KASAI PROCEDURE
EMAD KANDIL, MD
Preop Phenobarb
Post-op
- Hemodynamically stable
- Started on steroids
- Reported 1 greenish stools

**Total Bilirubin**

- mg/dL
- Generalized Normal High
- Generalized Normal Low

Graph showing the trend of total bilirubin levels from 12/17/2004 to 12/27/2004.
• no inflammation seen
PORTA HEPATIS

- fibrotic contain nerves and small blood vessels, no bile duct components
Liver Bx

- Bridging fibrosis
- Chronic and focal acute inflammation
- Marked cholestasis and giant cell transformation of hepatocytes c/W extrahepatic ducts dilation
KASAI PROCEDURE
EMAD KANDIL, MD
Biliary Atresia

• Obliteration or discontinuity of the extrahepatic biliary system

• MC cause of death as a result of liver disease in early childhood in the Western world

• MC surgically treatable cause of cholestasis encountered during the newborn period

• If not corrected surgically, 2ry biliary cirrhosis results

• First reported by Professor John Burns from University of Glasgow in 1817

Mowat AP, etal(Earlier identification of biliary atresia and hepatobiliary disease) Arch Dis Child 72:90-92, 1995
Biliary Atresia

TYPES

- subdivided into 2 distinct forms:
  - (1) isolated biliary atresia (postnatal form): (65-90%)
  - (2) Associated situs inversus or polysplenia/asplenia with or without other congenital anomalies (fetal/embryonic form): (10-35%)
Biliary Atresia

Types:

- **Type I**: atresia of the CBD, while the proximal ducts are patent.
- **Type II**: atresia of the hepatic duct, with cystic structures found in the porta hepatis.
- **Type III (>90%)**: atresia of the right-left hepatic ducts to the level of the porta hepatis.

Of great importance, these variants should not be confused with intrahepatic biliary hypoplasia, which comprises a group of distinct and surgically noncorrectable disorders.
Pathophysiology

- Poorly understood.
- Congenital malformation of biliary ductular system:
  - Failure of recanalisation
  - Ductal plate malformation
  - Imbalanced apoptosis
  - Disorganised cell turnover
  - Disordered epithelial-mesenchymal interaction
Pathophysiology

- Ischaemic insults
- Abnormal bile acid metabolism
- Pancreaticobiliary maljunction
- Immunologic dysfunction
- Type III (MC type) is characterized by a progressive inflammatory lesion, suggesting a role for infectious and/or toxic agents causing bile duct obliteration.

- Infectious agents:
  - Elevated antibody titers to:
    - Reovirus type 3
    - Rotavirus
    - CMV (25%)
Pathology

- 3 month old child died with extrahepatic biliary atresia
Pathology

- Macroscopic appearance of explanted liver showing large central nodules surrounded by cirrhotic liver (centimeter scale).
Pathology

- Microscopically, numerous brown-green bile plugs
Frequency

- **In the US:**
  - overall incidence of 1/10,000-15,000 live births.

- **Internationally:**
  - The incidence highest in Asian populations
  - more common in Chinese Vs Japanese infants.
Mortality/Morbidity

(Post Kasai):

- 47-60% at 5 years
- 25-35% at 10 years.
- Overall survival for > 20 y was reported as 22%.

- 30%, bile flow is inadequate following surgery, and these children succumb to complications of biliary cirrhosis in the first few years of life unless liver transplantation is performed.

• Nio M. The Outcome of Surgery for Biliary Atresia and the Current Status of Long Term Survivors.
• Tohoku J Exp M 1997
Race & Sex

- **Race:**
  - Asian populations.
  - Black infants $X^2 >$ white infants.

- **Sex:** Females $>$ males.
History

- Typical symptoms include variable degrees of jaundice, dark urine, and light stools.
- In most cases, acholic stools are not noted at birth but develop over the first few weeks of life.
- Appetite, growth, and weight gain may be normal.
Physical Exam

• No findings are pathognomonic for the disorder.
• These infants typically are full term and may manifest normal growth and weight gain during the first few weeks of life.
• Hepatomegaly may be present early, and the liver is often firm or hard to palpation.
• Splenomegaly (suggests progressive cirrhosis with portal hypertension).
• Direct hyperbilirubinemia (physiologic unconjugated hyperbilirubinemia rarely persists beyond 2W)
• Cardiac murmurs
• Bilirubin: direct bili > 2.0 mg% or 20% of T. bili
  • T. bili (6- to 12-mg%) range
• ALP, GGTP, AST, ALT:
  • no single test discriminates between biliary atresia and the other causes of neonatal cholestasis.
• Serum alpha1-antitrypsin with Pi typing:
  • Alpha1-antitrypsin deficiency MC inherited liver disease that presents with neonatal cholestasis
對 Neonatal Prolonged Obstructive Jaundice
治療、治療、計劃

Physiologic Jaundice 以後
有 Jaundice 之嬰兒集中觀察

Stool Color Yellowish
觀察治療 Neonatal Hepatitis

Stool Yellowish
繼續觀察治療 Neonatal Hepatitis

Stool Clay Color

Duodenal Juice Analysis

Duodenal Juice Yellowish
繼續觀察,治療 Neonatal Hepatitis

Duodenal Juice No color

Laparotomy 觀察治療

Atresia
Kasai’s Ope.
Washing of Bile duct
繼續觀察治療 Neonatal Hepatitis

Patent
Ultrasonography

- Exclude specific anomalies of the extrahepatic biliary system, particularly choledochal cyst. (Today, a diagnosis of choledochal cyst should be made in utero by fetal U/S).

- In biliary atresia, may demonstrate absence of the gallbladder.

- Sensitivity and Specificity do not exceed 80%
Triangular Cord Sign

Triangular Cord Sign

- Magd A. Kotb et al., PEDIATRICS Vol. 108 No. 2 August 2001, 416-420
Diagnostic Approach for Infantile Cholestasis

Biliary Atresia vs Neonatal Hepatitis

Ultrasonography

TC (+)
- Normal Gall Bladder
  - Tc-99m-DISIDA Scan
    - Excretion into Intestine: Surgery
    - No Excretion into Intestine: Conservative Rx

TC (-)
- Abnormal Gall Bladder
  - Liver Needle Biopsy
    - Inconclusive: Optional (Minilaparotomy or Re US/Bx)
    - Biliary Atresia: Surgery

Neonatal Hepatitis
Hepatobiliary Scintiscanning (DISIDA)

- Evidence of intestinal excretion of radiolabel confirms patency of the extrahepatic biliary system.
- Two cautionary notes:
  - Reliability of the scintiscan is diminished at very high conjugated bilirubin levels (>20 mg%)
  - 10% rate of false-positive/false-negative diagnostic errors.
Kasai Portoenterostomy

- Introduction in 1957.
- Not widely accepted by the western world until 1970s.
- The only palliative treatment for patients with biliary atresia.
- Increased 5-year survival from 0% to 60%.

Hepaticoportojejunostomy
Fig. 57.7 The Kasai 2 cutaneous enterostomy in which a stoma is fashioned in the Roux loop. The recommended lengths of bowel are indicated in cm.
Hepaticojejunostomy
Hepaticoporto-duodenostomy
Portocholecystostomy

Fig. 57.8 Portocholecystostomy. A patent gallbladder may be anastomosed to the transected tissue in the porta hepatis in some cases of type 3 atresia.
Factors Influencing Outcome

- Age (before 60 days)
- Hyaluronic Acid
- Experience or caseload of a surgical centre
- Preop Jaundice: no relationship with the outcome
- Serum transaminases and bilirubin have no predictive value
• Surgery done before age of 60 days is associated with favourable outcome.

• Some centres provide acceptable results with operation done between 60-90 days.

• Sendai series revealed a 10 years survival rate of 73% for those operated on before 60 days, but only 11% for those underwent surgery after 90 days of life.

Billirubin

- Serum transaminases and bilirubin have no predictive value on the outcome.
- However, the rapidity with which bilirubin returns to normal after Kasai operation is an important predictive factor for long-term survival.
- Serum bilirubin <1 mg/dL within 3 months after operation implicates good long-term outcome.

Fig 1. Kaplan-Meier cumulative patient survival curve. The total graph represents the overall survival rate for all 142 patients irrespective of whether bile drainage was achieved. The jaundice-free graph represents the patients whose bilirubin level decreased to 2.0 mg/dL at any time (months to years) after the Kasai operation. The jaundiced graph represents those whose bilirubin remained greater than 2.0 mg/dL.

Fig 3. Comparison of Kaplan-Meier cumulative patient survival rate between the success and jaundice-free groups. The difference becomes gradually significant over a decade ($P < .05$).
Hyaluronic Acid

- Serum level was found to be a useful early marker to predict the outcome of a patient after Kasai operation.
- HA is cleared rapidly from the circulation by the liver via receptor mediated endocytosis into sinusoids.
- During progressive liver disease, these cells undergo transformation → impairs the uptake of metabolites such as HA.
- >450g/L has similar predictive power as surgical age.

*Dhawan A. Serum hyaluronic acid as an early prognostic maker in biliary atresia. J Ped Surgery 2001;36:443-446*
Fig 1. Kaplan-Meier product-limit survival distributions. (A) Hyaluronic acid, cutoff ≤450, >450. (B) Age at Kasai, cut-off ≤9 wks, >9 wks.
Fig 2. Graph shows the relation between hyaluronic acid and age at Kasai. ● patients that were alive (5 years) and did not undergo transplant. ○ patients that died or underwent transplant.
Survival Data

• A nationwide survey in Japan revealed 16% out of 2013 patients have survived for more than 10 years. Only about half of these patients are jaundice free after 10 years.

• A similar survey in North America in 1989 reported long-term survival rate of 25%.

• Another, Japanese series produced the best result in terms of survival. Fifty-nine percents survived for 10 years after Kasai with >80% of them are jaundice free. Overall survival for > 20 y was reported as 22%.
Fig 1. Survival curves for 311 patients with biliary atresia treated with portoenterostomy at Tohoku University, Japan, between 1951 and 1998. The curves are presented in 6-year cohorts and illustrate the gradual improvement in long-term survival rates.

Overall Survival (without liver transplantation)
(GroupName by centre caseload)

- Group-A centres
  (>5 cases/year)

- Group-B centres
  (<5 cases/year).

Patrick J McKiernan, Lancet 2000
Overall Survival (Grouped by centre caseload)

- Group-A centres (>5 cases/year)
- Group-B centres (<5 cases/year).

Patrick J McKiernan, Lancet 2000

• Before 1999, infants born in the UK with suspected biliary atresia were investigated in regional centres, and, if confirmed, a Kasai operation was done there.

• Since 1999, all infants with suspected biliary atresia in England and Wales, UK, have been referred to one of three designated centres where both the Kasai operation and liver transplantation (if necessary) could be done.

Outcome of infants with Biliary Atresia (Jan, 1999, to June, 2002)

148 infants with biliary atresia

1 died

6 died after Kasai portoenterostomy

142 had Kasai portoenterostomy

5 had primary liver transplantation

52 received transplant

6 died after transplantation

46 alive with liver transplant

84 survived with native liver

5 alive with liver transplant


<table>
<thead>
<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>Overall Survival</td>
<td>85%</td>
<td>89%</td>
</tr>
<tr>
<td>Native Liver Survival</td>
<td>30%</td>
<td>51%</td>
</tr>
</tbody>
</table>

Our early results suggest that surgical outcome can be improved by centralization of care to supra-regional centers.

4-year Actuarial Survival rates

- overall survival: 89%
- 4-year survival with native liver: 51%

Postsurgical Complications

- **Unsuccessful Anastomosis**
  - MC complication
  - 1/3 of all patients, bile flow is inadequate following surgery, and then succumb to biliary cirrhosis in the first few years of life unless OLT is performed

- **Cholangitis**
  - 93% of patients before 1 year of age
  - 30-40% at 5 years post surgery
  - Some patients may present as late as 13 years after Kasai
  - The incidence is reduced by antibiotic prophylaxis
  - Early and prompt antibiotic administration helps in restoring good liver function.

  *Gottrand F. AJDC 1991;145:213-215*
**Postsurgical Complications (cont.)**

- **Portal Hypertension and Variceal Bleeding**
  - >60%
  - Recurrent uncontrolled variceal bleeding is an indication for transplantation

- **Hepatocellular Ca**
  - OLT is the only option for long-term survival.

- **Hepatopulmonary Syndrome**
  - Uncommon a/w chronic liver disease
  - Triad of liver dysfunction, arterial hypoxaemia and intrapulmonary vascular dilatation.
  - Dyspnoea, particularly orthodeoxia, and cyanosis.
  - Mortality rate 41%
  - OLT
Post Op Meds

- **Steroids:**
  - In the immediate postop
  - anti-inflammatory agent
  - Nonspecific stimulant of bile salt-independent bile flow.

- **Ursodeoxycholic acid (ursodiol):**
  - Enhance bile flow
  - may improve outcomes, and associated with minimal toxicity.

- **Bactrim:**
  - Prophylactic for cholangitis
Quality of Life

- 22 patients who survived > 20y
- 3 women were married and 1 had completed a normal pregnancy.
- Normal growth was achieved in all except 1 who had Turner syndrome.
- 2ry sexual characteristics were normal in all patients except the patient with Turner syndrome.
- School performance was normal in 8, 1 year below normal for 11, and 2-3 years subnormal for 7 patients.

# Quality of Life

<table>
<thead>
<tr>
<th>Satisfactory</th>
<th>16 of 21</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unsatisfactory</td>
<td>5 of 21</td>
</tr>
</tbody>
</table>

- Liver dysfunction (patient 16)
- Intrahepatic stones (patient 13)
- Cholangitis (patient 14)
- Cholangitis with hypersplenism (patient 17)
- Turner’s syndrome (patient 1)

*Nio M. Current Status of 21 Patients Who Have Survived More than 20 years since Undergoing Surgery for Biliary Atresia. J Ped Surgery 1996*
A recent comparison of quality of life in long-term biliary atresia survivors from King’s College and Tohoku University

The quality of life measurements were comparable between 2 centres except small reductions in the scores for general health and vitality among the Japanese.

## Table 6. Comparison of Quality-of-Life Standardized Scores Between Japan and UK Long-Term Survivors

<table>
<thead>
<tr>
<th></th>
<th>KCH-UK</th>
<th>Japan</th>
<th>95% CI for Standardized Mean Difference</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>Mean (SD)</td>
<td>No.</td>
<td>Mean (SD)</td>
</tr>
<tr>
<td>Body pain</td>
<td>21</td>
<td>0.022 (0.97)</td>
<td>25</td>
<td>-0.415 (1.47)</td>
</tr>
<tr>
<td>General health</td>
<td>21</td>
<td>-0.365 (1.16)</td>
<td>25</td>
<td>-1.08 (1.28)</td>
</tr>
<tr>
<td>Mental health</td>
<td>21</td>
<td>0.093 (1.09)</td>
<td>25</td>
<td>-0.315 (1.42)</td>
</tr>
<tr>
<td>Physical function</td>
<td>21</td>
<td>0.12 (0.80)</td>
<td>25</td>
<td>-0.08 (1.17)</td>
</tr>
<tr>
<td>Role emotional</td>
<td>21</td>
<td>0.04 (1.08)</td>
<td>25</td>
<td>0.495 (1.21)</td>
</tr>
<tr>
<td>Role physical</td>
<td>21</td>
<td>-0.32 (1.28)</td>
<td>25</td>
<td>-0.536 (1.41)</td>
</tr>
<tr>
<td>Social functioning</td>
<td>21</td>
<td>-0.23 (1.24)</td>
<td>25</td>
<td>-0.764 (1.66)</td>
</tr>
<tr>
<td>Vitality</td>
<td>21</td>
<td>0.50 (1.21)</td>
<td>25</td>
<td>-0.189 (0.99)</td>
</tr>
<tr>
<td></td>
<td>Mean Difference</td>
<td>95% Confidence Interval</td>
<td>( P ) Value (2-sided)</td>
<td></td>
</tr>
<tr>
<td>----------------</td>
<td>-----------------</td>
<td>-------------------------</td>
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<td></td>
</tr>
<tr>
<td>Albumin</td>
<td>1.85</td>
<td>((-1.06, 4.80))</td>
<td>.21</td>
<td></td>
</tr>
<tr>
<td>AST</td>
<td>(-1.88)</td>
<td>((-21.0, 17.23))</td>
<td>.84</td>
<td></td>
</tr>
<tr>
<td>Bilirubin</td>
<td>(-6.96)</td>
<td>((-24.60, 10.64))</td>
<td>.43</td>
<td></td>
</tr>
<tr>
<td>GGT</td>
<td>33.00</td>
<td>((-62.90, 129.00))</td>
<td>.49</td>
<td></td>
</tr>
<tr>
<td>Platelets</td>
<td>37.62</td>
<td>((-10.50, 85.70))</td>
<td>.12</td>
<td></td>
</tr>
</tbody>
</table>
Reoperation

- Infants who become jaundiced after an initial anicteric phase postoperatively
- Infants with favorable hepatic and biliary duct remnant histology at initial operation, who do not successfully drain bile
- Infants who may have had an inadequate initial surgery
Liver Transplantation

• Extrahepatic biliary atresia is MC diagnosis in children requiring OLT (>50% of patients with liver transplants in most series)

  • Consider OLT early in patients who do not achieve clearing of jaundice following Kasai.

  • However, in most series the primary indications for OLT are the symptoms of end-stage liver disease.

• OLT will salvage patients with failed Kasai with 10-year posttransplant survival of 71%.

Liver Transplantation

- Overall, a recent review demonstrated that 66% of infants undergoing the Kasai procedure ultimately required OLT, including more than 50% of patients who initially achieved bile drainage.

- OLT as the primary treatment for biliary atresia may be indicated only for patients > 120d of age with an enlarged and hard liver.

*With improved survival rate of 70-80% with liver transplantation, there are different opinions pertaining to the choice of treatment for BA. Some recommended primary liver transplantation as a curative approach.

* > 60% of infants undergoing the Kasai procedure ultimately require OLT

*Organ procurement problems??
Laparoscopic Kasai

Fig. 1 Porta hepatitis dissected with fine cautery needle

Laparoscopic Kasai

Fig. 2 Laparoscopic endportoenterostomy
Fig. 3 Transumbilical Roux-en-Y jejunal anastomosis with hand-sewn suture
Robot Surgery

- (A good surgeon must have the eyes of an eagle, a lion's heart and the hands of a lady)

Dr. L. Willoughby, 1935

- The da Vinci® robotic surgical cart
Computer-assisted robot-enhanced technology allows complex GI surgery to be performed using MIS.

Mariano ER, et al. (Anesthetic concerns for robot-assisted laparoscopy in an infant) Anesth Analg. 2004 Dec;99(6):1665-7,