Hepatitis B and C and the Healthcare Worker

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Percutaneous Injuries in Healthcare Workers (HCWs)

- Frequency has decreased over the last decade
  - in 1998 were 590164 reported percutaneous hospital-based exposures in the US. Is estimated that 39% were not reported making a total of 967500.
- Currently estimated at 384000 - 600000 percutaneous injuries per year at US Hospitals (> 1000/day)
  - Only 43% are reported.
- In 2004, the U.S. work-productivity cost was 188.5 million dollars.
- Highest rate is in OR Nurses (39.7 exposures/FTE/year).
- By the end of their training, 99% of surgical residents will have at least 1 needle stick injury; more than 50% will not be reported.
- Frequency with hollow-needles has decreased (due to safer devices) but with solid-needles has increased.

Percutaneous Injuries in Healthcare Workers (HCWs)

- Worldwide, in the year 2000, needle injuries caused:
  - 66000 cases of HBV,
  - 16000 cases of HCV, and
  - 1000 cases of HIV in HCWs.
- Factors that increase risk:
  - Poor organization climate or administrative support
  - High workload
  - Poor training in use of safer device
  - Belief that following precautions will place patient at risk
  - HCW's state of mental anguish or social dysfunction

Frequency of sharp injuries by surgeons in Teaching Hospitals - England 1992

Ann R Coll Surg 1996;78:447-449

Frequency	CT Surgery	OB/GYN Surgery	General Surgery	Other Surgery
> 1/month	60%	63%	54%	19%
< 1/month, > 1/year	40%	31%	23%	35%
< 1/year	0	6%	23%	47%
Always Reports	0	6%	14%	28%

Frequency of sharp-injuries and re-contact* exposure in Teaching Hospital – US 1992

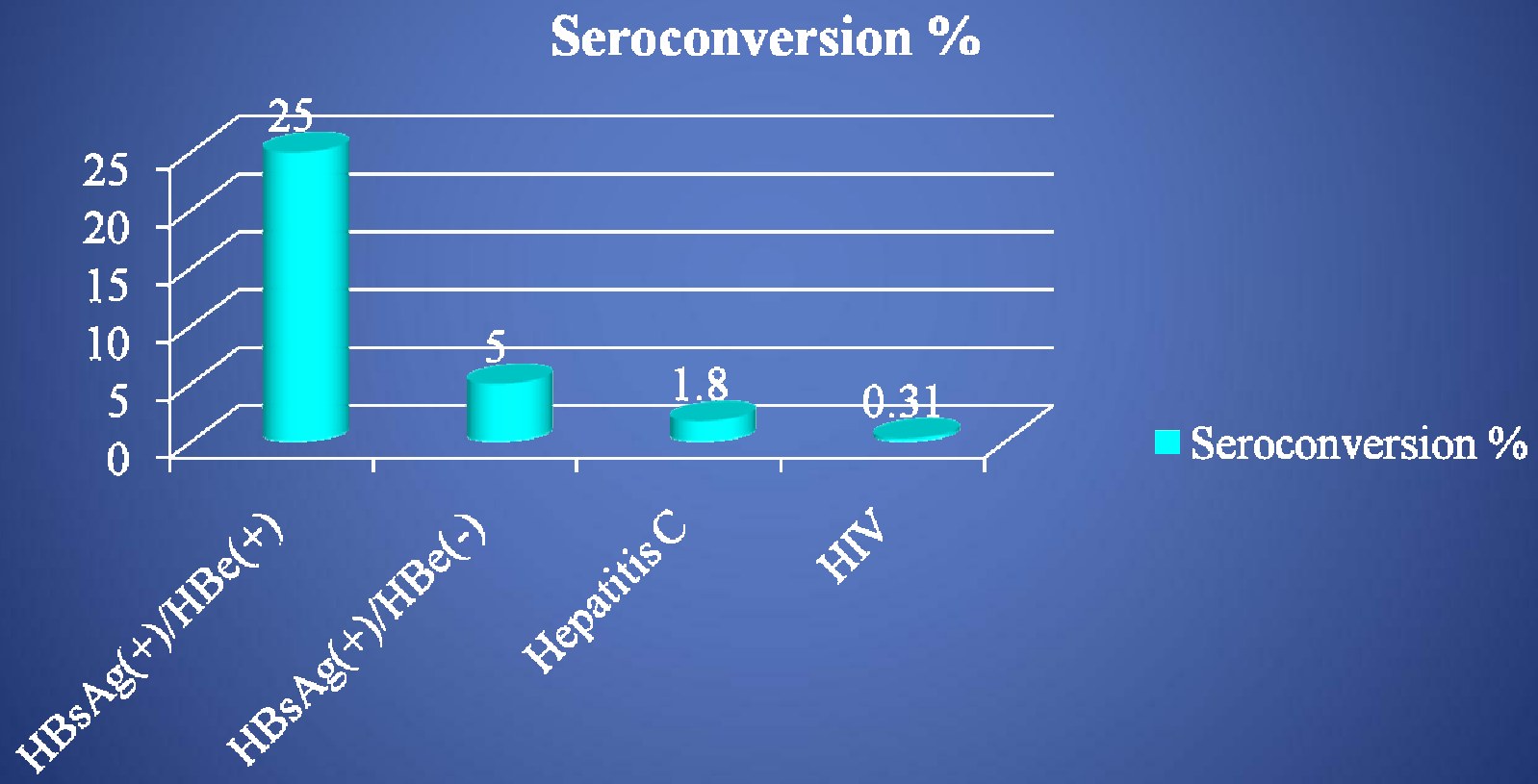
JAMA 1992;267:2899-2904

	CT Surgery	GYN Surgery	General Surgery	Orthopedic Surgery	Trauma Surgery
Procedures with Injury	9%	10%	8%	4%	5%
Re-contact*	3%	4%	1%	0.3%	3%

Re-contact: instrument contacted patient after HCW injury, or bone fragment or wire fixed to patient injured the HCW

Risk of Seroconversion after percutaneous exposure to infected source (without prophylaxis)

Epidemiol Rev 1994;16:437-450 & MMWR 1998;47(RR-19):1-39



Worldwide Cases of HCW-to-Patient HIV, HBV, or HCV Transmission 1991-2005

Am J Infect Control 2006;34:313-319

	# HCW	# Infected Patients	# Patients tested in look-back	% Infected Patients
HIV	3	3	3527	0.09%
HBV	12	91	3079	2.96%
HCV	11	38	9678	0.36%

Factors Affecting Viral Bloodborne Pathogens Transmission to HCWs

- Prevalence of the pathogen in the population served by the healthcare facility.
- Frequency of exposure
- Type of exposure (percutaneous, mucosal, nonintact skin)
- Infectivity of the virus (HBV > HCV > HIV)
- Titer of the virus in the body fluid or inanimate object.
- Availability of pre-exposure prophylaxis (HBV), and post-exposure prophylaxis (HBV, HIV)

Seroprevalence of HBV, HCV & HIV

Seroprevalence	HBV	HCV	HIV
General Population	0.42%	1.8%	0.31-0.42%
HCW population	Higher	Same	Same

Risk of Infection by Mode of Exposure to HCWs

	HBV	HCV	HIV
Percutaneous	6-30%	1.8%	0.2-0.5%
Mucosal	Transmission documented	Transmission documented	0.09%
Nonintact Skin	Transmission NOT documented	Transmission NOT documented	< 0.1%
Human Bite	Transmission documented	Transmission documented	Transmission documented

Infective Material Causing HCWs Infection

	HBV	HCV	HIV
Documented	Blood Blood products	Blood Immunoglobulins	Blood Blood products Body fluids
Possible	Semen Vaginal fluid Bloody fluids Saliva	Blood products Bloody fluids Semen Vaginal Fluids	Semen Vaginal fluid Cerebrospinal fluid Breast milk Serosal fluids Amniotic fluid Exudates Saliva in dental exam
Unlikely	Urine Feces	Saliva Urine Feces	Saliva Urine Feces

Risk Minimization

- All HCWs with reasonably anticipated exposure to blood or contaminated body fluids must receive from the healthcare facility:
  - yearly education about bloodborne pathogen transmission and risk minimization.
  - HBV vaccination (and post vaccination testing) at no cost. Quantitative anti-HBs titers should be tested 1-2 months after final (3^{rd}) vaccine dose.
  - If anti-HBs titer is < 10 mIU/mL, the 3-dose vaccination should be repeated, and anti-HBs titers repeated.
    - Failure to obtain titers > 10 mIU/mL after the second 3-dose vaccine series classifies the patient as “non-responder”.
  - If HCW refuses HBV vaccination, he/she must sign mandated declination form.

Risk Minimization
(healthcare facility must provide)

- engineering controls proven to reduce exposure risk
  - leak-proof containers to transport blood,
  - impervious needle-disposal containers,
  - needles IV medication systems,
  - blunted suture needles
- “Personal Protective Equipment”, that HCWs must use when performing procedures with blood exposure risk
  - impervious gowns,
  - gloves,
  - face/eye shields

Intra-dermal HBV Vaccination for Vaccine Non-Responders

Levitz RE, Cooper BW, Regan HC. *IC and H Epidemiology 1995;16:88-90. ;*
Fabrizi F, Andrulli S, Bacchini G, Corti M, Locatelli F. Nephrol Dial Transplant. 1997 Jun;12(6):1204-11.

- 1. Week 0: give adult hepatitis B vaccine Engerix B, 0.25cc intra-dermal in forearm
- 2. Week 2: give adult hepatitis B vaccine Engerix B, 0.25cc intra-dermal in other forearm
- 3. Week 4: draw HBsAb (post hepatitis B vaccine)
  - HBsAb > 10 mIU/mL = Immune, no further vaccine
  - HBsAb < 10 mIU/mL = repeat steps 1, 2, 3
- If HBsAb < 10 mIU/mL after second series of intradermal hepatitis B vaccine refer to Employee Health for counseling
  - some protocols give 16 weekly intradermal doses of 0.25 mL Engirex B (80 mcg total).

Postexposure Prophylaxis for Percutaneous or Mucosal exposure to HBV

	HBsAg(+)	HBsAg(-)	Not tested/ Unknown
Unvaccinated	HBIG 0.06 mL/kg or 5 mL IM x 1 dose Vaccinate (0,1,6,12 mo)	Vaccinate	Vaccinate
Vaccine responder	No treatment	No treatment	No treatment
Vaccine non-responder	HBIG 0.06 mL/kg or 5 mL IM x 2 dose, (30 d apart) Re-vaccinate	No treatment	If "high risk" source, treat as HBsAg(+)
Vaccinated; unknown response	Test anti-HBs titer If > 10 mIU/mL: No treatment If < 10 mIU/mL: HBIG 0.06 mL/kg or 5 mL IM x1 dose + Revaccinate x 3 doses and test titer	No treatment	Test anti-HBs titer If > 10 mIU/mL: No treatment If < 10 mIU/mL: Revaccinate x3 and test titer

Hepatitis B

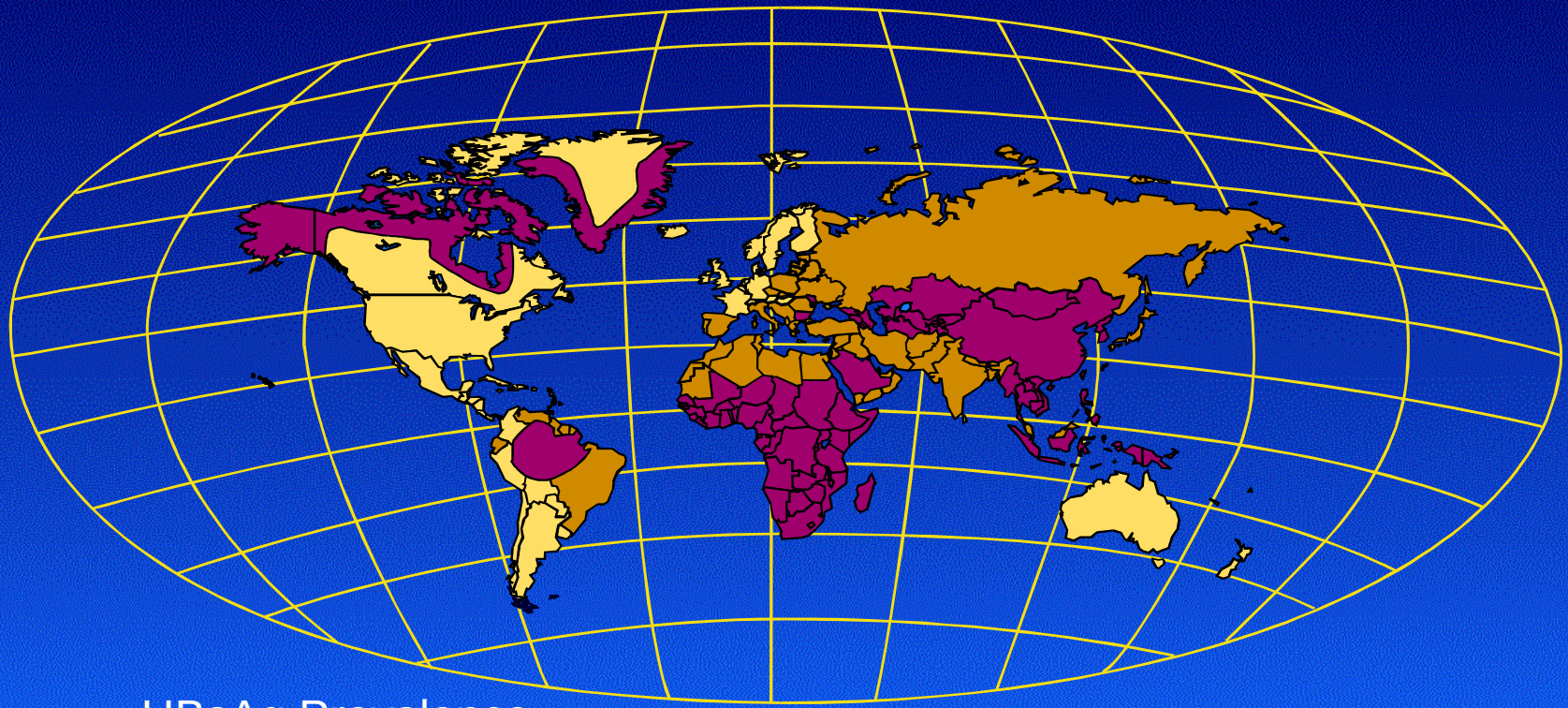
Hepatitis B

- 42 nm, partially double-stranded circular DNA virus.
- 350 million carriers world-wide; causes 250000 deaths a year.
- 1.25 million carriers in USA.(0.5 %); > 8% in Alaskan Eskimos.
- New infections: decreasing in frequency
  - 260,000/y in 1980's;
  - now 73,000/y
- Greatest decline among children & adolescents (vaccine effect).

Hepatitis B

- Highest rate of disease in 20 to 49 year-olds
- 20-30% of chronically infected Americans acquired infection in childhood.
- High prevalence in:
  - Asian-Pacific with 5-15% HBsAg(+) &
  - Eastern European immigrants
- **Transmission**: In USA predominantly sexual and percutaneous during adult age.
  - In Alaska predominantly perinatal.

Global Distribution of CHB Carriers



HBsAg Prevalence

Low < 2%

Intermediate 2-8%

High > 8%

Source: World Health Organization / Centers for Disease Control and Prevention.

Hepatitis B Transmission

- **Sexual**:
  - Heterosexual in 41% of acute cases.
  - Men having sex with men have 10% risk.
- **Percutaneous** (mostly illicit drug use):
  - 15% of acute HBV cases
- **Perinatal**:
  - 10% of acute cases (mother-child)
- **Transfusion**:
  - 1/63000 transfusions.
- **Other**: organ transplant, tattoo, piercing, acupuncture, …

Risk of HBV Infection in HCWs

- HBV is much more infectious than HCV and HIV.
- HBV can be transmitted by percutaneous, mucosal, or nonintact skin exposure.
- Inanimate objects (fomites) can transmit HBV: finger-stick devices, jet gun injectors, multi-dose vials, endoscopes.
- Infectious HBV can survive up to for 7 days in contaminated surfaces.
- OSHA-required HBV vaccination of HCWs since 1991, has decreased HBV infections by 95% between 1983 to 1995.
- Only 75% of HCWs have received HBV vaccination.

Acute HBV

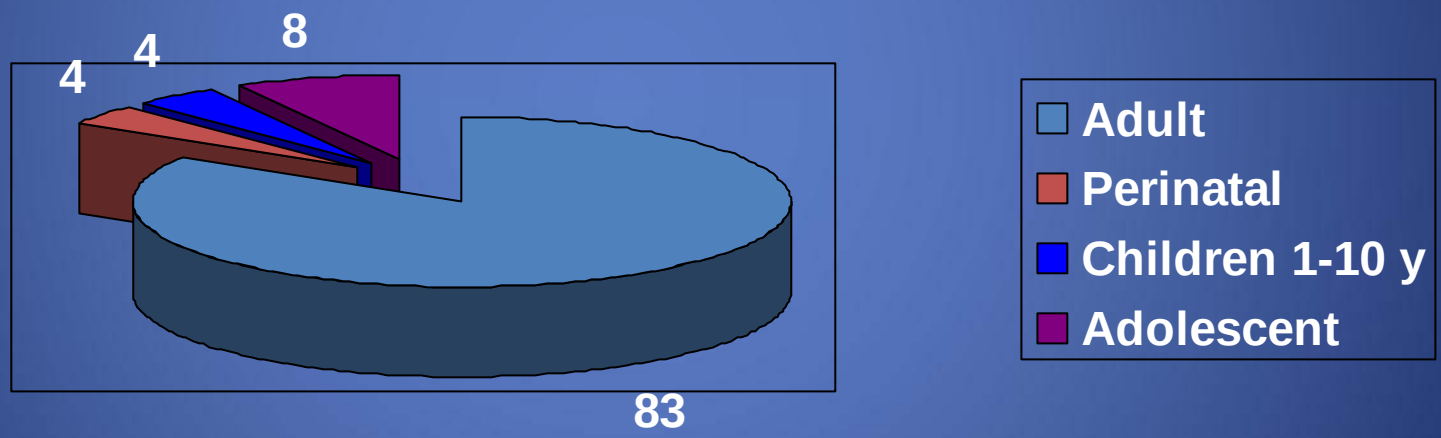
Acute Hepatitis B

- **Incubation**: 1-4 months
- **Prodrome**: arthralgia, arthritis, skin rash
- **Symptoms & Signs**: malaise, anorexia, jaundice, nausea, fatigue, low-grade fever, myalgia, change in taste and smell. Tender hepatomegaly in most patients; splenomegaly in 5-15%.
- Infrequently: confusion, edema, coagulopathy, coma (Fulminant Failure in 0.5%)

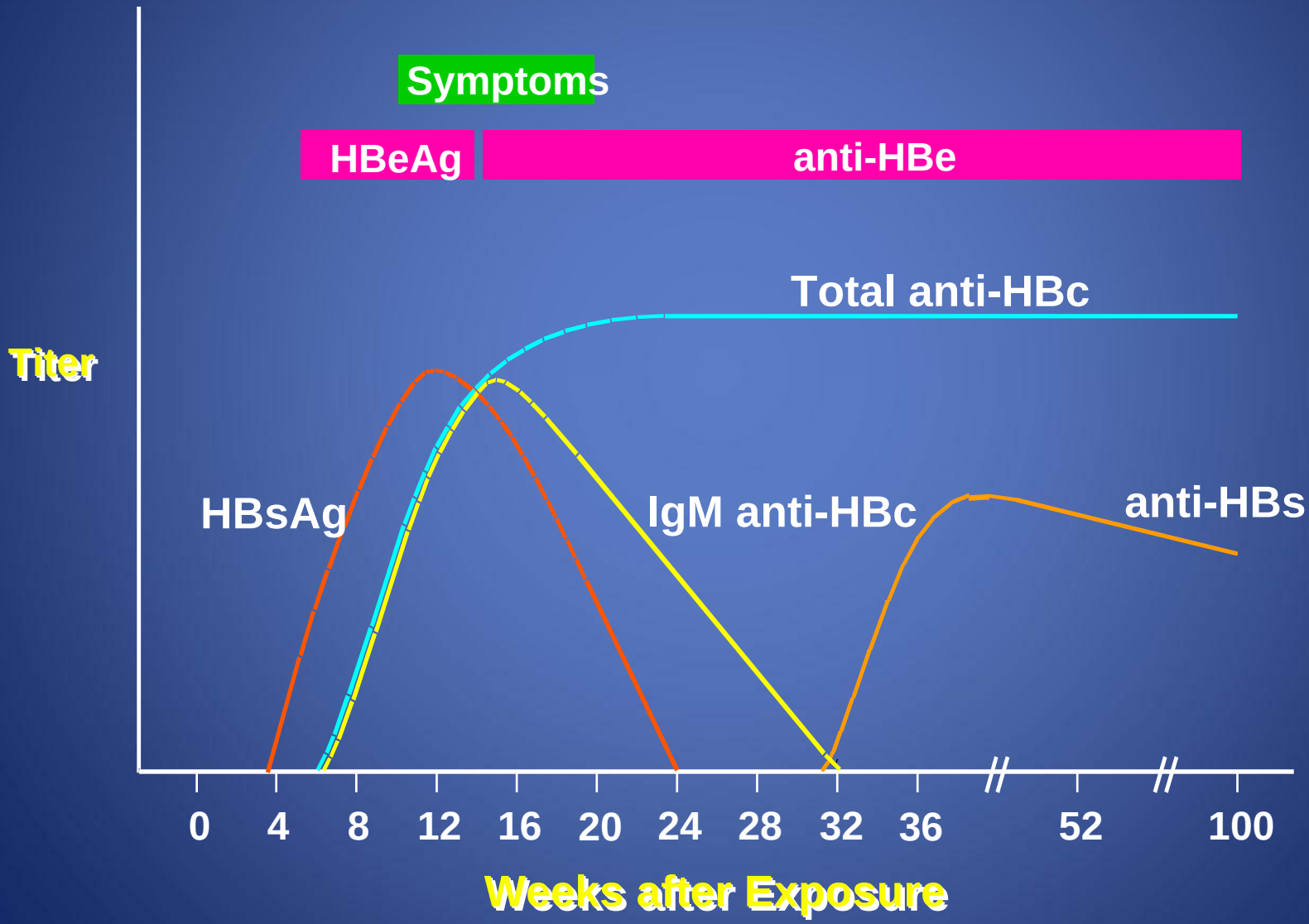
Acute Hepatitis B

- **Diagnosis**:
  - anti-HBc IgM antibody (+) usually with signal/noise ratio > 5.08
    - (s/n ratio </= 5.08 suggest reactivation of chronic infection);
  - Frequently HBsAg (+) in early phase and anti-HBs(+) in late phase.
  - HBV-DNA usually around 1000 IU/mL
    - (in reactivation of chronic HBV usually >/= 1 million IU/mL)
- **Evolution to Chronicity**:
  - a) Infants: 90%,
  - b) Children 1-5: 25-50% (**30%**) ,
  - c) Adults & older children: 5%
- **Treatment**:
  - Supportive;
  - Anti-virals in “protracted hepatitis”, or failure to regenerate/sub-massive necrosis.

Age of Acquisition of Acute Hepatitis B 1989 estimates



Acute Hepatitis B Virus Infection with Recovery
Typical Serologic Course



Chronic HBV

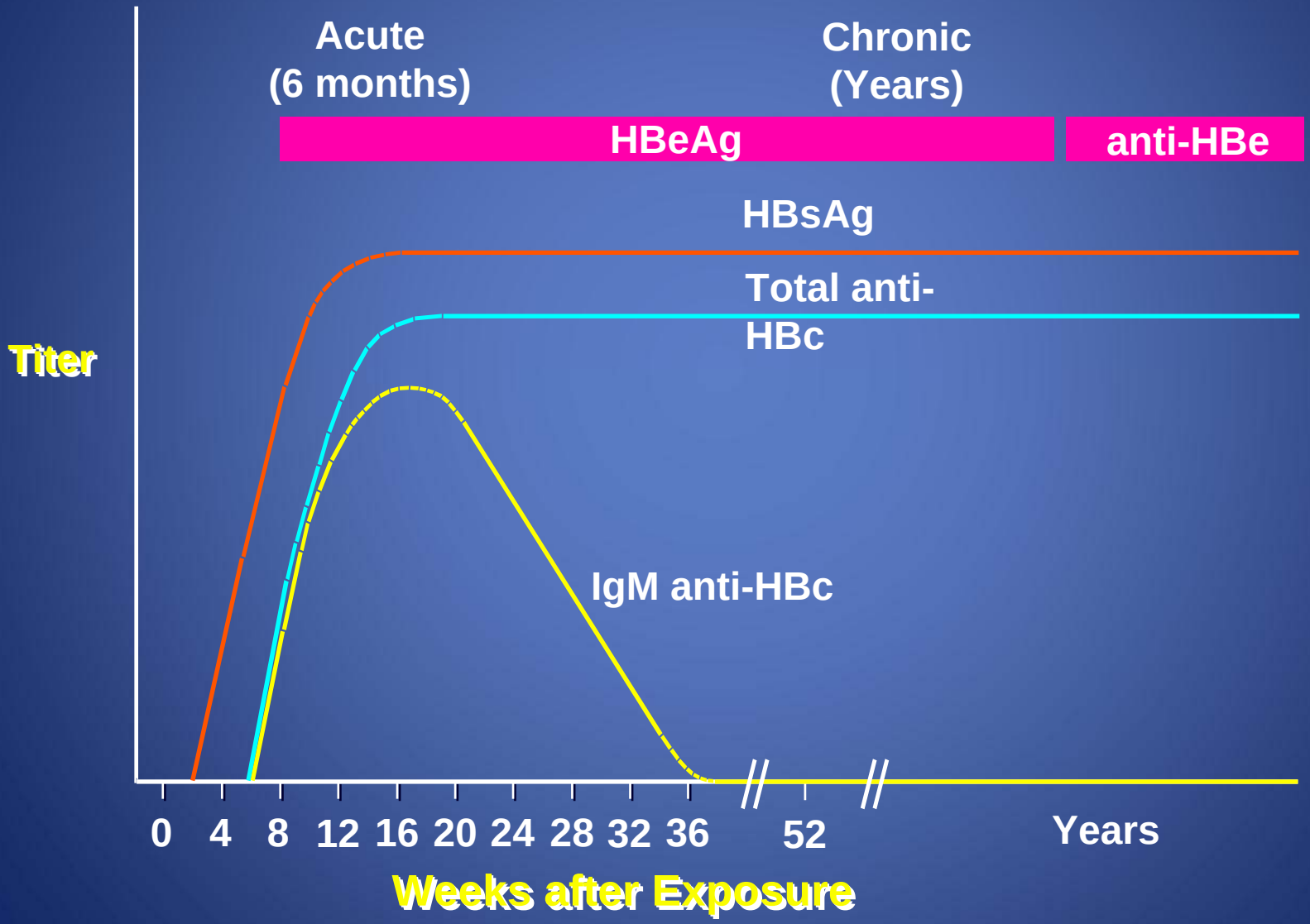
Chronic Hepatitis B

- In low prevalence areas (USA) 30-50% history of acute hepatitis (rare in high prevalence)
- **Symptoms**: frequently asymptomatic; sometimes RUQ or epigastric pain or acute-like hepatitis episodes.
- **Extrahepatic**: serum-sickness, polyarteritis nodosa, membrano- or membranoproliferative-glomerulonephritis, mixed cryoglobulinemia, IgA nephropathy, papular acrodermatitis.

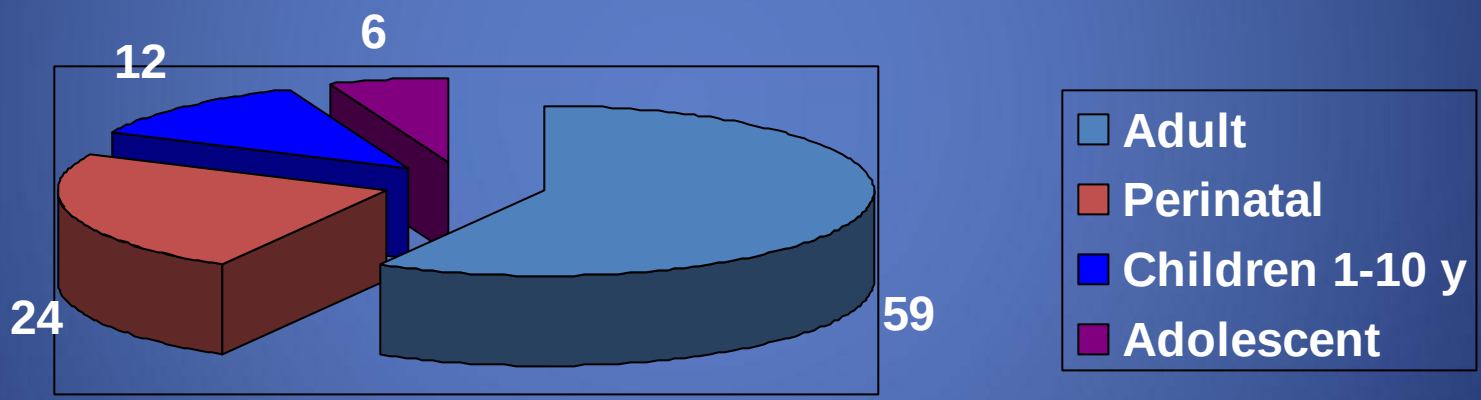
Chronic Hepatitis B

- Evolution to Chronicity after Acute HBV:
  - 90% of infants infected at birth
  - 30% of children infected at age 1-5 y
  - 6% of infected after age 5 y
- Death from chronic HBV liver disease
  - 15-25% of chronically infected
- USA yearly mortality from HBV
  - 5000 per year

Progression to Chronic Hepatitis B Virus Infection
Typical Serologic Course



Age of Acquisition of Chronic Hepatitis B 1989 estimates



Prognostic Factors For Progression To Cirrhosis

Factors	P-value
Older age	.0001
HBV-DNA persistance	.0001
Virus genotype C	.001
Recurrent acute flares	.001
Histologic Staging	.0002
Alcohol consumption	.001
HCV, HDV co-infection	.001
HIV co-infection	.02

McMahon et al. *Ann Intern Med.* 2001; 135: 759-768.

HBsAg(+) Healthcare Worker

- CDC says:
  - "Those who are HBeAg(+) should not perform exposure-prone procedures without previous counseling and advice from an expert review panel regarding under which circumstances they should be allowed to perform those procedures".
  - They should notify the patient about their HBV status prior to the procedure.
- In Europe different countries use HBV-DNA varying from 200 IU/mL to 20000 IU/mL to allow performance of exposure-prone procedures.

Hepatitis C

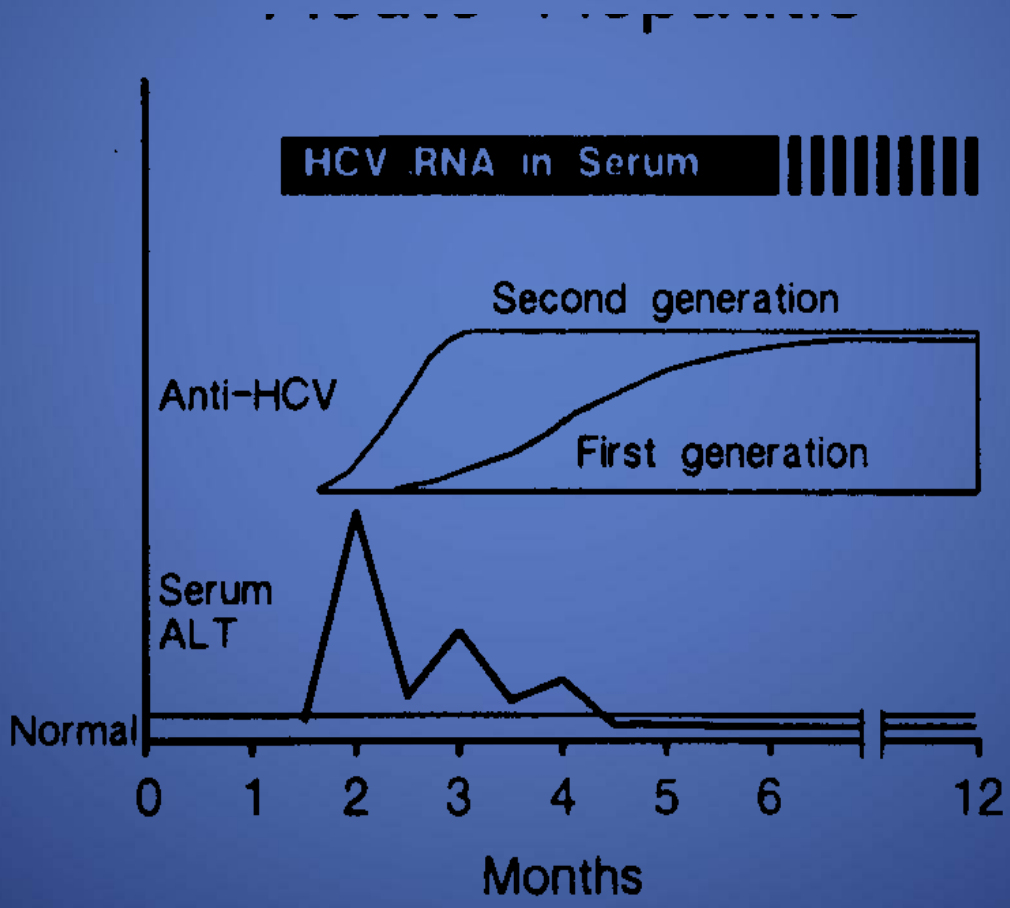
HCW exposure to HCV

- Prevalence of HCV in HCWs is similar to that of the general population.
- Testing for HCV in HCWs should be done after percutaneous, mucosal, and nonintact skin exposure to HCV(+) blood and potentially infectious body fluids.
- HCV can survive in environmental surfaces for > 16 hours, but < than 4 days.
- Baseline testing: anti-HCV, HCV-RNA quant, ALT
- F/U testing: ALT, HCV-RNA, anti-HCV @ wk 4, 12 & 24.
- If infection occurs and persists for >/= 12 weeks, treat as acute HCV.

Acute HCV

- **Incubation**: 2-26 weeks (usually 7-8)
- **Symptoms:** in < 30%, mild & last < 1month;
  - Usually: anorexia, arthralgia, myalgia, fatigue;
  - Rarely: jaundice, fever, or skin rash.
  - Extremely rare: FHF.
- **DX**: HCV-RNA (+) days to weeks after acquisition ; anti-HCV (+) in 6 weeks.
- **Spontaneous HCV clearance**: (within 12 weeks in adults)
  - Children < 2 y.o. & young women = 45%;
  - Others = 23%

Acute Hepatitis C Virus



Acute HCV Treatment

- If still HCV-RNA(+) 3 months after inoculation, spontaneous clearance is rare.
- Best regimen is unknown:
  - starting 3 months after inoculation, IFN 5 MU QD x 4 wks + 3 MU TIW x 20 wks gave 98% clearance;
  - the mildest & shortest effective therapy is unknown.
- Patients should be abstinent from alcohol (impairs treatment response) and drugs (anti-HCV is not protective against re-infection).

Treatment of Acute HCV @ 8,12, & 20 wks, Pegasys vs Rebetron x 12 wks

Kamal et al Abst # 37 AASLD, 2004

- 68 pts with Acute hepatitis C; 7 had spontaneous clearance.
- Treatment started at (time from acquisition):
  - A) Wk 8 (21),
  - B) Wk 12 (20),
  - C) Wk 20 (20)
- Rebetron vs Pegasys x 12 wks; if HCV-RNA still (+) at wk 12, treated 12 more wks.

Treatment of Acute HCV @ 8,12, & 20 wks, Pegasys vs Rebetron x 12 wks

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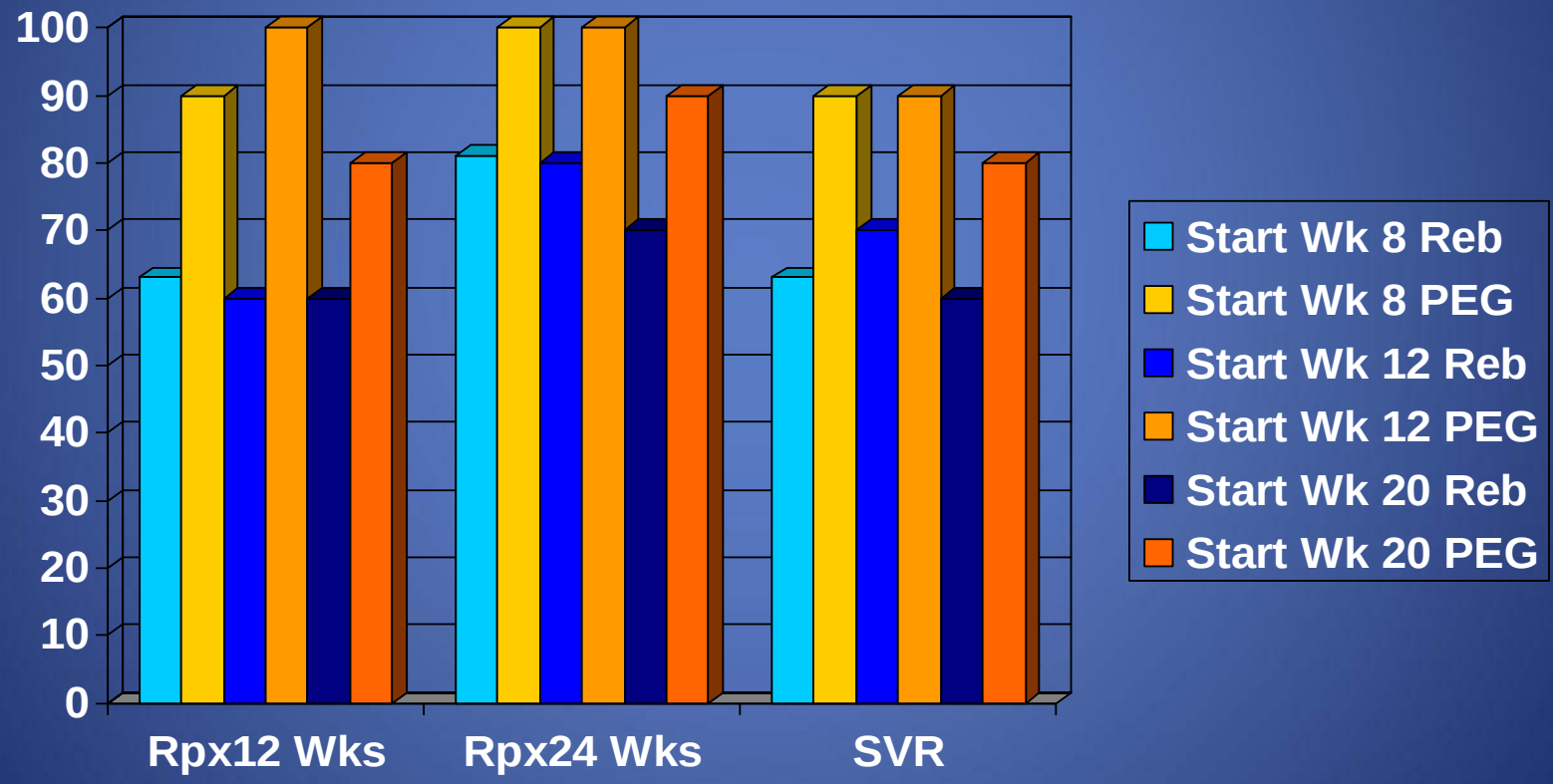

BLUE = Rebetron

ORANGE = Pegasys

Treatment of Acute HCV @ 8,12, & 20 wks, Pegasys vs Rebetron x 12 wks

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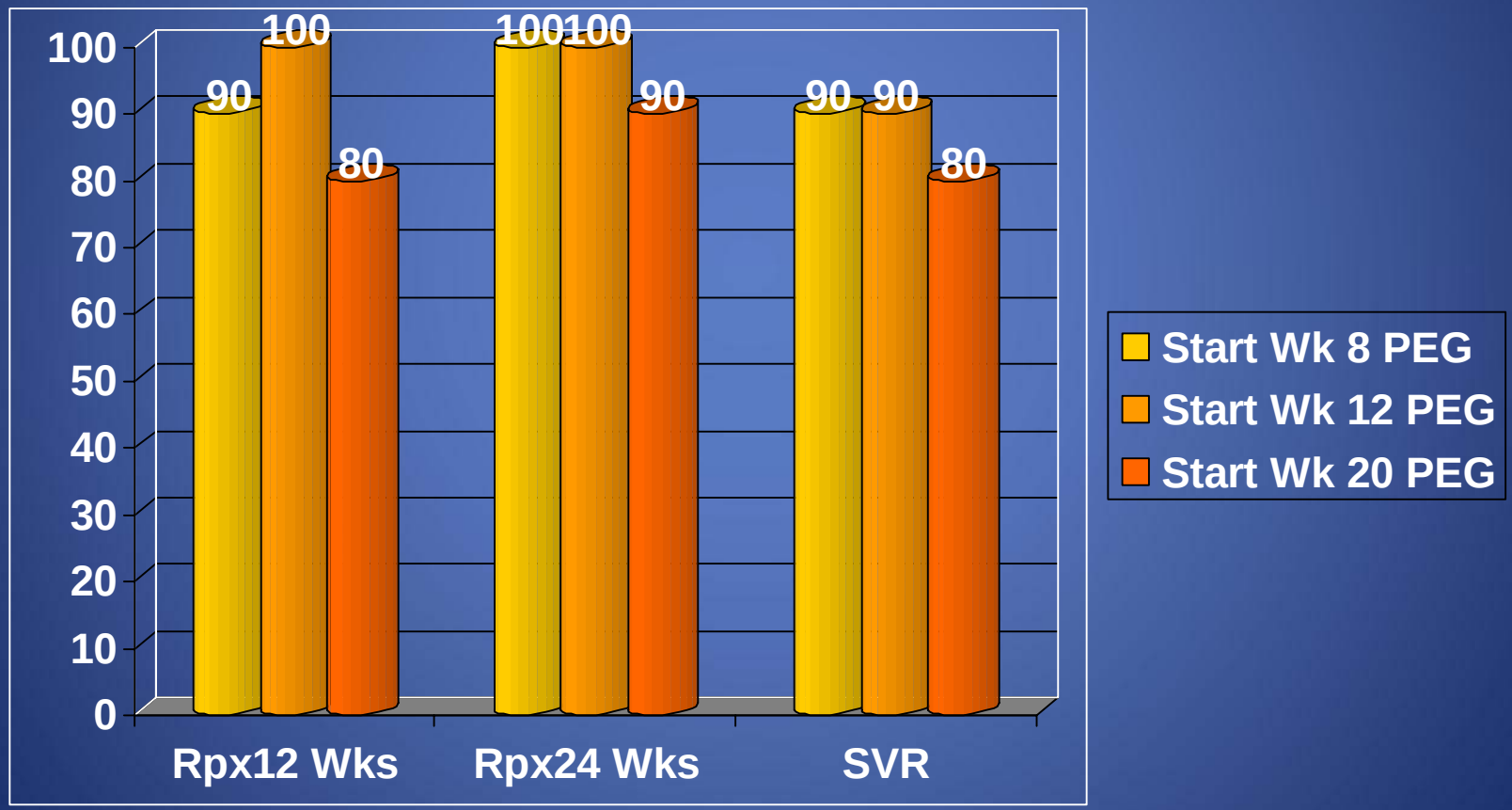

Treatment of Acute HCV @ 8,12, & 20 wks, Pegasys vs Rebetron x 12 wks

Kamal et al Abst # 37 AASLD, 2004

- Starting therapy at week 12 gave best results with SVR of 90%.
- Pegasys 180 mcg/week monotherapy x 12 weeks, was superior to Rebetron treatment x 12 weeks, in all groups.

Practical Approach to Treat Acute HCV

- Wait for 12 weeks from time of acquisition to see if spontaneous clearance occurs.
- Spontaneous clearance is more likely if patient is:
  - IL28B (rs12979860) CC regardless of symptoms or jaundice, or
  - IL28B CT and jaundiced.
- In absence of spontaneous clearance, treat with Peg-IFN + RBV (may improve outcome) for:
  - 3 months if HCV-RNA (-) at 4 weeks;
  - otherwise treat longer.

Spontaneous HCV Clearance in Acute HCV in 136 Young Women (25+/-4 y/o) by IL28B Genotype

Gastroenterology 2010;139:1586-1592