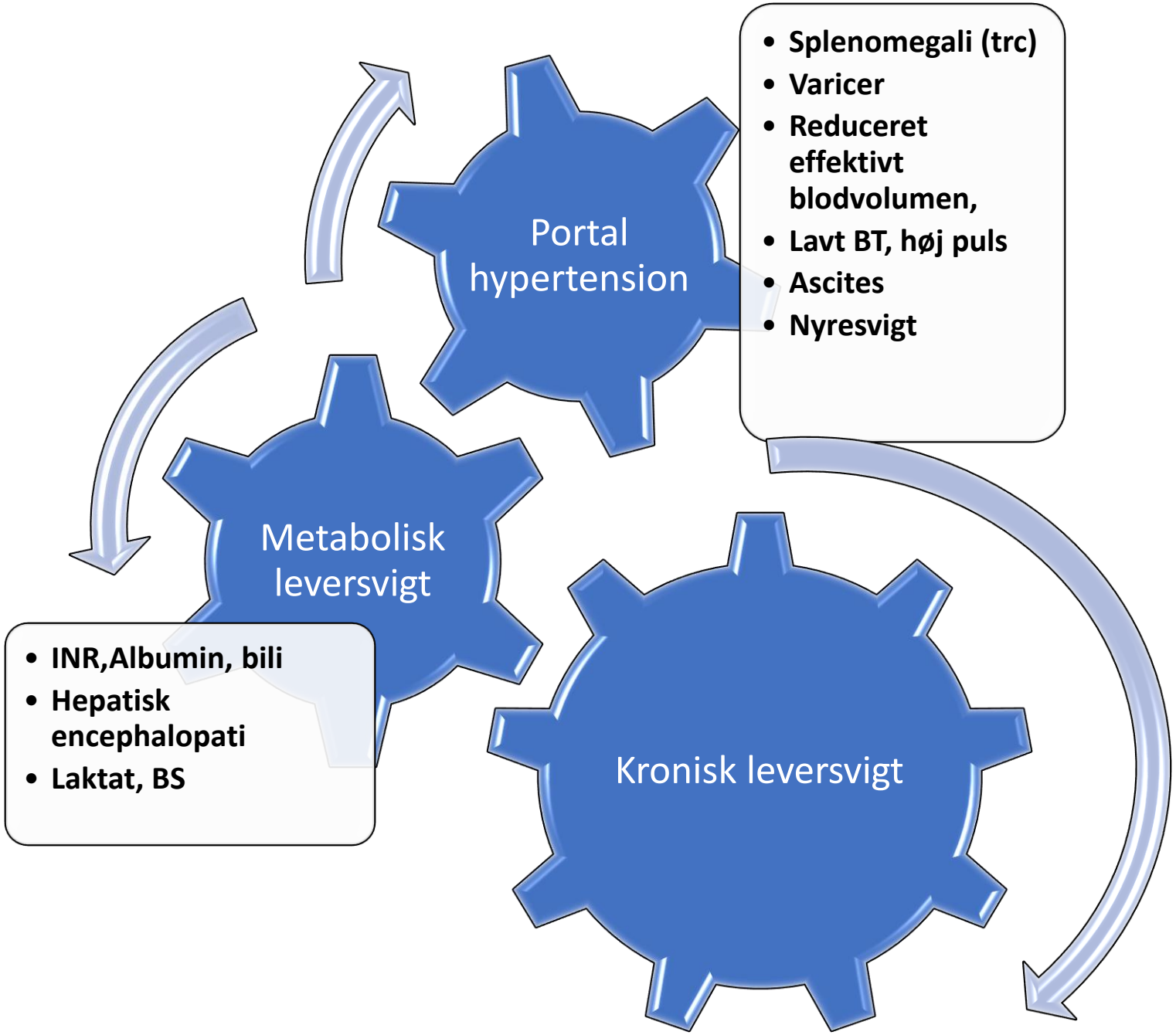
EASL guideline 2023




Cirrhotic liver

**Circulationen ved cirrose**




Portal hypertension
• Splenomegali (trc)
• Varicer
• Reduceret effektivt blodvolumen,
• Lavt BT, høj puls
• Ascites
• Nyresvigt
Metabolisk leversvigt
• INR,Albumin, bili
• Hepatisk encephalopati
• Laktat, BS
Kronisk leversvigt

# Child Pugh Score

| Measure | 1 point | 2 point | 3 point |
|---|---|---|---|
| Bilirubin (µmol/l) | <34 | 34-50 | >50 |
| Serum albumin (g/l) | >35 | 28-35 | <28 |
| INR | <1.3 | 1.3-1.5 | >1.5 |
| Ascites | Absent | Mild to moderate | Severe |
| Hepatisk Encephalopathy | Absent | I/II | >III |

| Points | Class | One year survival | Two year survival | Risk |
|---|---|---|---|---|
| 5-6 | A | 100 % | 85 % | 10 % |
| 7-9 | B | 80 % | 60 % | 30% |
| 10-15 | C | 45 % | 35 % | 80% |

Child et al 1964

# MELD

MELD = 3.78[Ln serum bilirubin (mg/dL)] + 11.2[Ln INR] + 9.57[Ln serum creatinine (mg/dL)] + 6.43

**3 month mortality is:**

- 40 or more — 71.3% mortality
- 30–39 — 52.6% mortality
- 20–29 — 19.6% mortality
- 10–19 — 6.0% mortality
- <9 — 1.9% mortality

Malinchoc M et al, 2000, Hepatology 31 (4): 864–71
Kamath PS et al, 2007, *Hepatology* 45 (3): 797–805.

## Cirrhosis with or without portal hypertension in pregnancy

### Pre-pregnancy counselling

**All women should receive pre-pregnancy counselling and discussion of risk based on risk stratification**

| Positive predictive factors | | | Negative predictive factors |
|---|---|---|---|
| **MELD score <6**<br>Risk of encountering a significant complication is minimal | **ALBI score <-2.7**<br>Predicts ↑ likelihood of live birth | **APRI score <0.84**<br>Predicts ↑ likelihood of reaching term | **MELD score >10**<br>Predicts ↑ likelihood of decompensation |

Has the women had a screening endoscopy (without varices identified) within 1-year of pregnancy?

| Yes | No |
|---|---|
| No further screening required in pregnancy | Screening endoscopy should be performed in pregnancy to assess for clinically significant varices and appropriate primary prophylaxis and endoscopic management provided |

### Endoscopy safety in pregnancy

- Safety of endoscopy in pregnancy:
  - Upper GI endoscopy may be safely performed in pregnancy
  - The usual left lateral position should be used
  - Can use midazolam judiciously where required

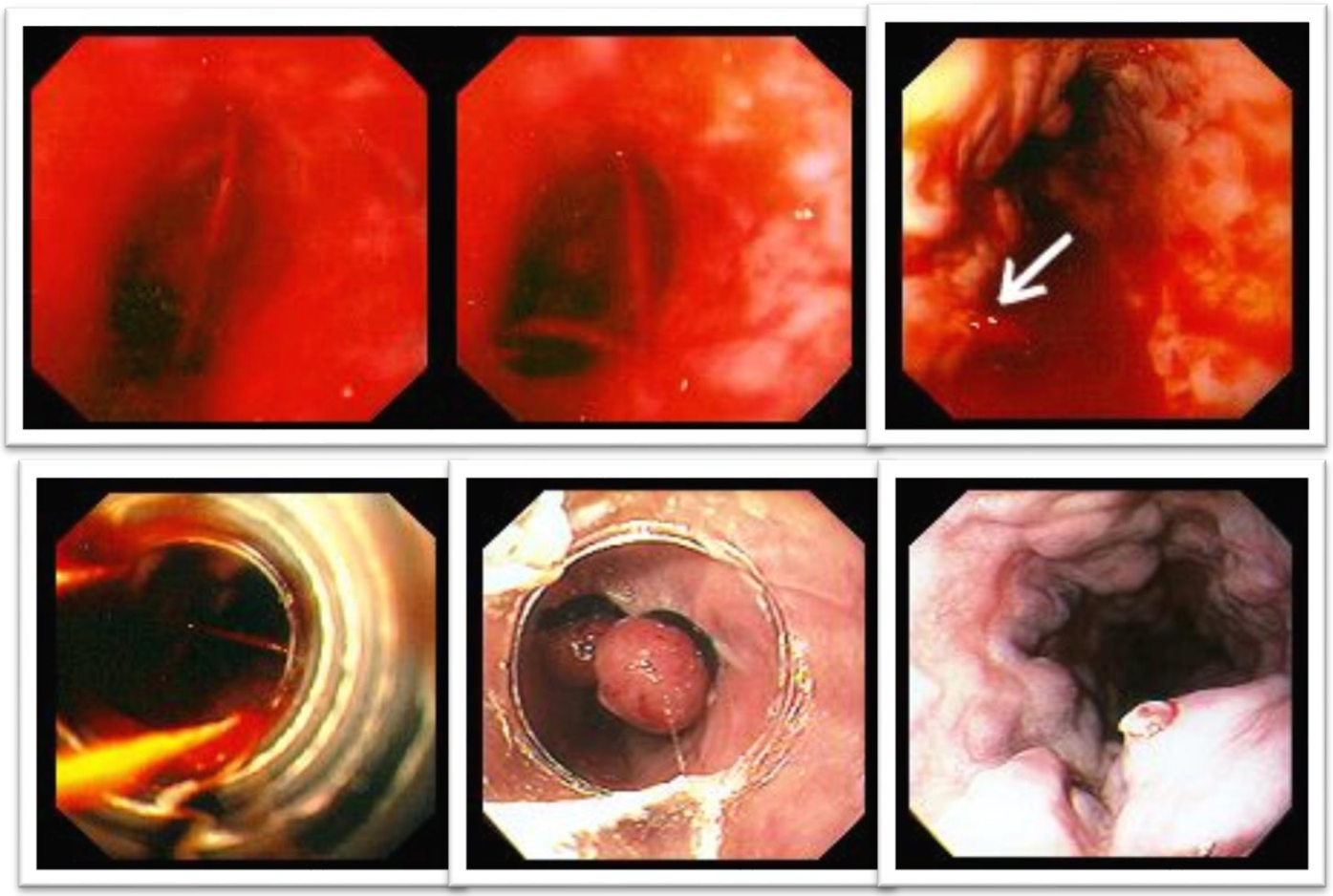
### Therapeutic safety-variceal bleed

| Safe | Caution |
|---|---|
| • Octreotide<br>• Broad-spectrum antibiotics<br>• Endoscopic band ligation remains gold-standard<br>• Cyanoacrylate glue may be used in life-threatening gastric variceal bleed<br>• TIPSS | • Terlipressin should be avoided unless endoscopic therapy and ocreotide have failed as may induce uterine contraction, spontaneous abortion or placental abruption<br>• Theoretical concern of shunting of toxic material to placenta with injection sclerotherapy |

### Delivery considerations

- Vaginal delivery preferred:
  - In the presence of varices shortened second stage/assisted second stage reduces need for repeated Valsalva and risk of bleeding
- In women requiring caesarean section for obstetric indications:
  - Correct coagulopathy/thrombocytopenia
  - MRI/US can be used to map intra-abdominal/pelvic varices
- The MDT should be involved in all cases

EASL guideline



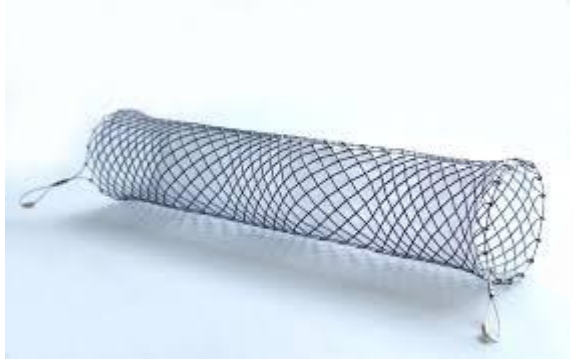
Bleeding from esophageal varices
6 weeks mortality 10-20 % on standard therapy

Baveno VI J hep 2015

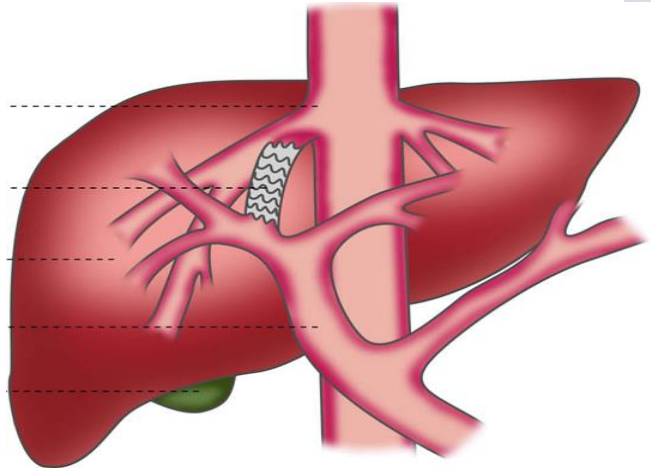
# HÆMOSTASE


Glue

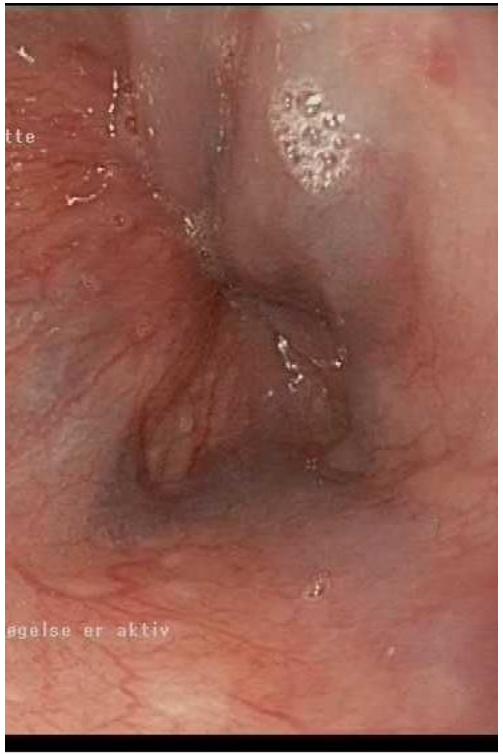
ELLA-stent

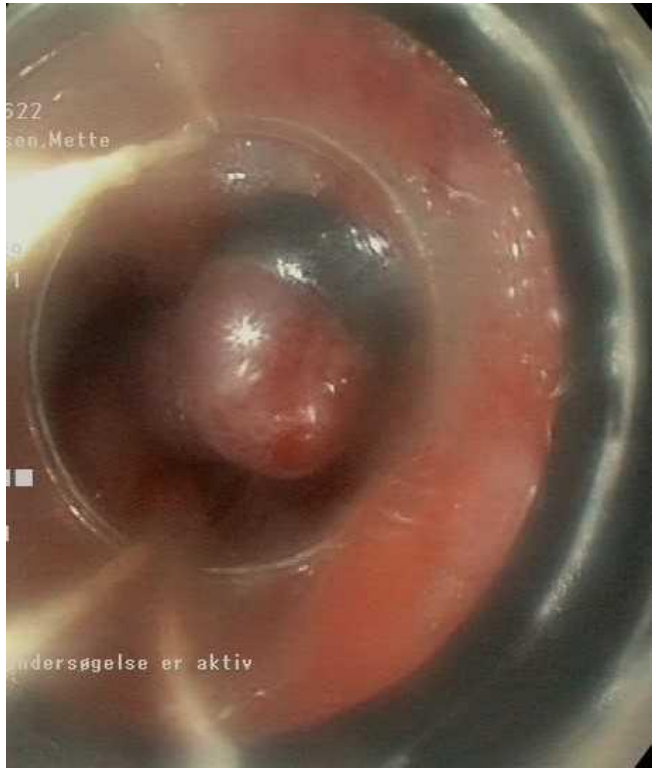


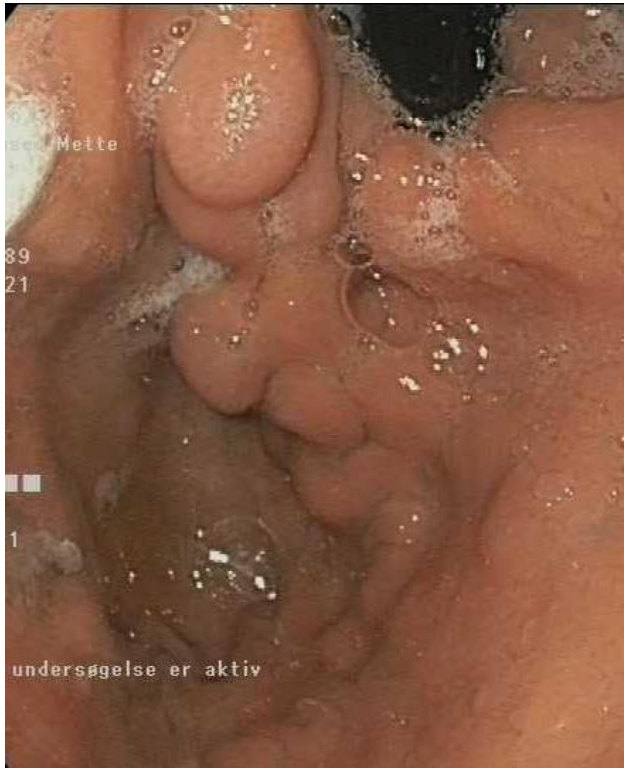
# REBLØDNING

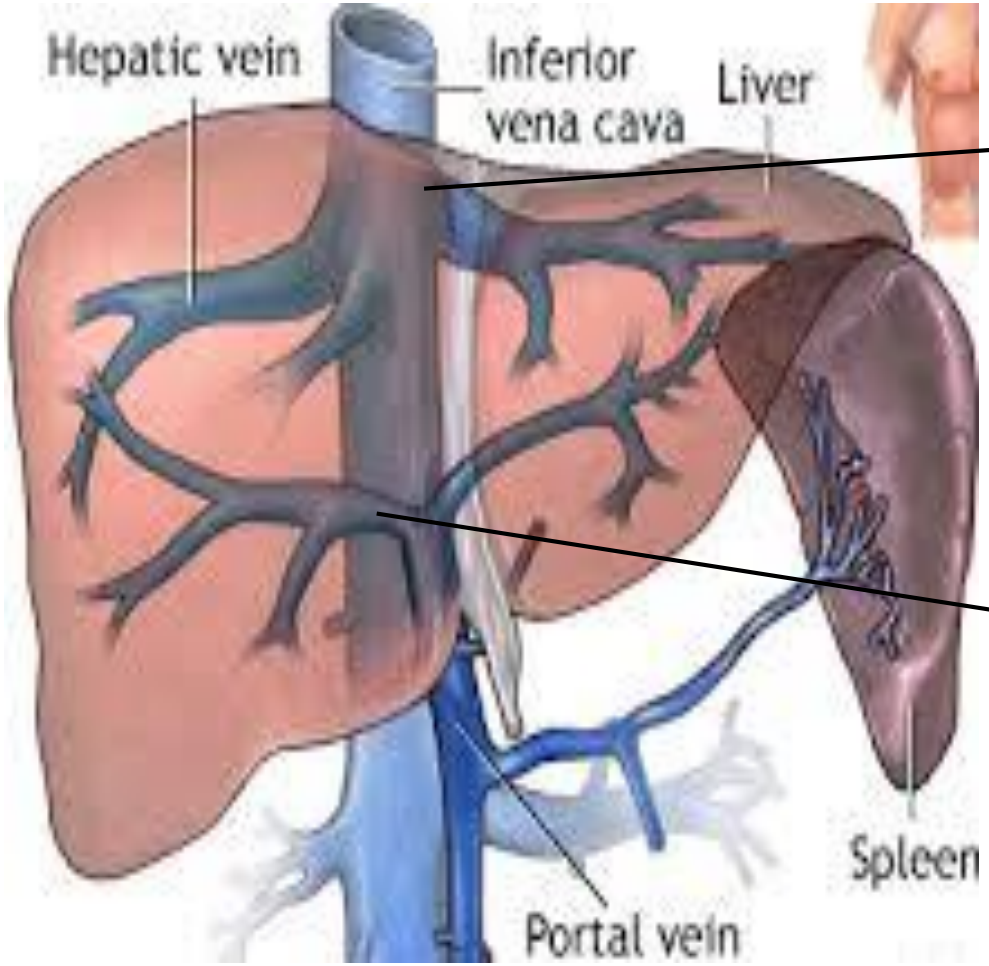
- PSC, cirrose
- 30 år
- Grav 1
- 2. trimester

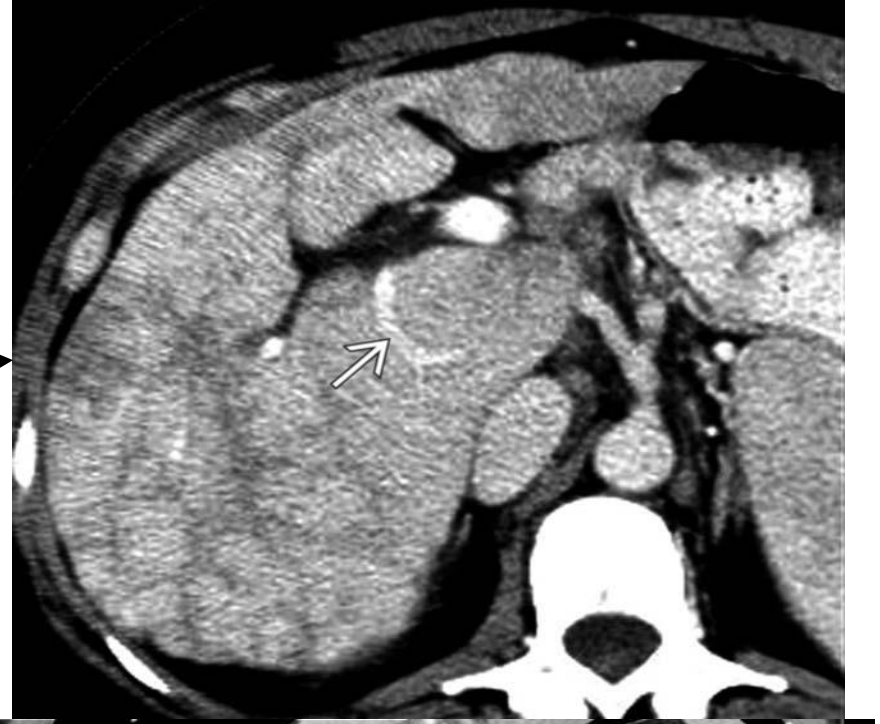


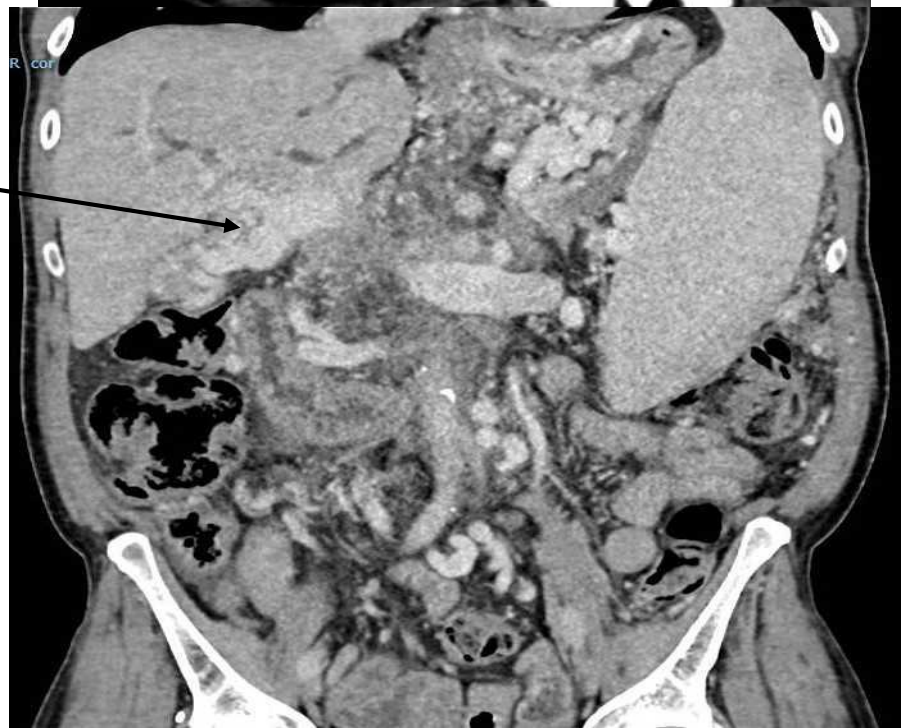



# Vaskulær leversygdom

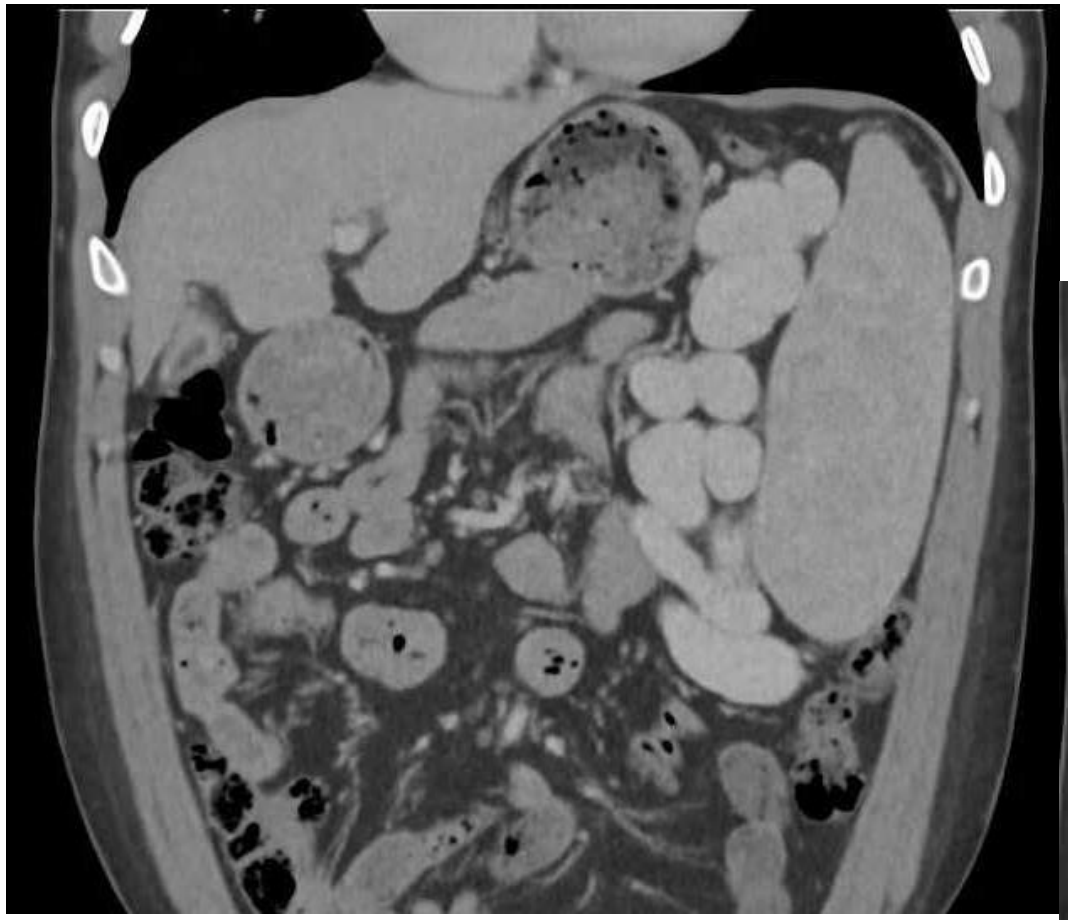


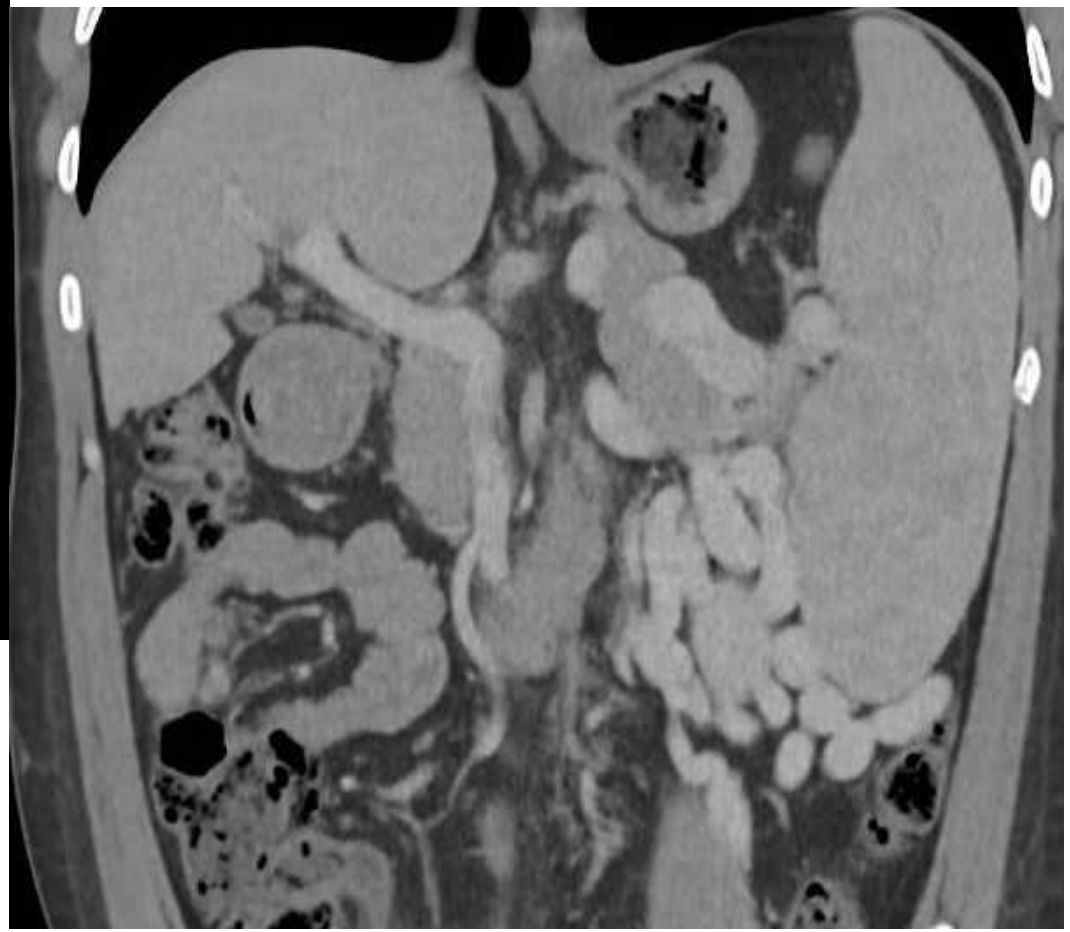





**KOAGULOPATI => AK BEHANDLING**
**MYELOPROLIFERATIV SYGDOM**

# Idiopatisk non cirrotisk portal hypertension





**HJÆLP !!**
23 år

Leveradenomer + FNH. 4-5 cm store, Skrumpet lidt ved vægttab
Tidligere vurderet til LTX, afstået fra dette
Noncirrotisk portal hypertension, nu grad 2 varicer.

Vil være gravid !