Paediatrics:
Case Discussions on Liver Dysfunction

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History

• The liver has fascinated mankind since the existence of medicine
• Humans were aware of the liver’s central role in nutrition – “principal instrument” of the body for Galen
• Capacity of liver to regenerate (Prometheus)
Role of the PA within Paediatric Hepatology

- Daily medical review of inpatients
- Accepting tertiary referrals
- Review of clinic patients
- Assessment & presentation of patients for transplantation assessment
  - Liver, Small Bowel, combined Liver & Bowel or Multi-visceral Transplant
- Presentation of patients in Radiology & Histology MDT meetings
- Review of patients attending for pre-admissions clinic
- Preparation of patients for transplantation
- Performance of specialised practical skills (paediatric blood sampling, stoma biopsy, ascitic tap)
Learning Objectives

i. Recognize the common presentations of liver dysfunction within children

ii. Identify key differences in the diagnostic approach and management of acute and chronic presentations in children

iii. Formulate a structured approach to the patient, identifying when to refer to specialist centers in a timely manner
Definitions

Jaundice
Hepatitis
Cirrhosis
Neonatal Cholestasis
Acute Liver Failure
Ascites
Portal Hypertension
Portosystemic Shunts
Anatomy & Physiology

• Two lobes
• Dual blood supply (Hepatic Artery & Portal Vein)
• Biliary system
Functions of the liver

- Production of clotting factors
- Role in immunity (Kuppfer Cells)
- Glycogen storage & metabolism
- Processing & excretion of toxins
- Production of Bile
  - Emulsification of fats to allow for absorption of dietary fats (Long Chain Triglycerides)
  - Absorption of fat soluble vitamins
- Role in production of serum proteins (notably albumin) and cholesterol
  - Regulation of fluid balance
- Drug metabolism
Bilirubin & Jaundice

• Bilirubin is a breakdown product of heme

• The hepatocytes take up bilirubin, conjugating it (in order to make it water soluble) and secreting it onto the bile ducts for excretion via the intestine

• Increased bilirubin causes jaundice
  • Pre-hepatic
    • Increased red cell break down (unconjugated hyperbilirubinemia)
  • Hepatic
    • Unable to metabolise the bilirubin (mixed)
      • Reduced conjugation
      • Unable to secrete bilirubin
  • Post-heptic
    • Obstruction to the excretion of bile (conjugated hyperbilirubinemia)
History

- Jaundice
- Pruritis
- Weight loss
- Diarrhoea & Vomiting
- Haematemesis/malaena
- Bruising/epistaxis
- Recent Drug History
- Recent travel history

- Family history, consanguinity
- School performance, clumsiness
- Developmental history
Examination

Acute liver dysfunction
- Jaundice
- Bruising/bleeding
- Hepatomegaly
- Splenomegaly
- Ascites
- Encephalopathy
- KF rings

Chronic liver disease
- Jaundice
- Spider naevi
- Palmar erythema
- Splenomegaly
- Acanthosis nigricans
- Ascites
- KF rings
Liver Function Tests

- Bilirubin – hepatocyte dysfunction/biliary obstruction
- Inflammation/Irritation
  - AST*/ALT - hepatocyte inflammation/damage
    - AST is an early marker of liver damage
    - ALT more liver specific but longer half life
  - ALP** - Biliary inflammation/damage/obstruction
  - GGT*** - Biliary inflammation/obstruction
- Synthetic function
  - Albumin - Chronic liver disease/poor synthetic function
  - PT - Chronic liver disease/poor synthetic function/vit K deficiency
  - Glucose - Acute/chronic liver failure/metabolic/hypopituitarism
  - Ammonia - Abnormal protein metabolism/urea cycle defect/inherited metabolic disorder
  - Lactate - Mitochondrial liver disease

* Found in liver, heart and muscles
** Found in liver, kidney, bone, placenta and intestine (isoforms)
*** Only present in biliary epithelia and hepatocytes (age dependent)
Common presentations

• The infant with jaundice
• The acutely unwell infant
• The infant with splenomegaly
• The older child with jaundice
• The older child who is acutely unwell
• Incidental abnormal liver biochemistry
• Isolated elevated ALP
The older child with jaundice

Differential Diagnosis

• Seronegative hepatitis
• Infection
  • Hepatitis viruses (A, B, E)
  • EBV
  • CMV
  • Parvovirus
  • HSV 1/2
  • VZV
• Autoimmune hepatitis
• Sclerosing cholangitis
• Wilson’s disease
• Alpha-1-antitrypsin deficiency
• Genetic (benign recurrent intrahepatic cholestasis aka BRIC)
• Drug induced liver injury
• Leukemia, lymphomia
The older child with jaundice

History:
- Contact with infection
- Tiredness, anorexia and vague abdominal pain
- Personal history of autoimmune conditions/FH of autoimmune disease (coeliac, diabetes, hypothyroidism)
- Personal history of ulcerative colitis
- Deterioration of school work and slurring of words
- Weight loss, pallor, bruising

Examination:
- Features of acute hepatitis (enlarged, tender liver, splenomegaly)
- Features of chronic liver disease (splenomegaly)

Investigations:
- Viral hepatitis: Hep A & E (acute hepatitis), Hepatitis B&C (CLD), HSV1/2, VZV, CMV, EBV, HHV6
- Autoimmune liver disease: Immunoglobulins, Autoantibody screen, pANCA, complement levels (C3/4)
- Wilsons disease: Copper, ceruloplasmin, urine copper, genetics (ATP7B mutation)
- Drug induced liver disease
- Malignancy: Bone marrow suppression - bi/pan cytopenia

Management:
- Supportive management for all conditions
  - Fat soluble vitamins
  - Nutritional support
  - Antiopruritics
- Treat underlying cause
  - Autoimmune hepatitis
  - Sclerosing cholangitis
  - Wilsons disease
Case 1

History
• 13 year old female
• Presenting complaint: nosebleed
• Previously fit & well
• Easy bruising, some weight loss, tiredness for past 4 months

Examination
• liver edge, no splenomegaly, some bruising

Initial Blood investigations:
• Transaminases: AST >1000
  ALT >800
  GGT 100
• Bilirubin: 56
• Albumin: 35
• PT: 17

Investigations
• Viral serology: Negative
• Copper: Normal
• Caeruloplasmin: Low
• Immunoglobulins: IgG = 29.6
• Auto antibody screen: ANA = 1:650;
  SMA = +ve
• FBC: Anaemia
Autoimmune Hepatitis

• 75% female preponderance
• Suggestion of genetic predisposition (associated with HLA B8/DR3 and DR4)
• Associated with other AI disorders:
  • in 20% of affected patients
  • in 40% of 1st degree relatives
• Variable age at onset (occasional presentation in infancy)
• Presentation:
  • insidious onset, with delay to presentation of many years
  • >50% present as acute illness, resembling acute viral hepatitis
  • 11% present as ALF
• Management: Corticosteroids, Azathioprine, alternative I/S (cyclosporin, tacrolimus, MMF), Liver transplantation
Case 2

History
• 15 year old female
• Presenting complaint: progressive jaundice & pruritus over 2/52
• Very active social life

Examination
• No hepatosplenomegaly

Initial Blood investigations:
• Transaminases: AST >600
  ALT >750
  GGT 100
• Bilirubin: 230
• Albumin: 35
• PT: 15

Investigations
• Viral serology: Negative
• Copper: Normal
• Caeruloplasmin: Normal
• Immunoglobulins: Normal
• Auto antibody screen: Normal
• FBC: Normal
Drug induced hepatitis/cholestasis

- Patient 2 was taking a combination of contraception and recreational drugs (XTC)
- Wide spectrum of severity of liver injury and can resemble all other forms of liver disease
- Diagnosis: high level of suspicion
- Occasionally presents with associated drug hypersensitivity features (rash, eosinophilia, fever)
- Management: Withdrawal of the offending agent, Steroids should be considered in children with DILI and hypersensitivity features (fever, rash, eosinophilia)
- Prognosis: Recovery can take weeks (av 44 days), if no signs of improvement after 4-5 days after agent withdrawal re-consider diagnosis
Common drugs causing liver injury

Cholestasis:
- Co-amoxiclav
- Erythromycin
- Sulphonamides
- Ketoconazole
- Carbamazepine

Damage to bile ducts:
- Flucloxacillin
- Tetracycline
- Ampicillin/amoxicillin
- Co-amoxiclav

Hepatocellular inflammation (aka hepatitis):
- Paracetamol
- NSAIDs
- Cephalosporin
- Tetracyclines
- Erythromycin
- Ketoconazole
- Carbamazepine
- Phenytoin
- Isoniazid
The older child who is acutely unwell

Differential Diagnosis

• Seronegative hepatitis
• Infection
  • Hepatitis viruses (A, B, E)
  • EBV
  • CMV
  • Parvovirus
  • HSV 1/2
  • VZV
• Autoimmune hepatitis
• Metabolic
  • Wilson’s disease
  • Glycogen storage disease
  • Mitochondrial disease
• Drug induced liver injury
• Paracetamol overdose
• Vascular anomalies (e.g. Budd-Chiari)
The older child who is acutely unwell

History:
• Previous medical history and medications
• Deterioration in school performance or changes in speech
• Developmental delay or neurological deterioration
• Known prothrombotic disorders
• Previous episodes of jaundice
• Recent sodium valproate

Examination:
• Features of acute hepatitis (enlarged, tender liver, splenomegaly)
• Features of chronic liver disease (splenomegaly)

Investigations:
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• Autoimmune liver disease:
  • Immunoglobulins, Autoantibody screen, pANCA, complement levels (C3/4)
• Wilsons disease:
  • Copper, ceruloplasmin, urine copper, genetics (ATP7B mutation)
  • Associated with low ALP, haemolysis, mildly raised immunoglobulins, ANA may be raised
• Metabolic conditions (GSD)
  • Hypoglycemia, increased urate and lactate
• Drug induced liver disease:
  • Diagnosis of exclusion!
• Paracetamol Overdose:
  • Paracetamol level
• Vascular anomalies (Budd-Chiari etc.)
  • Prothrombotic screen
  • Ultrasound
The older child who is acutely unwell

Management of Acute Liver Failure:

- Medications: Vitamin K, antacids, Lactulose, N-acetylcystine, Antibiotics, Antifungals, Antivirals
- No sedation (masks encephalopathy)
- Minimal handling
- Central venous access
- Regular monitoring: ECG, temperature, neurological observations, BMs, Acid-base balance inc. lactate, regular biochemistry, coagulation screen
- Fluid management: 50-75% maintenance fluid, dextrose to maintain BM, circulating volume maintained with colloid, ensure normal electrolyte and acid base balance
Monitor & manage complications:

- Hypoglycemia (<3.5mmol/L)
- Coagulopathy and bleeding: Daily dose of vit K, do not routinely correct PT unless bleeding (use FFP, cryo and platelets if required)
- Encephalopathy: head elevated at 20° no neck flexion, review fluid balance, ITU for elective ventilation, Mannitol, Thiopentone
- Convulsions
- Renal dysfunction
- Metabolic acidosis
- Sepsis
**Case 3**

**History**
- 12 year old male
- Presenting complaint: progressive jaundice (~3/52)
- Tiredness, weight loss, unable to cope at school, unusual outbursts/changes in behaviour

**Examination**
- liver edge, splenomegaly

**Initial Blood investigations:**
- Transaminases: AST 60
  ALT 85
  GGT 70
- Bilirubin: 190
- Albumin: 24
- PT: 36

**Investigations**
- Viral serology: Negative
- Copper: Normal
- Caeruloplasmin: Low
- Immunoglobulins: IgG = 19.6
- Auto antibody screen: ANA = +ve
  Rest = -ve
- FBC: Anaemia + Hemolysis
Wilson’s Disease

• Autosomal recessive disorder of copper metabolism (5/1,000,000)
  • Genetic mutations identified (>100 common)
  • Gene ATP7B at 13q14.3

• Copper accumulates in the liver, brain and cornea

• Seldom presents before 3 years
  • Younger children present with liver disease
  • Teenagers and adults present with neurological problems

• Management:
  • Medical: Zinc acetate as a chelation agent or Penicillamine (occasionally trientine)
  • Surgical: Liver transplantation (acute failure or non-response to therapy)
A note on paracetamol overdose

- **History:**
  - Time of overdose and whether it was staggered
  - Any other drugs or alcohol taken

- **Investigations:**
  - Paracetamol level
  - LFTs
  - Clotting
  - U&E
  - Venous Gas
  - Blood sugars

- **Monitoring:**
  - Clotting should be monitored 12h until the trend is stable or improved

- **Treatment:**
  - If significant overdose, delayed presentation or staggered overdose commence treatment before taking paracetamol levels
  - N-acetylcysteine
    - Stop NAC when PT is <18 (INR<1.5)
  - Ranitidine 3mg/kg TDS
  - Vitamin K 10mg IV OD

- **Indications for referral to a paediatric liver transplant centre:**
  - INR >2.5
  - Acidosis
  - Renal dysfunction
  - Encephalopathy
  - Hypoglycemia
Incidental abnormal liver biochemistry

Differential Diagnosis
• Non-alcoholic fatty liver disease (NAFLD)
• Sclerosing cholangitis
• A1AT deficiency
• Wilson’s disease
• First presentation of a multisystem disease
• Muscle disease
Incidental abnormal liver biochemistry

History:
• Obesity
• Hypertension
• FH of liver disease or emphysema
• Change in bowel habit, abdominal pain or blood in stool

Examination:
• Features of chronic liver disease
• Developmental delay
• Proximal muscle weakness

Investigations:
• A1AT:
  • Bloods: A1AT level & phenotype (PiZZ) if low

• Sclerosing cholangitis:
  • Bloods: pANCA +ve
  • Radiology: irregular bile ducts, beading on MRCP

• Wilson’s disease: as previous

• NAFLD:
  • Bloods: metabolic syndrome (elevated triglycerides, reduced HDL, raised fasting glucose)
  • Ultrasound: hyperreflective liver

Management:
• A1AT: manage cholestasis – fat soluble vitamins & ursodeoxycholic acid
• Sclerosing cholangitis: management of cholestasis, surgical procedures, liver transplantation
• Wilson’s disease: as previous
• NAFLD: lifestyle modification
Case 4

History
• 12 year old male
• Weight 110kg

Examination
• Acanthosis nigricans
• Spider Naevi

Initial Blood investigations:
• Transaminases:
  - AST 80
  - ALT 120
  - GGT 10

Investigations
• Bilirubin: <3
• Albumin: 40
• PT: 12
• A1AT level: Normal
• Cu & Ceruloplasmin: Normal
• pANCA: Normal
• US:
  - Fatty infiltration
• Hba1c: elevated
Non-alcoholic fatty liver disease (NAFLD)

- Non-alcoholic fatty liver disease is a condition in which fat builds up in the liver
- Spectrum of disease from mild fatty infiltration to cirrhosis
- Non-alcoholic steatohepatitis – inflammation of the liver caused by fatty infiltration
- Mainstay of treatment is through lifestyle modification
**Case 5**

**History**
- 24 month old male reviewed as an outpatient for poor weight gain

**Examination**
- No stigmata of liver disease present

**Investigations**
- Transaminases: ALT 475 IU/L; AST 429 IU/L
- US Abdomen: NAD

**Diagnosis? Most important investigation?**
Muscular Dystrophy

- Creatinine Kinase: 19,566 IU/L
- Diagnosis: Duchenne muscular dystrophy
- 7% of patients in whom muscular dystrophy is diagnosed may initially present with elevated liver enzyme levels
- Must assess development & assess for evidence of proximal muscle weakness

- Take home message: ALWAYS CHECK CK!!
A note on interpretation of isolated elevated ALP

• UNLIKELY PRIMARY LIVER PROBLEM!
• Sources of ALP: liver, bone, kidney, intestine, and placenta
• Review reference interval for lab
  • Reference intervals contain 95% of the population
  • 2.5% of the normal population have values above the upper reference limit
• Initially check GGT to confirm liver source
• If GGT normal evaluate for bone disease (Bone Profile, Vitamin D, PTH)
• If GGT elevated first exclude biliary obstruction (US abdomen) then investigate for intrahepatic causes of cholestasis
Physiological Jaundice

Physiological Jaundice occurs from day 3 after birth and resolves by 2 weeks of age.
Common presentations

• The infant with jaundice
• The acutely unwell infant
• The infant with splenomegaly
• The older child with jaundice
• The older child who is acutely unwell
• Incidental abnormal liver biochemistry
• Isolated elevated ALP
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High GGT cholestasis in an infant = biliary atresia until excluded
Neonatal Cholestasis

Definition: Jaundice which persists after 2 weeks of age (3 weeks if Ex-Prem, i.e. <37 weeks gestation)

History:
FH: Jaundice, neonatal deaths or miscarriages
Low or normal birth weight, failure to thrive or weight loss
Poor feeding & irritability
Hypoglycemic episodes
Vitamin K deficiency with bleeding

Examination:
STOOL PIGMENTATION
Dysmorphic features, arthrogryposis, cutaneous haemangioma
Cardiac murmur
Enlarged spleen
Ascites

Investigations:
Split Bilirubin
Conjugated hyperbilirubinemia
Unconjugated hyperbilirubinemia

Management:
Conjugated hyperbilirubinemia
Treat underlying cause
Manage cholestasis
Fat soluble vitamins
Ursodeoxycholic acid
Unconjugated hyperbilirubinemia
Phototherapy
Exchange transfusion
Phenobarbitone
Neonatal Cholestasis

Jaundice aged 2 weeks

Split Bilirubin

Conjugated Hyperbilirubinemia (25 µmol/L)

Requires urgent investigation for liver disease & discussion with liver centre

Unconjugated Hyperbilirubinemia

Unconjugated Bilirubin <250

Physiological Jaundice, Gilbert's Syndrome, Sepsis, Haemolysis, Hypothyroidism

Unconjugated Bilirubin >250 - 850

Crigler-Najjar

Treatment: Phototherapy & Reassurance

Unconjugated Bilirubin >250

Treatment: Phenobarbitone, Liver Transplantation
Conjugated hyperbilirubinemia

Pale stool
- Fasted ultrasound
  - Small gallbladder
  - Cyst
  - No abnormalities detected
  - Does not exclude BA!
  - Operative Cholangiogram
    - No flow into duodenum
    - Flow into duodenum
    - Requires further investigation

Small cyst
- No abnormalities detected
- Does not exclude BA!
- Operative Cholangiogram
  - No flow into duodenum
  - Flow into duodenum
  - Requires further investigation

Splenoegaly
- Referral & further investigation

Normal Spleen Size
- Investigate as per Local protocol

Pigmented stool
- Referral to tertiary centre if indicated i.e. progressive jaundice/hepatitis

First Stage Investigations

These should be performed on infants with prolonged conjugated jaundice who are clinically stable.

History
Birth weight, type of milk feed, maternal illness, family illness, exposure to infection, previous affected children, obstetric history, early neonatal history (prematurity, parental nutrition, sepsis, congenital heart disease).

Clinical examination
Particular attention should be made to document dysmorphic features, skin rash, head circumference, cataracts, hepatosplenomegaly, heart murmurs and stool colour.

Haematology
- Full blood count and reticulocyte count
- Blood group and Coombs test
- INR and prothrombin time: if prolonged, give a dose of intravenous vitamin K 300 micrograms/kg. Repeat the coagulation profile four hours later. If still abnormal, contact a liver centre urgently.
- APTT and fibrinogen

Biochemistry
- Blood Sugar and/or BMs pre-feed in first 24 hours of admission
- Na, K, urea, creatinine, serum lactate and bicarbonate
- Calcium, phosphate
- Bilirubin (total and conjugated)
- ALT+/AST, Alkaline phosphatase, GGT
- Albumin
- Cholesterol and triglycerides

Metabolic investigations
- Galactose-1-phosphate uridylyl transferase
- Alpha-1-antitrypsin level and phenotype
- Plasma and urine amino acids
- Urine organic acids (including succinyl acetone)
- Ward test urine for protein

Endocrine investigations
- Thyroid function
- Cortisol (ideally after four hour fast) if low: perform short synacthen test

Microbiology
- Blood and urine culture
- Urine for CMV
- Serology: TORCH, Hepatitis A, B, C and E
- Blood for HSV PCR, stool for enterovirus

Imaging
Ultrasound scan of abdomen should be performed in the fasting state: a four hour fast is usually adequate. Assessment should be made of liver size, texture and morphology, biliary tree, presence or absence of gall bladder, spleen size, presence of ascites and hepatic vessel patency.

Second Stage Investigations

These should be performed as appropriate, after considering the history, examination and first line investigation results. Discussion with a specialist centre is advisable.

Hepatobiliary scintigraphy / isotope excretion scan (eg HIDA)
Pretreatment with phenobarbitone 5mg/kg once daily (at night) should be completed for at least three days. Imaging should continue until 24 hours post isotope injection if there is no excretion seen at 4 hours

Liver Biopsy: This is seldom indicated, as other investigations may provide adequate information, and histology may be non-specific. Need for liver biopsy should be discussed with specialist centre, and only performed locally if there is sufficient expertise.

Molecular and extended virology: Syphilis serology and PCR for viruses on blood, stool or NPA may be indicated according to history

Ophthalmology assessment: To assess for evidence of Alagille syndrome (posterior embryotoxon), congenital infection (chorioretinitis), endocrine disorders (septo-optic dysplasia) or metabolic disorders (cataracts, retinal signs).

Spleen X-Ray: For evidence of Alagille syndrome (butterfly vertebrae)

Cardiology assessment and CXR: if heart murmur present, or other signs of Alagille syndrome.

Other investigations for rare disorders:

Blood:
- Lactate, ammonia, pyruvate, uric acid, carnitine and acyl carnitine
- Very long chain fatty acids or white cell enzymes (glucocerebroside or lysosomal storage disorders)
- Bile acids (quantitative and qualitative): ideally when OFF Ursodeoxycholic acid. If taking ursdo, specify on request form
- Alpha fetoprotein
- Transthyretin iso-electric focusing
- Feritin and transferrin saturation
- Blood spot for LAHD

Urine
- Qualitative bile acids: ideally when NOT taking ursdo. If on ursdo, specify on request form
- Urinary resorption of phosphate
- CSF: Protein and lactate: only after normalisation of coagulation

Tissue
- Muscle biopsy for mitochondrial cytopathy
- Bone marrow aspirate / trephine for storage disorders
- Skin biopsy for fibroblast culture

Imaging: MRI brain
- Genetic testing: DNA for cholestasis gene panel, mitochondrial DNA mutations and mtDNA depletion syndrome and/or perforin expression.
**Case 6**

**History**
- Term (BW 3.6kg), female
- Nil peri-natal concerns
- Well baby, jaundiced with pale stools
- Bottle fed, 50th centile

**Examination**
- Pale stool

**Initial Blood investigations:**
- Transaminases: AST 332, ALT 246, ALP 469, GGT 507
- Bilirubin: 198
- Albumin: 40
- PT: 12
Biliary Atresia

- A progressive obliterative cholangiopathy, preventing bile flow into the intestine

- Management:
  - Kasai portoenterostomy is a palliative surgical procedure
  - 90% of children with a successful Kasia develop portal hypertension and cirrhosis, requiring long term follow-up and liver transplantation
The acutely unwell infant

- **Infection**
  - Herpes Simplex
  - Adenovirus
  - Echovirus
  - Coxsacchie virus
  - Parvovirus

- **Immune mediated**
  - Gestational alloimmune liver disease (Neonatal haemochromatosis)

- **Haematological**
  - Familial haemophagocytic lymphohistiocytosis

- **Metabolic**
  - Mitochondrial disease
  - Galactosemia
  - Urea cycle disorders
  - Fatty acid oxidation defects
  - Organic acidemias
  - Glycogen storage disease
The acutely unwell infant

History:
- Consanguinuty
- Affected siblings
- Miscarriages
- Pregnancy & birth history
- Dietary and fasting history
- Difficulty in feeding/vomiting

Examination:
- Liver and spleen size
- Tachypnoea
- Abnormal neurology
- Intercurrent infection
- Urine colour (UCD)
Case 7

History
• 4 day old, term female (BW 3.6kg)
• Poor feeding & jaundice
• 1st pregnancy, normal pregnancy
• Mother well, no FH

Examination
• No organomegaly
• Jaundiced
• US: small, irregular liver

Initial Blood investigations:
• Lactate: 5
• Hb & WCC: Normal
• Platlets: Low
• Electrolytes: Normal
• Transaminases:
  • AST 62
  • ALT 30
  • ALP 469
  • GGT 46
• Bilirubin: 205 (100)
• Albumin: 28
• PT: 40
• Ferritin 3478
Neonatal Hemochromatosis

• This is a liver alloimmune disease resulting in iron overload
• The diagnosis is based on iron deposition in liver and extrahepatic organs
• Management:
  • Exchange transfusion
  • Immunoglobulins
  • Liver transplantation
The infant with splenomegaly

Differential diagnosis

- Infection – CMV, Toxoplasmosis, EBV, Rubella
- Haematological – Sickle cell, thalassaemia, immune mediated
- Malignancy – leukaemia, lymphoma
- Portal hypertension
- Storage disease – NPC, LAL-D
- Peroxisomal biogenesis disorder e.g. Zellweger’s
Learning Objectives

1. Recognize the common presentations of liver dysfunction within children

2. Identify key differences in the diagnostic approach and management of acute and chronic presentations in children

3. Formulate a structured approach to the patient, identifying when to refer to specialist centers in a timely manner
Any questions?