

# **LIVER TRANSPLANTATION IN ALAGILLE SYNDROME**

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# Treatment of Liver Disease in ALGS

- Improve bile flow
  - Ursodeoxycholic acid, 15-20 mg/kg/d
  - Rifampicin, sometimes cholestyramine or naltrexone
- Nutritional therapy
  - Prevent fat soluble vitamin deficiency
  - Special formulas to promote fat absorption
  - Other high calorie supplements
  - Monitor for zinc and iron deficiencies
- Partial cutaneous biliary diversion or ileal exclusion
- Liver transplantation

# Liver Transplant

## Timing: When to Transplant?



# Liver Transplant Evaluation

## Purpose of the Evaluation Process

- Confirm the Dx
- ? indication(s) for transplant
- Education
- Support
- Meet the transplant team
- Meet the patient & family



# What are the clinical indications for liver transplant?

- Acute liver failure & metabolic diseases
- Poor liver synthetic function-
  - coagulopathy (INR)
  - low albumin
  - high ammonia
  - cannot use bilirubin in ALGS
- Complications of portal hypertension:
  - Recurrent or significant GI bleeding
  - Ascites
  - Bacterial peritonitis
  - Growth failure
- Poor quality of life

# CANDIDATE SELECTION

## Indications

- Primary liver disease with life-threatening complications
  - Decompensated cirrhosis
  - GI bleeding, Ascites
  - Liver synthetic dysfunction, chronic hepatic encephalopathy
- Acute liver failure
- Metabolic liver disease

# CANDIDATE SELECTION

## Indications

- Primary liver tumor with limited disease
  - Hepatoblastoma
  - Hepatocellular carcinoma
- Non-progressive liver disease but with intolerable complications
  - Chronic cholestasis (ALGS)

# CONTRAINDICATIONS

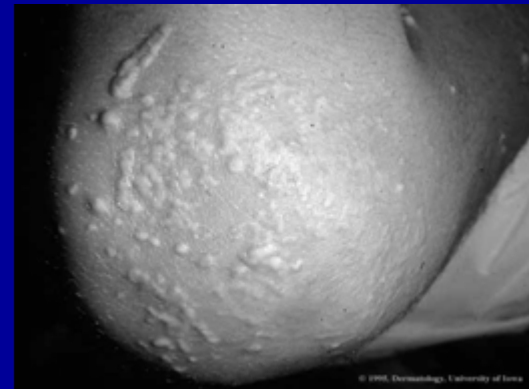
- Alternate therapy available
  - NTBC for tyrosinemia
- Disease state will not be reversed by hepatic replacement
- Pre-existing severe neurologic injury

# CONTRAINDICATIONS

- Uncontrolled infection
  - Systemic viral and fungal infections
- Multiple organ system failure
  - Pulmonary failure, pulmonary hypertension
- Metastatic tumor
  - Extension into extra-hepatic portal vein
  - Lung metastasis

# Indications for Liver Transplantation in ALGS

- Cirrhosis with end-stage liver disease (rare)
- Severe complications of cirrhosis unresponsive to treatment
- Extreme morbidity refractory to treatment, in the absence of cirrhosis
  - Itching, broken bones, cholesterol deposits, inability to gain weight
- In the absence of cirrhosis, the degree of morbidity must outweigh the risk of transplantation



# Liver Transplant Evaluation

- History & Physical
- Diagnostic W/P
- Routine Lab Work
- Exclude Infections
- ABO Blood Type
- Radiologic Studies
- Echocardiogram and Cardiology evaluation



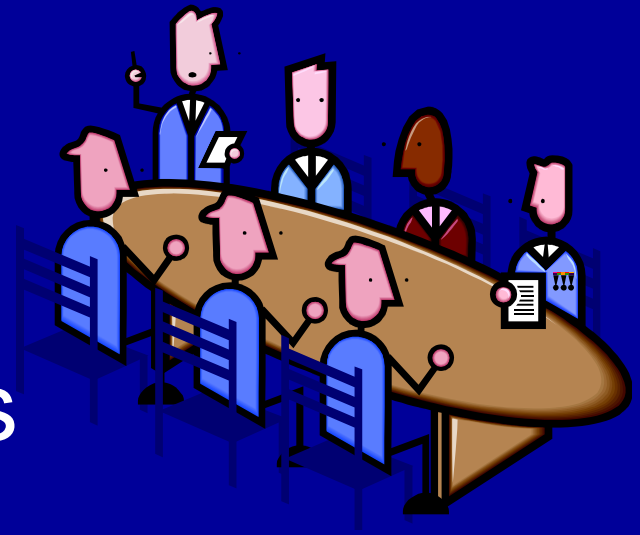
# Liver Transplant Evaluation: Consults

- Pediatrics or Medicine
- Transplant Surgery
- Anesthesia
- Nursing
- Nutrition
- Social Services
- Child Life
- Financial
- Other



# Liver Transplant Selection Committee

- Purpose
  - team review
  - prior to listing
  - authorization process
- Multidisciplinary



# Liver Transplantation Listing - Waiting



**UNOS**  
**UNET**

# 1998 DHHS Mandate

- **Guidelines for organ allocation**
  - organs should be allocated to transplant candidates in order of medical urgency
  - role of waiting times should be minimized
  - attempts should be made to avoid futile transplants and promote efficient use of scarce donor organs

# Waiting Time Disparities

- During the late 1990's, it became evident that there were marked differences in waiting times around the country
- National debate ensued about equalization of waiting times, assuming that waiting time was related to risk of death

# Waiting Time and Mortality

- Wait time was not considered to influence mortality
- What should take the place of waiting time?
- Sickest patients first?
  - Some are too sick to transplant
- Stratify by risk of death
  - What waiting time was originally supposed to do

# New System of Prioritization

- De-emphasizes wait time
- Use another measure to predict risk of dying
- Focuses on an illness severity scale
- Prioritize patients with this system rather than waiting time
- Started in 2002

**Development of the  
MELD/PELD**

# MELD PELD Listing Criteria

- Continuous disease severity scale
- Highly predictive of risk of dying from liver disease for pts awaiting LTx
- MELD for 12 years and older, PELD for under 12 years of age

# MELD/PELD Model Variables

- Bilirubin M and P
- Albumin P only
- Creatinine M only
- INR M and P
- Children: growth P only
- Age < 1 yr. P only
- cause of liver disease (exceptions)

# MELD PELD Priority Exceptions

- Hepatocellular carcinoma
- Hepatoblastoma
- Hepatopulmonary syndrome
- Familial amyloidosis
- Ornithine transcarbamylase deficiency (OTC) & other metabolic disorders
- Primary hyperoxaluria
- Crigler-Najjar syndrome type I

# Contraindications for Liver Transplantation in ALGS

## Transplantation is not a cure-all in ALGS

- All other treatment options to reduce morbidity and improve quality of life have not been fully exhausted
- The quality of life isn't bad enough to outweigh the risks associated with transplantation
- Severe heart disease

# Organs for Liver Transplantation

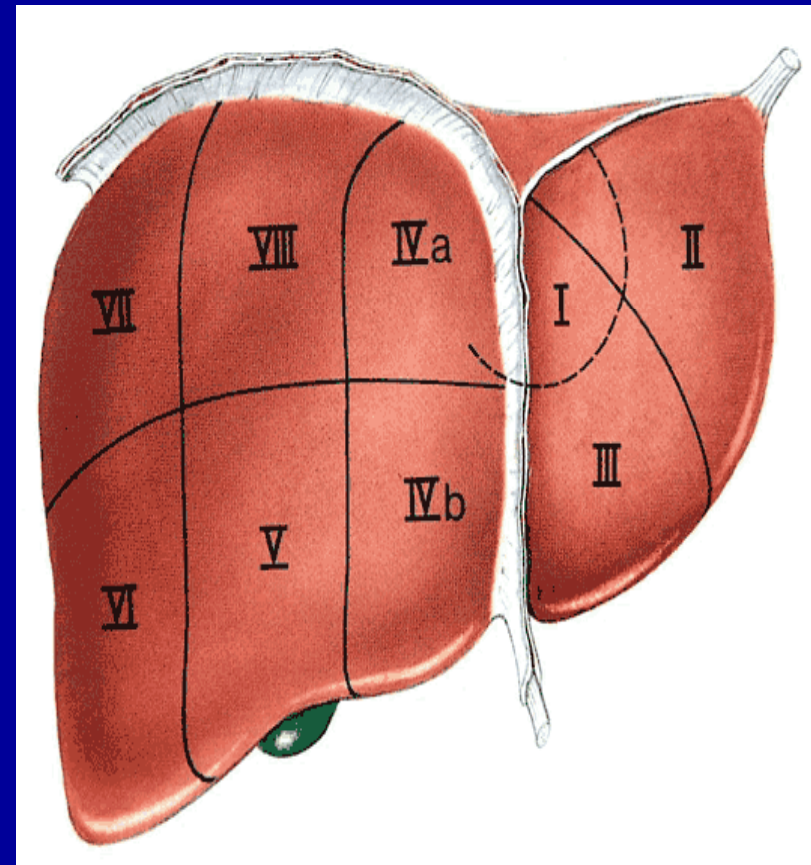
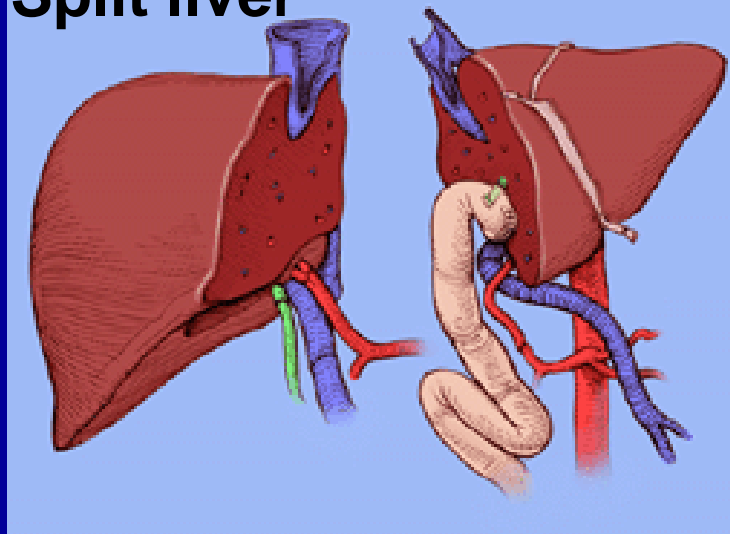
- Deceased Donor:
  - Whole organ
  - Left lobe
  - Left liver
  - Right liver
  - Split liver
- Living-related
  - Left lateral segment
  - Right lobe



# Liver Transplantation

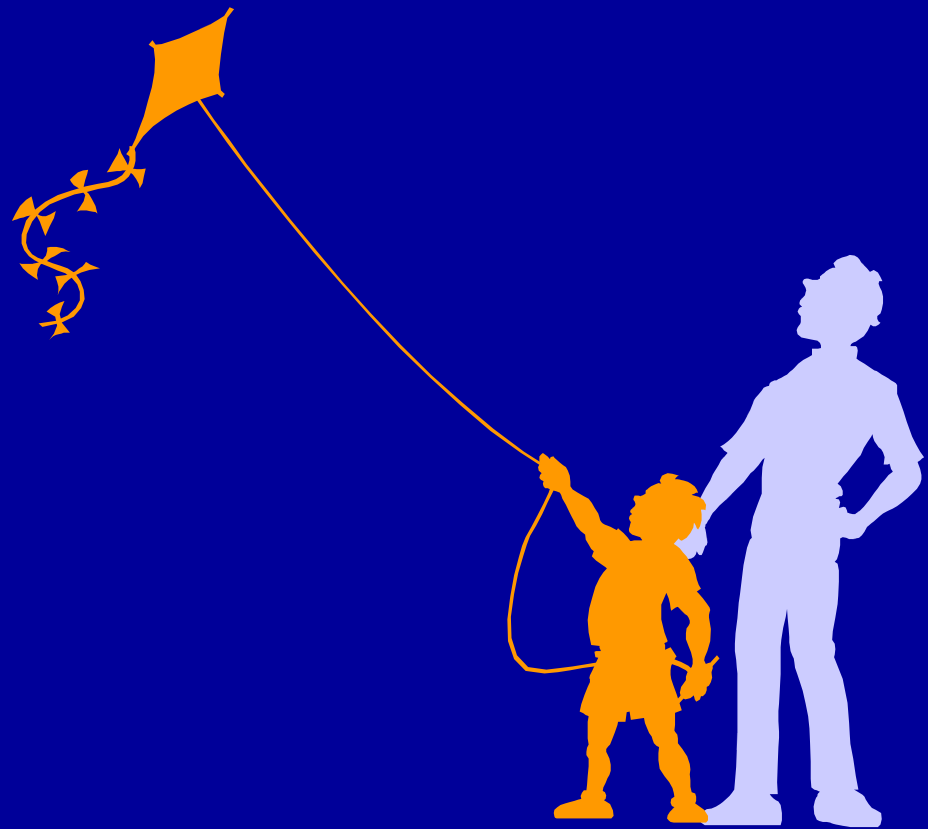
- Anatomical segments
- Living-related
- Split
- Reduced-sized

**Split liver**



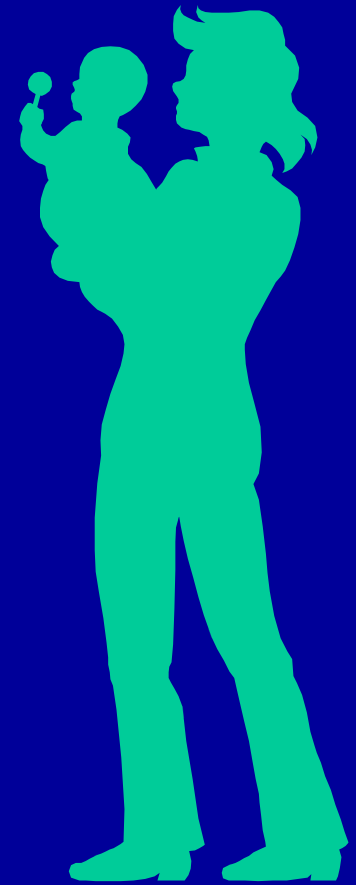
# Living-Liver Donors

- Parent
- Related
- Unrelated
- Altruistic



# Living Liver Donor Evaluation

- Education – support –counseling
- Discuss risk – benefits
- Ascertain willingness and effects on donor and their family
- Authorization for donor



# Living Donor Evaluation

- Phase 1: ABO
- Phase 2: lab, serology, UA, stool occult blood, tox screen, CXR, EKG, PFTs, PAP, > 35 mammogram
- Phase 3: H&P, additional consults incl. Psych
- Phase 4: abd US, CT with angio/cholangio
- Authorize for Tx and schedule
- Advocate for the candidate



# Living donor transplantation in ALGS

- LDLT is an option in ALGS patients
  - Lack of ESLD often precludes deceased donor transplant
  - Permits elective transplant
- Caution must be exercised when considering parental donors
  - ALGS must be excluded in donor
  - Biliary system must be carefully explored

# Assessment of Deceased Donor

## CLINICAL

- Age
- Precipitating events
- Physical examination
- Past history
- Hospital course

## LABORATORY

- Blood group  $\pm$  HLA
- Aminotransferases
- Bilirubin
- Coagulation profile
- Blood gases
- Serology
- Cultures
- Quantitative function tests

# Liver Transplant

## Outcomes

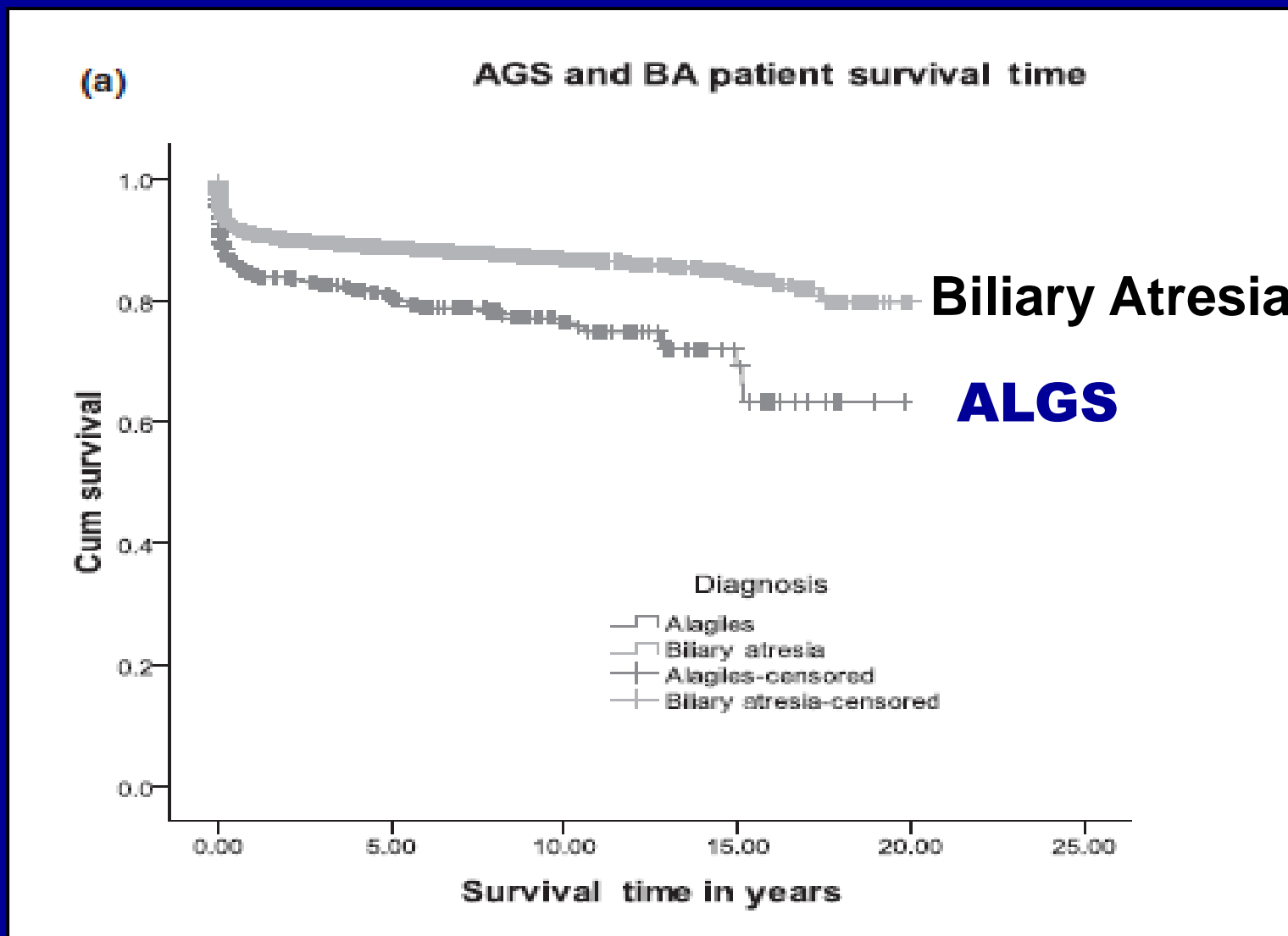


# Liver Transplant Outcomes for ALGS – UNOS Database

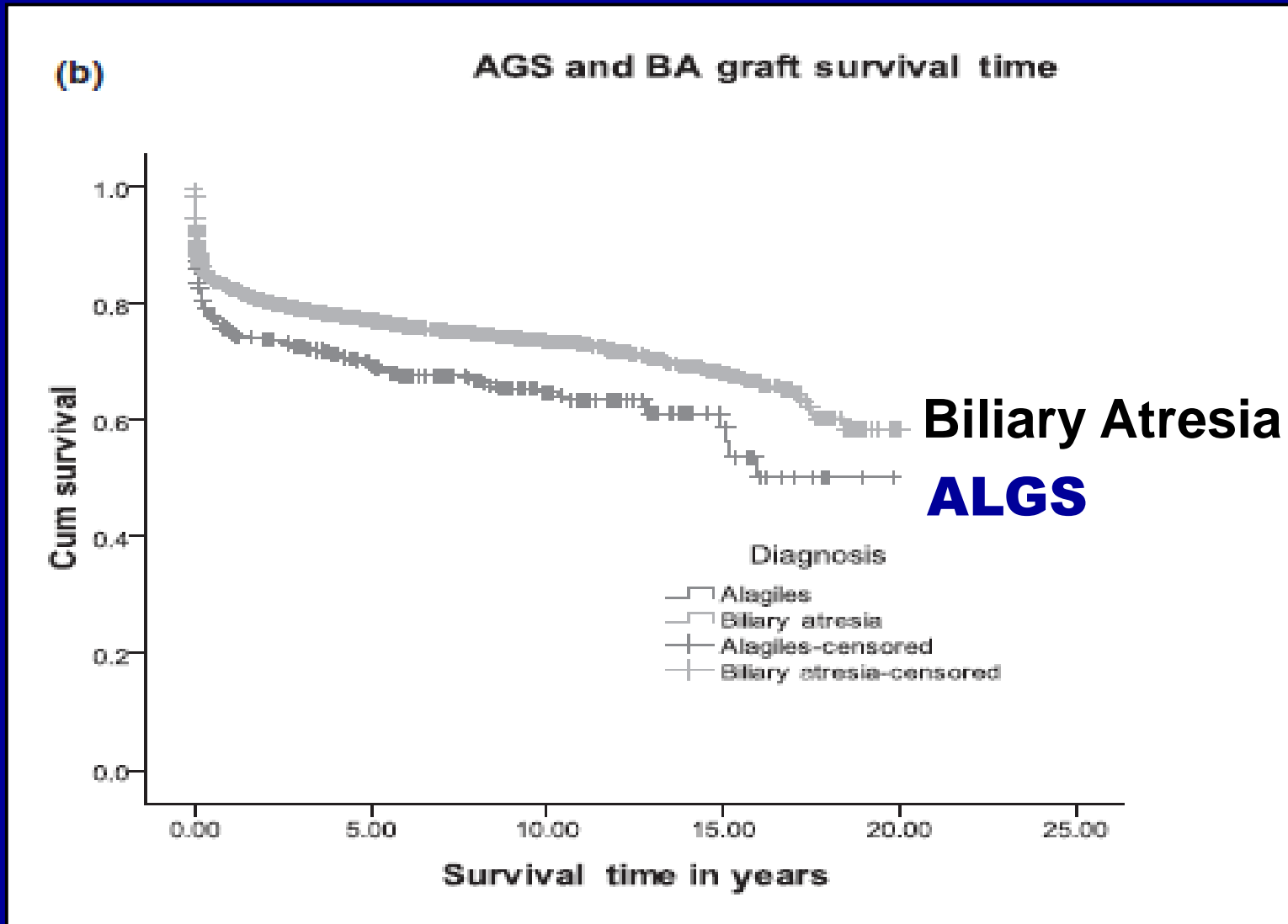
- Group at Mt. Sinai NYC
- Reviewed UNOS database for all LT in children for ALGS from 1987 to 2008:  
11,467
- 461 (4%) had ALGS
- Compared these to the 3,056 who had biliary atresia

***Pediatric Transplantation 2010; 14: 622***

# Patient Survival after Liver Tx



# Liver Graft Survival



# Graft Survival by Age

Table 5. Graft survival outcomes by age group (in percentages)

Age	1 yr survival			5 yr survival		
	AGS	BA	p-Value	AGS	BA	p-Value
<2	73.0	82.0	0.01	65.7	77.6	0.01
2-13	77.0	85.3	0.01	73.9	81.2	0.04
>13	80.8	84.3	ns	73.1	77.1	ns

# Outcomes by Era (over time)

Table 6. Outcomes over time for AGS and BA

	AGS		
	Transplants	Deaths (%)	Graft loss (%)
1987–1991	72	22 (30.6)	33 (45.8)
1992–1996	142	36 (25.4)	59 (41.5)
1997–2001	144	29 (20.1)	47 (32.6)
2002–2008	103	9 (8.7)	15 (14.7)

**91.3% Survival**

# Life can be very good after transplantation

- Liver-related morbidity is eliminated
  - no itching
  - no xanthomas
  - no jaundice
- Growth is usually improved but not complete
- Other nutritional problems resolved
- Quality of life after transplant averages 0.8-0.9 of normal

# Life after Liver Transplant in ALGS

- Take daily immunosuppressive drugs (1-3 )
- Blood Pressure medications
- Antibiotics/antifungals
- Frequent blood tests and doctor visits
- Mild increase risk for infections and tumors
- Watch kidney function carefully

# Summary

## Liver Transplantation in ALGS

- Appropriate candidate selection yields patient survival rates of >85% at 1 year
- Liver-related morbidity is eliminated
- Growth is improved
- Quality of life is good
- Must weigh the risks/benefits of liver transplantation for each patient

