



Hepatitis E: an emerging zoonosis?

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ULB

Case n°1: Mister A.M., 51 years

- Admitted on 20/04/2011
- Stayed in Pakistan from 10/03 to 04/04



- During the stay: diarrhea and vomiting
- Weight loss: 4 kg
- Symptomatic treatment
- Self-limited

Case n°1: Mister A.M., 51 years

- Back in Belgium
 - Persisting loose stools
 - Asthenia
 - Vomiting
 - Icterus → family doctor → Emergency Room
- Medical history:
 - Type 2 diabetes
- Current medication:
 - Metformine
 - Repaglinide

Case n°1: Mister A.M., 51 years

- Lifestyle
 - Independent in catering
 - Alcohol: 2 units/week
 - Tobacco: 1 pack/day
 - Native from Pakistan, lives in Belgium for years
- Anamnesis:
 - No alcohol consumption for a month.
 - No paracetamol nor other toxic.
 - Bottled water
 - Restaurants

Case n°1: Mister A.M., 51 years

Physical examination

- BP 110/60 HR 72 T° 37.4°C
- Weight: 70 kg (minus 9 kg)
- **Mucocutaneous icterus**
- No ascitis, no hepatosplenomegaly
- No lower limb oedemas
- No sign of hepatic encephalitis, flapping tremor negative
- No cirrhosis stigmata

Case n°1: Mister A.M., 51 years

	J0 – 20/04/2011	Normal values
PT	60%	70-130%
Leuco	10600 /mm ³	
Hb	15.0 g/dl	
Platelet count	174 000 /mm ³	
CRP	1.8 mg/dl	<1.0 mg/dl
Urea	27 mg/dl	
Creatinin	1.0 mg/dl	
Bilirubin	8.7 mg/dl	<1.2 mg/dl
Alcaline phosphatases	310 UI/L	
GGT	190	
ALAT	2443 UI/L	<34 UI/L
ASAT	2216 UI/L	
Albumin	3.4 g/l	

Case n°1: Mister A.M., 51 years

Investigations

- Hepatic imagery: normal
- Serologic tests HAV, HBV, HCV negative
- EBV – CMV: previous contact
- Auto-immunity markers negative
- Search for Wilson's disease negative
- Stool examination: negative for parasites

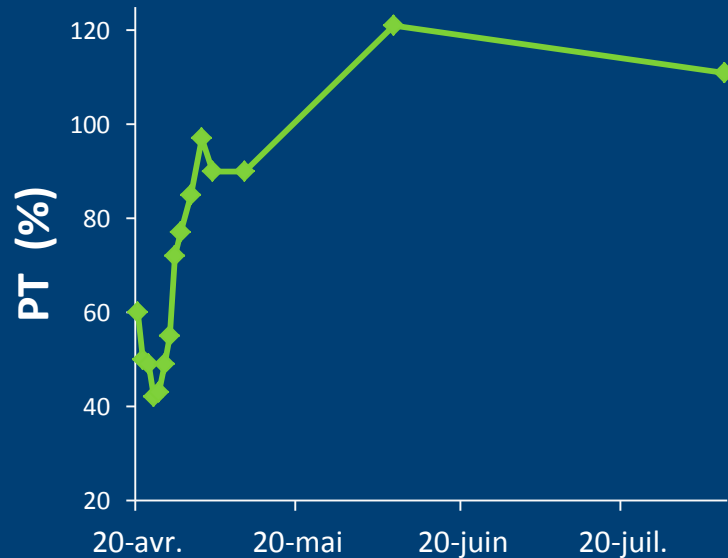
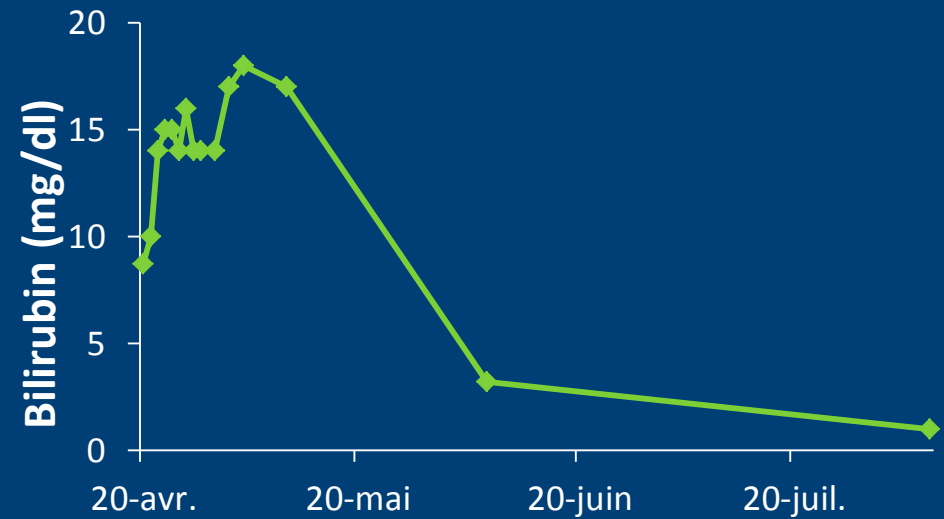
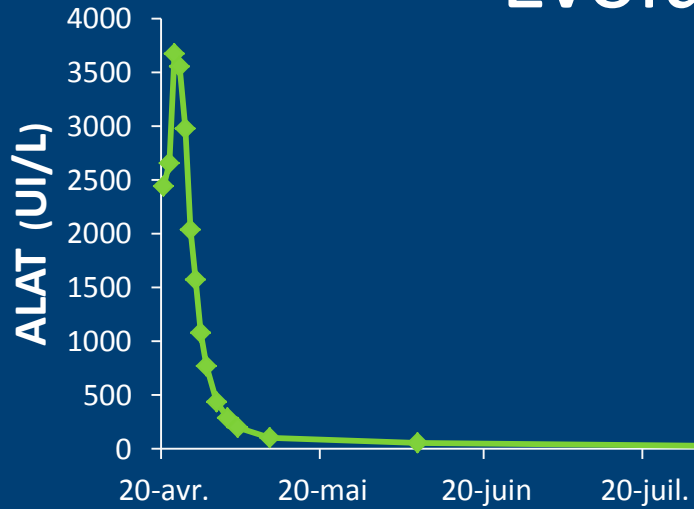
Case n°1: Mister A.M., 51 years

Investigations

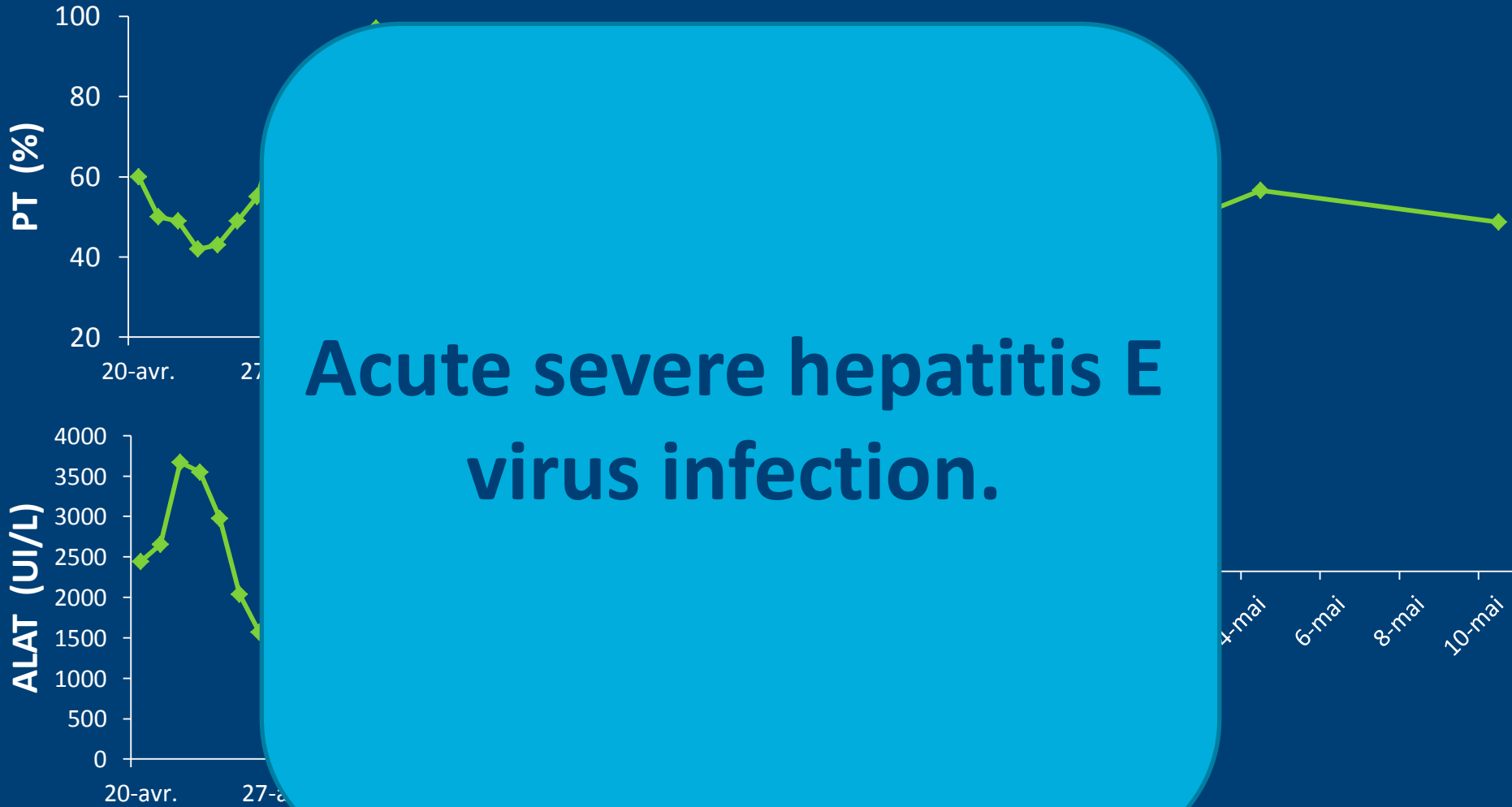
- Hepatic imagery: normal
- Serologies HAV, HBV, HCV négative
- EBV – CMV: previous contact
- Auto-immunity markers negative
- Search for Wilson's disease negative
- Stool examination: negative for parasites
- **HEV: IgG and IgM positive, PCR HEV positive in blood.**

Case n°1: Mister A.M., 51 years

Evolution

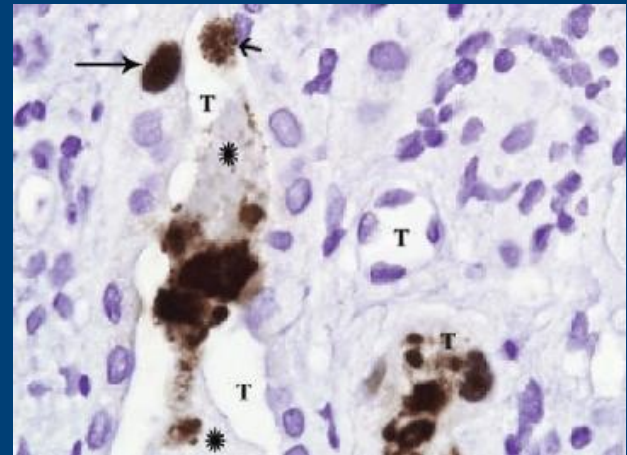


Case n°1: Mister A.M., 51 years



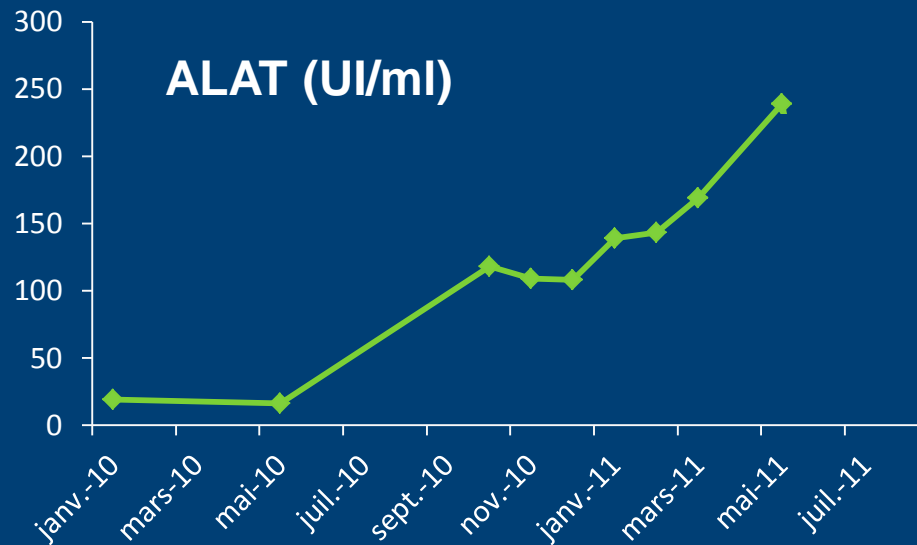
Case n°2: Mister D.C., 62 years

- Renal transplantation in 2005 for hepatorenal polycystosis.
- Chronic kidney failure (creat 1.9 mg/dl MDRD 36 ml /min)
 - Obstructive pathology of the transplant
 - BK Poliomavirus nephropathy
- No other medical history
- Current medication :
 - Tacrolimus (Advagraf® 1 mg)
 - Azathioprine (Imuran® 100 mg)
 - Methylprednisone 6 mg
 - Tamsulosine 0.4 mg



Case n°2: Mister D.C., 62 years

- Since october 2010: progressive transaminases elevation



- No cholestasis.
- Asymptomatic. Normal physical examination
- Hepatic imagery: not contributive in january 2011
- Liver biopsy in january 2011: mild aspecific hepatitis

Case n°2: Mister D.C., 62 years

Investigations

- Serologies HAV, HBV, HCV, HIV negative
- No travel abroad
- No toxic nor alcohol consumption
- Auto-immune markers negative
- No dysmetabolism

Case n°2: Mister D.C., 62 years

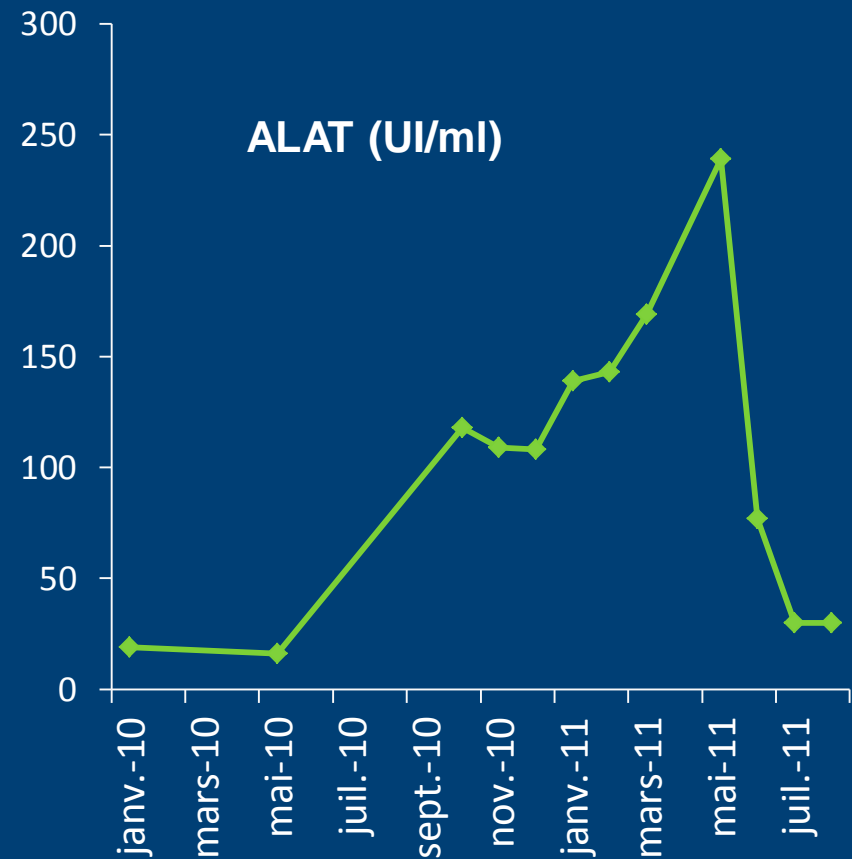
Investigations

- Serologies HAV, HBV, HCV, HIV negative
- No travel abroad
- No toxic nor alcohol consumption
- Auto-immune markers negative
- No dysmetabolism
- **PCR HEV positive!**

Case n°2: Mister D.C., 62 years

Evolution

- Ribavirin treatment: 400mg a day
 - Transaminases normalisation
 - PCR at two months: negative
 - General side effects
 - Leucopenia
 - No anemia
 - Better with 200 mg a day
 - Creatinine 1.6 mg/dl

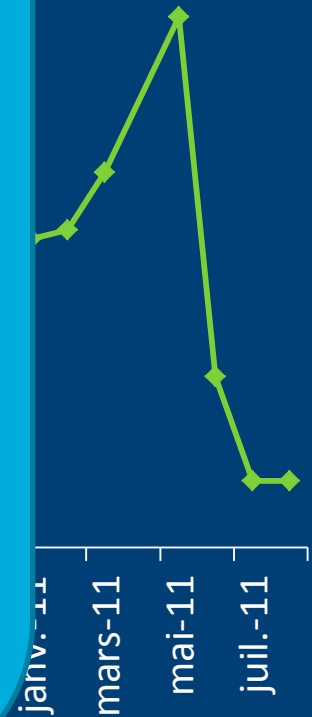


Case n°2: Mister D.C., 62 years

Evolution

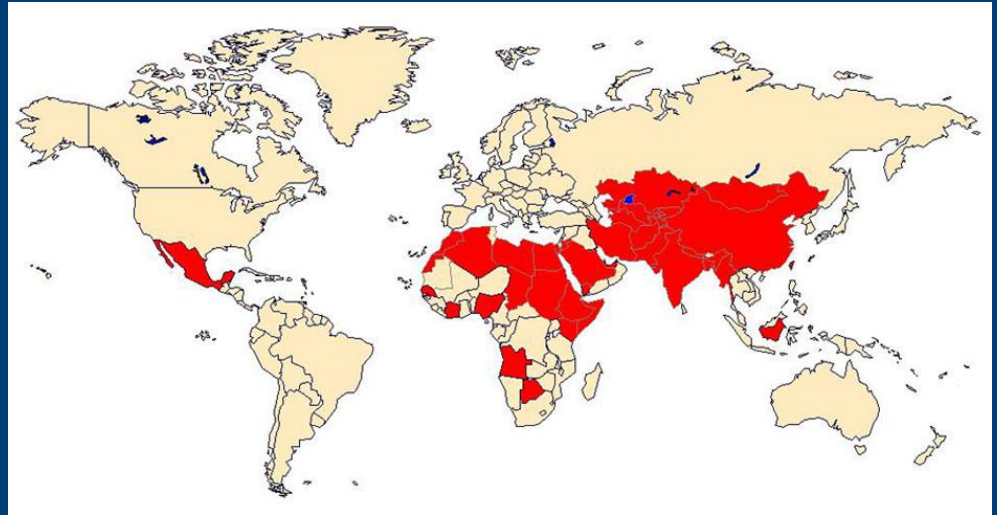
- Ribavirin treatment
 - Transaminases
 - PCR at 10⁶ IU/ml
 - Generalized pruritus
 - Leucopenia
 - No anaemia
 - Better renal function
 - Creatinine

**Chronic hepatitis E
virus infection.**



Hepatitis E virus infection

- Single stranded RNA virus, hepeviridae family, 4 genotypes, 24 subtypes.
- Enterically transmitted.
- Young adults.



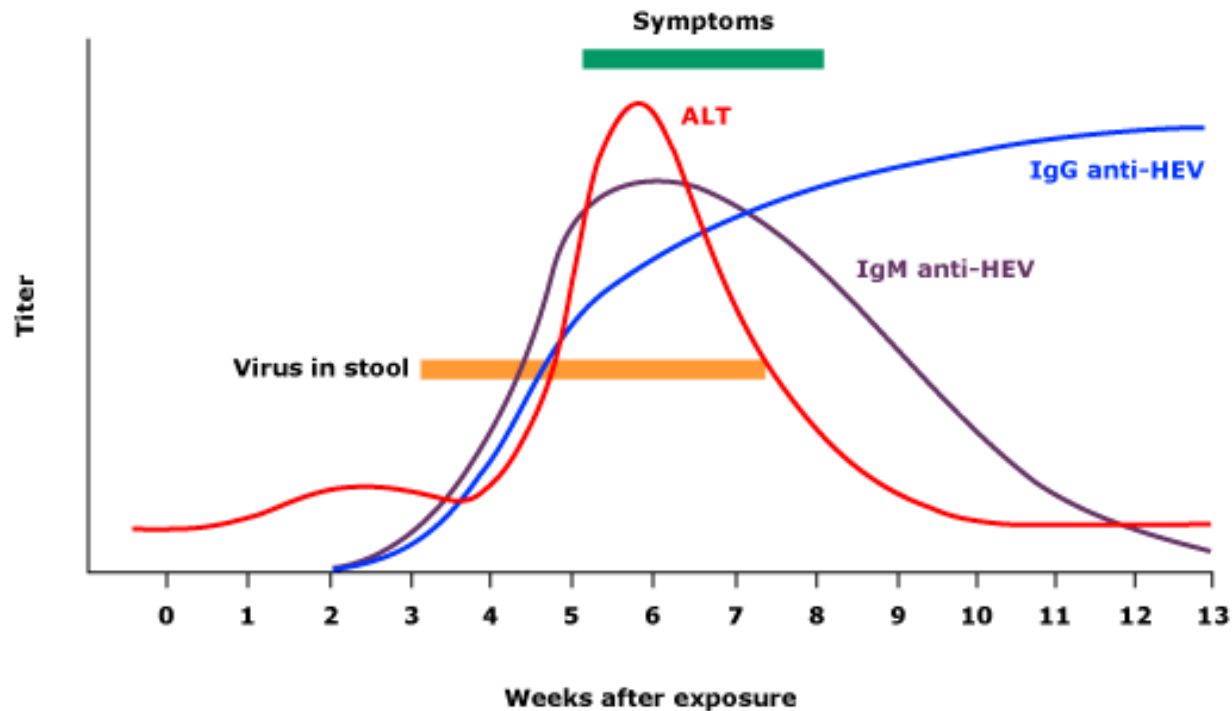
- « Imported » cases
- « Native » cases
 - Undercooked meat (pork, deer, wild boar), occupational contact with animals
- Overall seroprevalence of 21% (US – Third National Health and Nutrition Examination survey)

Hepatitis E: clinical features

- Self-limited acute hepatitis: aspecific symptoms or asymptomatic.
- Fulminant hepatitis: 1-2%
 - 10-20% during pregnancy
 - Pre-existing liver disease decompensation.
- Chronic infection: elevated liver enzymes and PCR + >6 months.
 - Solid organ Transplant recipients, Immunosuppression, HIV,...
 - Evolution to cirrhosis: 15%

Hepatitis E: Diagnosis

Hepatitis E virus infection typical serologic course



Reproduced from: Centers for Disease Control and Prevention.
<http://www.cdc.gov/hepatitis/index.htm>.

Hepatitis E: prevention

- Vaccines in development in endemic areas.
- No demonstrated efficacy of specific Ig.
- Classical hygienic measures.
- Solid organ transplant recipients should avoid undercooked pork and deer meat.

Hepatitis E: treatment

- **Acute infection:**
symptomatic and supportive treatment
- **Chronic infection**
 - Immunosuppressant dose reduction leads to viral clearance in 30% of cases.
 - Switch Tacrolimus to Cyclosporin
 - Peg-interferon (contra-indicated in kidney transplantation)
 - Ribavirin monotherapy
 - Adapted to creatinin clearance 400 to 800 mg a day in two doses.
 - Side effects: anemia, can necessitate EPO
 - Duration?

Take home messages

- HEV is a cause of acute hepatitis:
 - Back from endemic areas
 - Sporadic cases
- HEV is a cause of chronic hepatitis and cirrhosis in immunocompromised patients.
- Ribavirin monotherapy may be indicated in chronic forms.

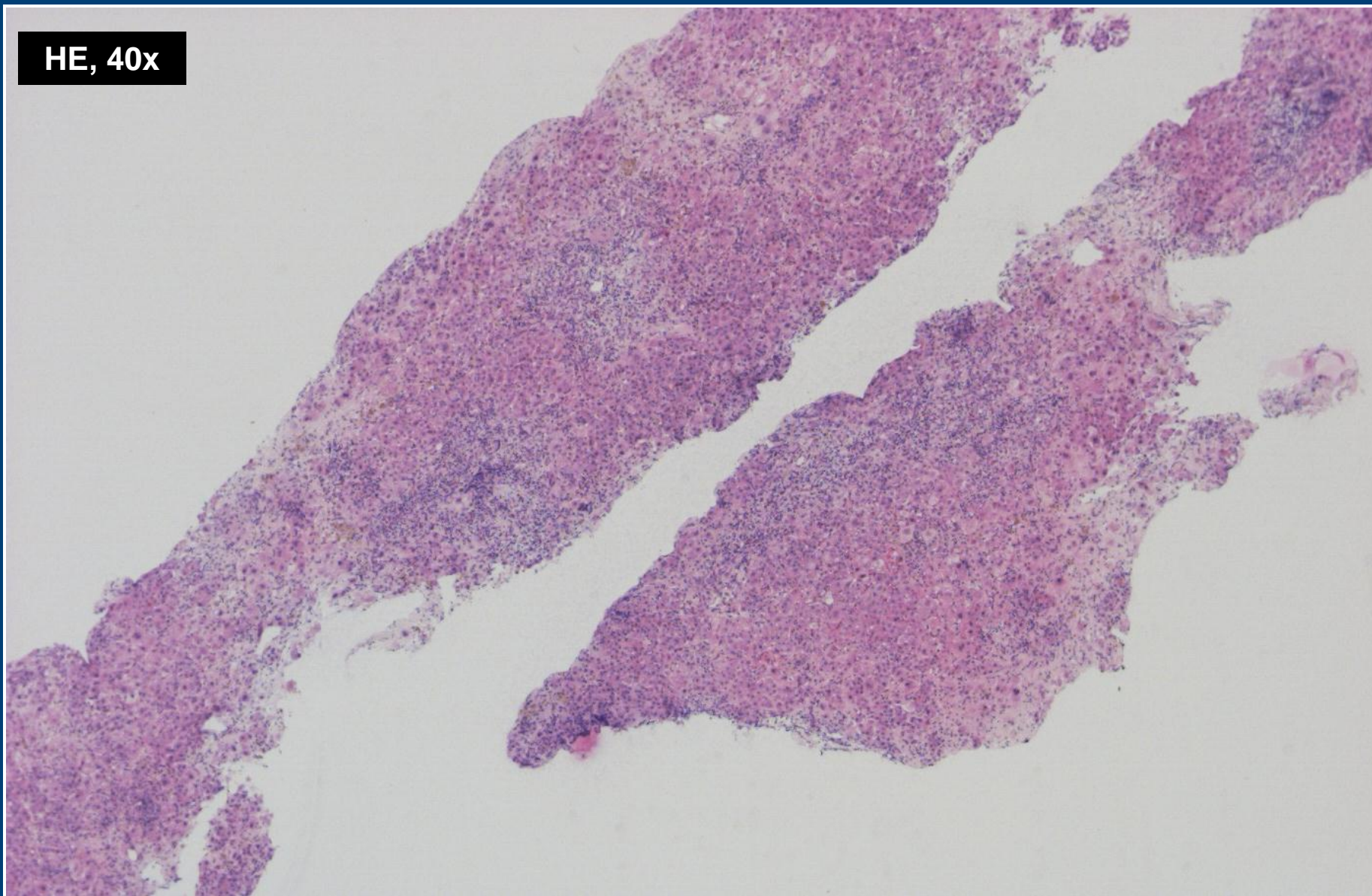
THANK YOU FOR YOUR ATTENTION!

BACK UP SLIDES

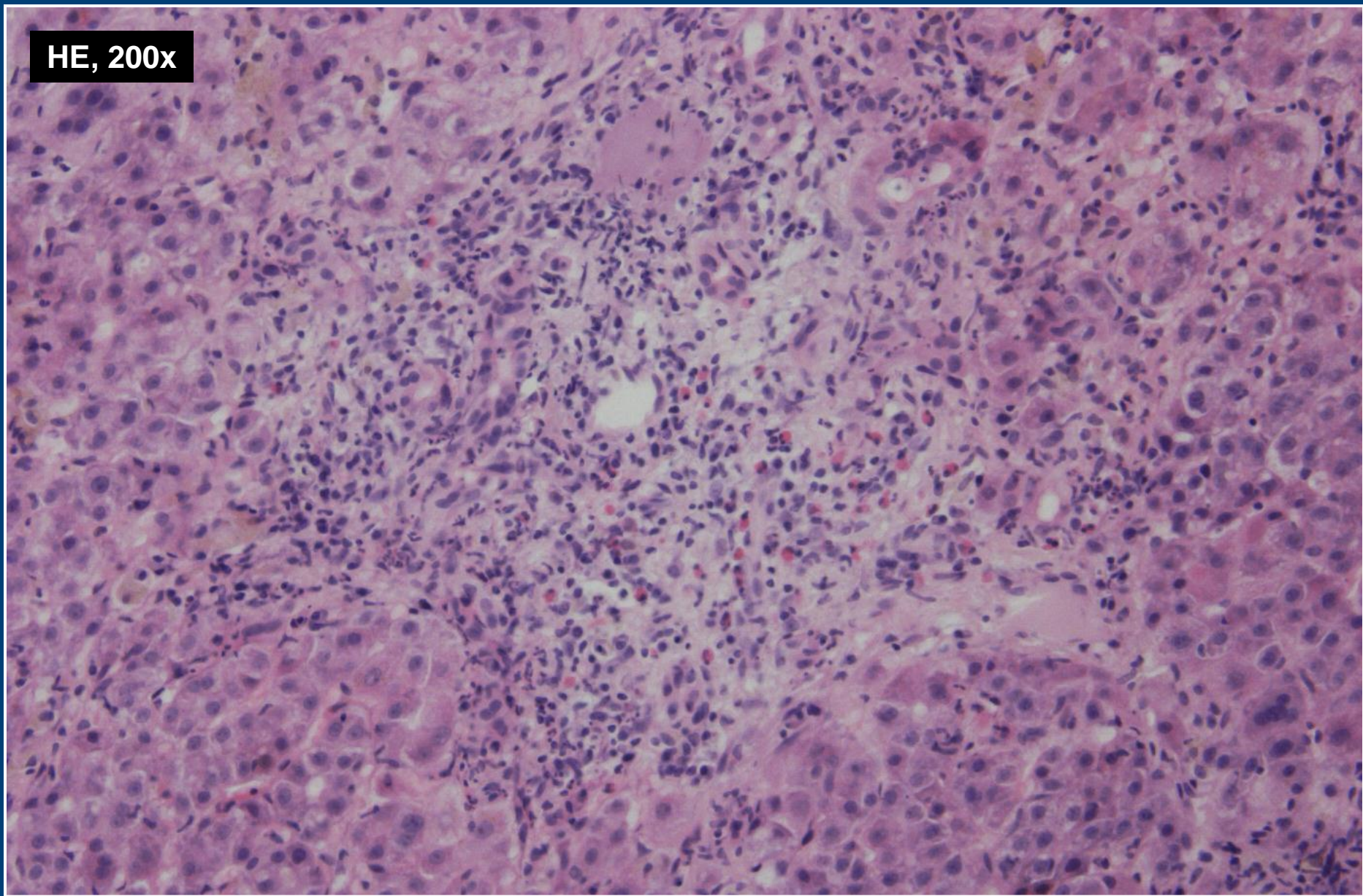
Bilan

- Imagerie banale
- BHTJ: pas d'hypertension sinusoidale
- Anapath:
 - Architecture lobulaire préservée
 - Infiltrat inflammatoire périportal + lame hépatique bordante
 - Souffrance péri-centrolobulaire
 - Infiltrat à prédominance lymphocytaire avec éosinophiles.
 - Fibrose sinusoidale

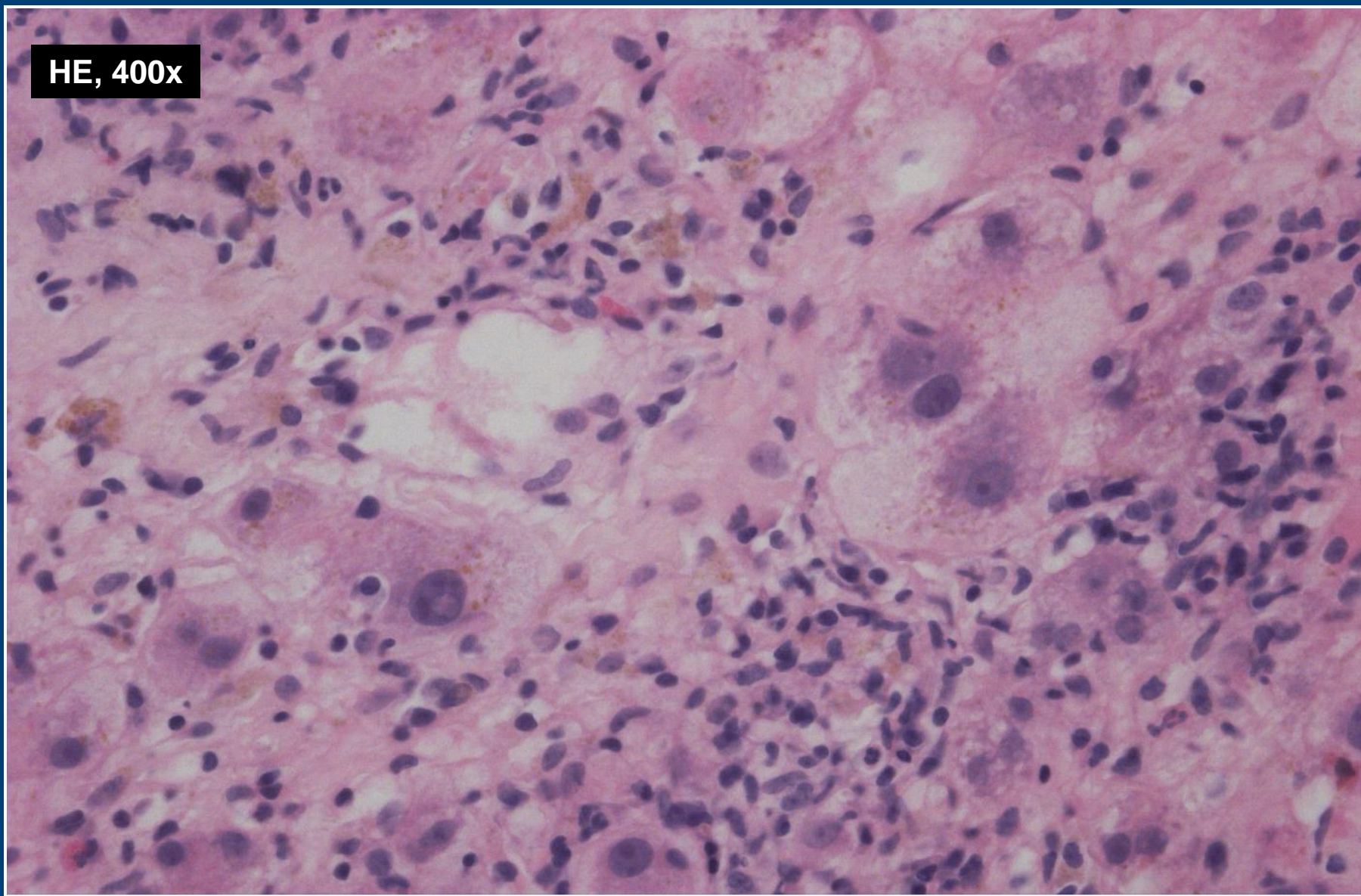
HE, 40x



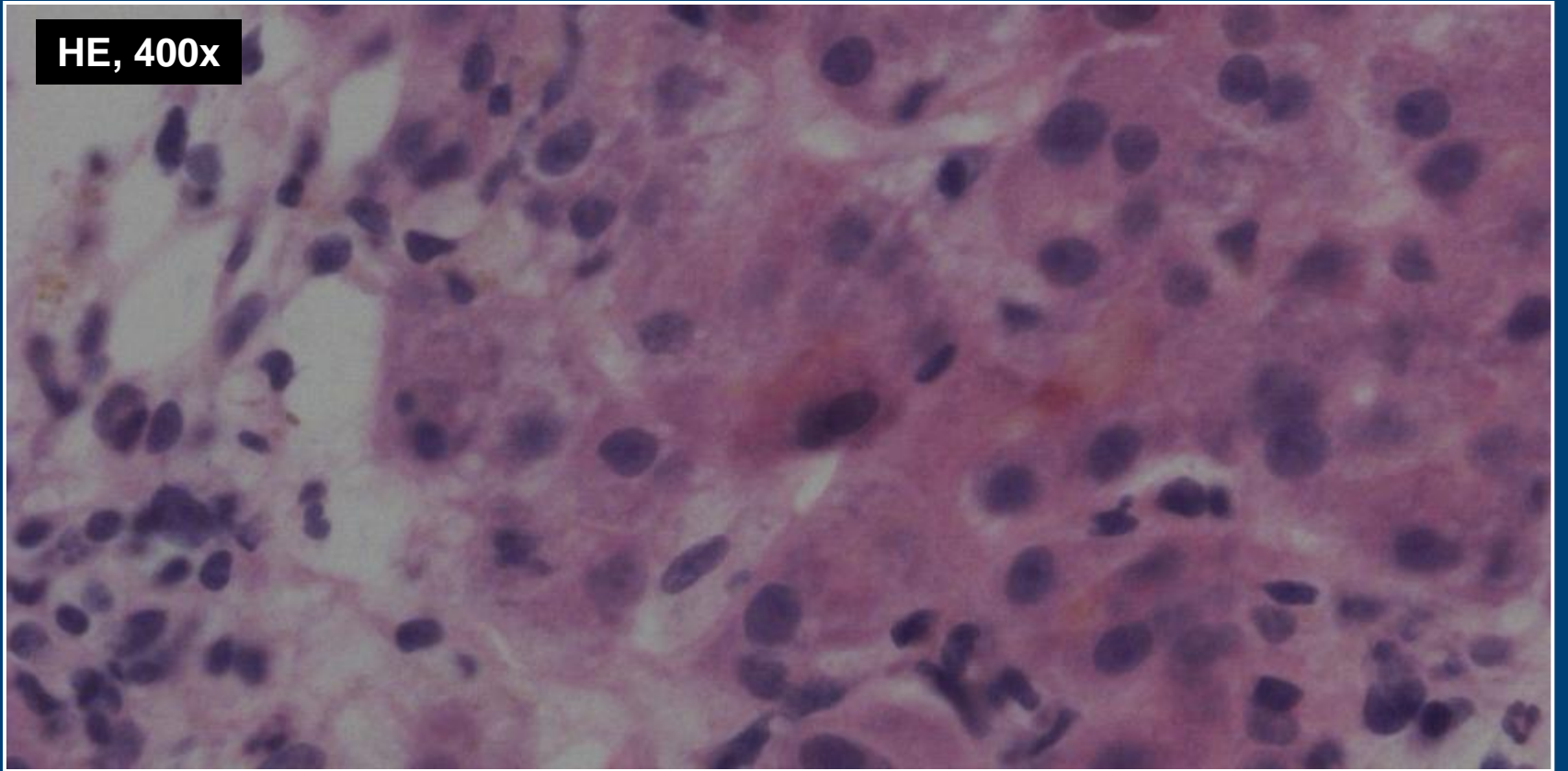
HE, 200x



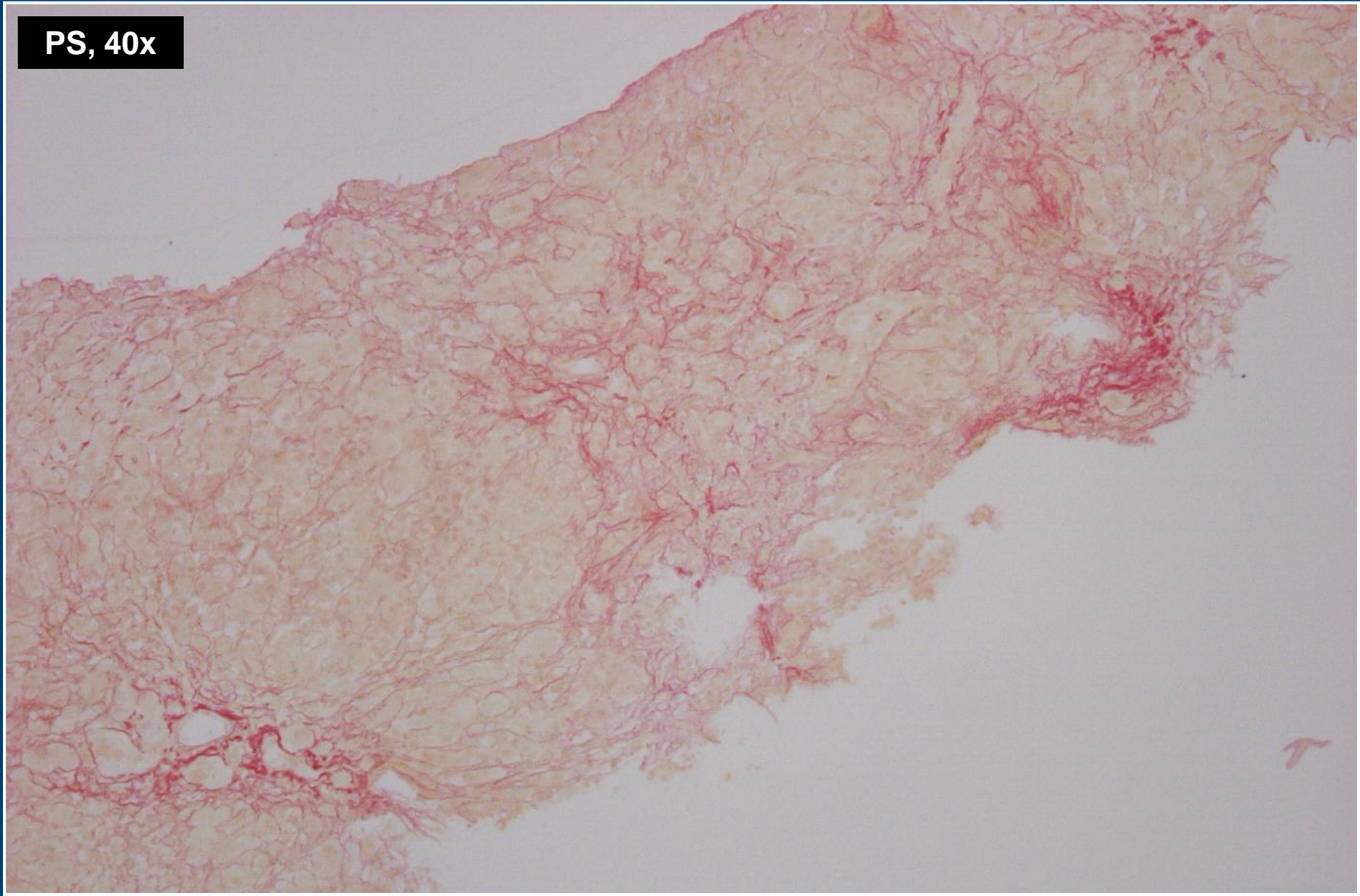
HE, 400x



HE, 400x

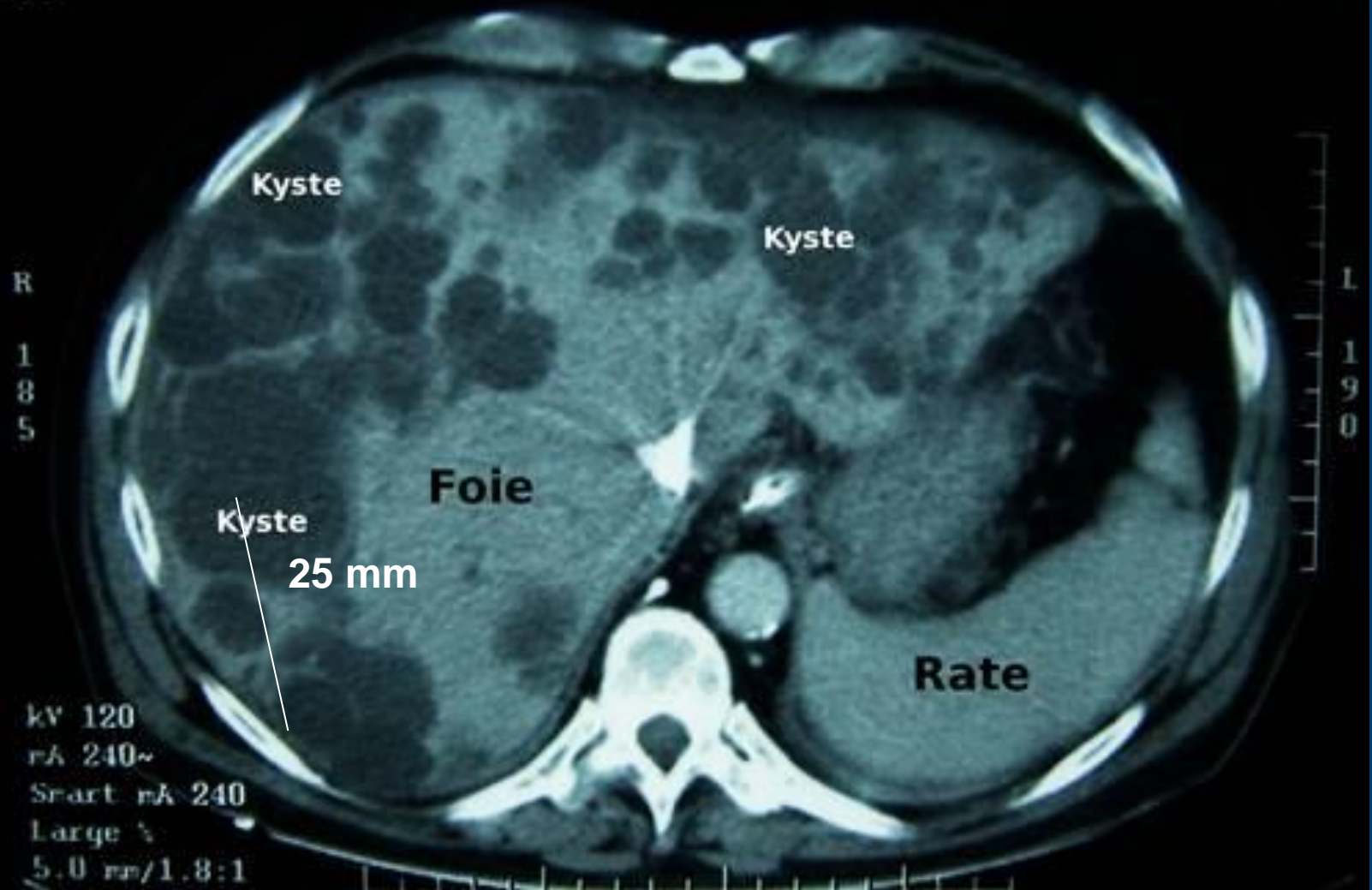


PS, 40x



SOFT

MF:1.3



Kyste

Kyste

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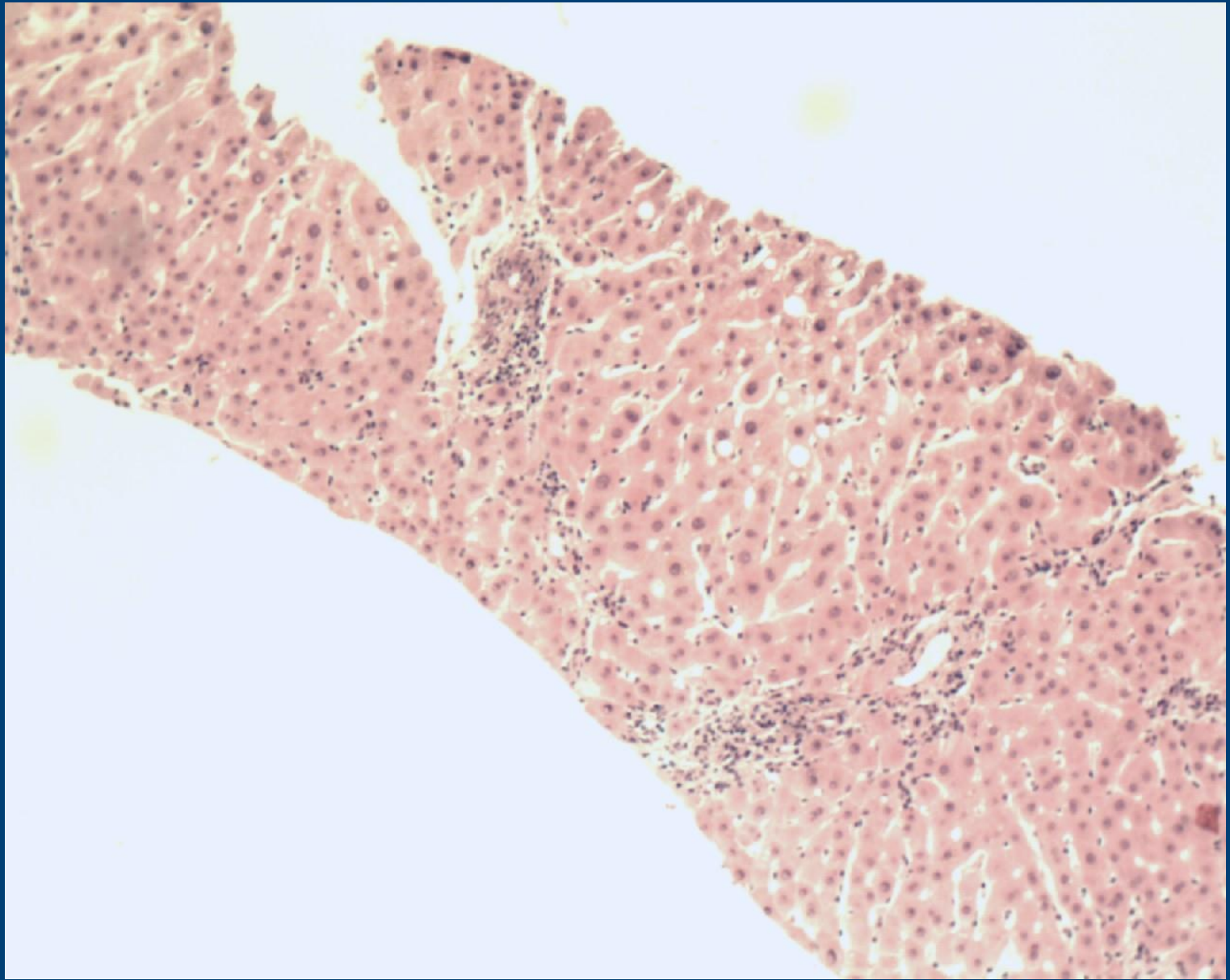
Foie

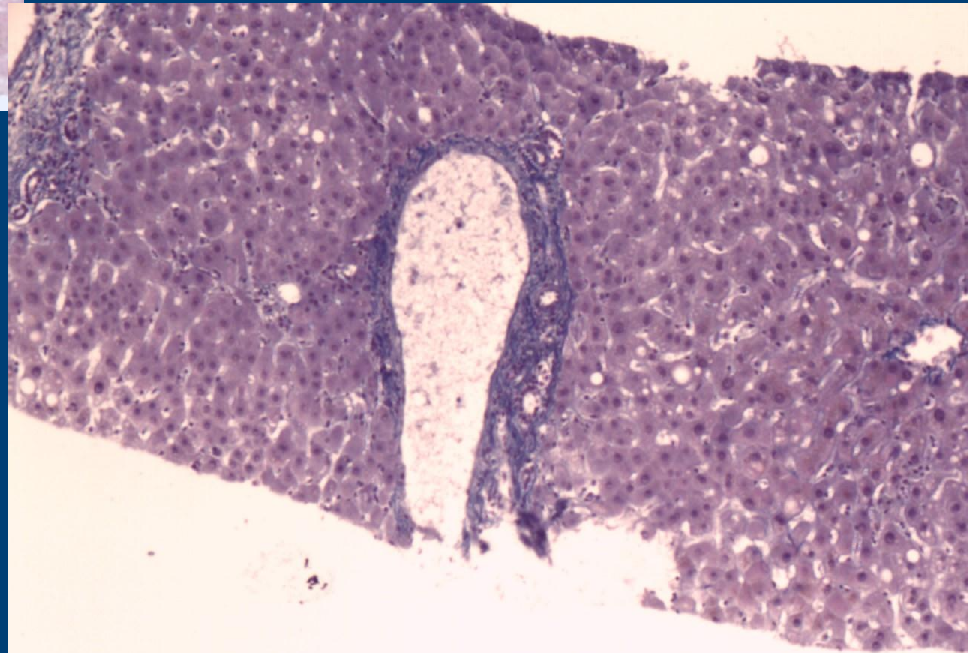
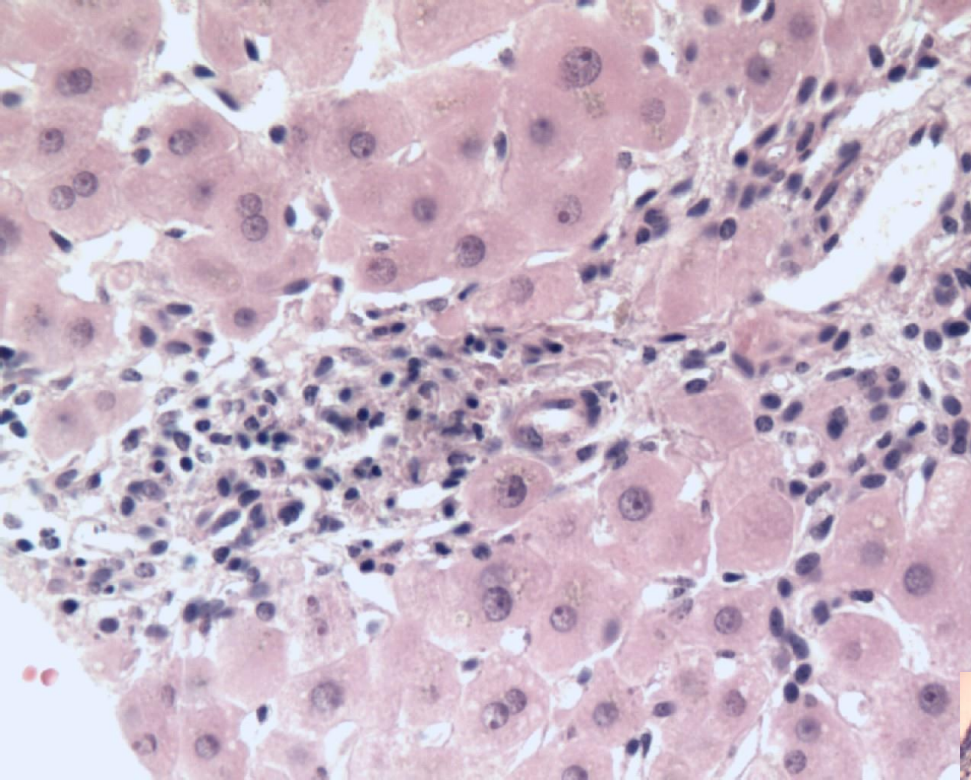
Kyste

25 mm

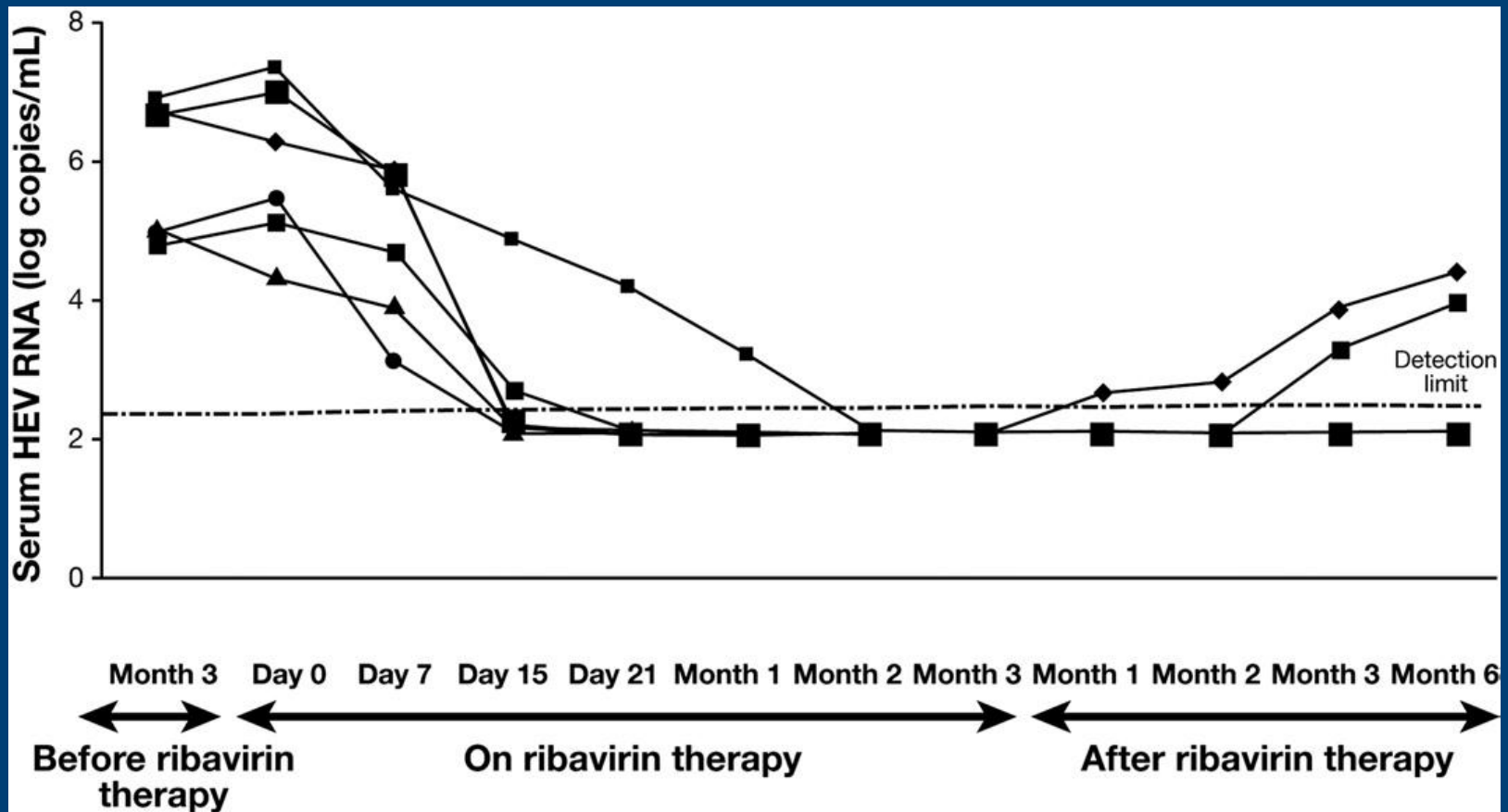
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mA 240~
Start mA 240
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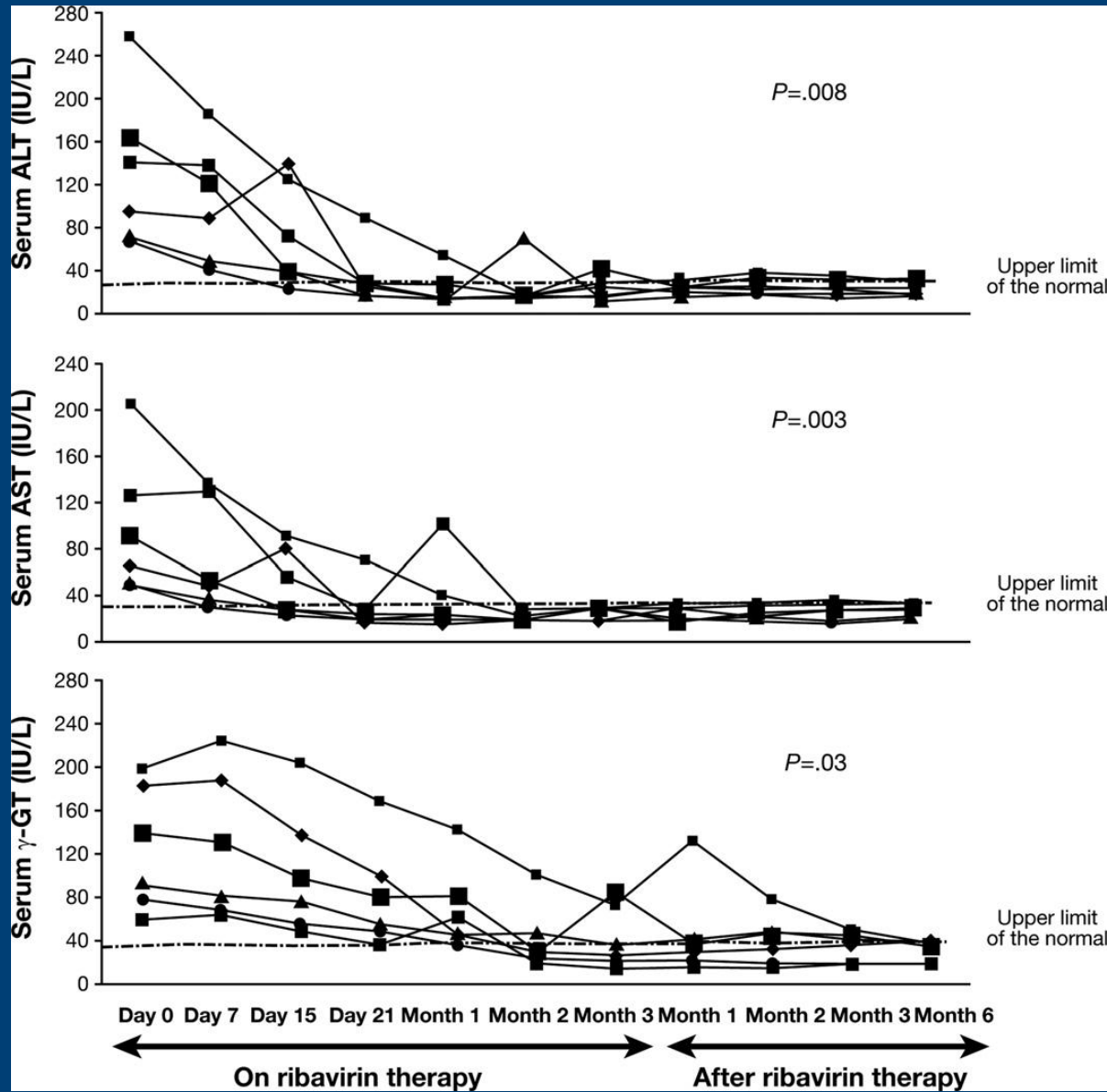




Trichrome de Masson



6 cas d'HEV chroniques chez transplantés traités par Ribavirine
 Kamar et al, Gastroenterology 2010;139:1612-1618



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