Management of Chronic Liver Failure

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ESPGHAN GOES TO AFRICA

CAPETOWN

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End Stage Liver Failure

Aetiology of Chronic Liver Disease

- Neonatal liver disease
- Chronic hepatitis
- Metabolic
- Fibropolycystic liver disease
- Drugs

Neonatal Cholestasis

Extrahepatic:- Biliary atresia

Neonatal Hepatitis Syndrome (NHS)

- Intrauterine infection
- Inborn error of metabolism
- Biliary hypoplasia (Alagille/PFIC)
- Inborn errors of bile salt metabolism
- Prematurity
- Endocrine

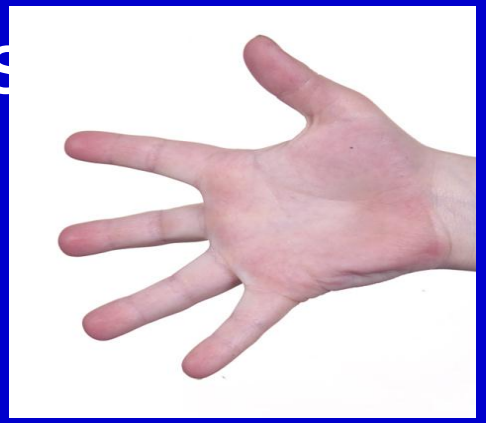
TPN cholestasis

Chronic Liver Disease

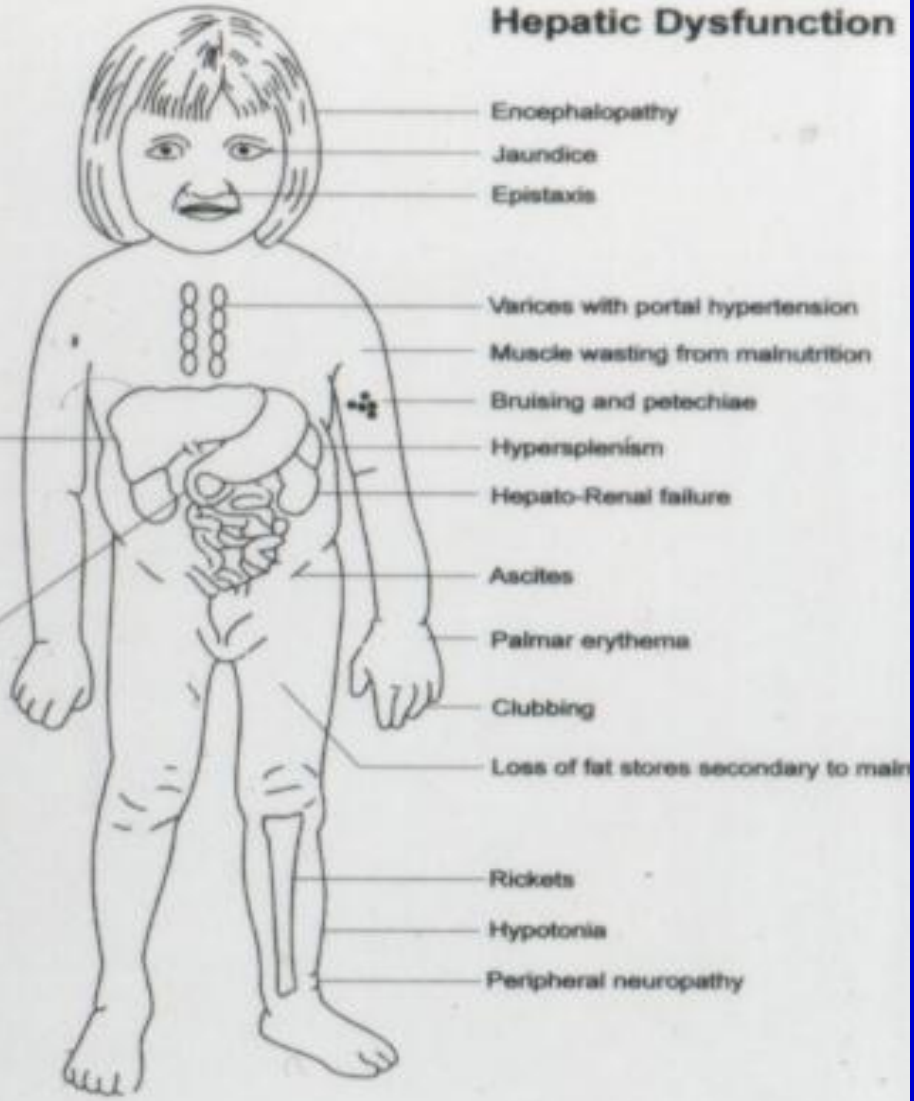
- Chronic viral hepatitis (B&C)
- Autoimmune hepatitis
  - Type I (ANA, SMA +ve)
  - Type II (LKM +ve)
  - Sclerosing cholangitis
- Metabolic liver disease
  - Alpha-1-antitrypsin deficiency
  - Cystic fibrosis
  - Wilson's disease
- Non Alcoholic Fatty Liver Disease
- Drugs

Chronic Liver Disease

- Jaundice may be absent
- Malnutrition
- Stunting
- Hypersplenism
  - Low Hb, white cells and platelets
  - Bruising/petechiae/epistaxis
- Hepatosplenomegaly



Multi-organ involvement in Liver Disease



Hepatic Dysfunction

- Encephalopathy
- Jaundice
- Epistaxis
- Varices with portal hypertension
- Muscle wasting from malnutrition
- Bruising and petechiae
- Hypersplenism
- Hepato-Renal failure
- Ascites
- Palmar erythema
- Clubbing
- Loss of fat stores secondary to malnutrition
- Rickets
- Hypotonia
- Peripheral neuropathy

Functions of the Liver

Carbohydrate, Protein & Fat metabolism
Synthesis of coagulation proteins
Drug metabolism
Degradation of Hormones
Bilirubin conjugation

Cholestasis

Malabsorbtion of longchain & fat soluble vitamins, leads to: -

- Pruritus
- Pale stools
- Dark urine

Viral Hepatitis B & C

- World wide disease
- Perinatal transmission
- Chronic Asymptomatic Infection
- Acute Infection
  - Rare in childhood
- Significant risk of chronic liver disease
- Hepatocellular Carcinoma

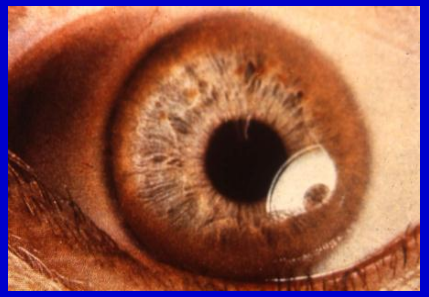
Wilson's Disease

- Autosomal recessive:
- Incidence of 1:30,000 live births.
- The gene is on chromosome 13
- Encodes a copper transporting P-type ATPase-ATP7B ATPase.

Wilson's Disease

- Hepatic presentation < 12 years
  - Acute or chronic hepatitis/Failure
  - Haemolysis
  - Low alkaline phosphatase

- Neurological > 12 years
  - Slurred speech/Tremor /poor co-ordination
- Kayser Fleischer rings



Tyrosinaemia Type I

Incidence 1:50,000

Deficiency of fumaryl-aceto-acetase

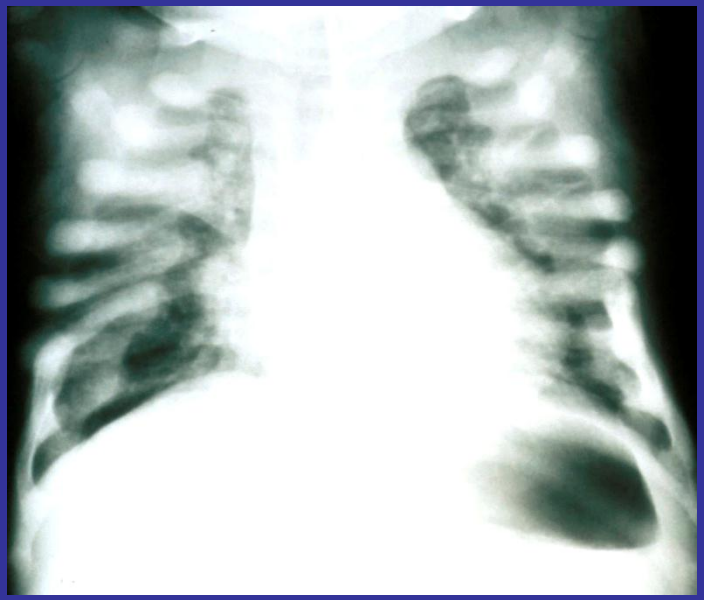
Δ Succinyl acetone in urine

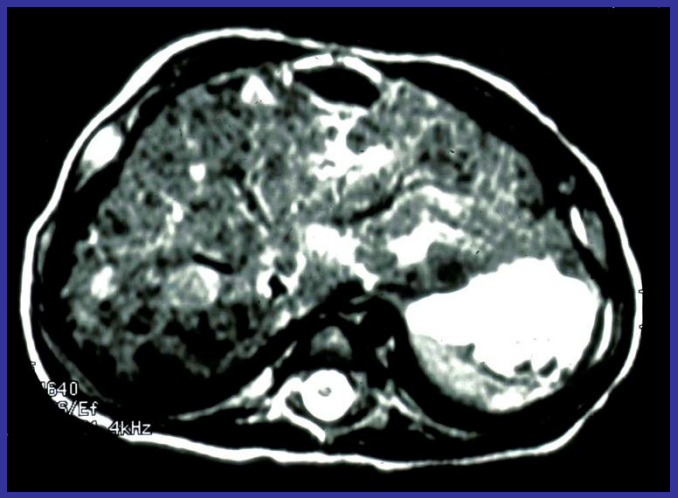
Deficiency of FAA in fibroblasts

Clinical Presentation of TTI

Chronic Liver Failure

- Failure to thrive
- Hepatosplenomegaly
- Rickets
- Cardiomyopathy
- Renal failure
- Neurological symptoms





Fatty Liver Disease

Definitions:

Non Alcoholic Fatty Liver Disease (NAFLD)

- hepatic steatosis without inflammation

Non Alcoholic Steatohepatitis (NASH)

- hepatic steatosis with hepatocellular injury
  +/- fibrosis/cirrhosis

Fatty Liver Disease

Increasingly common cause of

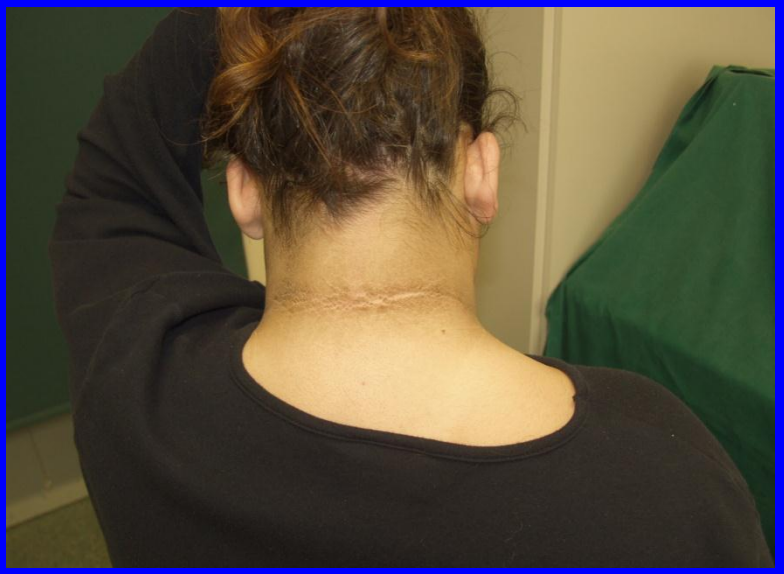
- elevated transaminases
- hepatomegaly
- “bright” liver on ultra sound

Associated with Insulin Resistance

Diabetes type 2
Alstrom Syndrome
Bardet – Biedl Syndrome
Polycystic Ovary
Turner Syndrome
Lipodystrophy

Clinical features of Fatty Liver Disease

- Children more likely to be symptomatic
  - RUQ pain
  - Fatigue/malaise
- Most present coincidentally
  - Hepatomegaly
  - ↑ ALT/AST (1.5 – 5 times normal)
  - ALT/AST ratio > 1 in most NAFLD
  - elevated triglycerides
  - acanthosis nigricans
  - insulin resistance



Treatment for Fatty Liver Disease

- **WEIGHT LOSS**
  - Diet and Exercise
  - cannabinoid receptor blockade (Rimonabant/Acomplia)
  - Lipase inhibition Orlistat

- **ANTIDIABETIC THERAPY – *Insulin sensitizer***
  - Glitazone
  - Metformin

- **ANTIOXIDATIVE THERAPY**
  - Vitamin E

- **ANTI LIPID THERAPY**
  - Statin

- **URSODEOXYCHOLIC ACID**

Hepatocellular Dysfunction in Children

Multi-organ failure

Primary:	Cardiac (Alagille, HOCM)
	Renal (RTA)
	Cerebral (mitochondrial disease)
Secondary:	Encephalopathy
	Functional renal failure
	Cardiac failure
	Coagulopathy

Chronic Liver Disease in Children

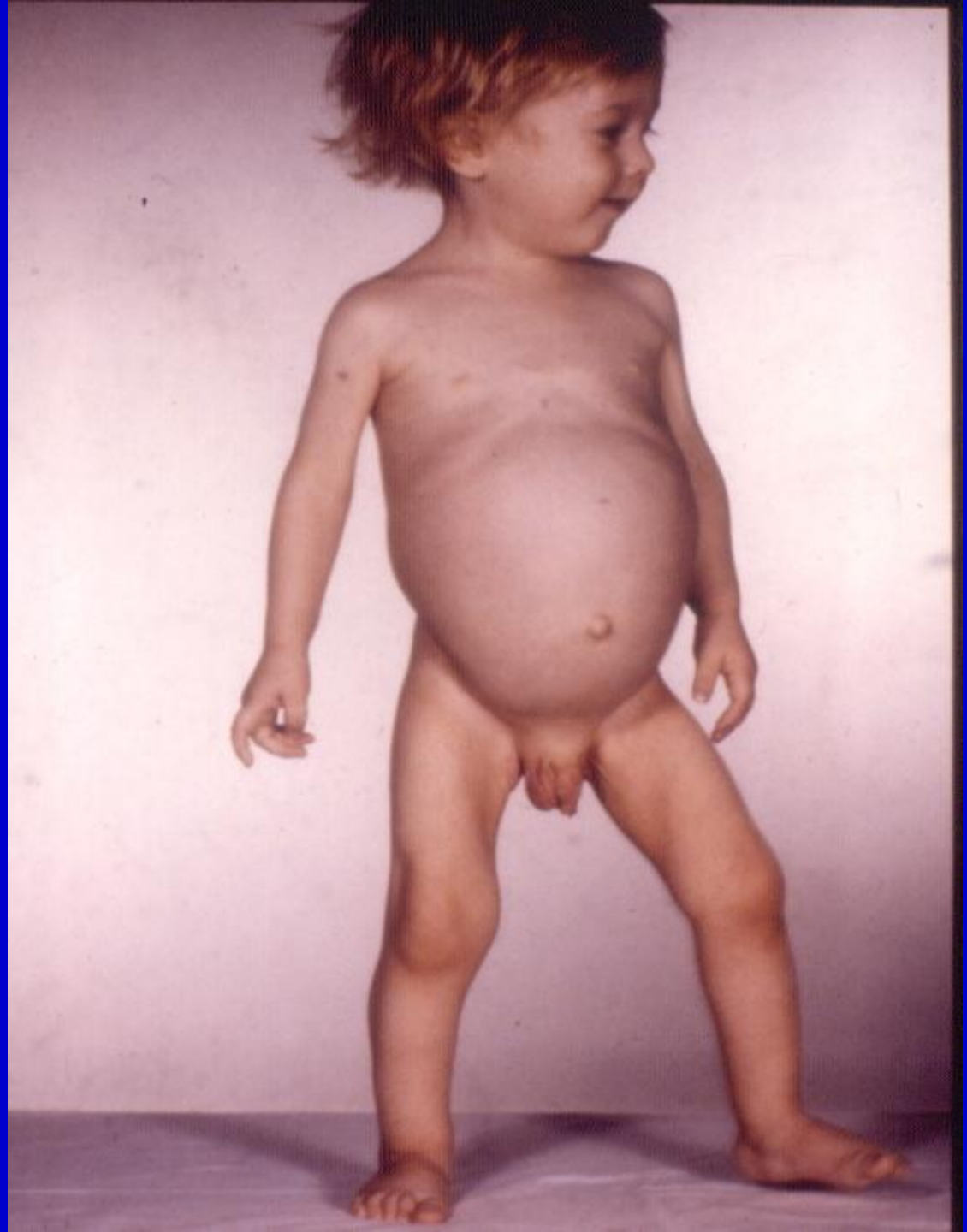
Persistent liver disease (>8 weeks)

- Sustained hepatic dysfunction
- Biochemical/histological
- Functionally
  - Jaundice
  - Coagulopathy
  - Hypoglycaemia
  - Portal hypertension
  - Malnutrition

Effect of Hepatic Dysfunction

Cholestasis

- Pruritus
- Steatorrhoea
- Fat soluble vitamin deficiency
- Malnutrition



Management of End Stage Liver Failure

Supportive:

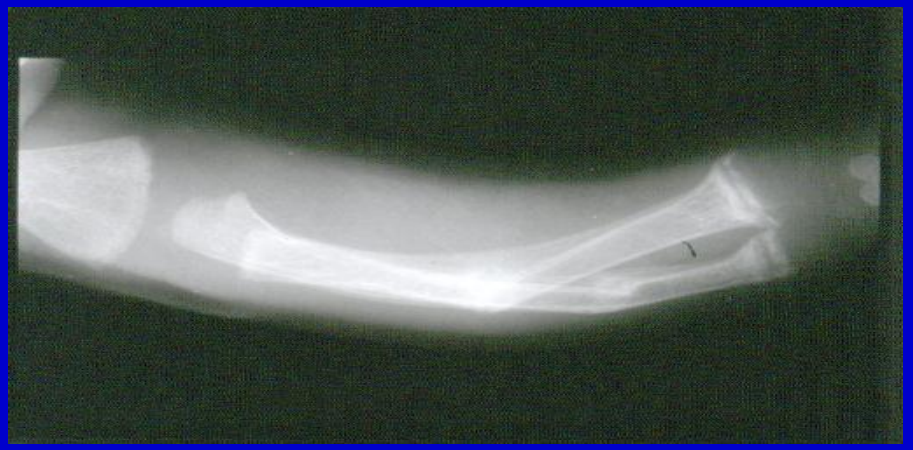
Prevention therapy:-

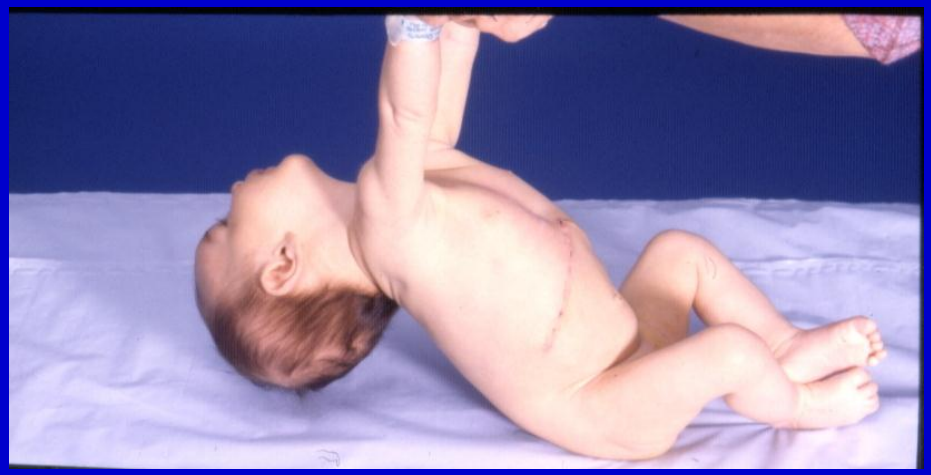
- Hepatic complications
- Sepsis

Nutritional support

Psychosocial

- child/family





Nutritional Management of End Stage Liver Failure

Modular feed: High protein/CHO

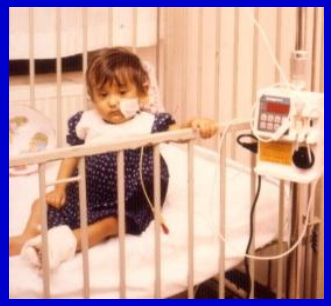
Balanced MCT/LCT

Low salt

150% RDA

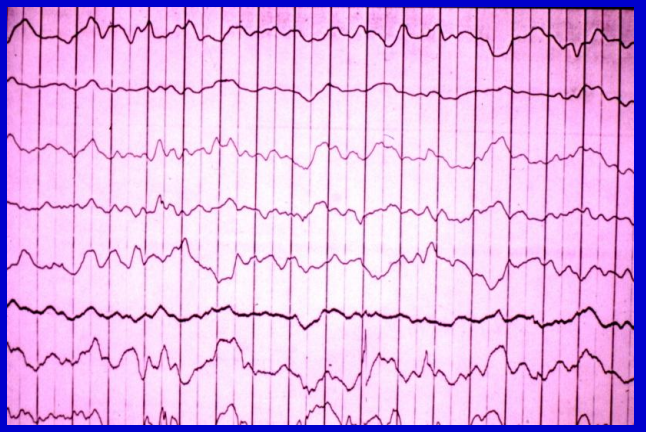
Fat soluble vitamins A, D, E, K

- Oral
- Nasogastric
- Parenteral



Management of End Stage Liver Failure

Hepatic Encephalopathy



- Low protein diet (2g/kg)
- Lactulose 5.20 ml/day
- Neomycin 0.5 g TID
- Rifaxamine

Prompt treatment of sepsis/haemorrhage

Hepatocellular Dysfunction in Children

Fluid Management

Pathophysiology: Na/water retention

Ascites

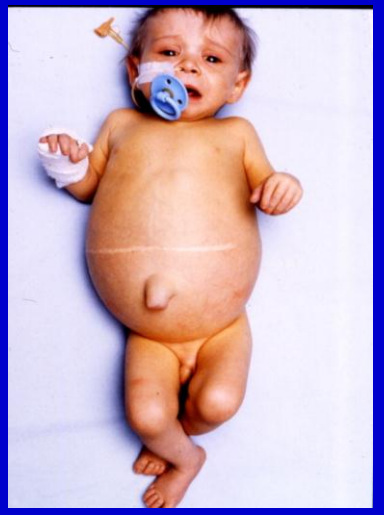
Fluid overload

Management: Fluid restriction

Calorie requirement

Management of End Stage Liver Failure Ascites and Fluid Retention

- Fluid and salt restriction
  - (2/3 maintenance)
- Diuretics: Spironolactone 3mg/kg
  Frusemide 1-2 mg/kg
- Ascitic tap/drainage
- Haemofiltration/Dialysis



Management of Pruritus

Enzyme inducers:-

- Phenobarbitone (5-15 mg/kg)
- Rifampicin (3 mg/kg)

Bile Diversion:-

- Ursodeoxycholic acid (20 mg/kg)
- Cholestyramine (1-4G/d)
- Biliary diversion

Central:-

- Naloxone
- Ondansetron

Management of End Stage Liver Failure

Coagulopathy:

Vitamin K 2-10 mgm/kg

Fresh frozen plasma 10 ml/kg

Cryoprecipitate

Platelets

Anaemia:

Oral iron

Transfusion

Management of End Stage Liver Failure

Specific:

Immunosuppression	(CAH)
Penicillamine	(Wilsons)
Ursodeoxycholic acid	(CF)
Anti-viral therapy	(Hep B/C)
Diet	
Liver Transplantation	

Hepatocellular Dysfunction in Children

Portal Hypertension:

- Varices
- Portal gastropathy
- Hypersplenism

Implications for a normal life:

- School
- Contact sports

Managing Portal Hypertension in Children

Medical Therapy

- Diagnostic endoscopy and therapy
- Drug therapy
- Transjugular intrahepatic porto-systemic stent shunt (TIPSS)
- Prophylaxis

Pharmacological Treatment of Portal Hypertension

Hepatic vascular resistance

Reduced by	-	nitric oxide
		prostacyclin
		adrenergic antagonists
		calcium channel blocker

Portal blood flow

Reduced	-	vasopressin/glypressin
		Somatostatin/octreotide
		propranolol

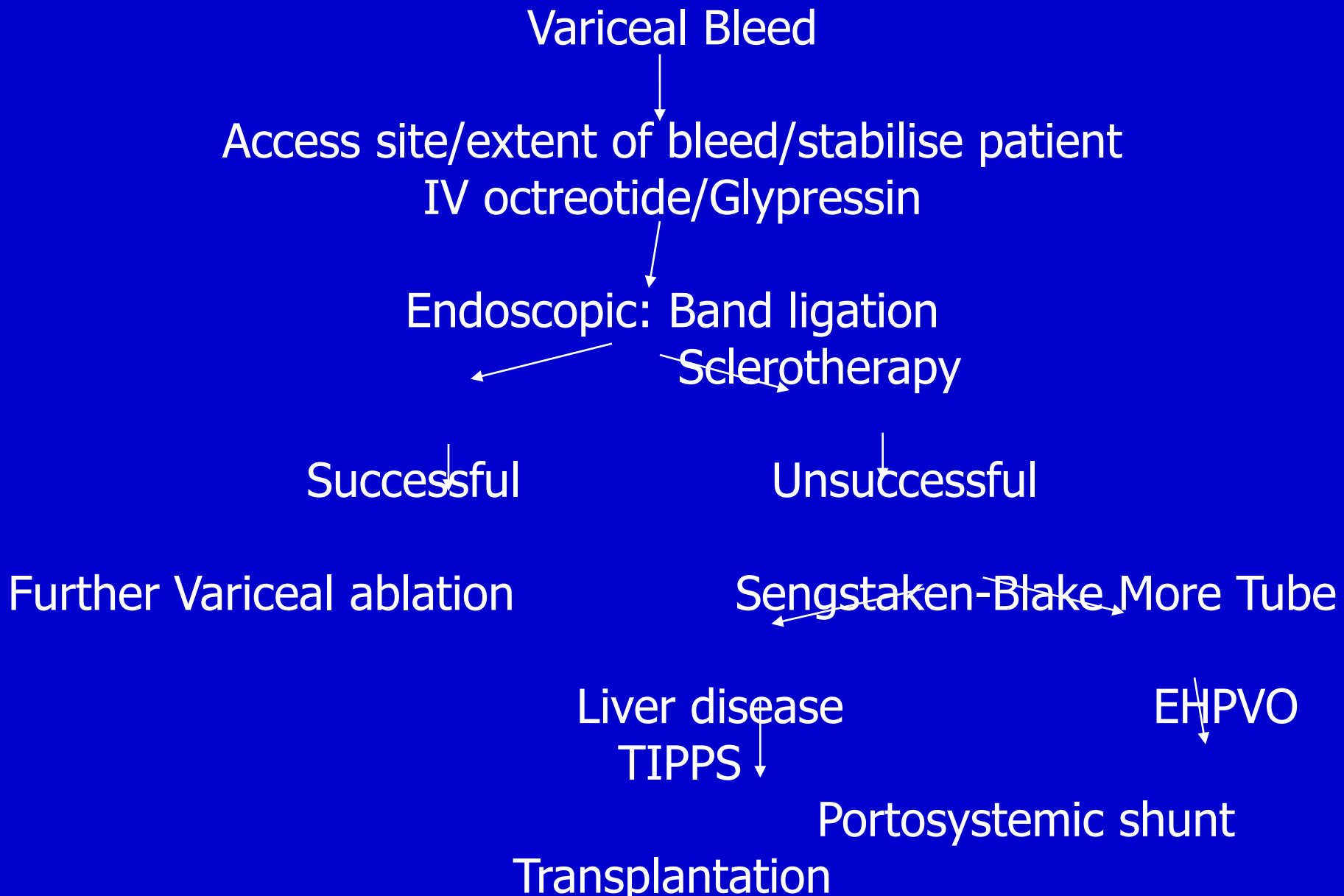
Prophylaxis of Portal Hypertension in Children

Drug therapy:

- Beta-blockers:
  - Propranolol, Nadolol
- 3 small studies in children
  - Bleeding in 15-33%
- No trials in children with CF
- ? Propranolol contraindicated in CF
- ? Losartan - angiotensin II receptor antagonist
- No trials of prophylactic band ligation in CF

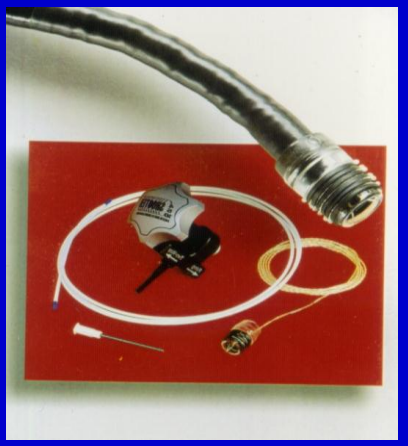
Shashidar et al 1999; Ozsoylu et al, 1985, 2000

Management of Acute Variceal Bleed in Childhood



Results of Variceal Band Ligation in Children

	N	Ablation	Rebleeding
Price	18	70%	30%
Fox	7	100%	28%
Karrer	7	100%	15%



Limitations of TIPPS Procedures in Children

Age/size of child

Size of portal vein (<2mm)

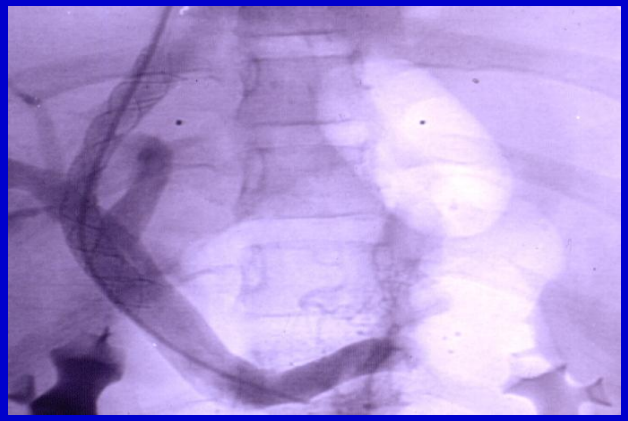
Size of stent (5-6 mm diameter)

Length of stent:- allow for growth

<u>Long Term Outcome:</u>

Encephalopathy

Occlusion/infection



Prognosis of Chronic Liver Disease

Depends on:-

- Aetiology
- Severity of insult
- Progression to cirrhosis
- Portal hypertension

Access to liver transplantation

Indications for Transplantation in Chronic Liver Failure

Laboratory Indices

Serum cholesterol <2.6 mmol/l (100 mg/dl)

Indirect bilirubin >100 μmol/l (6mg/dl)

Serum albumin <35 g/l (3.5 mg/dl)

Prothrombin ration (INR) >1.4

Portal vein reverse flow on ultrasonography

Indications for Transplantation in Chronic Liver Failure

Clinical:-

Severe portal hypertension

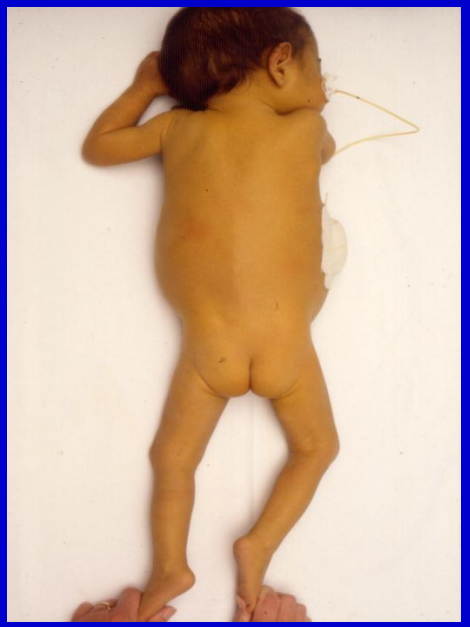
Recurrent variceal bleeding

Refractory ascites

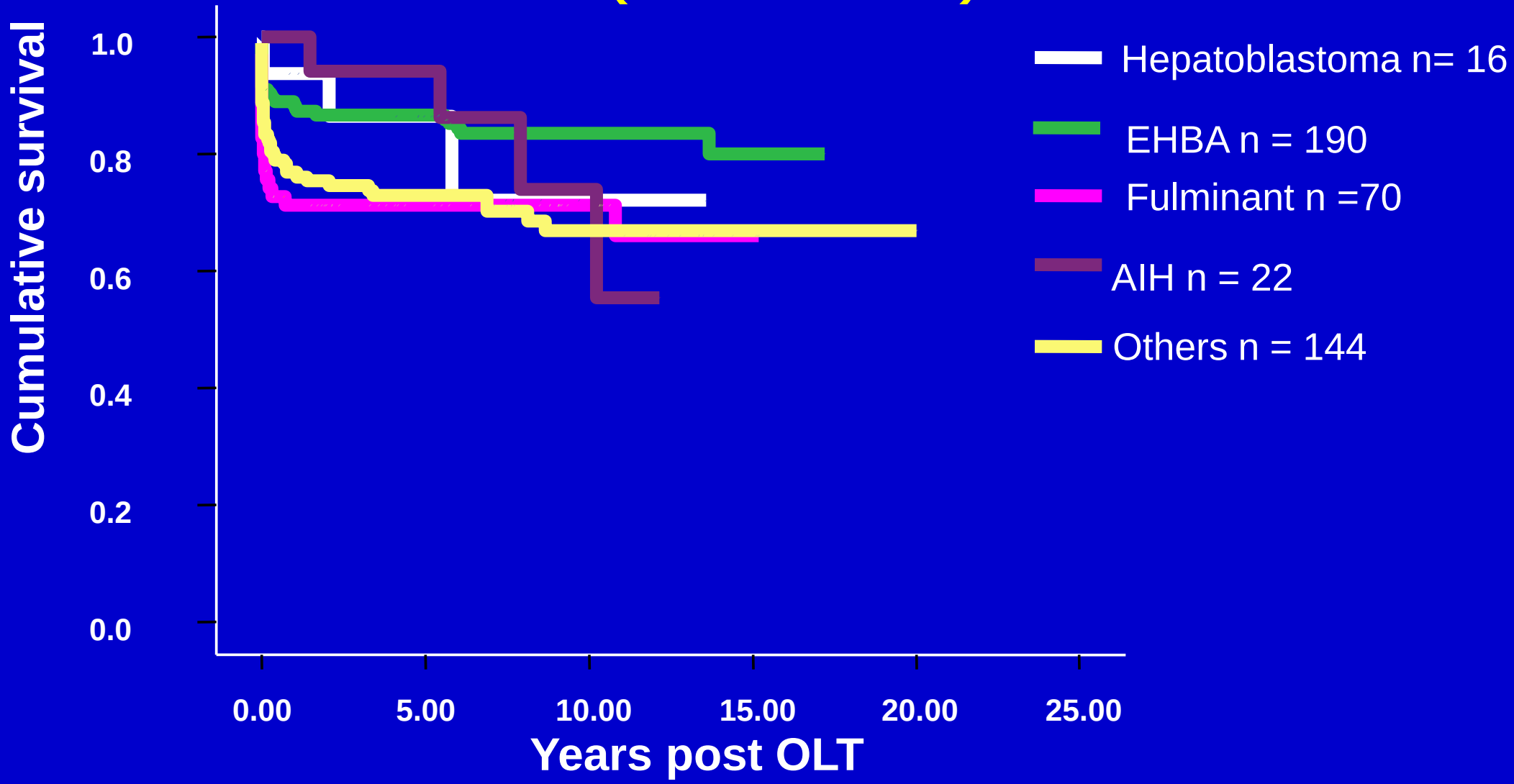
Intractable pruritus

Growth retardation

Unacceptable quality of life



Survival post transplant by disease (1989-2005)



Chronic Liver Disease

Chronic liver disease

Early referral and recognition of liver disease

Referral to Specialist centre

- Early diagnosis
- Consideration of Treatment
- Improve outcomes for children