AN INTERESTING CASE OF LIVER FAILURE

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PEDIATRIC HEPATOLOGY AND GASTROENTEOLOGY

APOLLO CHILDREN'S HOSPITAL

HISTORY

- Ms. A, a 9 year old girl,
- First born of non consanguineous marriage
- From Tripura
- Intermittent fever for 15 days and yellowish discoloration of the sclera for 10 days

- No history of diarrhoea
- No history of abdominal pain
- No history of high grade fever with chills, anemia, vomiting, abdominal distension
- No history of seizures

- No history of TB contact
- No history of encephalopathy/ sleep disturbances
- No history of GI bleeds(hemetemesis/ melena)
- No history of edema

- No history of any treatment(herbal supplements) given outside
- No history of recent blood transfusion, needle stick injury

- She was the first born of non consanguineous parents
- No family history of liver diseases/ deaths.

- Antenatal period / Perinatal period was uneventful
- Vaccination as per the national immunisation program

ON EXAMINATION

- Alert, GCS-15/15
- Icteric
- No stigmata of chronic liver disease

- Liver palpable 4cm below the right costal margin, firm, smooth surface, margins well felt
- Spleen palpable 1 cm below the left costal margin
- No KF ring (s/b ophthalmologist)

SYNOPSIS

- 9 year old girl with fever and jaundice of recent onset, with mod Hepatomegaly with no overt bleeds or encephalopathy

INVESTIGATIONS

- Hb-13.1
- TC-8600
- PLt-3.29
- PT-31/11
- INR-2.8

LIVER FUNCTION

- Total bili - 26.5 (upto1mg/dl)
- Direct bili - 18.2 (upto0.2mg/dl)
- Total protein - 6 (6-8g/dl)
- Albumin - 3.6 (3.8-5.4g/dl)
- SGOT - 975 (15-55U/L)
- SGPT - 725 (5-45U/L)
- ALP - 376 (<300U/L)

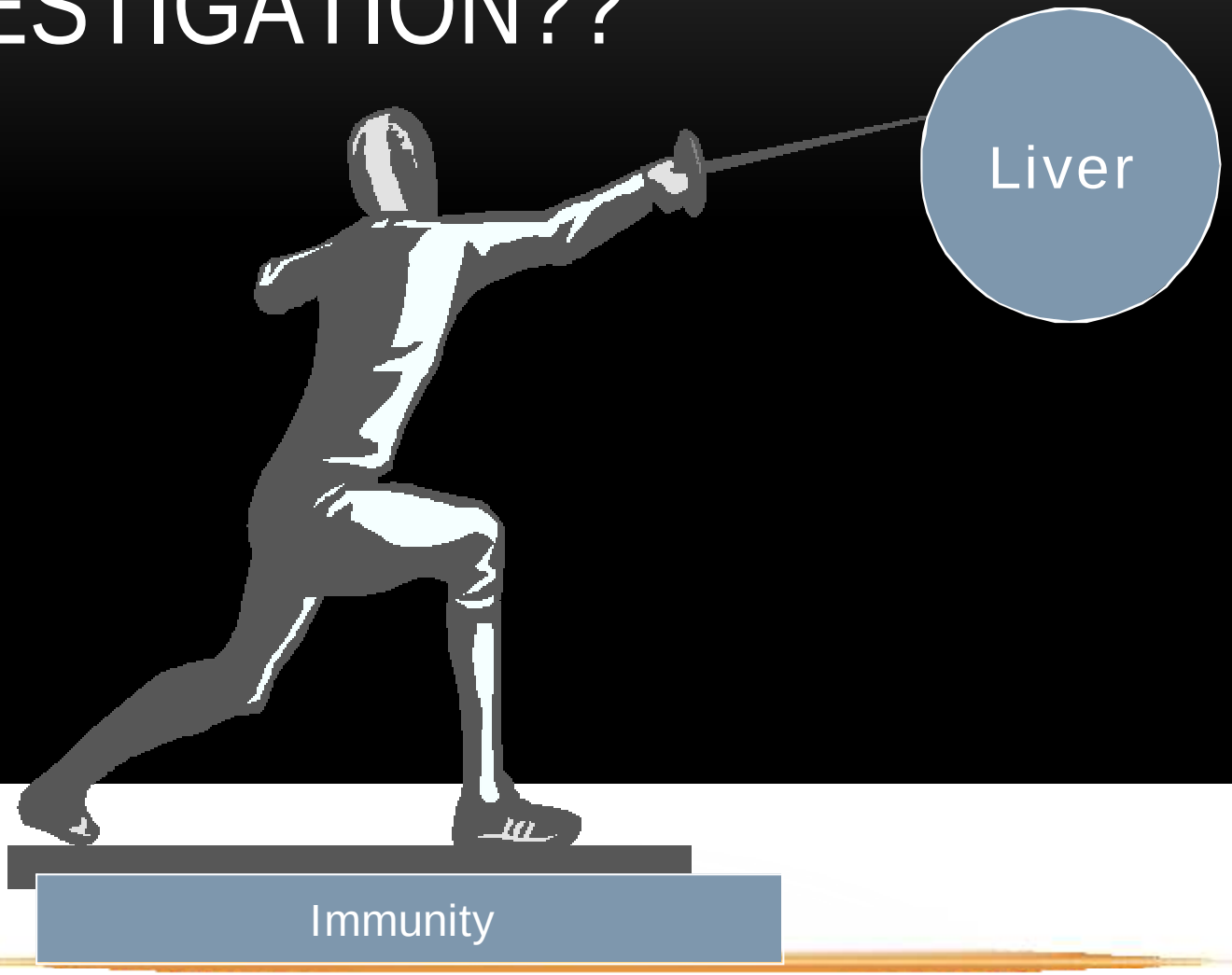
WORK UP TOWARDS ETIOLOGY

- Hepatitis A IgM - negative
- Hep B surface Ag - negative
- Hep E IgM - negative
- Hep C RNA PCR - negative
- CMV/ EBV/ Lepto Igm - negative
- Serum copper - 96.9 (90-190)
- [illegible]
- [illegible] was elevated 1930(400-1590)

- USG abdomen – mildly enlarged liver, prominence with thickening of intra hepatic biliary radicles in both lobes. Multiple, enlarged peripancreatic and periportal LN noted, s/o active hepatitis
- Bilateral renal pelvic prominence, rest normal

• Cultures	-	no growth
• ANA	-	negative
• ANCA	-	negative
• ASMA	-	negative
• Liver biopsy	-	deferred in view of high PT /INR

THE DIAGNOSTIC INVESTIGATION??



- DCT - positive
- Anti LKM - positive
- Anti LC-1 - positive
- Anti M2-PDH - negative
- Anti SLA - negative

DIAGNOSIS

- AUTO IMMUNE HEPATITIS

DEFINITION

chronic hepatic inflammatory process

- elevated serum aminotransaminase concentrations
- liver associated serum autoantibodies
- hypergammaglobulinemia

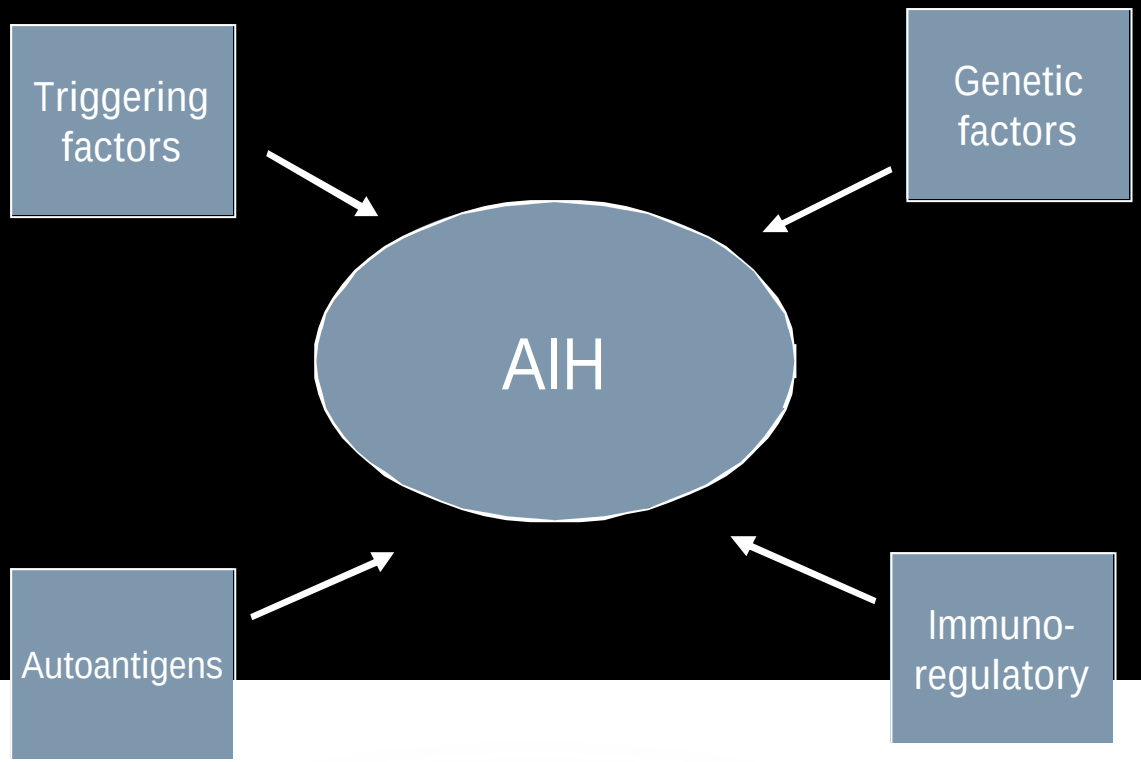
EPIDEMIOLOGY

- INCIDENCE: 1.9 cases per 100,000 persons per yr
- PREVALENCE: 16.9 cases per 100,000 persons per yr
- Females account for 70% of cases, 50% $\leq$ 40 years
- Cause of chronic liver disease: 11-23%
- AIH accounts for 2.6% and 5.9% of liver transplants in Europe and U.S. respectively

NATURAL HISTORY

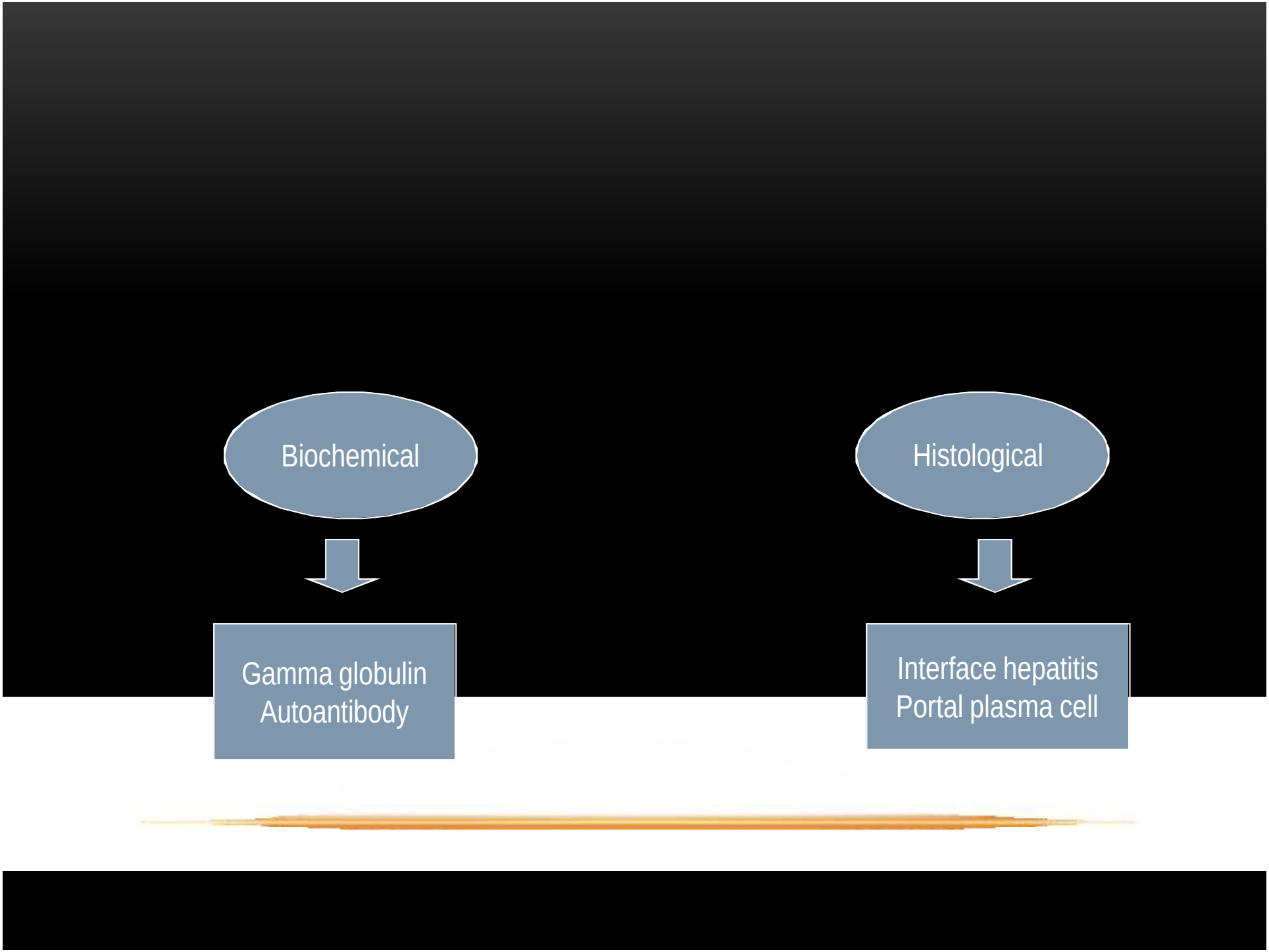
- Severe disease (untreated)
  - 40% die within 6 months of diagnosis
  - 40% of survivors develop cirrhosis
  - 54% of cirrhotics develop varices within 2 years of diagnosis of cirrhosis
  - 20% of patients with varices will bleed

PATHOGENESIS



- Genetic factors
  - Antigen presentation/immunocyte activation
  - DRB1 encodes for MHC II antigen binding grooves (antigen presentation to T cells)
- Triggering factors
  - Infections (HAV, HBV, HCV, HSV, EBV, measles)?
  - Medications (ABX, statins, NSAIDs etc.)?
  -
  - Molecular mimicry?

- Antibody-dependent cellular cytotoxicity
  - Antibodies directed against ASGPR
  - Suppressor T cell defect
  - Binding of NK cell to antigen-antibody complex followed by hepatocyte destruction
- Cell-mediated cytotoxicity
  - IL-12 and IL-2 released
  - [illegible]
  - [illegible] T cell destruction of hepatocyte


Biochemical
Histological
Gamma globulin
Autoantibody
Interface hepatitis
Portal plasma cell

INTERNATIONAL AUTO IMMUNE HEPATITIS GROUP CRITERIA

- Gender
- AP/AST, ALT ratio
- Serum globulins/IgG
- ANA, ASMA, LKM-1
- AMA positive
- Viral serologies
- Drug history/Alcohol intake
- Liver histology
- Other autoimmune diseases
- HLA DR3/DR4

SIMPLIFIED CRITERIA

- Autoantibodies
  - ANA, ASMA, LKM-1, SLA
- IgG
  - Typically elevated in autoimmune hepatitis
- Histology
  - Interface hepatitis, lymphocytic or lymphoplasmacytic infiltrate, rosettes
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AIH TYPE 1

- Age: 10-20yrs
- Female: 78%
- γ-globulin elevation: marked
- Autoantigen: asialoglycoprotein receptor?
- Autoantibodies: ANA, ASMA
  - Others: pANCA, actin, ASGPR, SLA/LP
- HLA-A1-B8-DR3 or HLA-DR4
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AIH TYPE 2

- Age: 2-14 years
- Female: 90%
- γ-globulin elevation: Mild
- Autoantigen: CYP450 IID6
- Autoantibodies: LKM-1
  - Others: LC-1, SLA/LP
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- Severity: more severe than type 1

HISTOLOGY

- Piecemeal necrosis (interface hepatitis)
- Panacinar inflammation or collapse
- Lymphoplasmacytic infiltrates
- Eosinophils
- Rosette formation
- Fibrosis or cirrhosis
- Absence of portal lymphoid aggregates and steatosis

SEVERE DISEASE

- AST ≥ 10 NORMAL
- AST ≥ 5 NORMAL + IgG >2 NORMAL
- Bridging necrosis
- Multilobular collapse
- HLA B8, DR3
- African American males

MORTALITY WITHOUT LIVER TRANSPLANTATION

- 50% at 3 years & 90% at 10 years

HITOLOGY AND PROGNOSIS

- Interface hepatitis
  - 17% risk of cirrhosis at 5 years
  - Normal survival
- Bridging or multilobular necrosis
  - 82% risk of cirrhosis at 5 years
  - 45% 5-year mortality
- Cirrhosis
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TREATMENT OPTIONS

IMMUNOSUPPRESANTS

- STEROIDS
- AZATHIOPRINE

- Prednisone
- initial dose of 1-2 mg/kg/24 hr - UNTIL aminotransferase values return to less than twice the upper limit of normal.
- The dose should then be lowered in 5 mg decrements
- over 2-4 mo until a maintenance dose of 0.1-0.3 mg/kg/24 hr is achieved.

SECOND LINE AGENTS (CENTRE BASED PROTOCOL)

- Mycophenolate
- Cyclosporine
- Tacrolimus
- Budesonide
- Methotrexate
- Cyclophosphamide

REMISSION

- Disappearance of symptoms
- Normalization or near normalization of AST to < 2 normal
- IgG and bilirubin: normal
- Minimal or no hepatic inflammation
- 65% and 80% of patients within 18 months and 3 yrs of initiation of Rx respectively
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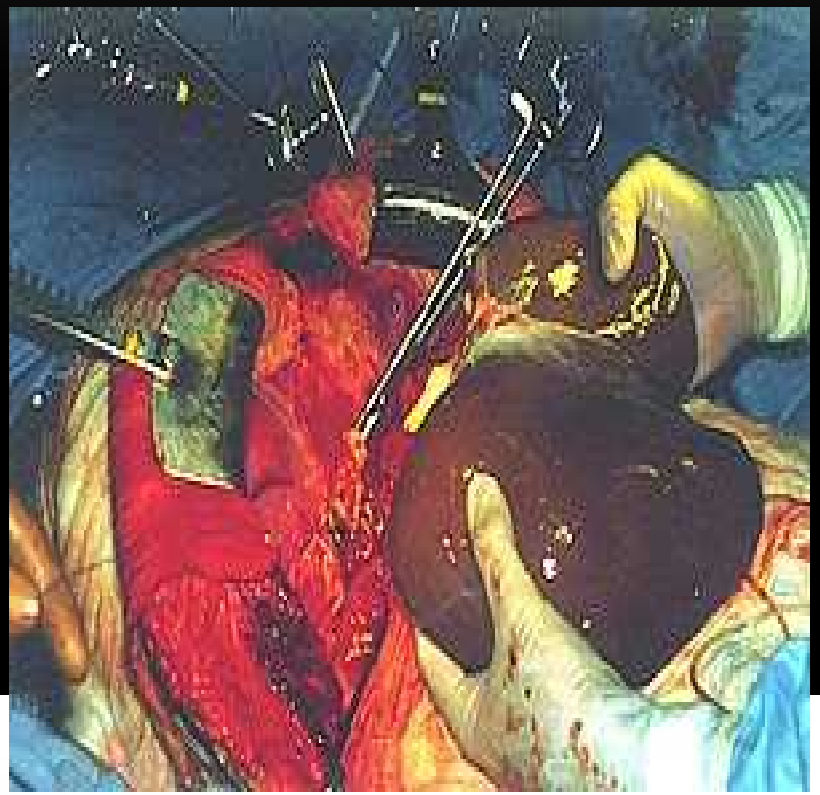
TREATMENT END POINTS

- Disease remission
- Relapse after treatment withdrawal
- Treatment failure
- Incomplete response
- Drug toxicity

LIVER TRANSPLANTATION

- In End-stage liver disease
- In Fulminant liver disease



- Results
  - 5 yr pt and graft survival: 80-90%
  - Recurrence: 15-40%
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COURSE OF MS A.

- Clinically well
- Started on 2mg/kg prednisolone – slowly tapered and is on 0.2mg/kg/day dose
- On follow up for 9 months now.

- Present LFT:
- Total bili - 0.6
- Direct bili - 0.3
- Albumin - 4.0
- SGOT - 56
- SGPT - 54
- ALP - 312
- [redacted]
- PT/INR 14/1.3

TAKE HOME MESSAGE

- Clinical presentation is variable
- Diagnosis based upon LFTs, serology, gamma globulins, and histology
- Early diagnosis is crucial (death if undiagnosed)
- Timely referral to the specialist (esp aculte liver failure or coag not correcting with vitamin k)
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THANK YOU