

# **Liver Transplantation for Viral Liver Disease in Israel**

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**Ministry of Health**

**The West Galilee Medical Center**

# Liver Transplantation in Israel

- **Since 1991**
- **Three liver transplantation centers:**
  - **The 'Rabin' Medical Center**
  - **The Tel-Aviv Medical Center**
  - **The 'Hadassah' Medical Center**

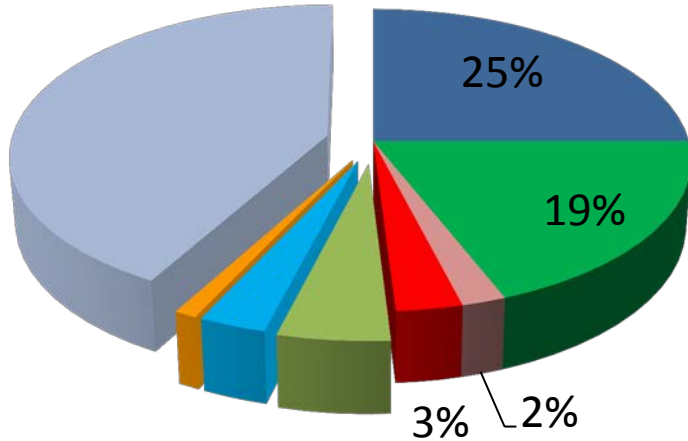
# Liver Transplantation in Israel

- **840 liver transplantations**
- **Allocation scheme:**
  - **1991-2002: Local**
  - **2002- current: Central:**
    - **2002-2005 The New England score**
    - **2005-Current: The MELD score**

# Etiology for Liver Transplantation

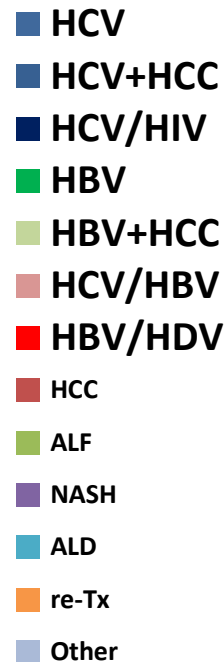
\* 1991-1999

\*Shaharabani E. et al Harefuah, Sep. 2000



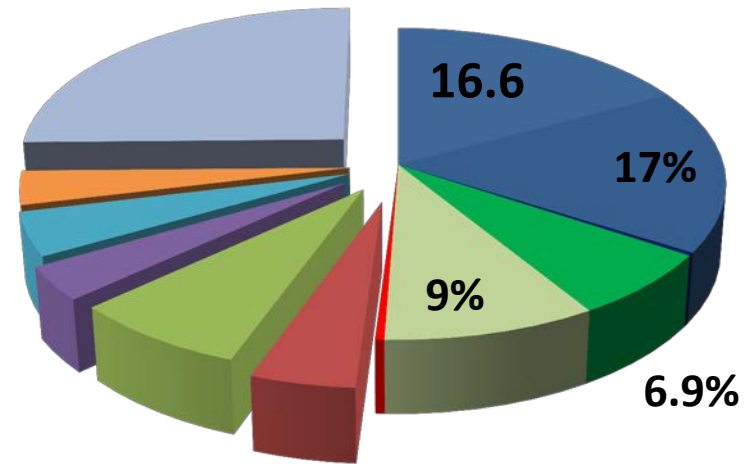
**Chronic Viral Hepatitis: 49%:**

- HCV: 25%
- HBV:19%
- HBV/HCV 2%
- HBV/HDV 3%



2006-2011\*\*

\*\* Carmiel-Haggai M. Harefuah, Dec. 2012



**Chronic Viral Hepatitis: 50.7%:**

- HCV: 33.6% (HCC: 17%)
- HBV: 15.9% (HCC:9%)
- HCV/HIV 0.4%
- HBV/HDV 0.4%

# Liver Transplantation for Hepatitis C:

- Men: 61.3%
  - Average age<sup>1,\*</sup>
    - Until 2006: 50.8<sub>±</sub>10.4
    - 2006-2011: 56.8<sub>±</sub>7.75
- \*(p=0.015)
- Demographic (candidates on waiting list<sup>2</sup>)
    - Eastern Europe: 58%
    - Native Jews: 16%
    - Native Arabs: 10%
    - North Africa: 8%
    - North America/ Europe: 8%

<sup>1</sup>The Israeli National Transplant Center

<sup>2</sup>Carmiel et al IA SL meeting; 2009;

# Liver Transplantation for Hepatitis C

## Survival (1998-2009)

	Patient Survival		Graft Survival	
	1 year (%)	3 year (%)	1 year (%)	3 year (%)
Non-HCV patients (n=78)	83%	80%	80%	78%
HCV patients (n=65)	81%*	74%*	81%	71%*

\* p<0.05

Early (90 days) mortality: 12.3%

Late mortality :

- **HCV related graft failure: 37.5%%**
  - **Recurrent HCV cirrhosis: 25%**
  - **Fibrosing cholestatic hepatitis: 12.5%%**
- Non-HCV related liver failure: 12.5%
- Other : 50%

# Recurrence of Hepatitis C

- Evidence of recurrence: 63-72%<sup>\*/\*\*</sup>
- Median interval to recurrence: 117 days (19-488 days)
- Early stage HCV @ diagnosis: 96%<sup>\*</sup>
  
- Response to treatment:
  - Introne + Ribavirin : SVR 1:10 (10%)
  - Peg-interferone + Ribavirin :
    - Intent to treat SVR 5:20 (25%)
    - Per protocol SVR 5:11 (45.5%)
  - Treatment with anti HCV Direct Acting Agents?

**60% of responders had increased fibrosis  
despite SVR**

•Carmiel et I IA SL meeting; 2009

\*\*Shaharabani E. et al Harefuah, Sep. 2000

# Liver Transplantation and Hepatitis C: Related Policy

- No re-transplantation for HCV related liver failure
- Exemption - rare

## HCV (+) DONOR

- Use of anti HCV(+) donors for anti HCV(+) recipients



# Liver Transplantation for Hepatitis B

- **Prevalence among liver transplant recipients:**
  - **1991-1999: 19%( HDV 3%)\***
  - **2006-2011 : 15.9% (HDV 0.4%)\*\***
- **Demographics:**
  - **Native Arabs: 44%**
  - **Native Jews 12%**
  - **Eastern Europe: 13%**
  - **North Africa: 25%**
  - **Africa 6%**

\*Shaharabani E. et al Harefuah, Sep. 2000

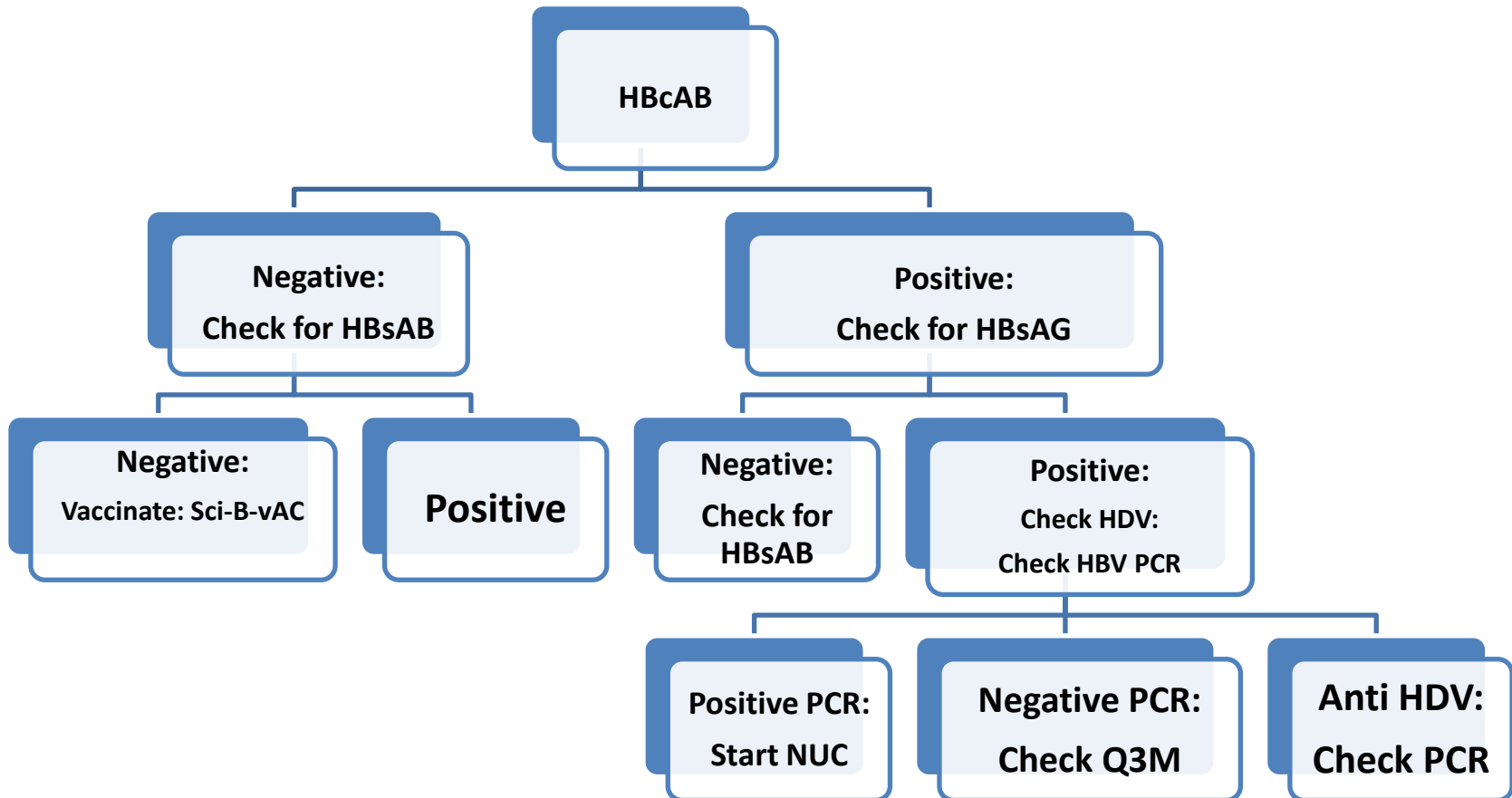
\*\* Carmiel M. Harefuah, Dec. 2012

\*\*\*The Israeli National Transplant Center

# Re-infection with Hepatitis B:

- **Pre nucleotide/side analog (NUC) era:**
    - **Incidence of 35%\* graft re-infection:**
      - **Mortality due to liver failure: 30%**
      - **YMDD mutation early after starting Lamivudine**
  - **Since 2000:**
    - **Re infection: rare**
  - ***De Novo* Hepatitis B: Reported 5 cases:**
    - **HBcAB+ donor: 2**
    - **Iatrogenic: 1**
    - **Sexually transmitted: 1**
    - **Unknown:1**
- Shaharbani E.et al. Harefuah, 2000, 139(6)  
•Ben-Ari Z. Liver Transpl 2001, 7(2)

# Candidates Evaluation for HBV Infection



# Preventing HBV Re-Infection

## NUC Protocol

- Continue NUC previously given
- Naïve HBsAg (+) , HBV DNA(-): start Lamivudine
- Repeat HBV DNA check

## HBIG Protocol

- Un-hepatic phase
- 3-7 days post operative
- According to HBsAB levels repeat when:
  - High risk pts. ] <500 u/ml
  - First year ]
  - After 1<sup>st</sup> year → <100-150 u/ml
- Check repeatedly for HBsAg + DNA

# Liver Transplantation and Hepatitis B: Related Policy

- Pre transplantation HBV DNA – mandatory for non-urgent cases

## Use of HBcAb + Donors

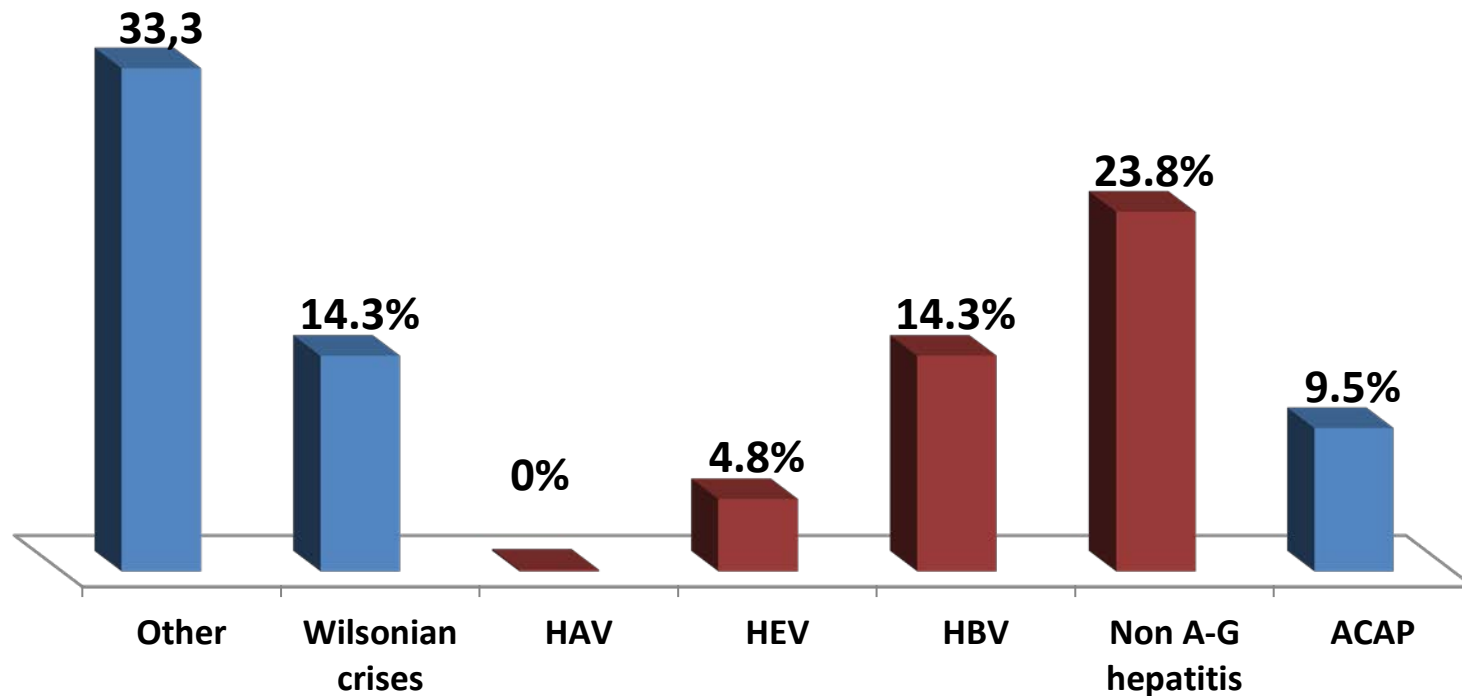
	HBsAg+	Isolated HBcAb	HBcAB+ ;HBsAb+ HBsAg –	HBcAb – , HBsAb+	HBcAb – HBsAb –
HBcAb+; HBsAg– HBsAb +	Yes	yes	yes	Yes*	+/-**
Isolated HBcAB	Yes	Yes*	yes	Yes*	+/-**
HBsAg +	Consider Bx	no	no	no	no

•F/U HBsAb  
\*\* Nuc Rx.  
vaccinate.,  
f/u HBcAb

Donor

# Urgent Liver Transplantation due to Viral Hepatitis

Etiology for Urgent Liver Transplantation  
(Tel-Aviv Medical Center 2003-2009)



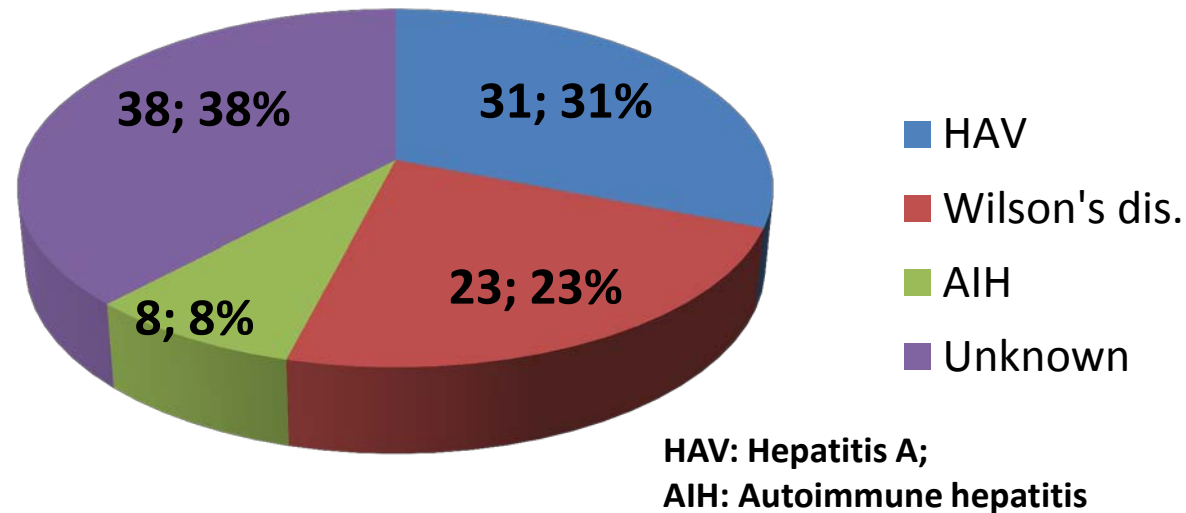
# Urgent Liver Transplantation due to Viral Hepatitis: Pediatric

- Hepatitis A: Leading cause for pediatric urgent liver Tx.

- All HAV cases before 1999

- No HAV induce liver failure was reported (March 2013)

Etiology for Urgent Pediatric Liver Transplantation 1996-2007



# Liver Transplantation for Viral Hepatitis in Israel: Future

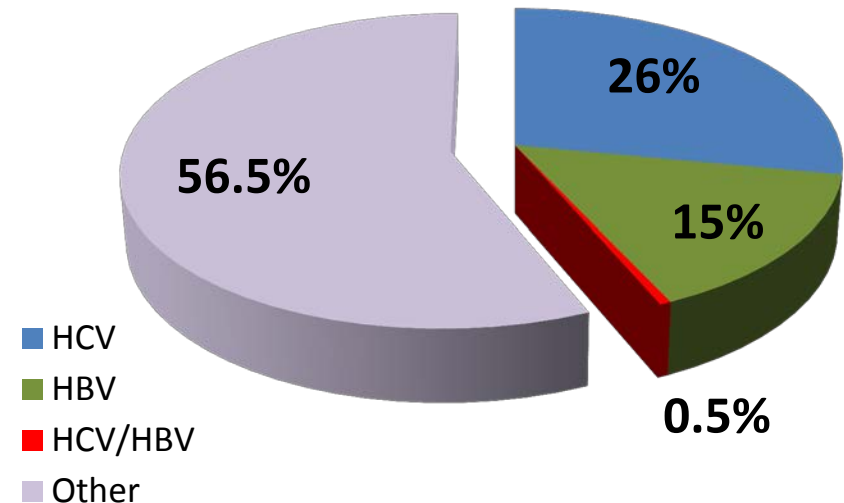
## Hepatitis C:

- Leading liver disease
- Older recipients

## Post transplantation

- Universal recurrence
- New direct acting agents
- HCIG??

Candidates for Liver  
Transplantation March 2013





# Liver Transplantation for Viral Hepatitis in Israel: Future

## Hepatitis B:

- **Excellent outcome after transplantation**
- **Entecavir/Tenofovir:**
  - **Better viral control:**
    - Less need for transplantation?
    - Lower incidence of HCC ?
    - NUC mono-therapy to prevent re-infection?

# Liver Transplantation for Viral Hepatitis in Israel: Future

## Acute Liver Failure:

- Eradication of HAV
- Screening and preventive therapy for HBsAg + immune- compromised patients

# Liver Transplantation is a Team Work

**Tamar Ashkenazi and Rona Ben-Simon**  
**The Israeli Transplant Center**  
**Ministry of Health**

**Oren Shibboleths and Helena**  
**Katchman**  
**Liver Unit**  
**Tel-Aviv Medical Center**

**Rifaat Safadi**  
**Liver Unit**  
**Hadassah Medical Center**

**Marius Braun**  
**Liver Unit**  
**Rabin Medical Center**

**Eitan Mor**  
**The Organ Transplantation**  
**Center**  
**Rabin Medical Center**

**Riki Shapira**  
**Pediatric Liver**  
**Transplantation Unit**  
**Schneider Children Hospital**  
**Rabin Medical Center**