Neonatale cholestase

Geneeskundige Dagen van Antwerpen
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Zoals u al wist …

- Verlengde icterus (>2-3 weken)
- Geconjugeerd versus niet geconjugeerd.
- Ontkleurde stoelgang of niet

Universal Screening for Biliary Atresia Using an Infant Stool Color Card in Taiwan

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***Hepatology*, 2008**

- **All** newborns screened in 2004 & 2005
- Total of 422,273 infants
- Mothers sent home with stool color card

- Outcome:
- 279 cards returned
- mean age of 27 days

- 75 diagnosed with BA (1:5600)

- Detected with the card < 60 days
  - 2004: 29/40 (72 %)
  - 2005: 34/35 (97 %)

- Kasai operation performed < 60 days:
  - 1976-2000 47%
  - 2004 60%
  - 2005 74%

Infant Stool Color Card

Abnormal 1 2 3 Normal 4 5 6

Careful Observation of Stool Color Is Helpful in Early Diagnosis of Biliary Atresia in Early Infancy

Though neonatal jaundice is very common, some babies may suffer from cholestasis if the jaundice is prolonged after the 3rd or 4th week of life. Cholestasis can be divided into intra-hepatic and extra-hepatic type. The most common intra-hepatic cholestasis is neonatal hepatitis, while the most common extra-hepatic cholestasis is biliary atresia. The infants with biliary atresia should be diagnosed within 50 days of age, and undergo surgery as quickly as possible before 60 days of age. The stasis of bile in the liver tends to result in liver cirrhosis, and most die before 2 years of age if left untreated.

How to Assist in Early Screening for Infantile Cholestasis?

The parents should observe the baby's skin and stool color. When the skin and sclera color becomes yellowish, it's necessary to carefully observe the baby's stool color. The color in pictures No. 4–6 above, belong to the normal stool color group. The color of stools without a mixture of bile will be light yellow or clay-colored, as in pictures No. 1–3 above. These colors belong to the abnormal stool color group. Babies with abnormal stools should be sent to a professional pediatric physician for consultation and transferred to a pediatric gastroenterologist if necessary, as early as possible.

The baby's stool color is most like photo No.:____

The date when this kind of stool was first noticed:

Name of the baby:_____ Date of Birth:_____

Mother's Name:_____ Tel.:_____

Address:_____

The hospital or clinic where the baby was born:

If the baby's stool most closely resembles photos No. 1–3, please inform us by phone or fax immediately. We will provide you with related information and advice.

Fax: 02-2388-1799

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Biliaire atresie

- Gezonde zuigelingen, goede gewichtstoename
- Icterisch, hepatomegalie
- Geen klinische tekenen van leverlijden
- Ontkleurde stoelgang
- Soms presentatie met bloeding
- Biochemisch: gestegen direct bilirubine, vaak ook GGT
- Verdere diagnostiek: de tijd dringt
  - Echografie (sens 80%, spec 80%)
  - Leverbiopsie (sens 95%, spec 95%)
  - Intra-operatieve cholangiografie (= gouden standaard)

OBSTRUCTIEF

- Biliary atresia
- Choledochal cysts
- Inspissated bile
- Lithiasis

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NIET-OBSTRUCTIEF

- Infectious
- Endocrine
- Metabolic
- Genetic
- Toxic
- Immune
- Idiopathic

Alagille syndrome

- 1/100.000, A Dom
- *JAG1* or *NOTCH2*
- Cardiac, Renal, Ocular, Vertebra, Dysmophism
- Paucity of bile ducts
- Pruritus!
- Liver transplantation

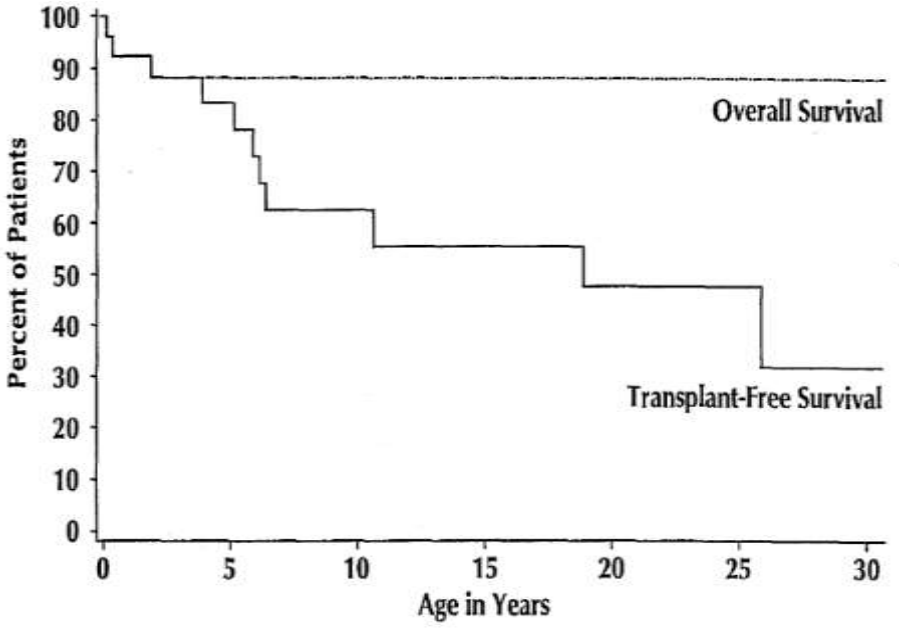

Figure. Kaplan-Meier plot of data on 26 index patients with sPILBD. Overall survival rate is shown by the *dotted line*. Early death is caused by extrahepatic manifestations of the disease, such as congenital heart disease or intracranial hemorrhage. The *solid line* represents transplant-free survival. The predicted probability of attaining 19 years of age without liver transplantation is about 50% *(solid line)*. With liver transplantation the probability of long-term survival is 87%.

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- Alagille
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- Immune
- Idiopathic

α1-antitrypsin deficiency

- A Rec, 1/2500-1/5000
- *SERPINA1*: PiZZ, (PiSZ)
- Longziekte als volwassenen
- 10% zuigelingen krijgt leverziekte
  - 5% LTx <4j
  - 95% normaliseert, goede QoL
    - 25% geen leverziekte
    - 50% biochemisch abnl
    - 25% cirrhose, LTx <20j
- 2e indicatie voor pediatrische levertransplantatie

Infectious

- Toxoplasma
- Rubella
- CMV
- Herpes
- Syfilis

- Bacterial sepsis (UTI)
- HHV6, entero, adeno, Parvo B19, VZV, HIV, …

Endocrine

- Hypothyroidism
- Panhypopituitarism
- Hypocortisolaemia

Metabolic

Substantie

- Suikers: galactosemia
- AZ: tyrosinaemia
- VZ

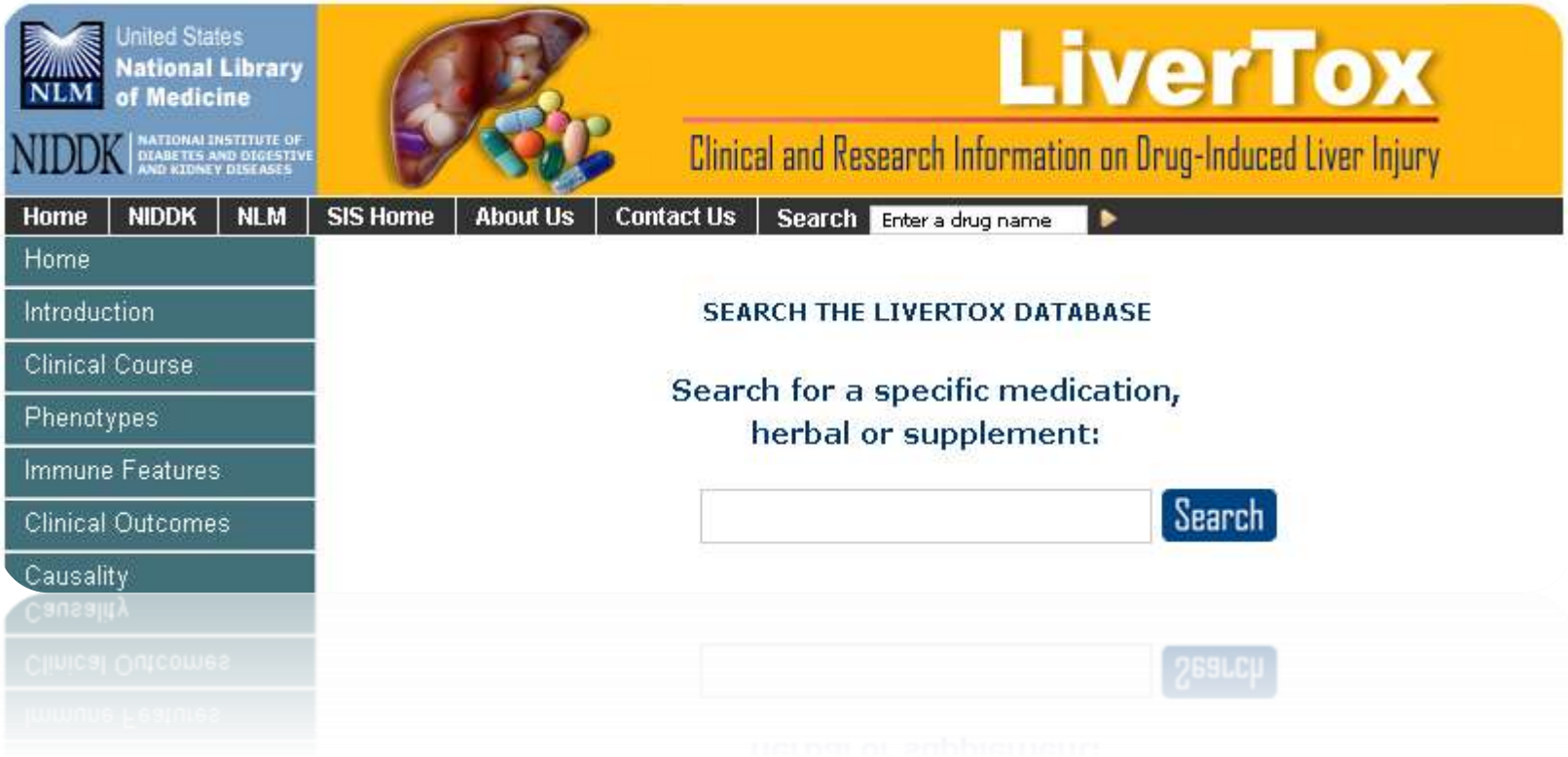
Organel

- Peroxisomale (Zellweger)
- Mitochondriale (Alpers)
- Lysosomiale (Wolman)

Genetic

- Chromosomal disorders
- Cystic fibrosis
- α1-antitryspin deficiency
- PFIC 1-3
- (Bile acid synthesis disorders)

Toxic



- Antibiotics
- PNALD
- Chloral hydrate
- Foetal alcohol syndrome

- Premature infants: ‘multifactorial’

Immune

- Neonatal haemochromatosis
- AIHA met giant cell hepatitis
- Familial haemophagocytic syndrome

Idiopathic neonatal hepatitis

- 10-15 % geen ethiologie gevonden
- Normale kleur van stoelgang
- Prematuriteit, IUGR, ...
- Biopsie: verstoorde lobulaire architectuur, giant cell hepatitis
- Prognose: goed> 90%, normaliseert < 1 jr

OBSTRUCTIEF

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- Infectious
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- Alagille

Acuut leverfalen

Pediatric Acute Liver Failure Study Group:

1. Acute onset of liver disease with no known evidence of chronic liver disease
2. Biochemical / clinical evidence of severe liver dysfunction:
    1. Encephalopathy + PT 15-19.9s (INR 1.5-2.0)
    2. PT>20 sec (INR>2) (no correction with Vit K iv, no sepsis)

Acuut leverfalen

- Neonatal: lactose-free milk, Aciclovir
- Acute liver failure = referral to transplant center
- In pediatric age (*Kings College Criteria)*:
  - *INR ≥ 4*
  - *Bilirubin ≥ 13mg/dL*
  - *age < 2 y*
  - *wbc > 9 x 10^9/L*
- Don’t correct PT, correct glycemia

Neonatale cholestase : Praktische aanpak

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Practical approach

- History
- Clinical examination
- Lab investigations
- Ultrasound

• Geconjugeerd bilirubine
• Levertesten: ALT, AST, GGT, Alk Phos
• Leverfunctietesten: PT, glc, albumine, ammonia, cholesterol
• FBC

WORK-UP

→ **Infections**

Blood cultures
Urine culture and CMV
Serology (IgM to Toxoplasma, rubella, CMV, Herpes)
Hepatitis A, B, and C serology

Metabolic

Sweat test
Galactose-1-phosphate uridyl transferase
α1 antitrypsin level and phenotype
Plasma and urine aminoacids
Urine organic acids (succinyl acetone)

Endocrine

Thyroid function tests
Cortisol (preferably after 4 hour fast)

Practical approach

- History
- Clinical examination
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- Ultrasound

- Uitsluiten biliaire atresie

Exclude treatable

Table 4. Causes of the neonatal hepatitis syndrome which require specific treatment

Condition	Treatment
Hypopituitarism	Hydrocortisone, thyroxine ± growth hormone
Galactosaemia	Galactose free diet
Fructosaemia	Fructose free diet
Tyrosinaemia type 1	(2 (2 nitro-trifluoromethylbenzoyl)-1,3-cyclohexenedione) – NTBC
Bile acid synthetic disorders	Cholic acid ± chenodeoxycholic acid ± UDCA
Autoimmune haemolytic anaemia with giant cell hepatitis	Immune suppression

Lactosevrije voeding tot galactosemie is uitgesloten!

Practical approach

- History
- Clinical examination
- Lab investigations
- Ultrasound

- Uitsluiten biliaire atresie
- Lactosevrije voeding + MCT
- Vetoplosbare vitamines nooit vergeten