LIVER TRANSPLANTATION

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Liver Transplantation

- First attempts: 1963
- Reasonable mortality: early 1980s
  - Organ preservation
  - Immunosuppression
  - Patient selection
  - Surgical technique
- Current:
  - 1 Year Survival ≥ 85%
  - 5 Year Survival ≥ 70%

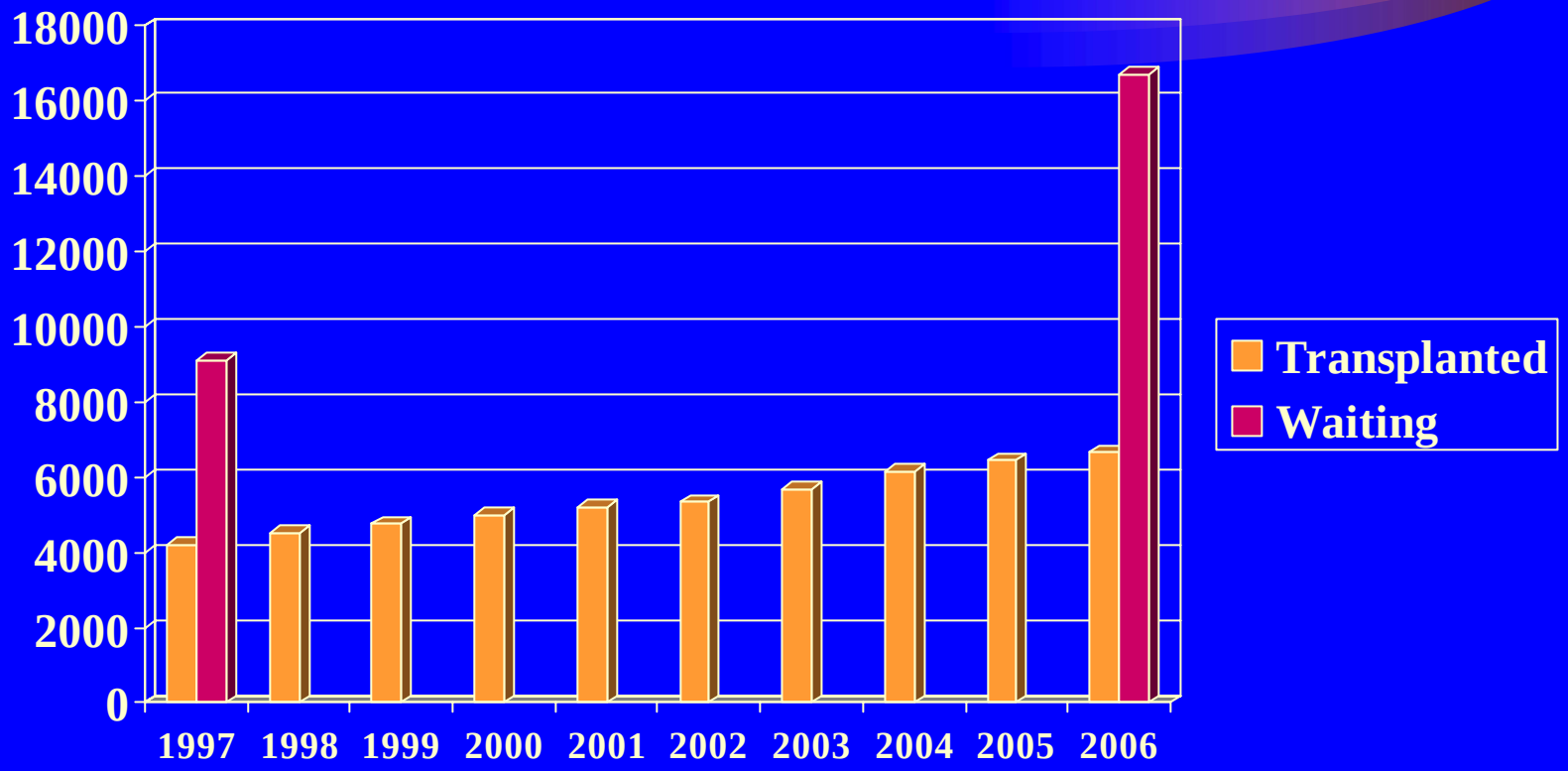
Frequency & Need

- 1983 NIH Consensus Conference:
  Therapeutic Modality for End-Stage Liver Disease
- More than 6650 Liver Transplants in 2006.
- More than 100 Liver Transplant Centers
- 16,700 Liver Transplant Candidates in waiting list in 2006

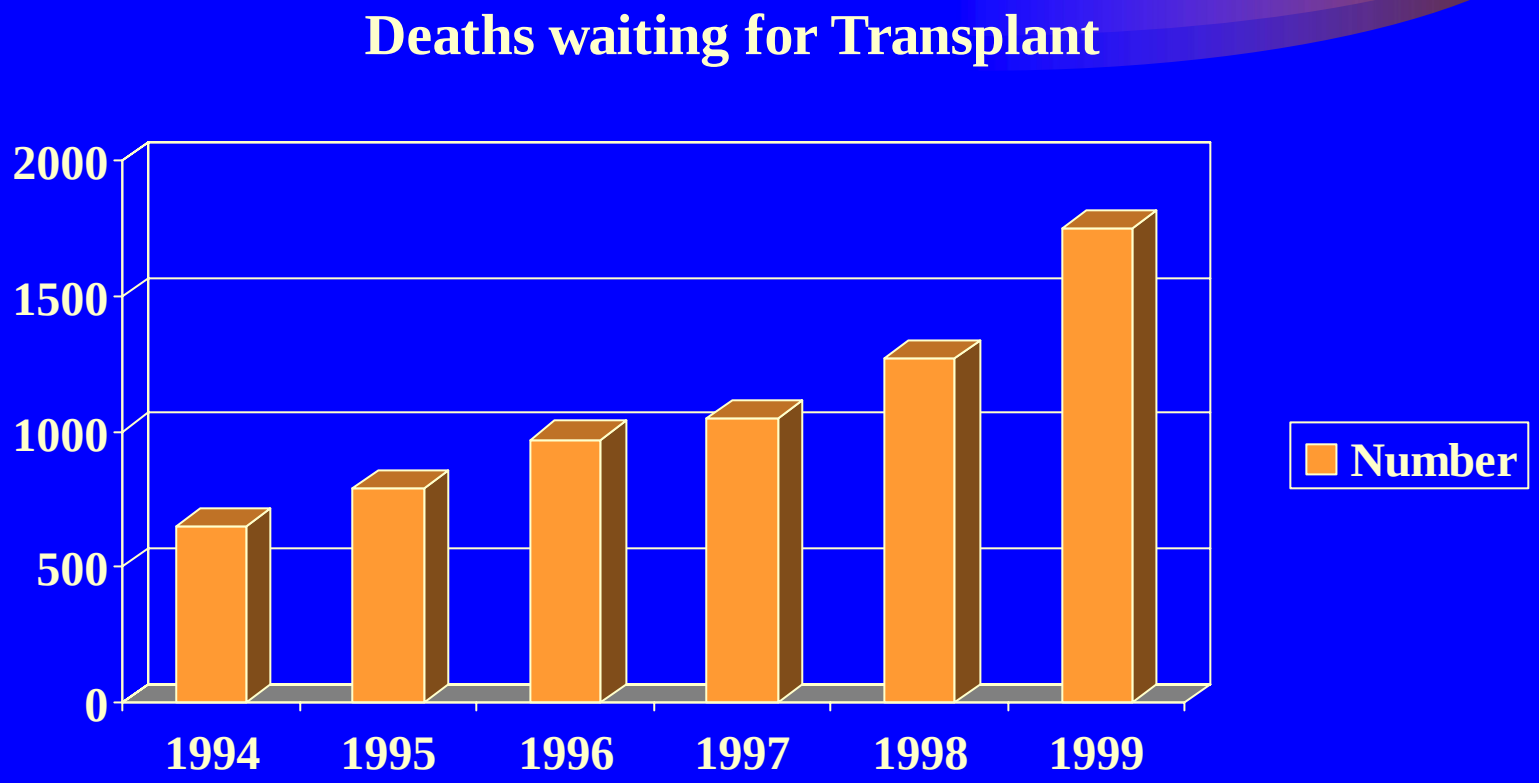
Consequences

- Longer waiting time
- Greater “waiting-list mortality”
- More pressure to use “suboptimal” organs
- Maximal utilization of organs: split livers
- Need for living donors
- Tighter selection of recipients
- Need for early referrals

Liver Transplants per Year

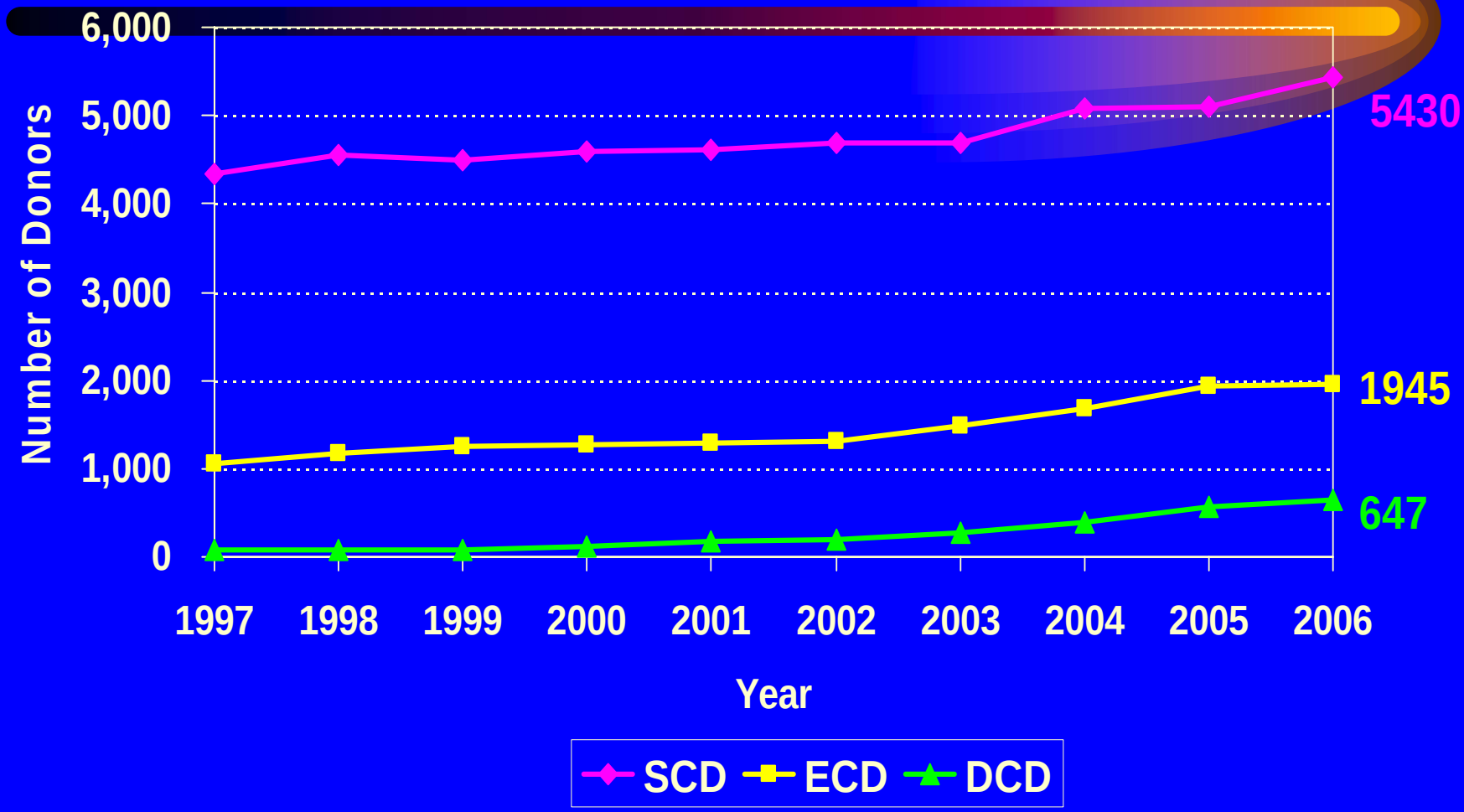


Liver Transplant Waiting List Deaths



Deceased Donors by Type

1997 - 2006



Indications for Liver Transplantation

- End Stage Chronic Liver Disease
- Fulminant Hepatic Failure
- Neoplastic or Metabolic Disorder located only or dominantly in the liver and associated with shortened life-expectancy.

Non-Disease-Specific Minimal Listing Criteria

Liver Transpl Surg 1997;3:628-637

- Immediate need for Liver Transplantation
- Estimated 1-year Survival < 90%
- Child-Pugh score = or > 7 (Child B or C)
- Portal HTN Bleed or single episode of SBP, irrespective of Child class

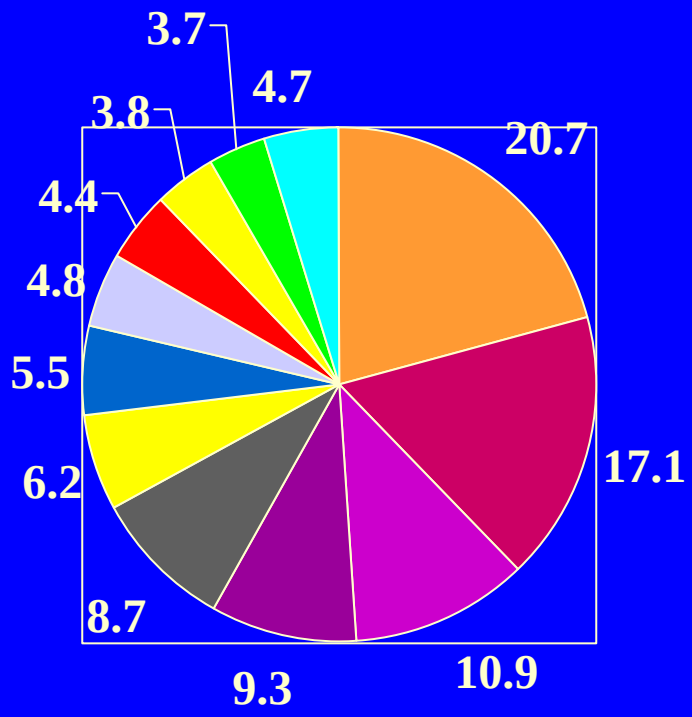
Indications

End-Stage Chronic Liver Disease

- **Hepatocellular Disease:**

	Child-Pugh B (7-9) or C (10-15)		
	1	**2**	**3**
Encephalopathy Grade	None	1-2	3-4
Ascites	None	Mild	Moderate
Bilirubin (mg/dL) <	1-2	2.1-3	≥ 3.0
(Cholestasis)	(< 4)	(4-10)	(>10)
Albumin (mg/dL)	≥ 3.5	2.8-3.5	≤ 2.7
Protime elevation or	1-4	4.1-6	≥ 6.1
(INR <)	(<1.7)	(1.7-2.3)	(> 2.3)

Etiology of Liver Disease
Adult Liver Transplant Recipients



Fulminant Hepatic Failure
Definitions & Incidence

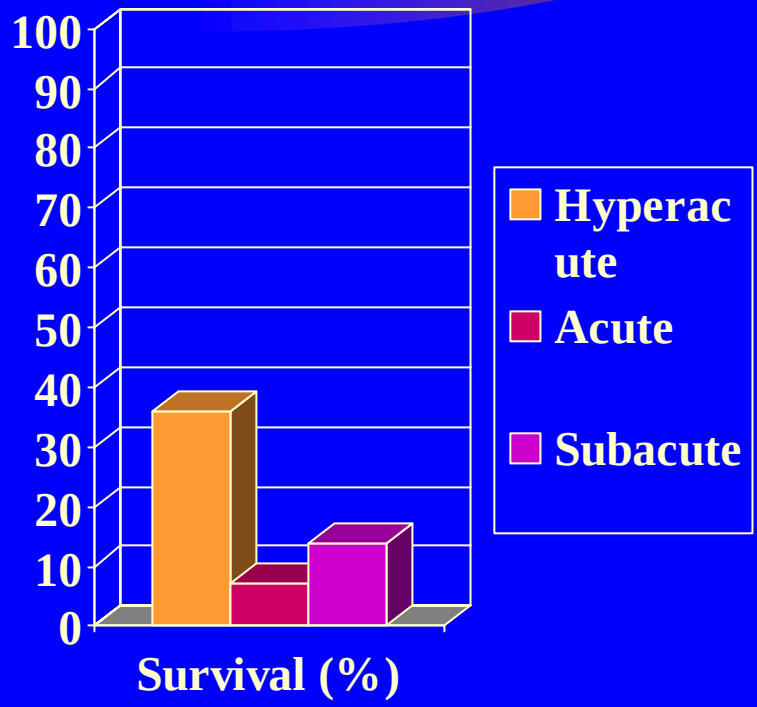
- ***Classic:*** Development of hepatic encephalopathy within 8 weeks of initiation of *symptoms* in a patient without known chronic liver disease.
- ***Practical:*** Development of hepatic encephalopathy and coagulopathy (INR > 1.5) within 26 weeks from the onset of *jaundice*, in patient without known chronic liver disease.
- ***Incidence***: 2300-2800/ year in USA;
  - 6% of adult transplants;
  - 6% of liver-related deaths;
  - 0.1% of deaths in USA.

Fulminant Hepatic Failure & Liver Transplantation

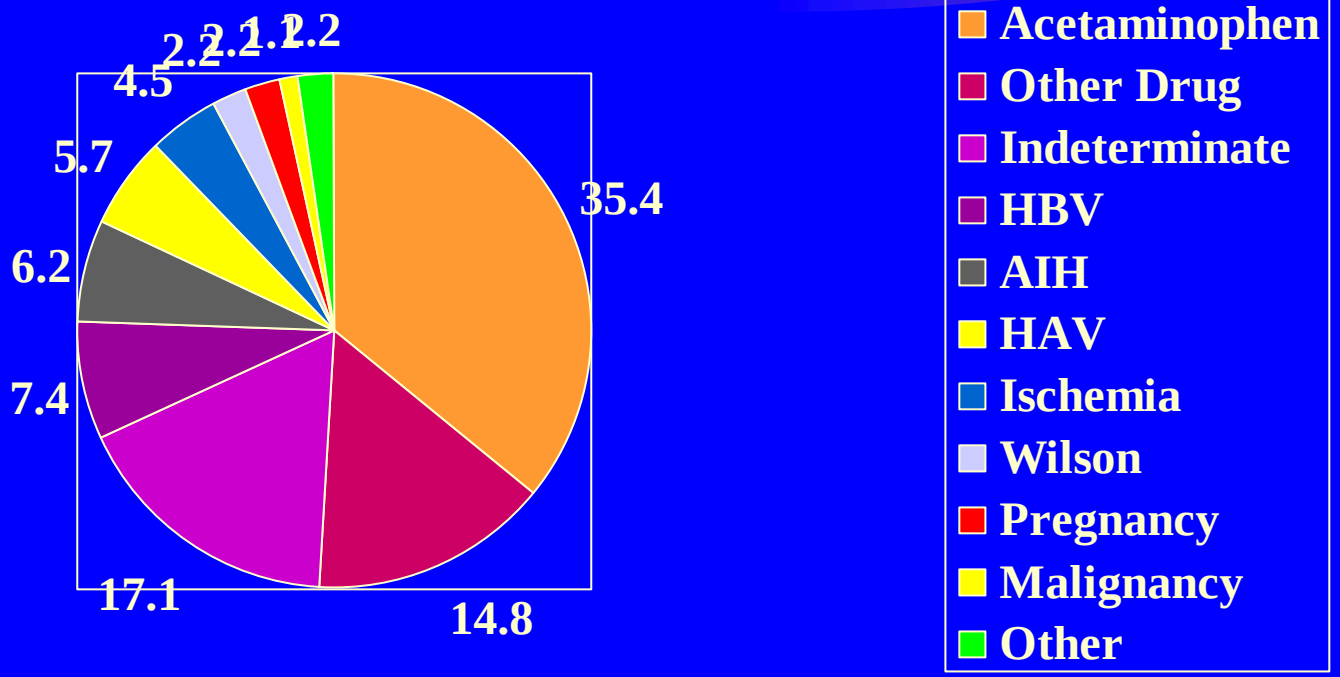
- 75% mortality with grade III-IV encephalopathy
- Median age = 28 (vs. 44 for chronic ESLD)
- Mean waiting time = 5.3 days
- Receive ABO incompatible liver = 11%
  (1.9% in chronic ESLD)
- Patient survival: 1 year = 63% (82%: 2000-2003)
  (78-85% in chronic ESLD)
- Graft survival: 1 year = 53% (75%: 2000-2003)
  (70% in chronic ESLD)

Subtypes of (Fulminant) Hepatic Failure

- ***Hyperacute***: encephalopathy in < 8 days from jaundice.
- ***Acute:*** encephalopathy from 8 – 28 days.
- ***Subacute:*** encephalopathy from 29 days to 26 weeks after onset of jaundice



Etiology of Acute Liver Failure 1998-1999



Indications
Fulminant Hepatic Failure

- Fulminant Hepatic Failure:

  Encephalopathy ≤ 8 (**26**) Weeks

  No pre-existing liver disease

  – ***Acetaminophen*** ***(PPV 0.95, NPV 0.78)***

    - pH < 7.3 or
    - PT with INR > 6.5 + creatinine > 3.4 mg/dL

Indications
Fulminant Hepatic Failure

- ***Non-Acetaminophen*** ***(PPV 1, NPV 0.3)***
  - Age < 30 & Factor V < 20 mg/dL, or
  - Age > 30 & Factor V < 30 mg/dL
  - Patient with INR > 6.5, or
  - Three of the following:
    - NANB, Age < 10 or > 40
    - Halothane or Idiosyncratic drug reaction
    - Jaundice > 7 days before encephalopathy
    - PT with INR > 3.5
    - Bilirubin > 17.6 mg/dL

Wilson's Disease

- Modified Nazer's score for WD & OLTx
- Validated in children (Liver Transpl 2005;11:441-448) & adults (Liver Transpl 2007;13:55-61)
- Score =/> 11, or INR =/> 7 needs OLTx; all other can receive chelation therapy.

Points	Bili	AST	INR
0	**<5.84**	**<100**	**<1.3**
1	**5.85-8.7**	**100-150**	**1.3-1.6**
2	**8.8-11.6**	**151-200**	**1.6-1.9**
3	**11.7-17.5**	**201-300**	**1.9-2.4**
4	**>17.5**	**>300**	**>2.4**

FHF
Expected Survival by Etiology

	%
• Wilson's dz	**0**
• Cryptogenic	**< 20**
• Idiosyncratic	**< 20**
• Halothane	**< 20**
• Hep A/B+brain edema+ARF	**30**
• Hep A/B+brain edema	**50**
• Hep A/B+ HE 3/4 (no brain edema)	**67**
• Tylenol+brain edema+ARF	**53**
• Tylenol+brain edema	**71**
• Tylenol+ HE 3/4 (no brain edema)	**100**

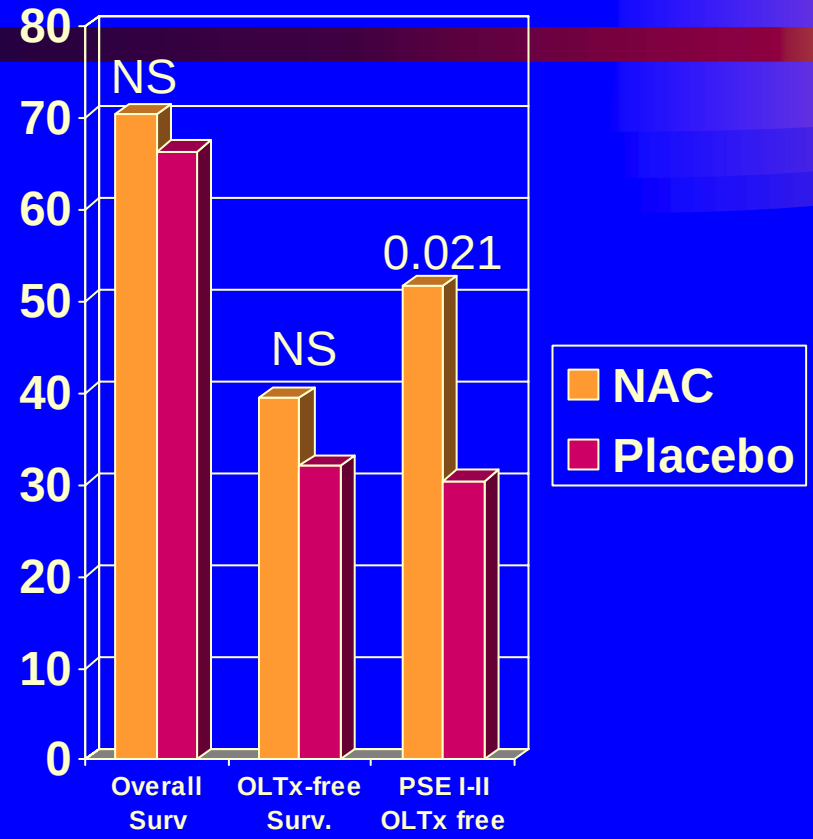
IV NAC in Non-Acetaminophen ALF

Lee WM et al. AASLD Abstr. # 79, 2007

- **Patients:**
  - 848 adults screened,
  - 173 qualify and randomized.
- **Stratification:**
  - PSE I-II vs
  - PSE III-IV
- **Intervention:**
  - IV NAC x 72h (82 pts) vs
  - Placebo (92 pts).
- **End point:**
  - 1: survival,
  - 2: OLTx free survival.
- **Diagnosis:**
  - Drug 26%,
  - Indeterminate 24%,
  - HBV 21%,
  - AIH 15%,
  - Other 14%.

IV NAC in Non-Acetaminophen ALF

Lee WM et al. AASLD Abstr. # 79, 2007



CONCLUSION: In Early Non-Acetaminophen ALF, NAC improves Spontaneous Survival

Indications
Neoplastic or Metabolic

- Neoplastic or Metabolic Disorder located only or dominantly in the liver and associated with shortened life-expectancy.
  - Familial Amyloidotic Polyneuropathy
  - Primary Hyperoxaluria type 1
  - Hereditary Hemorrhagic Telangiectasia
  - Polycystic Liver Disease
  - Cholangio Ca (for UNOS approved protocol with neoadjuvant therapy)
  - Carcinoid Neuroendocrine tumors, after removal of primary tumor, and without extrahepatic disease.
  - Hepatic Epithelioid Hemangioendothelioma, despite extrahepatic disease.

Indications
Neoplastic or Metabolic

- Neoplastic or Metabolic Disorder located only or dominantly in the liver and associated with shortened life-expectancy (continuation).
  - Adenoma in patient with Glycogen Storage Disease
  - Tyrosinemia type 1
  - Crigler-Najjar type 1
  - Homozygous Familial Hypercholesterolemia
  - Maple Syrup Urine Disease (domino LT)
  - Mitochondrial defects confined to liver
  - Disorders of Fatty Acid metabolism.

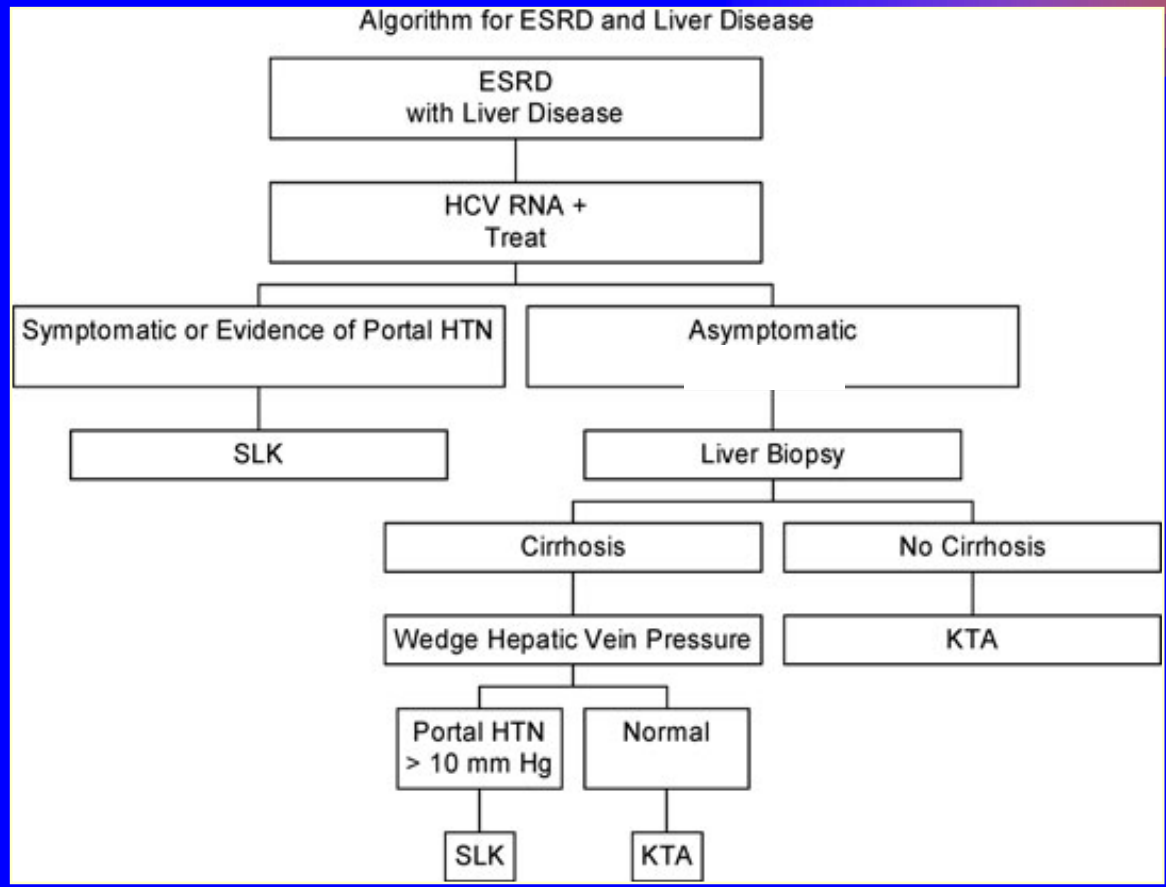
Indications for Simultaneous Liver-Kidney Transplant (SLK)

Am J. Transplant 2008;8:2243-2251

- Automatic approval
  - CKD stage IV or V + cirrhosis + symptomatic portal HTN or HVWPG >/= 10 mm Hg
  - Liver failure + CKD with eGFR </= 30 mL/min for > 90 days
  - Liver failure + AKI or HRS with creat > 2 mg/dL + dialysis >/= 8 weeks
  - Liver failure + CKD + Kidney Bx with > 30% glomerulosclerosis or > 30% interstitial fibrosis.
- MELD exception by Regional Review Board
  - All other cases; comorbidities like DM, HTN, other pre-existing kidney disease, age > 65 will increase potential benefit for SLK.

Algorithm for ESRD & Liver Disease

Am J. Transplant 2008;8:2243-2251



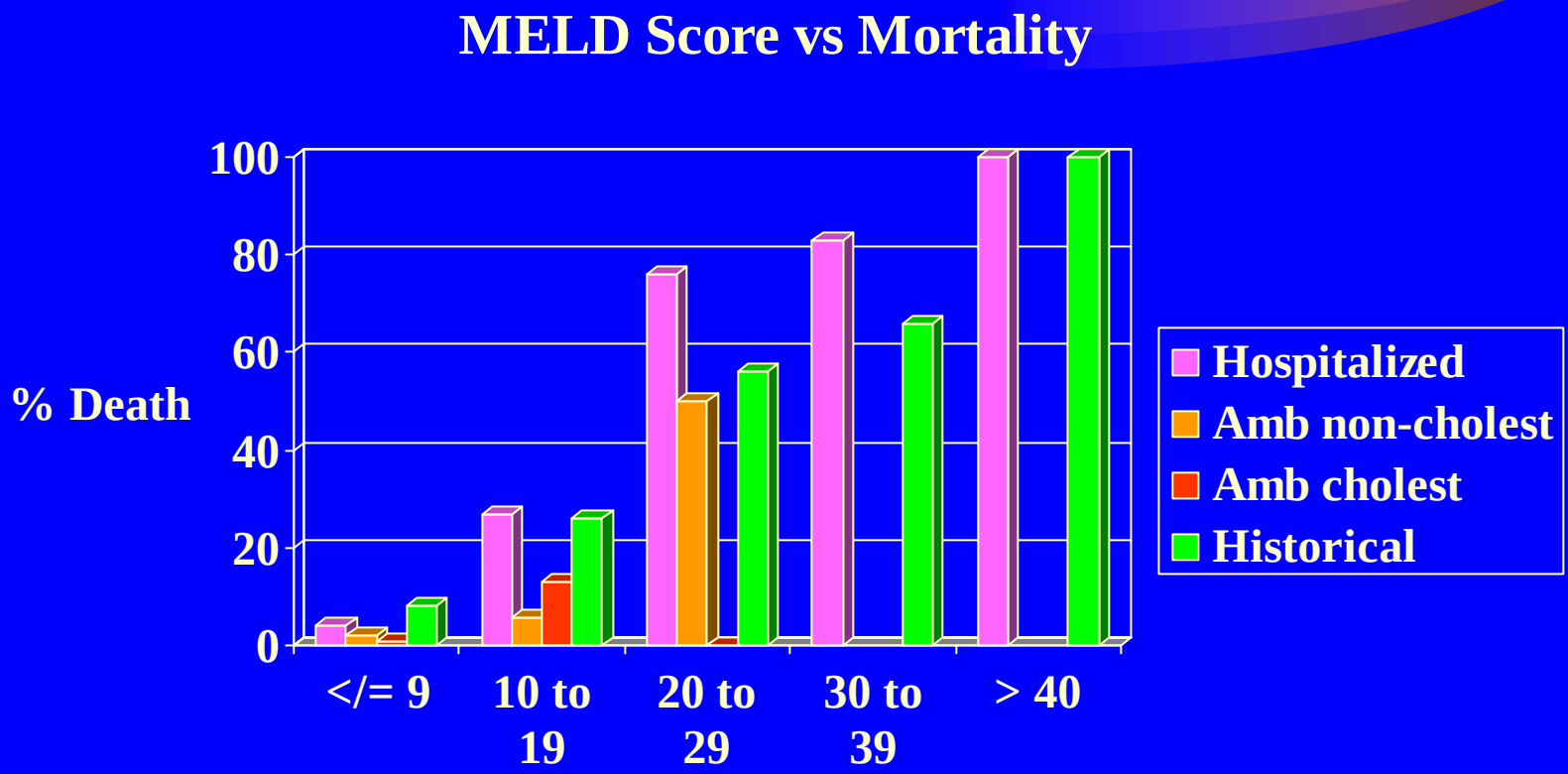
Model for End-stage Liver Disease (MELD)

Hepatology 2001;33:464-470 & Gastroenterology 2003;124:91-96

- Predicts 3-month & 1-year mortality for:
  - a) Hospitalized,
  - b) Ambulatory non-cholestatic,
  - c) Ambulatory cholestatic (PBC)
- No affected by: SBP, PSE, Ascites, or Variceal bleed
- ***MELD = 3.78 log(e) bili (mg/dL) + 11.2 log (e) INR + 9.57 log(e) creatinine (mg/dL) + 6.43***
- ***3-month mortality =*** 0.98465exp(MELD score-10)*0.1635
- www.mayo.edu/int-med/gi/model/mayomodl.htm

MELD

Three-month Death Rates



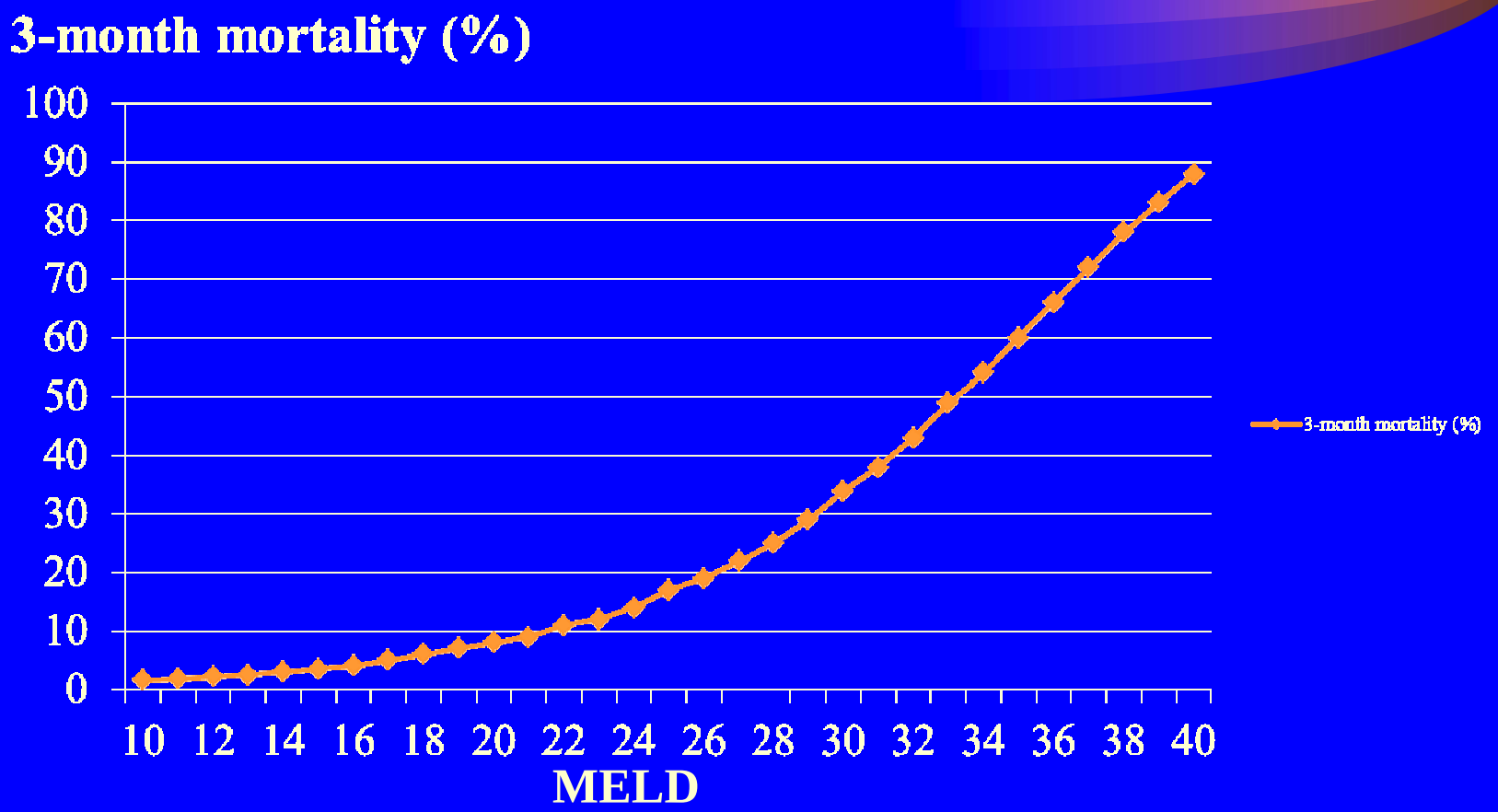
3-month Mortality in Cirrhosis by MELD Score

Wiesner R et al. Gastroenterology 2003;124:91-96

MELD	3-month mortality (%)	MELD	3-month mortality (%)
10	1.6	**26**	19
11	1.8	**27**	22
12	2.2	**28**	25
13	2.5	**29**	29
14	*3*	**30**	34
15	*3.5*	**31**	38
16	*4*	**32**	43
17	*5*	**33**	49
18	*6*	**34**	54
19	*7*	**35**	60
20	*8*	**36**	66
21	*9*	**37**	72
22	*11*	**38**	78
23	*12*	**39**	83
24	*14*	**40**	88
25	*17*		

3-month mortality in 3437 patients by MELD

Wiesner R et al. Gastroenterology 2003;124:91-96



MELD 15-17 is equivalent to surgical death-rate

Factors that may Modify MELD points

- Hepatocellular Carcinoma:
  - single lesion > 2cm & < 5cm, **OR**
    up to 3 lesions </= 3 cm each, **OR**
    [chronic liver disease + AFP > 500ng/mL]
  - increases the MELD to 22
- Refractory Ascites:
  - Definition = massive ascites **AND** 2 of the following:
    1) =/>3 therapeutic paracentesis > 2 L each in last 60 days;
    2) =/> 2 episodes of SBP;
    3) Persistent despite previous TIPS;
    4) Unresponsive to Spironolactone 400 + Furosemide 160,
    5) =/> 2 therapeutic thoracentesis;
    6) Serum Na =/< 125 mEq/L
  - At the discretion of Regional Review Board.

MELD Exceptions

Liver Transpl. 12:S85-136, 2006

- Bacterial Cholangitis (PSC, Caroli's, ischemic cholangiopathy, etc):
  - =/> 2 culture(+) bacteremia over 6 months, **OR** any septic complication (liver/biliary abscess, endocarditis, meningitis, osteomyelitis, fungemia), not related to PTC/ERCP, without stent/tube, and not suppressed despite antibiotic therapy, in the absence of correctable lesion.
  - At Regional Review Board discretion. Add points to MELD equivalent to 8% death-risk now and every 3 months.
- Cystic Fibrosis:
  - Liver alone: If FEV_1<40%: add MELD points equivalent to 10% mortality now and every 3 months.
  - Liver-Lung: If FEV_1<40%: 40 MELD points.

MELD Exceptions

Liver Transpl. 12:S85-136, 2006

- Familial Amyloidotic Polyneuropathy:
  - Diagnosis confirmed by TTR gene mutation by DNA analysis or mass spectrometry in tissue
  - Initial MELD of 15% mortality, then MELD increase equivalent to 10% mortality every 3 months (for “domino transplant”.)
- Hepatopulmonary Syndrome:
  - Sitting-up ABG@RA with PaO_2< 60 mmHg, **AND** (+) Echo bubble study, with normal CXR & PFTs. If CXR or PFTs are abnormal, must have MAA scan with shunting > 20%.
  - PaO_2 56-59 mmHg = MELD 22;
    PaO_2 51-55 mmHg = MELD 24;
    PaO_2 =/< 50 mmHg = MELD 26 baseline, plus 2 points every 3 months.

MELD Exceptions

Liver Transpl. 12:S85-136, 2006

- Portopulmonary HTN:
  - PP hypertension defined as: MPAP >25mmHg, AND PVR >240dynes/sec/cm^{-5}, AND [MPAP-PCWP >12mmHg]
  - At Regional Review Board discretion.
    If MPAP > 35 mmHg AND 12 wks of therapy (prostacyclin) achieve: MPAP <35 mmHg AND PVR <400 dynes/sec/cm-5, AND satisfactory RV function;
    MELD of 26, with additional points after 6 months.
- Refractory Portal HTN GI bleeding:
  - Apply if: bleeding >6 units in 24h, **OR** >2 units/d for 3 days, **OR** >2 units/week for >6 weeks in patient with patent TIPS or in whom TIPS is contraindicated (bili >5 mg/dL, portal v. thrombosis, portopulmonary HTN)
  - MELD exception according to Regional Review Board.

MELD Exceptions

Liver Transpl. 12:S85-136, 2006

- Small-for-Size Syndrome:
  - Four of 6 criteria: 1) >5 days post-LDLT; 2) Bili >10 mg/dL without obstruction/rejection; 3) Bile-duct ischemia/leak; 4) INR =/>1.5; 5) Significant ascites; 6) Liver Bx with centrilobular ballooning, necrosis, and cholestasis.
  - MELP/PELD equivalent to 50% mortality, with increase of 10% mortality every 3 months.
- Primary Hyperoxaluria type 1:
  - Proven deficiency of alanine:glyoxylate aminotransferase (AGT) by liver Bx analysis
  - a) Less than 1y/o: PELD 40;
    b) > 1y/o with ESRD on HD, for Liver-Kidney: MELD/PELD equivalent to 15% mortality, with increase in 10% mortality every 3 months;
    c) OLTx before renal injury or Liver-Kidney before ESRD: MELD/PELD equivalent to 10% mortality, with increase in 10% mortality every 3 months.

MELD Exceptions

Liver Transpl. 12:S85-136, 2006

- Hereditary Hemorrhagic Telangiectasia:
  - Diagnosis: by abdominal CT with characteristic changes (diffuse heterogeneous enhancement & enlarged hepatic artery)
  - At Regional Review Board discretion; consider MELD 40 for acute biliary necrosis, and MELD 22 for intractable heart failure.
- Polycystic Liver Disease:
  - Massive PLD (cyst/parenchyma ratio > 1), **AND** have cachexia, ascites, variceal bleeding, hepatic outflow obstruction, biliary obstruction, albumin < 2.2mg/dL, low Mid-Arm Circumference (<23.1 in females, <23.8 cm in males), cholestasis, or recurrent cyst infection.
  - At Regional Review Board discretion.
    1) Without renal insufficiency: initial MELD of 15; add 3 points every 3 months ***with reapplication***.
    2) With renal insufficiency CrCl < 30: initial MELD 20; add 3 points every 3 months ***with reapplication***.

MELD Exceptions

Liver Transpl. 12:S85-136, 2006

- Cholangio Ca can get 22 MELD points if all 3 apply:
- Diagnosed by:
  - Positive Bx or brush cytology, or
  - Elevated CA 19-9 > 100 U/mL + dominant stricture or enhancing mass in cross-sectional imaging, or
  - Aneuploidy in FISH analysis due to (+) polysomy, + dominant stricture or enhancing mass in cross-sectional imaging.
- Unresectable hiliar cholangio Ca, less than 3 cm in largest diameter, without metastasis to regional lymph nodes or elsewhere
- Completed pre-transplant chemoradiation + pre-transplant staging laparotomy + regional lymph node sampling

Other MELD Exceptions

Liver Transpl. 12:S85-136, 2006

- Cholangio Ca (for UNOS approved protocol with neoadjuvant therapy)
- Carcinoid Neuroendocrine tumors, after removal of primary tumor, and without extrahepatic disease.
- Hepatic Epithelioid Hemangioendothelioma, despite extrahepatic disease.
- Adenoma in patient with Glycogen Storage Disease
- Tyrosinemia type 1
- Crigler-Najjar type 1
- Homozygous Familial Hypercholesterolemia
- Maple Syrup Urine Disease (domino LT)
- Mitochondrial defects confined to liver
- Disorders of Fatty Acid metabolism.

No MELD Exceptions

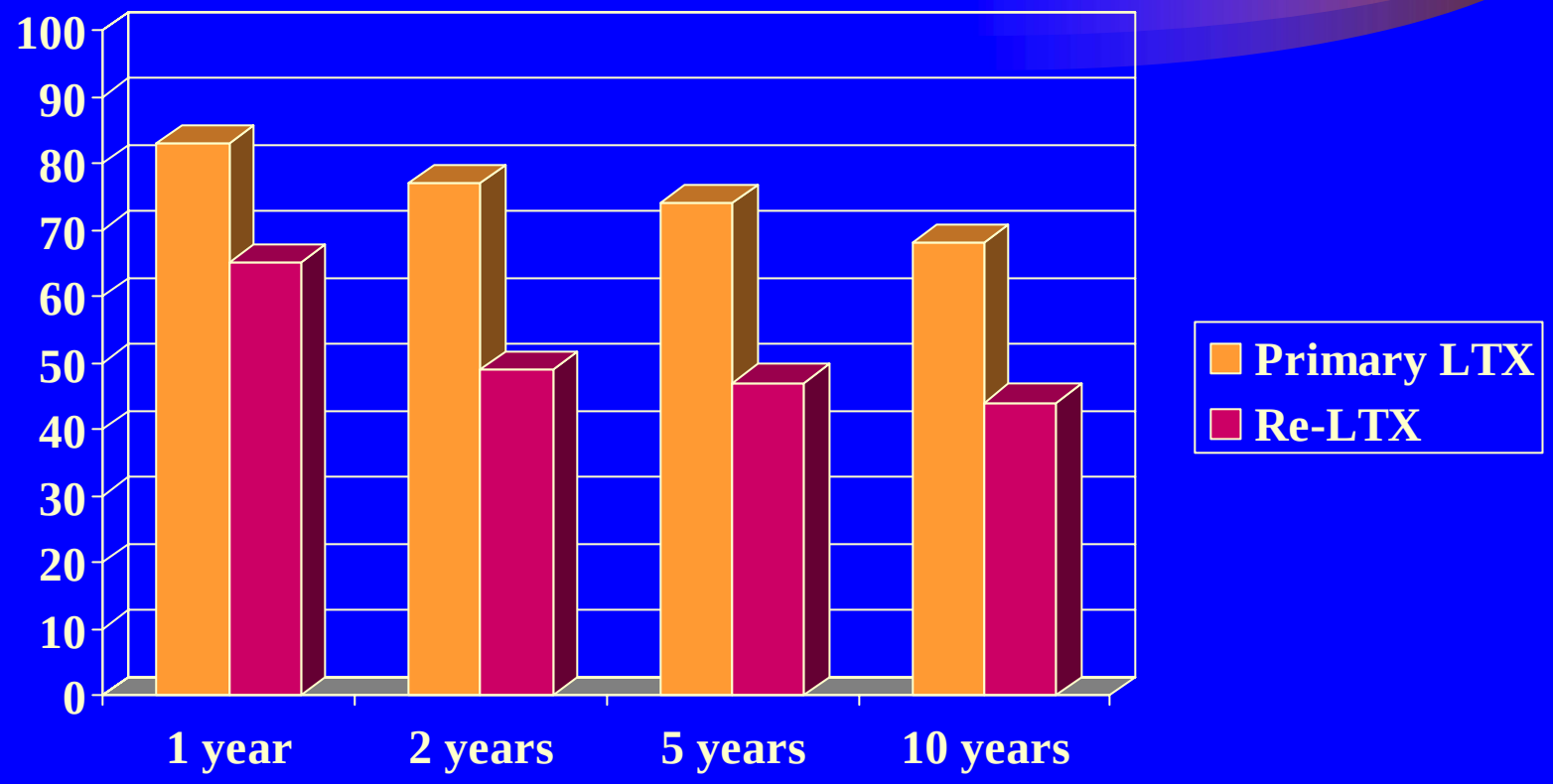
Liver Transpl. 12:S85-136, 2006

- Hepatic Encephalopathy
- Biliary Dysplasia in PSC
- Intractable pruritus
- Budd-Chiari Syndrome
- Non-carcinoid Neuroendocrine tumors
- Biliary Cystadenocarcinoma

Effects of MELD implementation

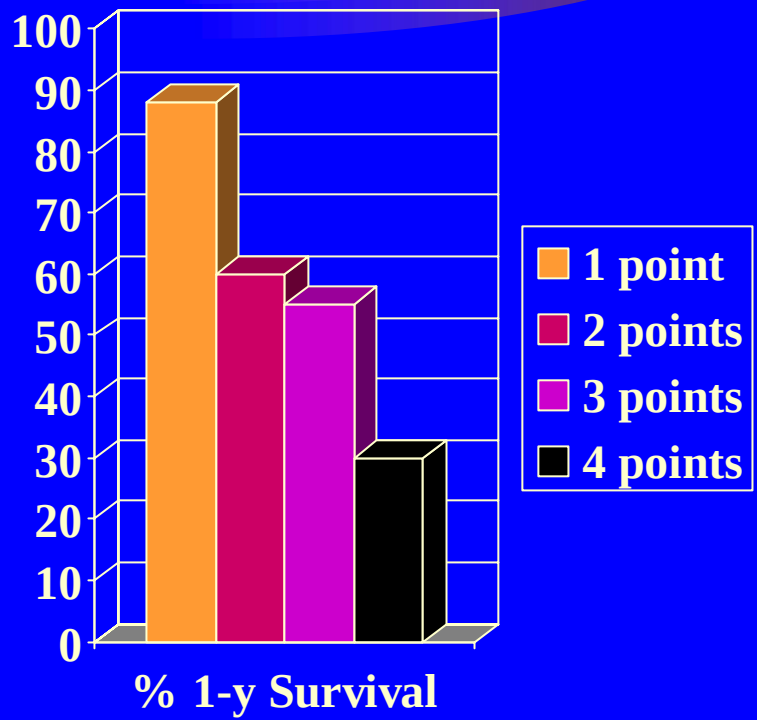
- MELD score at OLTx is higher than in pre-MELD era.
- Removal from list due to “death/too sick” decreased from 25.9% to 6.7%
- Patient survival: no-change/slightly better.
- OLTx for HCC has increased from 7% to 22%
- Waiting time for HCC decreased from 2.3 to 0.6 y

Survival after Liver Transplant & Re-Transplant



Re-LTX 1-year Survival by UCLA Class

- **POINTS (1 each)**
- Age > 18
- Liver ischemia > 12 h
- Pre-op in ventilator
- Creatinine > 1.6mg/dL
- Bilirubin > 16mg/dL



Transplant Candidacy Psychosocial Aspects

- Non-compliance is responsible for 25% of late deaths post organ transplant.
- Adherence has several components: medication use, clinic visits, lab tests, self-monitoring, exercise, use of harmful substances.

Transplant Candidacy Psychosocial Aspects

- **Factors affecting adherence:**
  - hostility,
  - poor caregiver-support,
  - poor friend-support,
  - lack of active coping strategies,
  - use of avoidant coping strategies;

  Risk of non-adherence:
    - **0-1 factor: 30%,**
    - **2-3 factors: 50%,**
    - **>/=4 factors: 80%**

Psychosocial Aspects
Social Support

- Should be able to provide: basic care, transportation, medication verification, & emotional support.
- Sources of support: family, friends, work relations, faith & community organizations.
- More than one support person must be identify.
- Must be willing to be involved during evaluation, hospital care, & post-operative care.
- **Good support correlates with: better adherence, low recidivism, less depression, better graft survival.**

Psychosocial Aspects
Alcohol Abuse & Dependence

- Chronic medical problem with relapsing-remitting course.
- Only 75% of patients transplanted for ALD have alcohol dependence.
- Dependence requires 3 or more within 12 mo:
  - 1. Tolerance,
  - 2. Withdrawal Syndrome,
  - 3. Larger amount & longer use than intended,
  - 4. Persistent desire to cut down,
  - 5. Excessive time using,
  - 6. Important activities affected b/o use,
  - 7. Use continues despite physical/psychological problem.

Psychosocial Aspects Alcohol Abuse & Dependence

- **Stable sobriety**: if lasting > 5 years.
- **Relapse rate in LTx waiting-list**: up to 25%
- All relapses are serious; very few can go to "social use": Complete abstinence (even from "non-alcoholic beer/wine" is recommended
- Pre- & post-LTx patients should have routine alcohol screening
- **Post-LTx severe medical complications from alcohol**:
  - 10-15% of patients.
- **Any relapse post-LTx**:
  - 1 year = 8-22%;
  - 5 years = 30-50% (vs 60-80% in non-LTx alcoholics)

Psychosocial Aspects Alcohol Abuse & Dependence

- **Predictors of post-LTx alcohol use**:
  - Alcohol dependency
  - Short pre-Tx sobriety
  - Hx polysubstance abuse
  - Family Hx alcoholism
  - Previous addiction rehabilitation
  - Personality disorders

Psychosocial Aspects Alcohol Abuse & Dependence

- Sobriety < 6 months does not consistently predicts alcohol relapse.
- **Patterns of alcohol relapse post-LTx**:
  - complete abstinence: 69%,
  - occasional (<14 units/wk): 10%,
  - heavy (>14 units/wk or > 4 units/d for any period): 21%
- No difference in 8-y survival among the 3 groups, but alcohol contributed to death in 15% of "heavy" group.

Predictors of Alcohol Relapse Recent study (Kelly 2006)

- Depression
- Lack of stable partner (family & friends)
- Tobacco use
- Lack of insight
- Amount of alcohol (gm/day) before evaluation
- **LENGTH OF ABSTINENCE WAS NOT A PREDICTOR**

Urine Tests for Drugs of Abuse

Test Drug	Detectability duration	False Positives
Amphetamines	2-3 days	Ephedrine, Pseudoephedrine, phenylephrine, selegiline, chlorpromazine, trazodone, bupropion,desipramine, amantadine, ranitidine
Cocaine	Light: 2-3 days; heavy: 8 days	Topical anesthetics with cocaine
Marijuana	Light: 1-7 days; heavy: 1 month	Ibuprofen, naproxyn, dronabinol, efavirenz, hemp seed oil, pantoprazole.
Opiates	1-3 days	Rifampin, fluoroquinolones, poppy seeds, quinine in tonic water
Phencyclidine	7-14 days	Ketamine, dextrometorphan

High Dose Nicotine-Patch Therapy

Dosing Based on Smoking Rate or Cotinine Levels

Cigarettes per Day	Plasma Cotinine (ng/mL)	Nicotine-Patch Dose (mg/d)
< 10		7-14
10-20	< 200	14-21
21-40	200-300	21-42
> 40	> 300	42+

Dale LC et al. JAMA 274:1353, 1995 & Mayo Clin Proc 75:1311-1316, 2000

Psychosocial Aspects
Prescription-Drug Abuse

- May be using medication to treat the wrong indication (narcotic for anxiety), or at excessive dose.
- Chemical dependency program is recommended.
- Should:
  - get controlled substances from only one prescriber,
  - use single pharmacy,
  - be followed by psychiatrist or addiction specialist

Psychosocial Aspects Prescription-Drug Abuse

- Remember that Methadone once a day is appropriate for opioid dependency but not for pain control (q 3-6 hours for pain control)
- Tapering Methadone in “stable methadone-maintained opioid addicts”, results in relapse of up to 80%.
- Relapse of illicit-opioid use < 10% in “methadone patients”, and LTx outcome and nonadherence to medication is similar to “non-methadone patients”.

Psychosocial Aspects
Mood & Personality Disorders

- Up to 63% of cirrhotics have depression.
- Depression increases physical complaints & pain, decreases quality of life & coping skills.
- Treatment of depression can help compliance
- Patients with suicidal ideation or attempt need intense evaluation from all sources; isolated act is not contraindication for LTx; patterns of self-destructive behavior are contraindication for LTx.
- Schizophrenia, schizoaffective disorder, bipolar disorder, and personality disorder which are stable, controlled, with good adherence, good family support, and good working relation with the transplant team, are not contraindication for LTx.

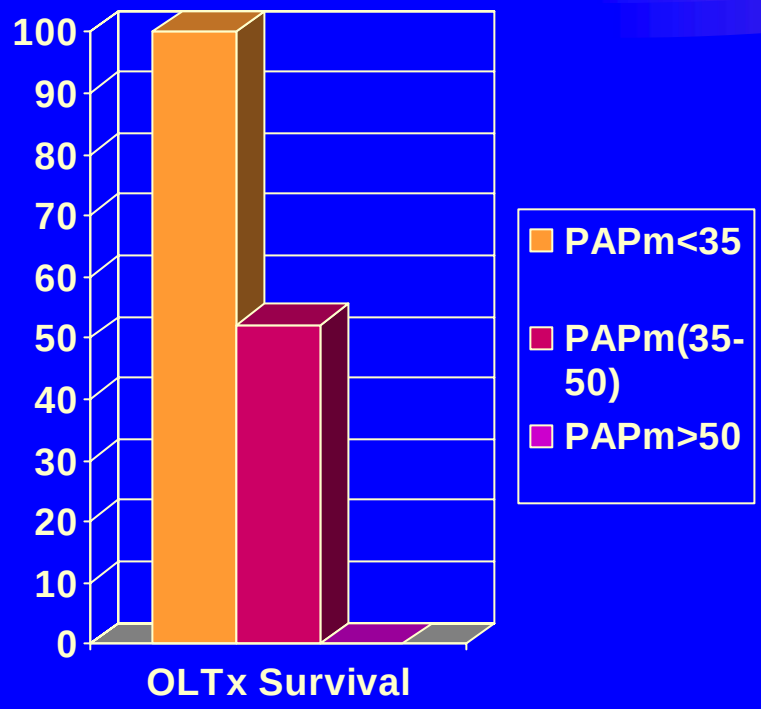
Contraindications

- *Absolute*
- *Relative*

Contraindications: Absolute

- Extrahepatic Malignancy (except in Hepatic Epithelioid Hemangioendothelioma)
- Cholangiocarcinoma (unless in approved special protocol)
- Hemangiosarcoma
- Uncontrolled Sepsis
- Portopulmonary HTN with PAPm > 35 mmHg despite therapy

Transplant Survival in PPHTN



Expected Survival less than 62% are a contraindication for OLTx

Contraindications: Absolute

- Active Alcoholism/Substance Abuse
- Advanced Cardiac or Pulmonary Disease
- Inability to Comply w. Immunosuppression
- Anatomic Abnormality Precluding Treatment
- Irreversible Neurologic Complication
  (ICP > 50 mmHg x 2h, or cerebral perfusion pressure < 40 mmHg x 2h)

Contraindications: Absolute

- BMI 40 or higher
- BMI 35-39.9 + [Diabetes Mellitus OR Hyperlipidemia] + any of the following:
  - Macroalbuminuria
  - Microalbuminuria > 300 mg/L
  - Renal Insufficiency (other than HRS)
  - Retinopathy
  - Coronary Artery Disease
  - Peripheral Vascular Disease
  - TIA / Stroke
  - Autonomic Neuropathy

Obesity and OLTx

- 20% of OLTx recipients are obese.
- Obesity increase risk of HCC & other tumors
- Severe obesity: higher infections, respiratory failure, systemic vascular complications, hospital LOS, & cost.
- Mortality in Obese (BMI 30-34.9) & Severely-Obese (BMI 35-39.9) is similar to non-obese when adjusted by co-morbidities.
- Morbid-Obesity (BMI > 40) increases mortality.

Contraindications: Relative

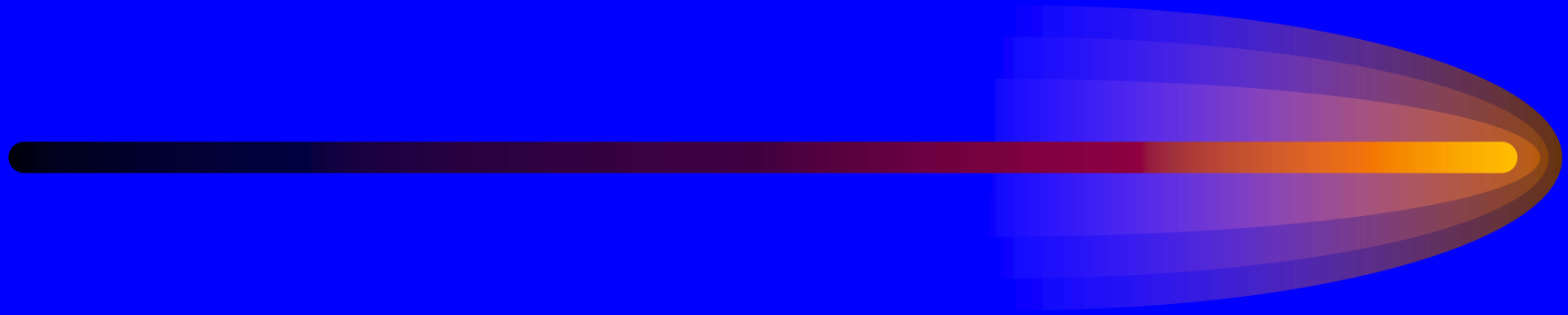
- AIDS
- Advanced age: well motivated and active 65-70
- Poor social support
- Previous extrahepatic malignancy:
  - 2 years free in most malignancies.
  - 4-5 years free in melanoma, breast ca, colon ca
  - Send consult to: Israel Penn International Transplant Tumor Registry (www.ipittr.uc.edu)
- Hepatopulmonary S with $PaO_2 < 50$ mmHg

Hepatopulmonary Syndrome

- Extra MELD points may be given (24 points) if PaO_2 < 60mmHg
- Worsens 5 mmHg PaO_2 per year.
- LTx mortality increases to 34% with PaO_2 < 50 mmHg or MAA shunt > 20%; data is not conclusive yet.
- TIPS is controversial; Coil embolization of discrete A-V fistulas may help (but is uncommon)

Contraindications: Relative

- Prior portosystemic shunt
- Renal failure
  - FHF = higher mortality
  - ESLD = if requiring dialysis or liver-kidney Tx
    $\rightarrow$ higher mortality, ICU stay and cost
- Obesity: more wound infections (BMI > 35)
- Malnutrition: increases L.O.S., cost and mortality



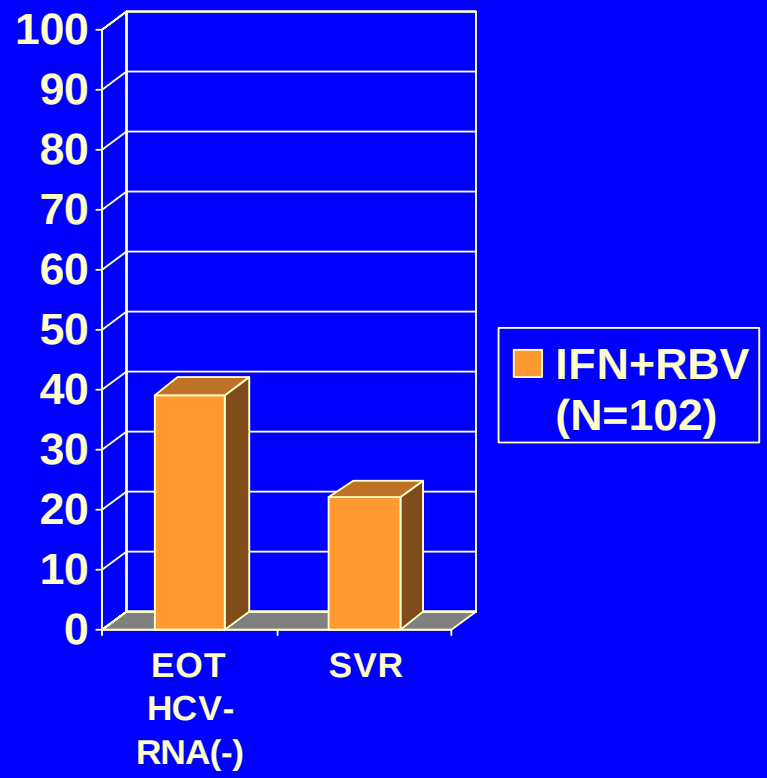
Treatment of HCV in the "waiting list"

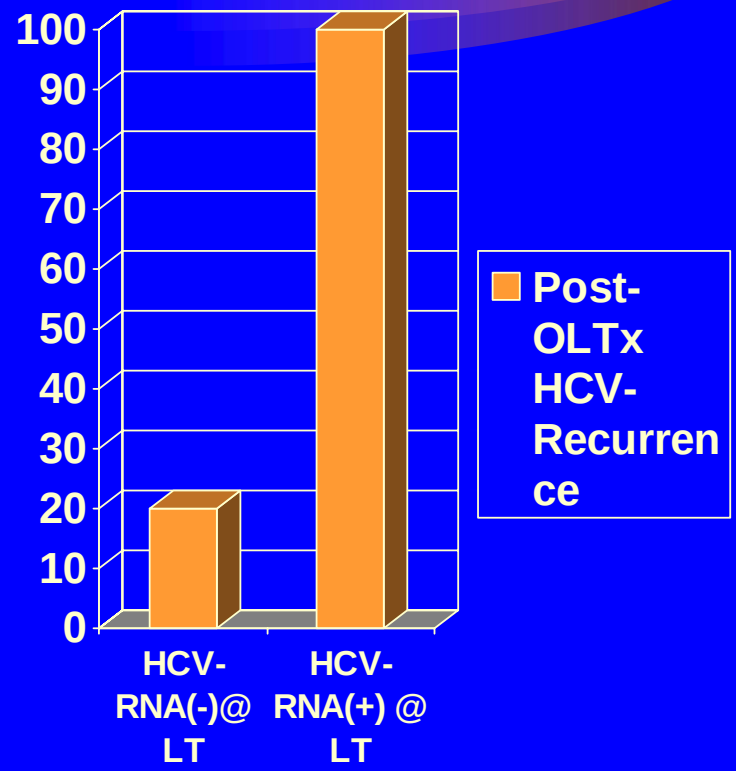
Pre-LTx Treatment of HCV-Cirrhosis Candidates

- **Best Candidates:**
  - **Child-Turcotte score =/< 7**
  - **MELD =/< 18**
- **Best response:**
  - **genotype 2 & 3**
- Patients with Child-Turcotte 8 to 10, or MELD 18 to 24 are controversial.
- **Patients with Child-Turcotte =/> 11, or MELD =/> 25 are not treatment candidates.**

Effect of pre-LT Therapy on Post-OLTx Outcome in Cirrhotics listed for LT

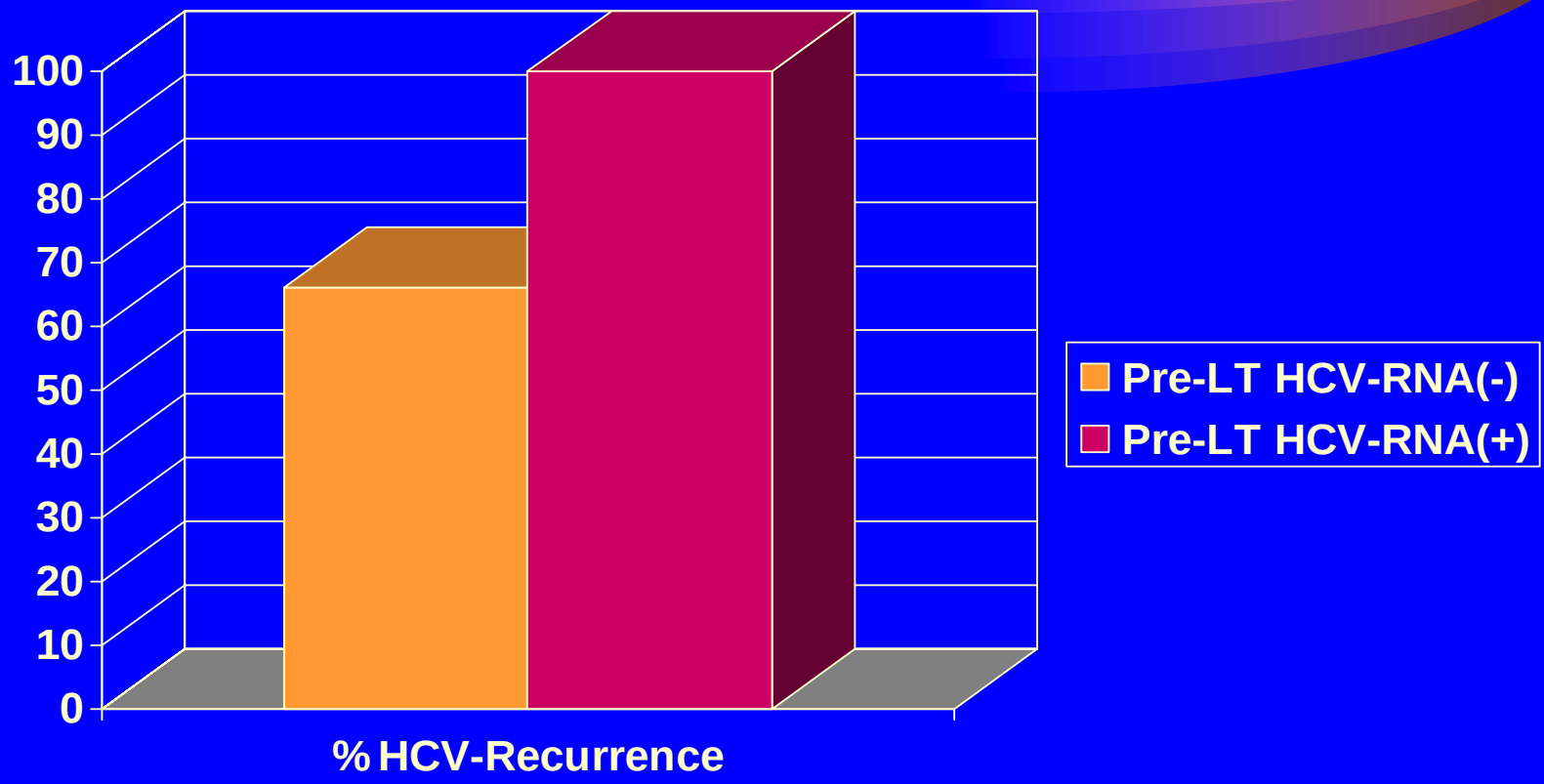
Everson et al. Rev. Gastrointest Disord 2004;4 Suppl 1:S31-38

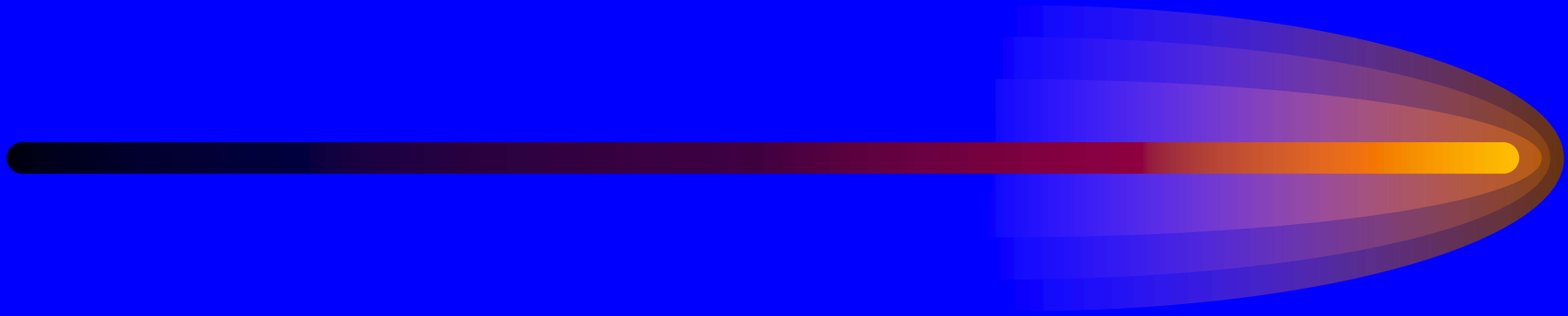




Post OLTx HCV-Recurrence in Listed Cirrhotics Treated with Daily IFN Monotherapy

Thomas et al. Liver Transpl 2003;9:905-915





Live-Donor Adult Liver Tx

Live-Donor Adult Liver Tx

- 5% of transplants in USA. (learning curve = 20 cases)
- Donor: (30-45% of potential donors donate; aborted hepatectomy in 5%)
  - 30% offspring, - 20% sibling,
  - 20% parent, - 20% unrelated,
  - 10% other relative/unknown.
- Donor age: 50% > 50 years old.
- Donor risk: (14 death, 1 vegetative state, 2 LT/ 6-7000 live-donors)
  - 0.4% mortality,
  - 0.4-0.6% catastrophic complication, &
  - 35% morbidity
- Patient survival: equal to cadaver-donor.

Live-Donor Adult Liver Tx
Disease-Specific Considerations

- HCC: Must fulfill Milan Criteria
- HCV: Is acceptable indication, but appropriate timing needs further investigation (not too early).
- FHF: Acceptable indication for emergency transplantation.

Live-Donor Adult Liver Tx
Donor Evaluation

- Complete history & physical with “ideal & actual body weight”.
- CBC, CMP, serologic testing, comprehensive coagulation profile, markers of liver disease, other tests as indicated by Hx & PE.
- Psychosocial evaluation.
- Radiology: liver volume & vascular anatomy; biliary anatomy pre-op or intra-op.
- Pre-op liver Bx is controversial (do if: abnl. enzymes, or steatosis by imaging, or BMI > 30, donor genetically related to patient with AIH, PSC, or PBC)

Live-Donor Adult Liver Tx
Donor Evaluation

- Donor age-limit of 60 is considered appropriate.
- BMI > 30 may increase risk to donor, but is not absolute contraindication.
- Volumetric imaging analysis may overestimate liver volume by 10%.
- Calculated donor-remnant should be at least 30% of original liver volume & with complete venous drainage.
- Graft-liver-volume to recipient-body-weight ratio (GWBWR) should be =/> 0.8%.

Live-Donor Adult Liver Tx
Donor Evaluation

- ABO compatibility is recommended.
- ABO incompatible only in:
  - a) infants,
  - b) child < 1y/o without isoagglutinins,
  - c) emergency situation where no deceased-donor available
- Lab contraindications: HIV, HCV, HBsAg(+), anti-HBc(+)
- Thromboembolism prophylaxis recommended.
- Autologous blood storage should be offered.

"Small-for-Size" Syndrome (SFSS)

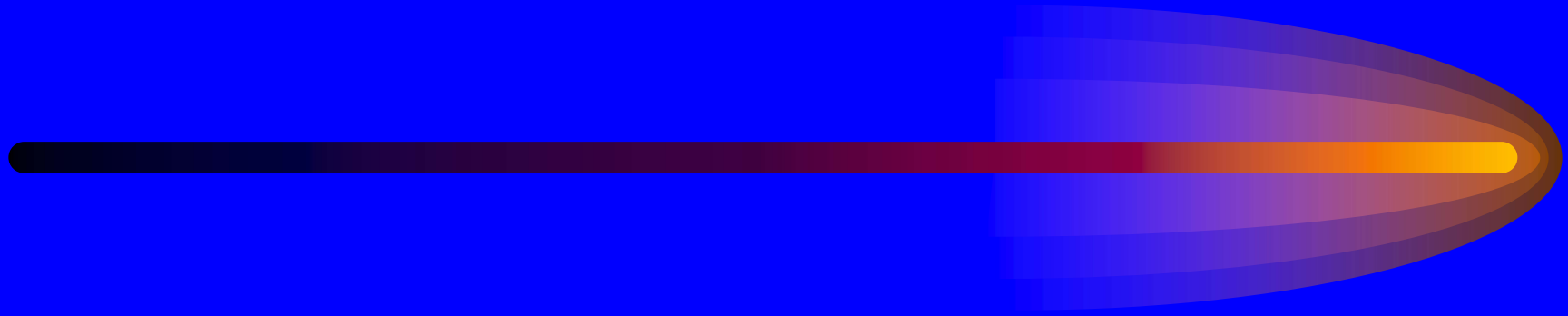
- Partial liver graft unable to meet functional demands of recipient: poor early graft function in absence of ischemia.
- Prevention: in cirrhotic GWBWR must be =/> 0.85%
- Manifestations:
  - Poor bile production
  - Prolonged cholestasis
  - Significant ascites
  - Coagulopathy

"Small-for-Size" Syndrome

- Biochemical profile:
  - Elevated Direct (& total) bili
  - Mild/moderate elevation of ALT & AST
  - Prolonged PT
- Histologic Features:
  - Cholestasis with "bile plugs"
  - Areas of regeneration & ischemia with patchy necrosis.
- Prognosis: 50% of recipients will die of sepsis within 4-6 weeks.

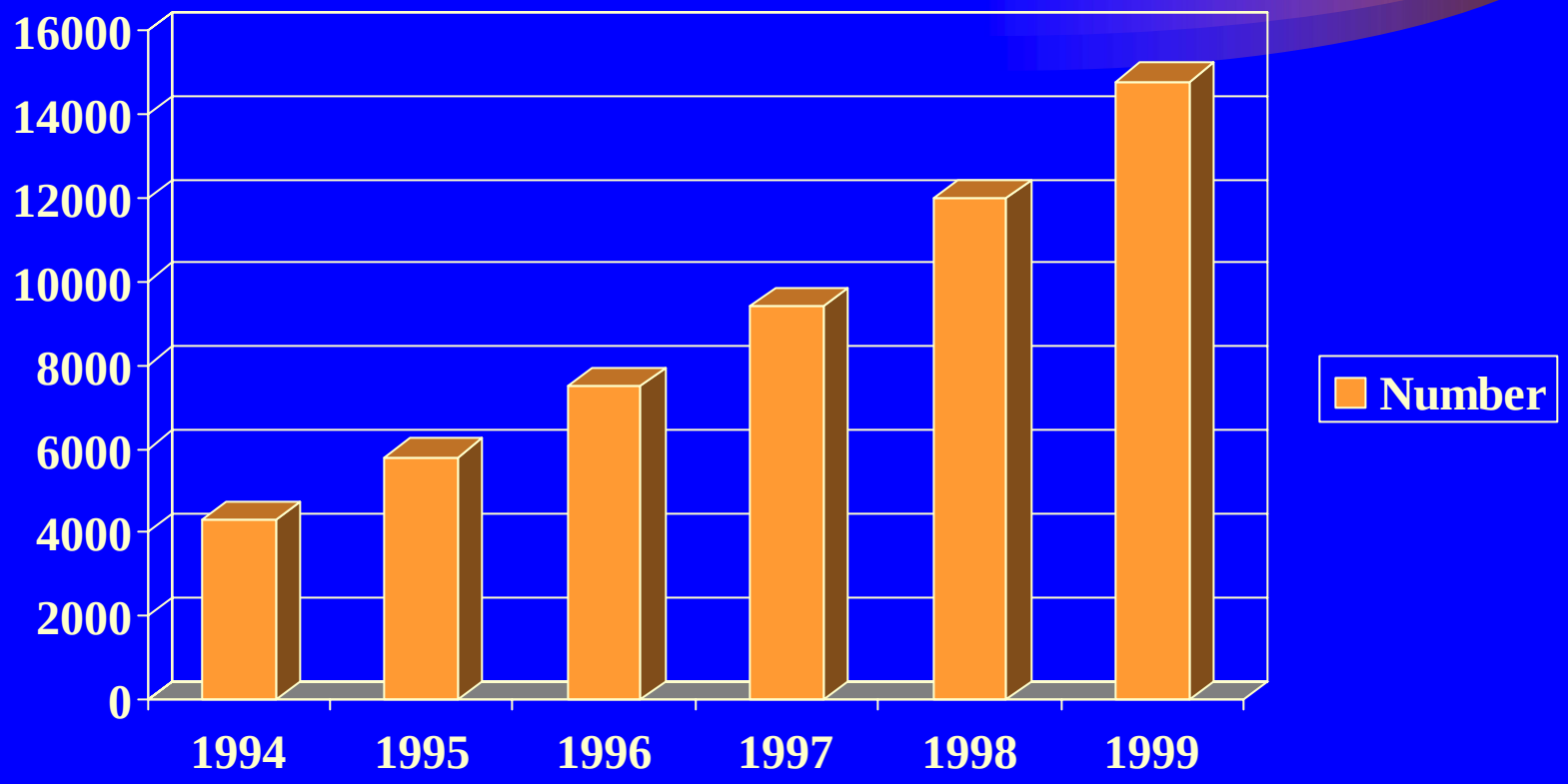
"Small-for-Size" Syndrome

- Recipient Factors Predictive of poor-outcome/ SFSS
  - Graft mass
  - Poor metabolic & physical recipient condition
  - Advanced chronic liver disease & severe portal hypertension
  - Impaired venous inflow and/or outflow.



Questions ?

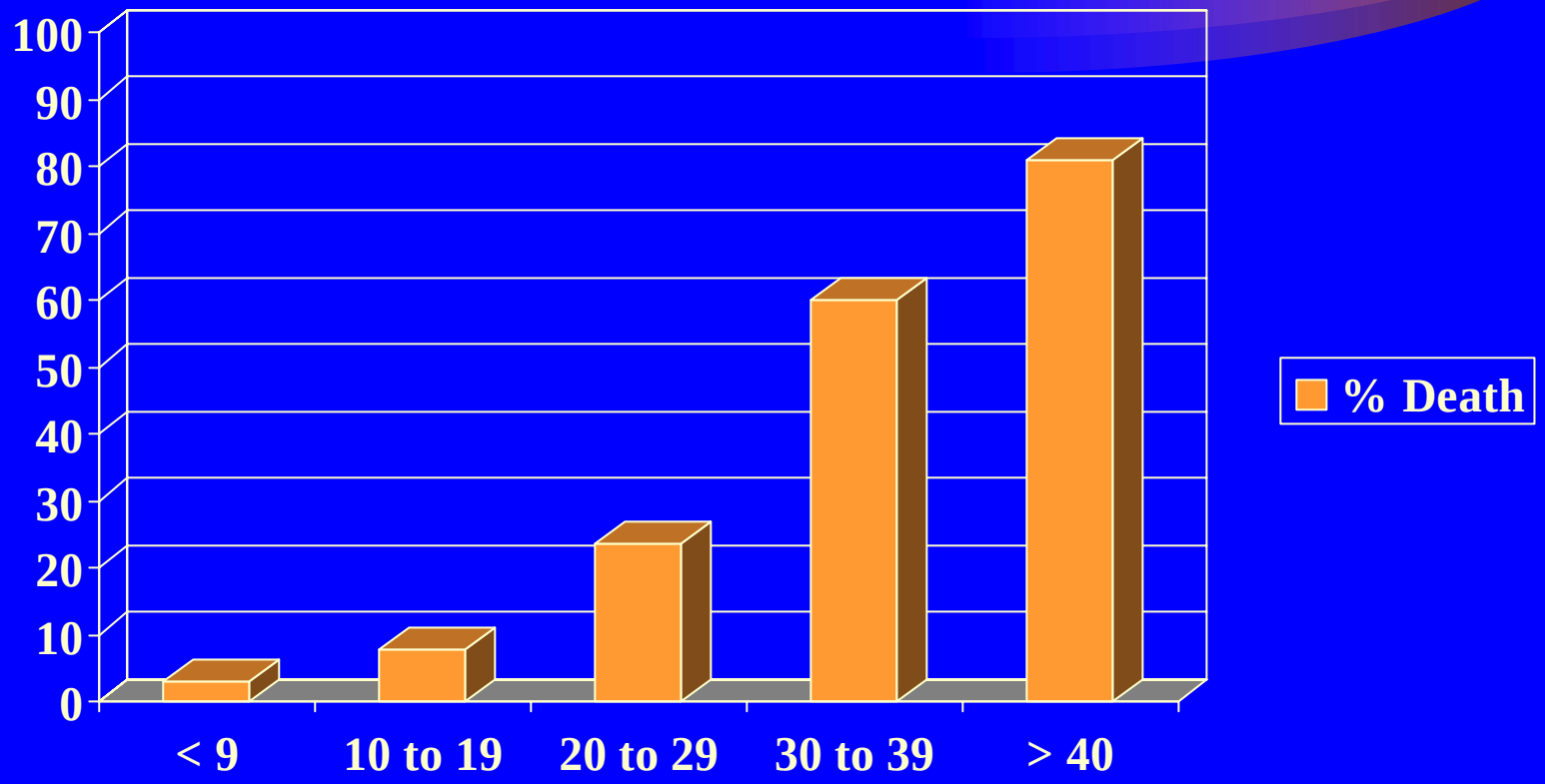
Liver Transplant Waiting List



MELD - 3437 patients

Three-month Death Rates

Wiesner R et al Gastroenterology 2003;124:91-96



MELD 15-17 is equivalent to surgical death-rate