بسم الله الرحمن الرحیم

Emerging Diseases

Epidemiology of Hepatitis C

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Definition and Importance

Viral Hepatitis / C

- **Systemic infection affecting predominantly the liver**
- **Six categories of viral agents :**

(A, B, C, D, E, G)

Viral Hepatitis / C

- **Persistent infections and chronic liver disease common to the bloodborne types**
- **Chronic hepatitis has increased risk of hepatocellular carcinoma**
- ***One of the most common cause of chronic liver disease***

➢Definition and public health importance

· Hepatitis C has been compared to a "viral time bomb".

· WHO estimates that about

200 million of the world's population, are infected,

130 million of whom are chronic HCV carriers at risk of developing liver cirrhosis and/or liver cancer.

➢Definition and public health importance

- It is estimated that 3-4 million persons are newly infected each year,
- 70% of whom will develop chronic hepatitis.
- HCV is responsible for 50–76% of all liver cancer cases, and two thirds of all liver transplants in the developed world

➢Current situation of hepatitis C (2017)

- **Globally, an estimated 71 million people have chronic hepatitis C infection.**
- **A significant number of them will develop cirrhosis or liver cancer.**
- **Approximately 399 000 people die each year from hepatitis C, mostly from cirrhosis and hepatocellular carcinoma.**

➢Current situation of hepatitis C (2017)

- **Antiviral medicines can cure more than 95% of persons with hepatitis C infection, thereby reducing the risk of death from liver cancer and cirrhosis, but access to diagnosis and treatment is low.**
- **There is currently no vaccine for hepatitis C; however research in this area is ongoing.**

Hepatitis C Virus

- **Family: *Flaviviridae***
- **Genus : Hepacvirus**
  - **+ ssRNA**
    - RNA virus isolated in 1988
- **Antigenicity**
  - **Frequent mutation**

HCV Genetic Heterogeneity

- **Six major genotypes**
  - **Iran population (Genotype 1,2, 4, 5?)**
  - **Predict treatment outcome**
- **Multiple quasispecies within a single person**

There is no vaccine , no passive immunoprophylaxix and no chemoprophylaxis

Descriptive epidemiology

&

Occurrence

Clinical epidemiology of Hepatitis C

- Definition and public health importance
- Etiologic agents

OCCURRENCE

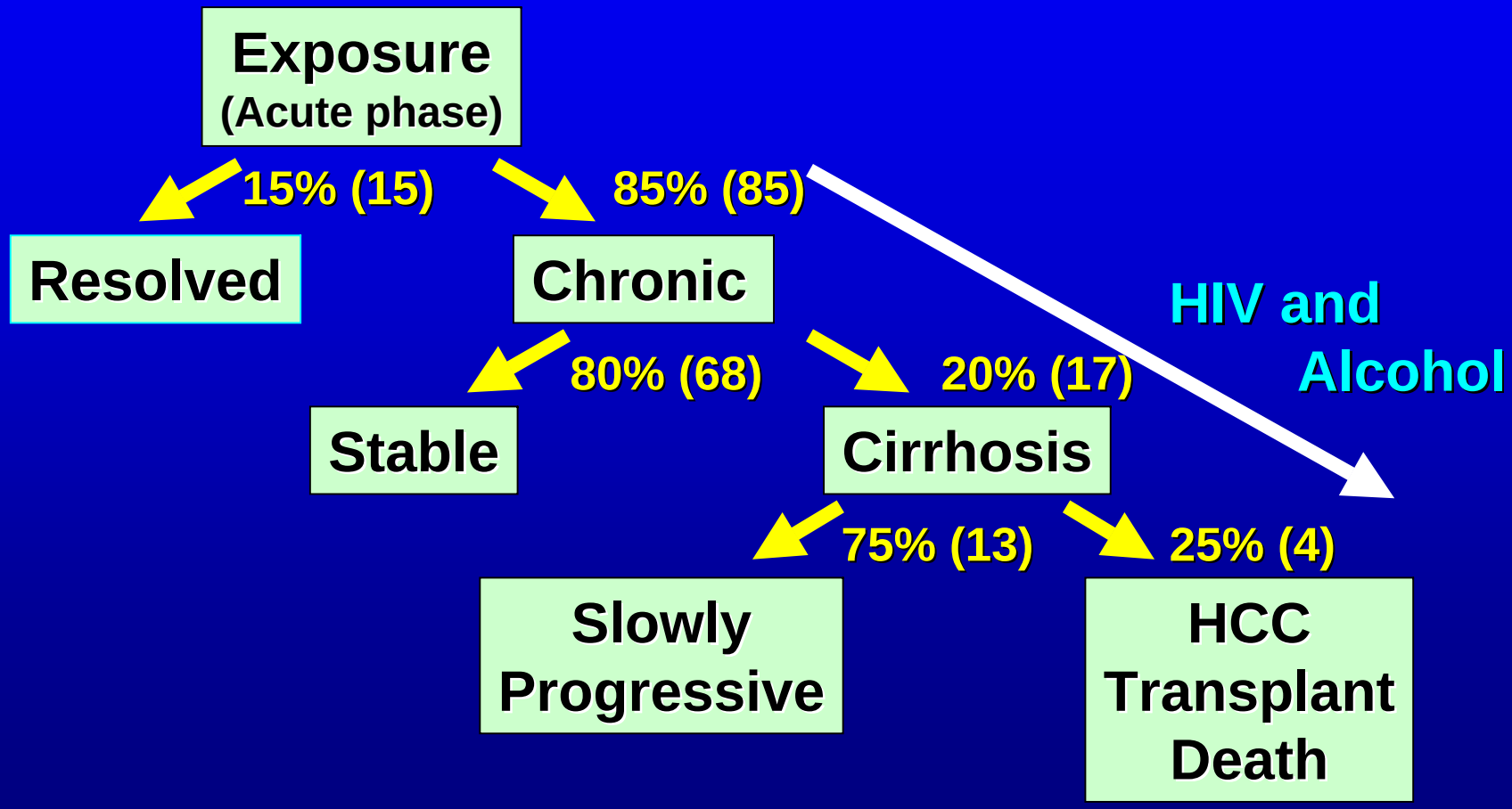
1) Incubation period
2) Natural course
3) Geographical distribution
4) Timeline trend
5) Age, Gender, Occupation, Social situation
6) Predisposing factors
7) Susceptibility & Resistance
8) Secondary attack rate
9) Modes of transmission, period of communicability

- Prevention : primary, secondary, tertiary

1 -Incubation Period

- Average 45 days
- Range 15-150 days

2 - Natural course



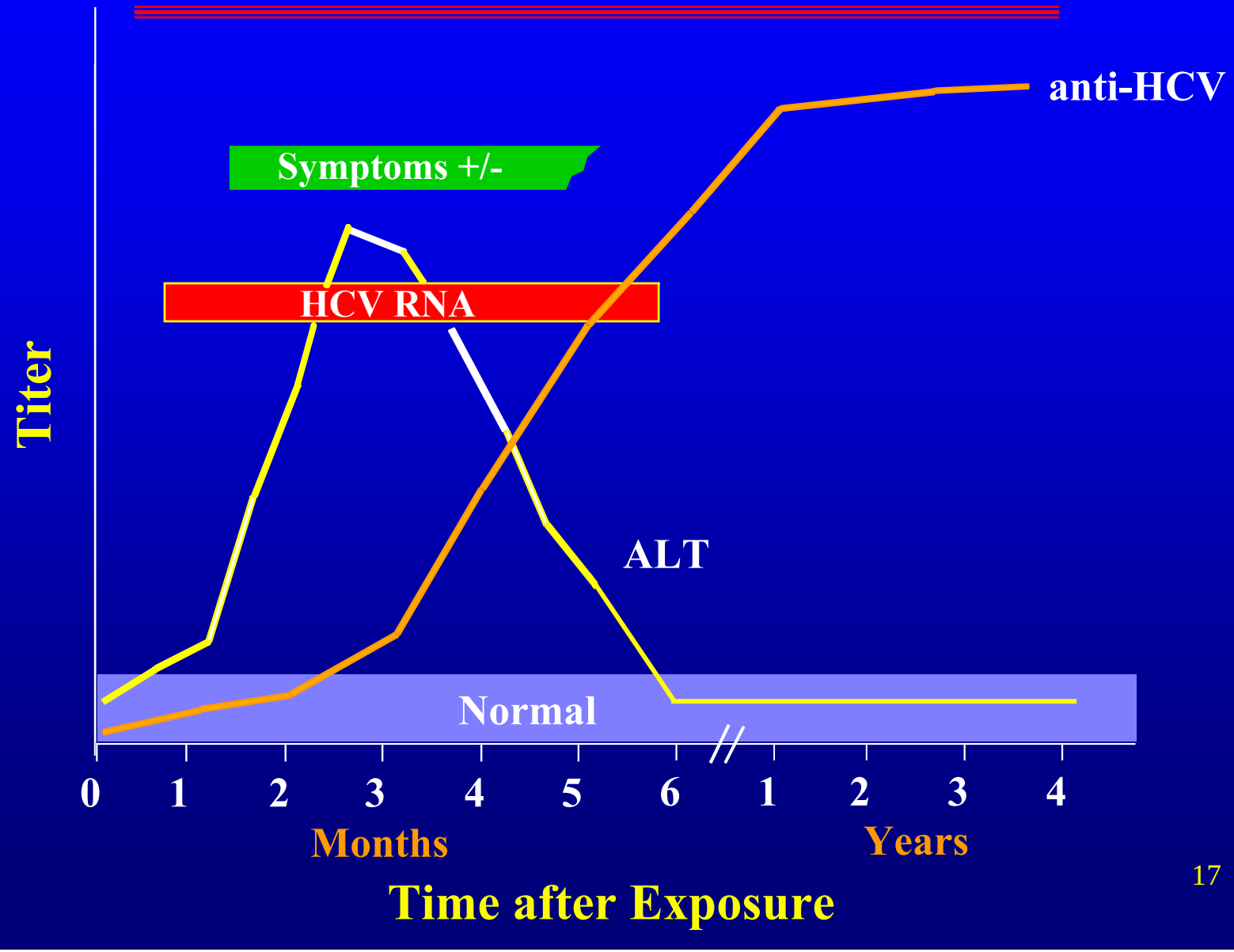
Natural History of Hepatitis C

- Asymptomatic in early stages of infection
- Morbidity and mortality rates are:
- Low during the first twenty years of the disease
- Increase after the second decade

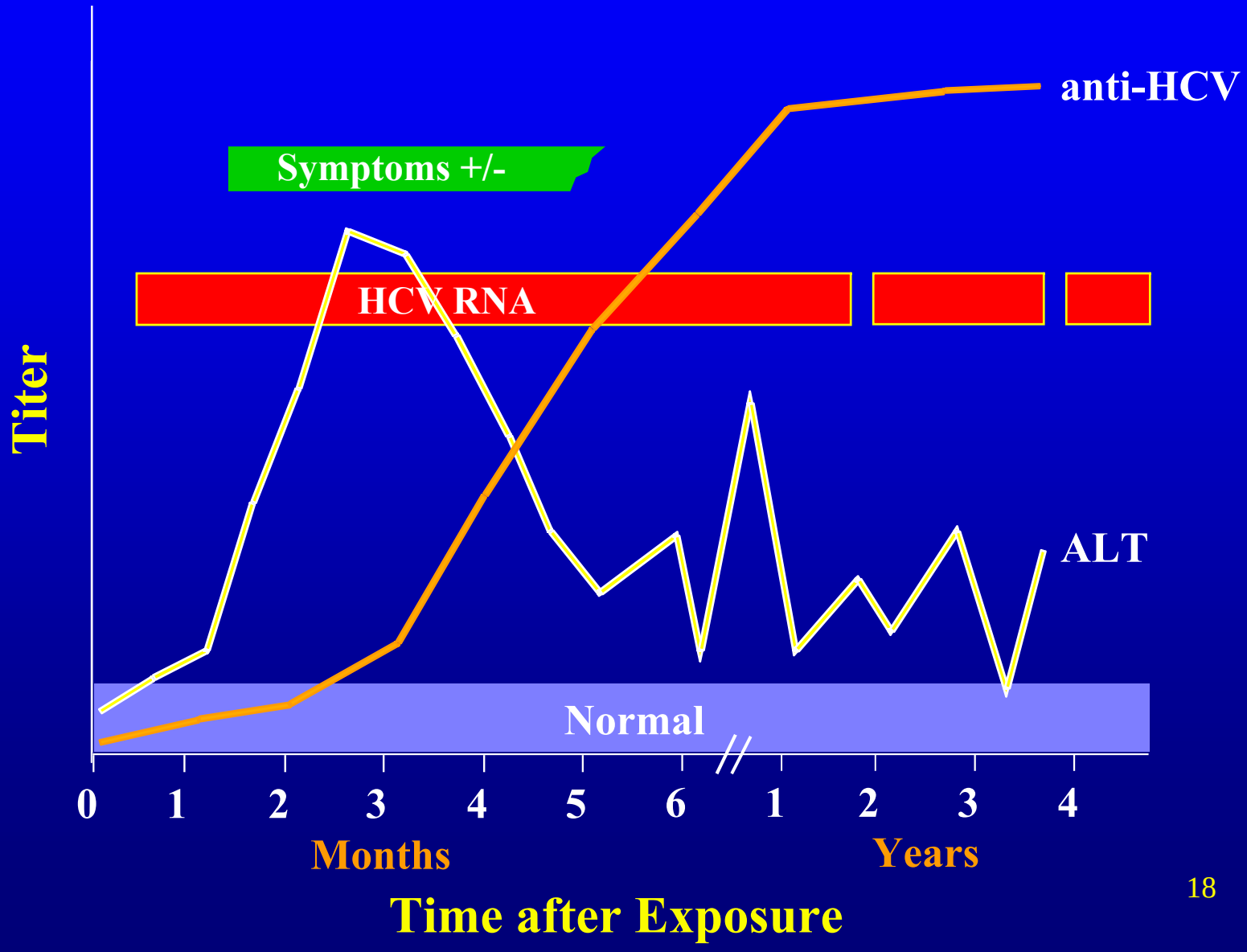
Natural course of Hepatitis C
Extrahepatic syndromes:

- Porphyria **cutanea tarda**
- Cryoglobulinemia
- Membranoproliferative **glomerulonephritis**
- Polyarteritis **nodosum**

Serologic Pattern of Acute HCV Infection with Recovery



Serologic Pattern of Acute HCV Infection with Progression to Chronic Infection

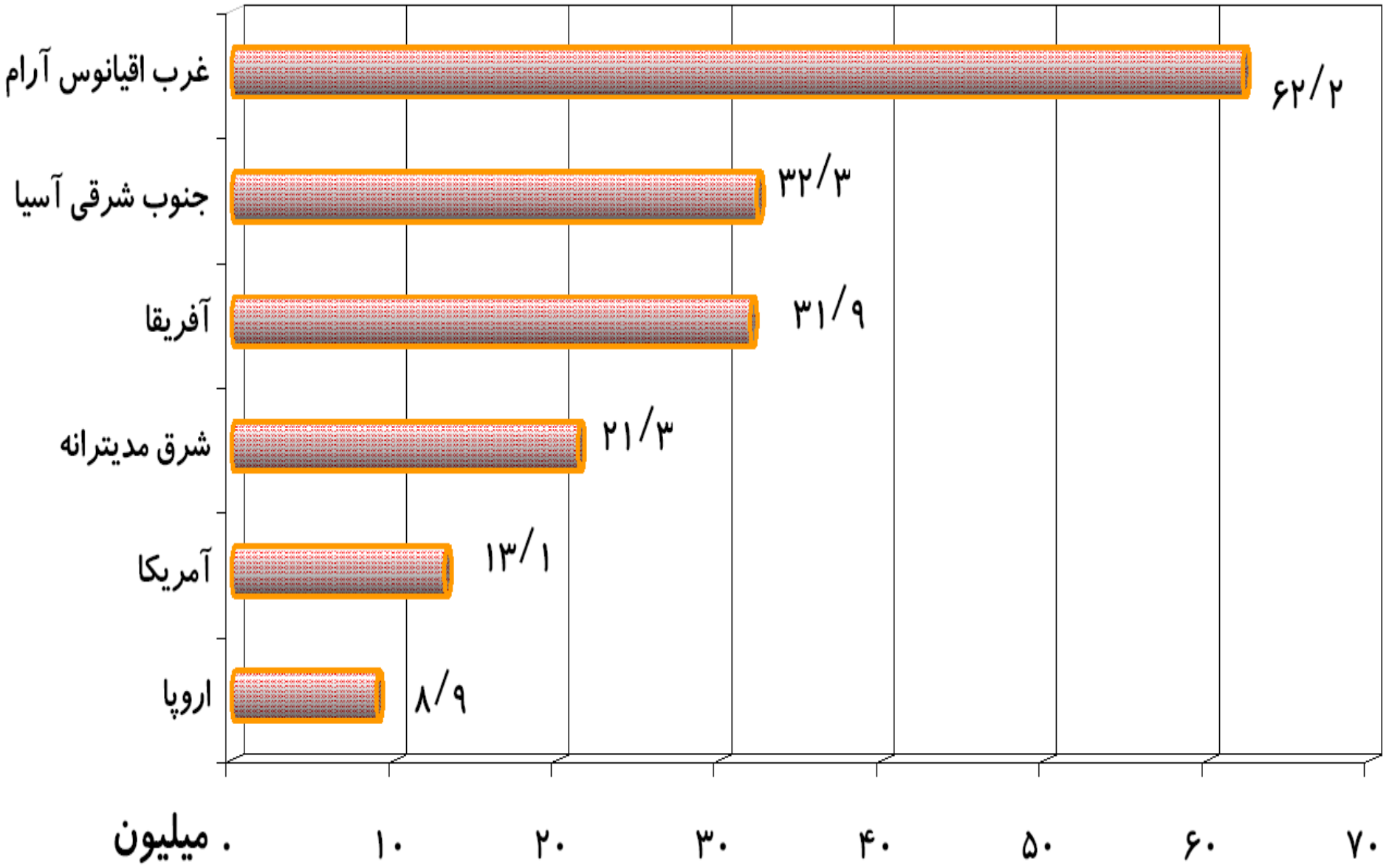


3 – Geographical distribution

170-200 Million Carriers Worldwide

World Health Organization, 1999.

3 – Geographical distribution



Hepatitis C estimated prevalence and number infected by WHO Region (WHO)

WHO Region	Total Population (Millions)	Hepatitis C prevalence Rate %	Infected Population (Millions)
Africa	602	5.3	31.9
Americas	785	1.7	13.1
Eastern Mediterranean	466	4.6	21.3
Europe	858	1.03	8.9
South-East Asia	1 500	2.15	32.3
Western Pacific	1 600	3.9	62.2
Total	**5 811**	**3.1**	**169.7**

Hepatitis C Virus Infection, IRAN

Hepatitis C seroprevalence among Intravenous Drug Users in Tehran, Iran

- Hepatitis C (HCV) is increasing worldwide including Iran
- HCV is more prevalent among intravenous drug abusers (IDU), especially if imprisoned, mostly due to needle sharing
- 518 subjects 75% prisoners; 90% males
- Overall 66% tested positive for HCV Ab
- (287 males (68%), 21 females (50.0%)

Hepatitis C Virus Infection, IRAN

Hepatitis C seroprevalence among Intravenous Drug Users in Tehran, Iran

- HCV seropositivity was higher among prisoners (78% vs. 32%)
- Older IDU (78% vs. 54%,)
- Association between HCV seropositivity and :
  - Imprisonment
  - Sharing syringes
  - Duration of intravenous drug use

Table 1- Sociodemographic characteristics and risk factors associated with HCV infection among IDUS in Tehran

Variables	Prisoner/Non-Prisoner	HCVinfection		P-Value
		Positive	Negative	
Imprisonment	Prisoner	78.1	21.9	P<0.001
	Non-Prisoner	30.6	69.4	
Gender(male)	Prisoner	81.8%	18.2%	(P<0.014)
	Non-Prisoner	30,5%	69.5%	
Frequency of injecting per day	Prisoner	3.6	3.3	0.1
	Non-Prisoner	3.7	2.9	0.08
Sharing equipment	Prisoner	82.7%	17.3%	P<0.004
	Non-Prisoner	41.7%	58.3%	P<0.009
Mean age (years)	Prisoner	36.06± 8.2	32.1± 8.3	0.015
	Non-Prisoner	33.0 ±8.6	32.1±3.8	0.014
Mean duration of injecting (years)	Prisoner	5.1±4.7	3.3 ±3.8	0.001
	Non-Prisoner	6.1±5.4	2.6±0.9	0.001

Table ٢- Prevalence of HCV infection according to sexual behavior

Sexual Behavior			HCVAb		Total
			Positive	Negative	
Heterosexual			No(%)	No(%)	No(%)
	Yes	Prisoner	136(81.9)	30(18.1)	166(100.0)
		Non-prisoner	29(34.9)	54(65.1)	83(100.0)
	No	Prisoner	135(74.6)	46(25.4)	181(100.0)
		Non-prisoner	8(21.1)	30(78.9)	38(100.0)
Homosexual					
	Yes	Prisoner	19(79.2)	5(20.8)	24(100.0)
		Non-prisoner	5(22.7)	17(77.3)	22(100.0)
	No	Prisoner	252(78.0)	71(22.0)	323(100.0)
		Non-prisoner	32(32.3)	67(67.7)	99(100.0)
Bisexual					
	Yes	Prisoner	16(80.0)	4(20.0)	20(100.0)
		Non-prisoner	6(27.3)	16(72.7)	22(100.0)
	No	Prisoner	255(78.0)	72(22.0)	327(100.0)
		Non-prisoner	31(31.3)	68(68.7)	99(100.0)

Table ٣- Risk factors associated with HCV infection

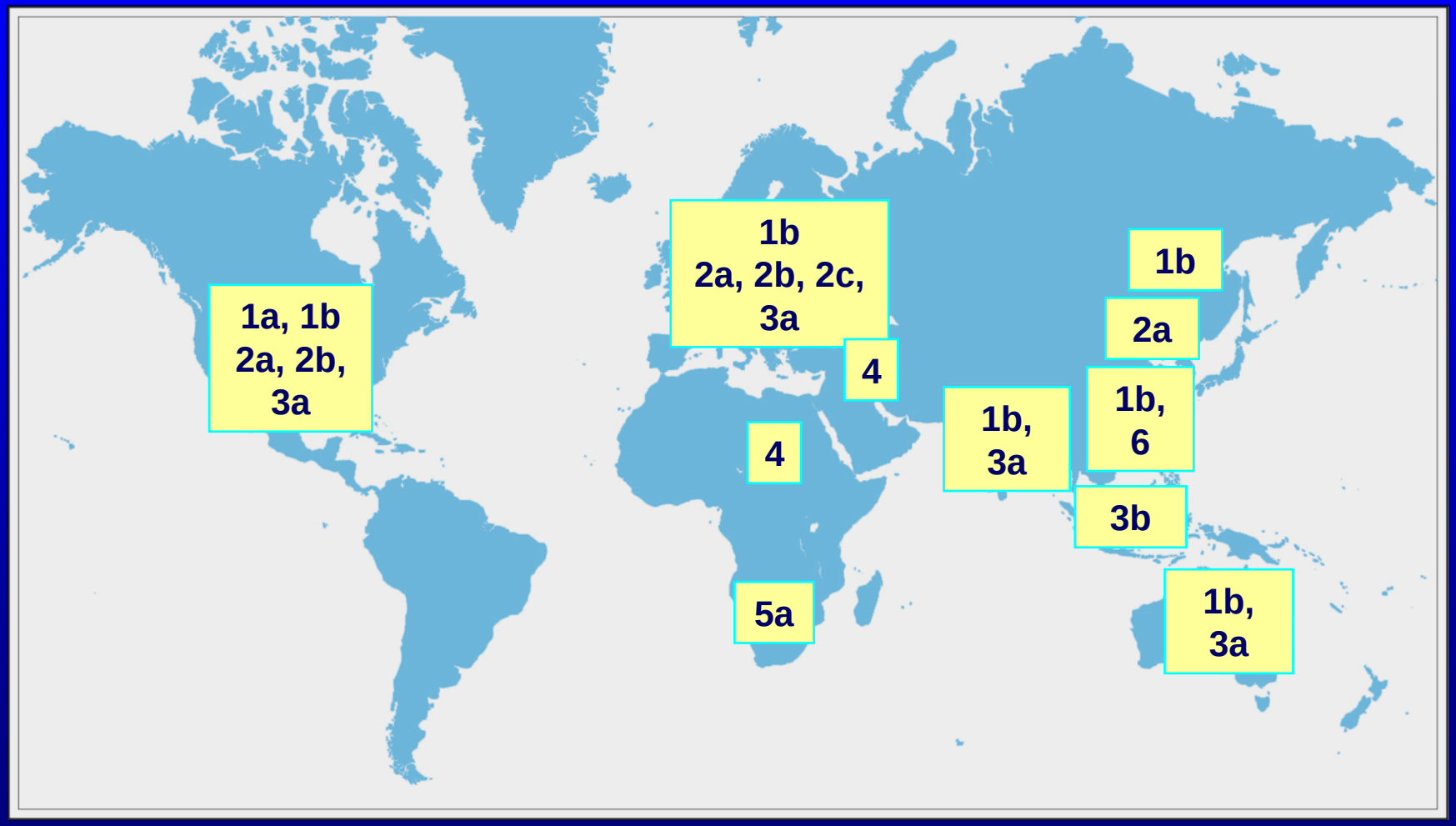
Risk Factors		HCV Ab		Total
		Positive	Negative	
Tattooing	Yes	178(71.8)	70(28.2)	248
	No	130(59.1)	90(40.9)	220
Blood Transfusion	Yes	35(60.3)	23(39.7)	58
	No	273(66.6)	137(33.4)	410
Surgery	Yes	124(66.6)	64(34.0)	188
	No	184(65.7)	96(34.3)	280
Dental procedure	Yes	257(67.1)	126(32.9)	383
	No	51(60.0)	34(40.0)	85
Cupping	Yes	64(58.7)	45(41.3)	109
	No	244(68.0)	115(32.0)	359
Ear piercing	Yes	12(52.2)	11(47.8)	23
	No	296(66.5)	149(33.5)	445
Heterosexual	Yes	165(66.3)	84(33.7)	249
	No	143(65.3)	76(34.7)	219
Homosexual	Yes	24(52.2)	22(47.8)	46
	No	284(67.3)	138(32.7)	422
Bisexual	Yes	22(52.4)	20(47.6)	42
	No	286(67.1)	140(32.9)	426
H/O Jaundice	Yes	54(65.1)	29(34.9)	83
	No	254(66.0)	131(34.0)	385

نتایج بعضی از مطالعات در ایران

- ۳٪ اهداءکنندگان خون در تهران
- در ۲۱٪ مبتلایان به بتاتالاسمی ماژور
- ۸۰٪ ساکنین اردوگاه پیربنو شیراز

مهم ترین و شایع‌ترین علّت هپاتیت مزمن و سیروز کبدی، نزد بیماران ایرانی مبتلا به هموفیلی، تالاسمی و نارسایی کلیه (دیالیزی) محسوب می‌شود

HCV Infection: Worldwide Genotype Distribution



Hepatitis C virus genotypes in Iran: a preliminary study.

- Serum samples from 21 HCV infected
- Type I/1a in 7 cases,
- Type II/1b in 3 cases and
- Type V/3a in 4 patients. 1 sample disclosed Type 4.

East Mediterr Health J. 2000 Mar-May;6(2-3):372-7.Zali MR, Mayumi M, Raoufi M, Nowroozi A.

Molecular epidemiology of hepatitis C virus in Iran

- 125 Iranian patients by phylogenetic analysis
- Subtypes 1a and 3a were predominant accounting for 47 and 36%,
- Subtypes 1b and 4 accounted for 8 and 7%.
- This subtype distribution differs from that of Turkey and Pakistan, where subtypes 1b and 3a dominate
- And also from neighboring Arabic countries where subtype 4 is the prevalent genotype.

J Med Virol. 2004 Oct;74(2):246-52.Samimi-Rad K, Nategh R, Malekzadeh R, Norder H, Magnius L.

Molecular epidemiology of hepatitis C virus in Iran

- The Iranian 1a and 3a strains indigenous to Iran.
- Subtype 1a was frequent in South Iran (70%), while 3a was more prevalent in North-West Iran (83%),
- Patients infected by blood products had more frequently subtype 1a (57%),

  while younger drug users had more frequently subtype 3a (54%).

J Med Virol. 2004 Oct;74(2):246-52.Samimi-Rad K, Nategh R, Malekzadeh R, Norder H, Magnius L.

Molecular epidemiology of hepatitis C virus in Iran

- **Genotype 4 was over-represented among haemodialysis patients in Tehran**
- **One strain, most similar to genotype 5,**

J Med Virol. 2004 Oct;74(2):246-52.Samimi-Rad K, Nategh R, Malekzadeh R, Norder H, Magnius L.

Seruprevalence of Hepatitis C virus in Iran:

- Iran 0.3%
- Sistan 1.5%
- Fars 0.2%

با زندانی شدن افراد در ایران خطر ابتلاء به این بیماری و میزان مثبت شدن آزمون سرمی مربوطه به ۱۱۸۱ برابر، افزوده می‌گردد

- The most important cause of chronic hepatitis and cirrhosis in haemophilics, thalacemics, renal failure & specially HIV infection

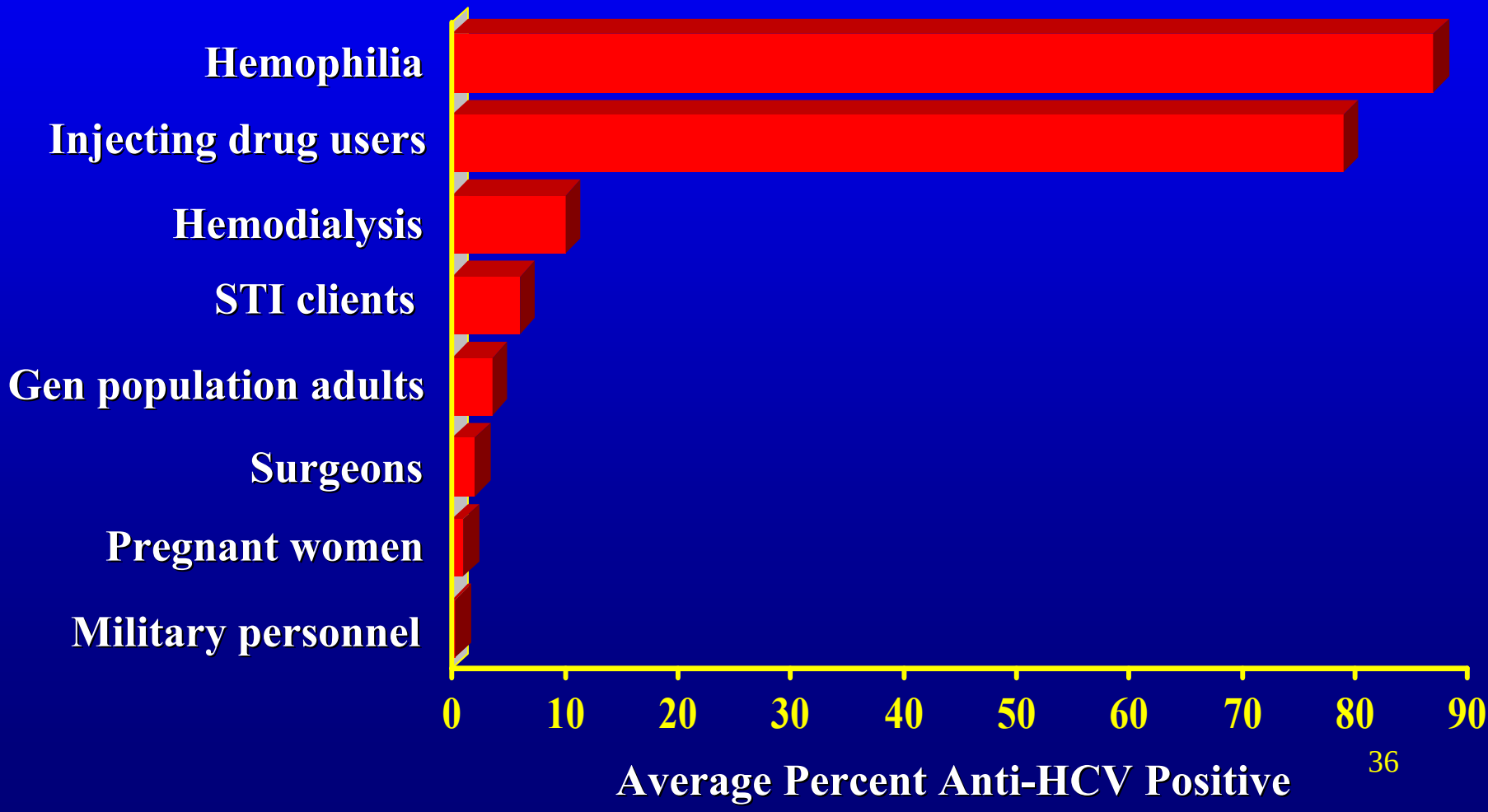
East Mediterr Health J. 2000 Mar-May;6(2-3):372-7.Zali MR, Mayumi M, Raoufi M, Nowroozi A.

4 - Timeline trend

- Pandemics
- Epidemics
- Outbreaks
- Seasonality

5 – Age, Gender, Occupation, Social situation

HCV Prevalence by Selected Groups USA



تاثیر سن، جنس، شغل و موقعیت اجتماعی

- معمولا در سنین بالاتر، عارض میشود
- احتمال پیشرفت آن در جنس مذکر بیشتر است
- کارکنان حرفه‌های پزشکی تا حدودی در معرض خطر بیشتری هستند

6 – Predisposing factors

Factors Associated with Disease Progression in HCV Infected Patients

- Age > 50 years
- Duration of infection
- Male gender
- Iron overload
- Alcohol
- Coinfection with HBV
- Coinfection with HIV

Not associated:

- HCV "viral load"
- HCV genotype
- Serum ALT
- ? Smoking

HCV/HIV Co-infection

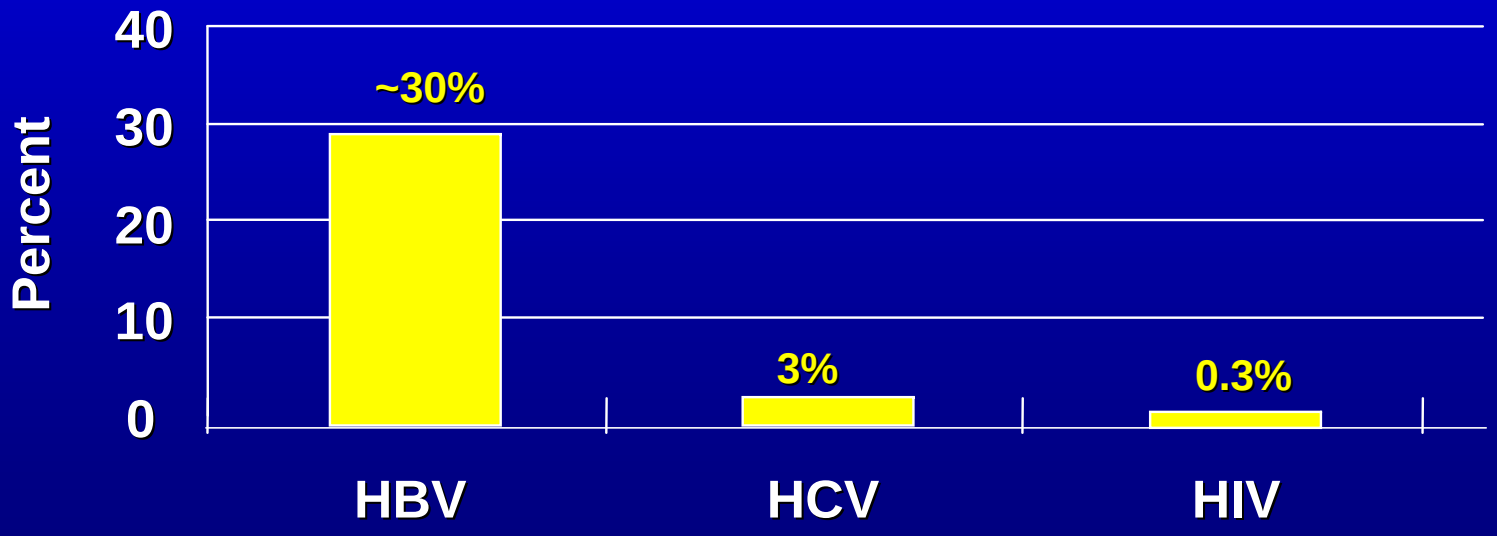
- HIV both accelerates and increases risk of HCV progression
- Liver disease is increasing as a cause of death in HIV+ persons
- Impact of HCV on HIV continues to be investigated- impact
- may be greater in post- HAART era

7 – Susceptibility and Resistance

- Susceptibility is general
- The degree of immunity following infection is not known
- Repeated infections have been demonstrated in an experimental chimpanzee model

8 – Secondary attack rate
HCV and Healthcare Workers

Risk of Transmission by Single Needle Stick to Susceptible Healthcare Workers



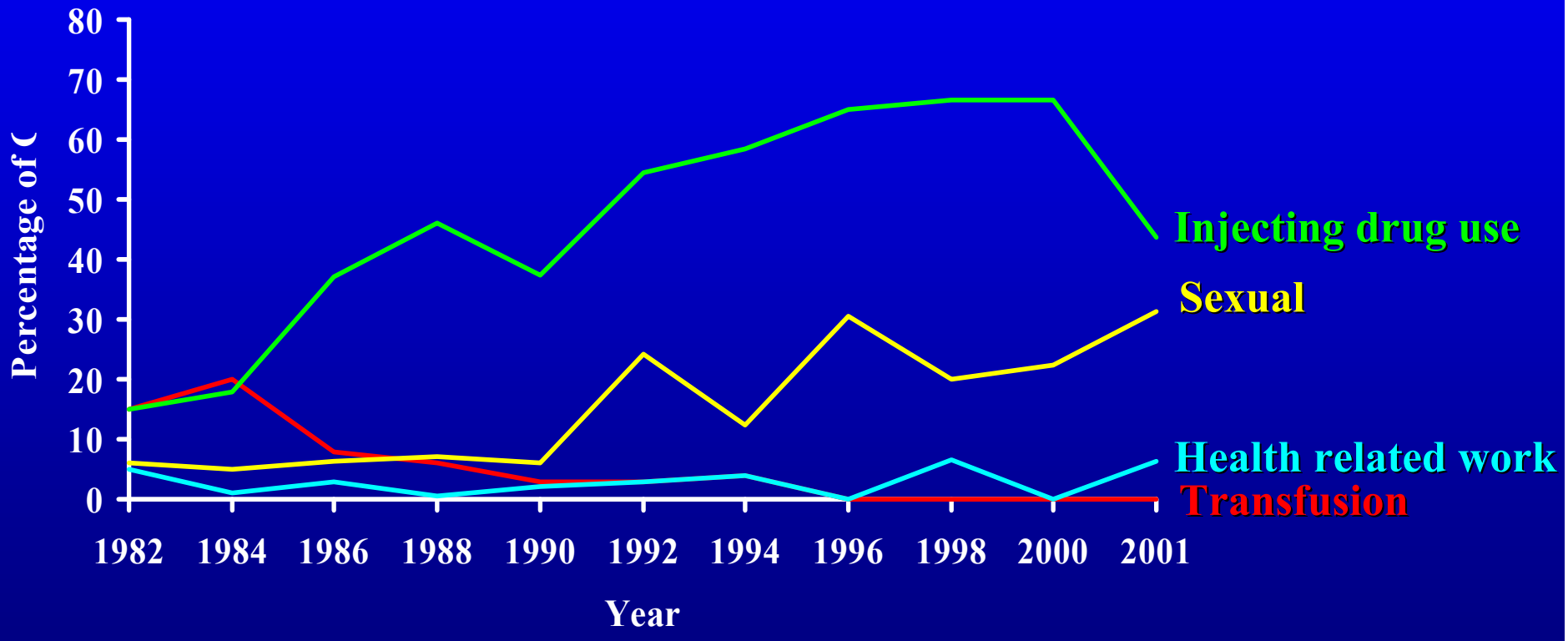
میزان حملات ثانویه

- کمتر از نوع B است
- در تماس‌های خانوادگی کمتر است
- در تماس پریناتال، ۶٪ است
- در مادران HIV+ ، ۱۷٪ است

9 - Transmission

- Injecting drug use
- Transfusion, transplant from infected donor
- Occupational exposure to blood
  - Mostly needle sticks
- Iatrogenic (unsafe injections)
- Birth to HCV-infected mother
- Sex with infected partner
  - Multiple sex partners

Reported Cases of Acute Hepatitis C by Selected Risk Factors, USA



Injecting Drug Use and HCV Transmission

- **Highly** efficient
- **Rapidly acquired after initiation**
  - 30% prevalence after 3 years
  - >50% after 5 years
- **4 times > HIV**

Occupational Transmission of HCV

- Inefficient
- Average incidence 3%
- Blood splash to eye
- Prevalence 1-2% among HCWs
  - Lower than adults in the general population
  - 10 times lower than for HBV infection

Perinatal Transmission of HCV

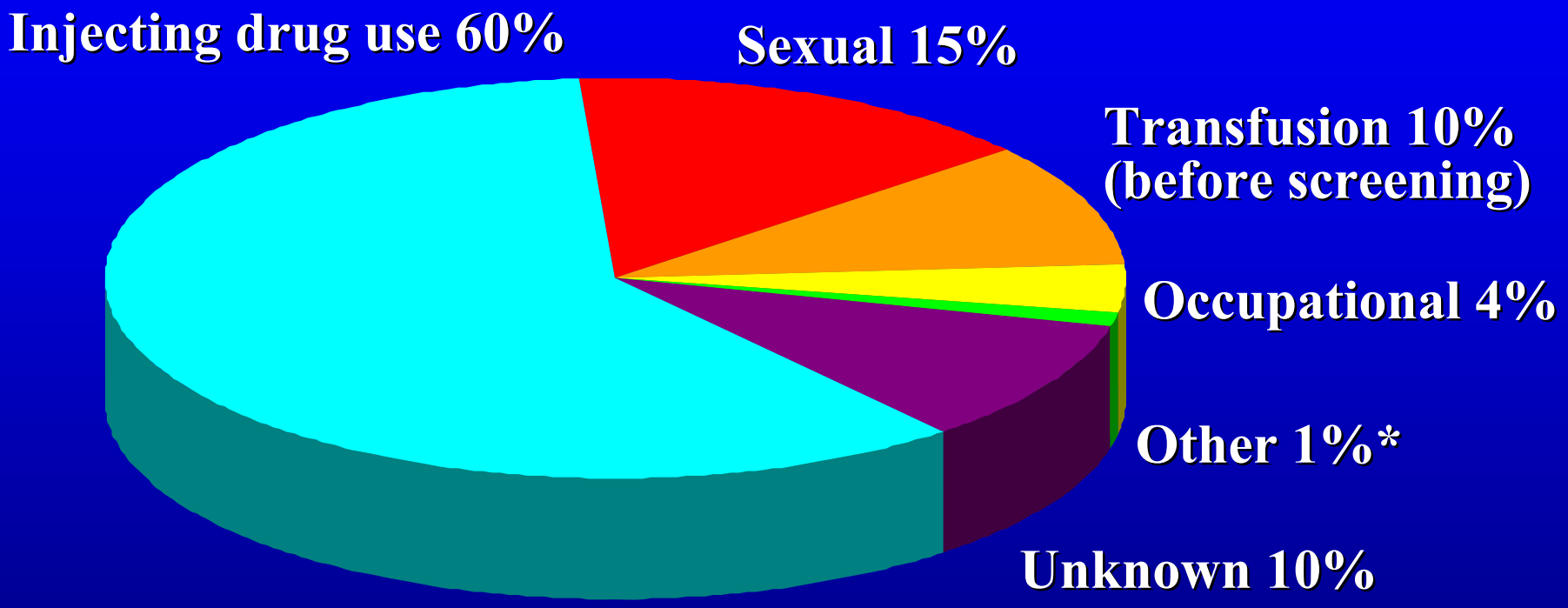
- From women HCV-RNA positive at delivery
  - Average rate of infection 6%
  - Higher (17%) if woman co-infected with HIV
- No association with :
  - Delivery method
  - Breastfeeding

Household Transmission of HCV

- Rare but not absent
- Could occur through percutaneous/mucosal exposures to blood
  - Theoretically through sharing of contaminated personal articles (razors, toothbrushes)

احتمال انتقال این ویروس بین همسران یا زوج‌های جنسی، به ازای هر سال تماس، کمتر از ۱٪ برآورد گردیده (۲)

Sources of Infection for Persons With Hepatitis C



* Nosocomial; iatrogenic; perinatal

Source: Centers for Disease Control and Prevention

هپاتیت بعد از انتقال خون (PTH)

- تقریباً از هر یک هزار نفری که خون دریافت می‌نموده‌اند ۱۰-۵ نفر، دچار این بیماری می‌شده‌اند
- امروزه به کمتر از ۱ نفر در هر صدهزار نفر تا یک نفر در هر یک میلیون و ششصدهزارنفر، کاهش یافته است

Prevention and Control

Prevention and Control

- **Primary Prevention:**
  - Prevention of disease in “well” individuals
- **Secondary Prevention:**
  - Identification and intervention in early stages of disease
- **Tertiary Prevention:**
  - Prevention of further deterioration, reduction in complications

1 – Primary Prevention:
Reduce or Eliminate Risks for Acquiring HCV Infection

- Screen and test donors
- Virus inactivation of plasma-derived products
- Counseling
- Safe injection

HCV Testing Routinely Recommended

- Ever injected illegal drugs
- Received clotting factors made before 1987
- Received blood/organs before 1992
- Ever on chronic hemodialysis
- Evidence of liver disease
- HCWs after needle stick/mucosal exposures
- Children born to HCV-positive women

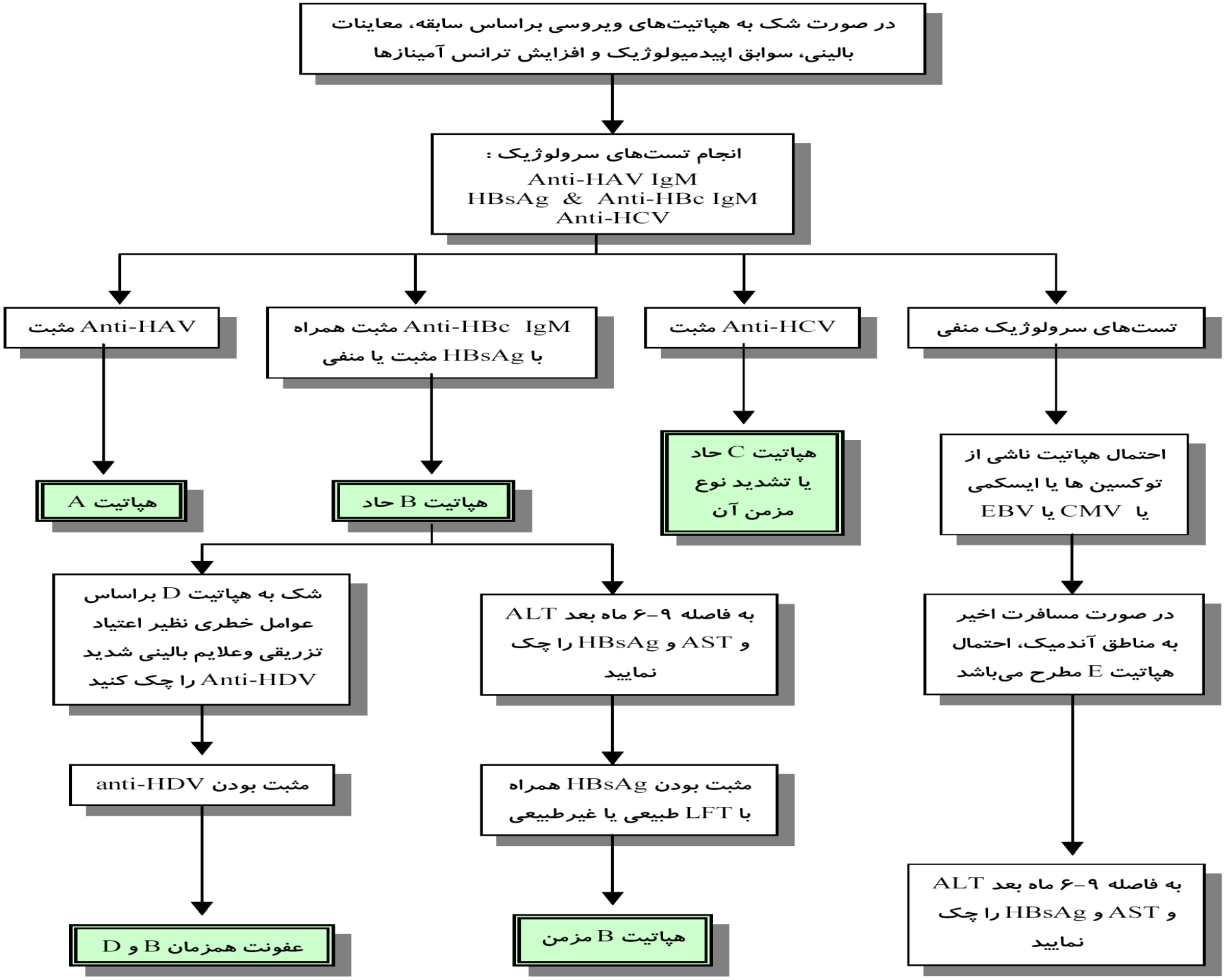
Postexposure Management for HCV

- IG, antivirals not recommended for prophylaxis
- Follow-up
  - Test source for anti-HCV
  - Test worker if source anti-HCV positive
    - Anti-HCV and ALT at baseline and 4-6 months later
    - For earlier diagnosis, HCV RNA at 4-6 weeks
  - Confirm all anti-HCV results with RIBA
- Medical evaluation and management

Mother-to-Infant Transmission of HCV

- No need to avoid pregnancy or breastfeeding
- No need to determine mode of delivery based on HCV infection status
- Test infants born to HCV-positive women
  - –>15-18 months old

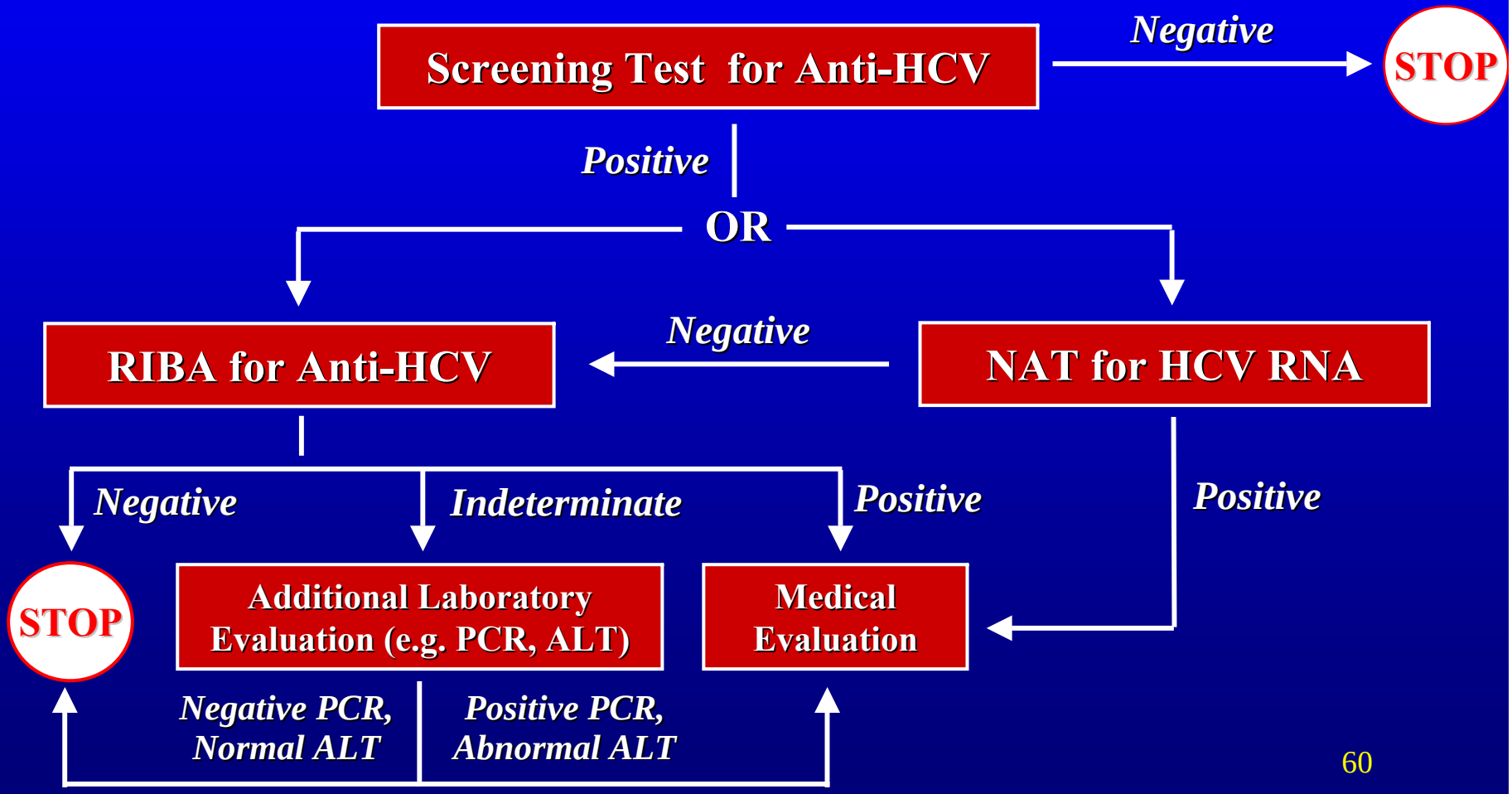
2 - Secondary Prevention:


در صورت شک به هپاتیت‌های ویروسی براساس سابقه، معاینات بالینی، سوابق اپیدمیولوژیک و افزایش ترانس آمینازها
انجام تست‌های سرولوژیک :
Anti-HAV IgM
HBsAg & Anti-HBc IgM
Anti-HCV
Anti-HAV مثبت
Anti-HBc IgM مثبت همراه با HBsAg مثبت یا منفی
Anti-HCV مثبت
تست‌های سرولوژیک منفی
هپاتیت A
هپاتیت B حاد
هپاتیت C حاد یا تشدید نوع مزمن آن
احتمال هپاتیت ناشی از توکسین ها یا ایسکمی یا CMV یا EBV
شک به هپاتیت D براساس عوامل خطری نظیر اعتیاد تزریقی وعلایم بالینی شدید Anti-HDV را چک کنید
به فاصله ۹-۶ ماه بعد ALT و AST و HBsAg را چک نمایید
در صورت مسافرت اخیر به مناطق آندمیک، احتمال هپاتیت E مطرح می‌باشد
مثبت بودن anti-HDV
مثبت بودن HBsAg همراه با LFT طبیعی یا غیرطبیعی
به فاصله ۹-۶ ماه بعد ALT و AST و HBsAg را چک نمایید
عفونت همزمان B و D
هپاتیت B مزمن

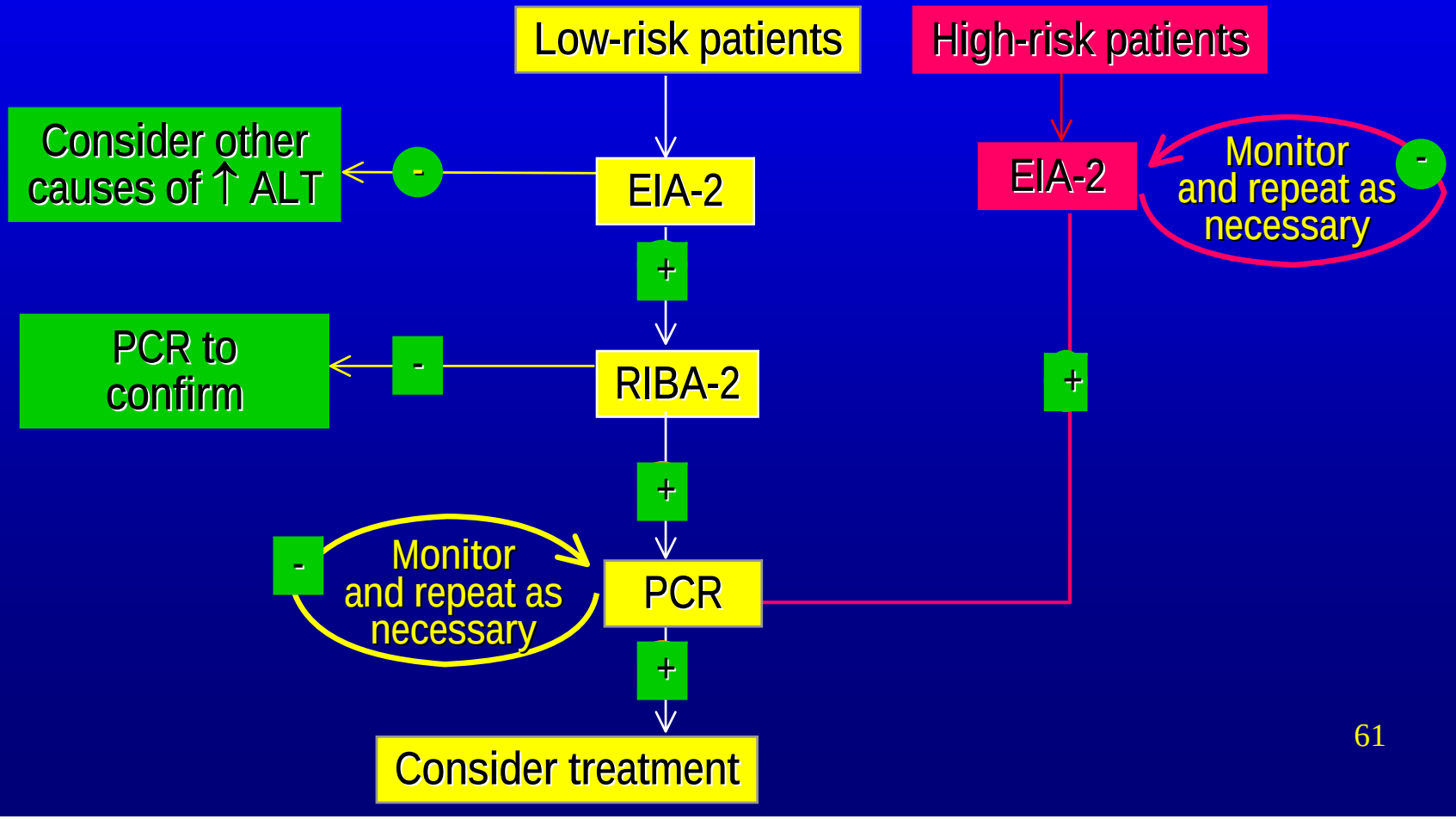
Treatment

- Weekly pegylated interferon with daily oral Ribavirin for 24-48 weeks;
- Side effects: often very debilitating
  - Flu-like syndrome, hair-loss, thyroid dysfunction
  - Depression and other psychiatric disorders
  - Anemia, retinal bleeding

HCV Infection Testing Algorithm for Diagnosis of Asymptomatic Persons



Diagnostic Algorithm for HCV:
Modified NIH Algorithm



Laboratory Tests to Diagnose HCV

- **Hepatitis C antibody (EIA-2 or EIA-3)**
  - 95% sensitivity and specificity
  - Immunosuppressed patients may exhibit false negative
- **RIBA-2**
  - Confirmatory assay
  - Has become less relevant
- **PCR**
  - Always necessary to confirm ongoing HCV infection
  - > 90% sensitive and specific

Is Liver Biopsy Important?

- Establishes disease stage and prognosis
- HCC screen for patients with cirrhosis
- Affects management decisions
  - Not needed to confirm diagnosis
  - Not required to initiate therapy
  - Some patients (e.g. Genotype 2 or 3) may not need liver biopsy prior to treatment

Does ALT Still Matter?

Not as much as it used to, but it still does

- **Some correlation with degree of activity**
- **Normal ALT patients have milder histology, but not always**
- **Degree of inflammatory activity correlates with risk of progressive fibrosis**
- **Still useful to monitor during therapy**

Evaluating the Hepatitis Patient

- **HCV EIA for diagnosis and HCV RNA testing to confirm chronic infection**
  - **ALT and HCV load are not reliable indicators of disease severity**
- **Liver biopsy to stage liver disease**
  - **Predicts prognosis and influences treatment decisions**
  - **Not "required" to treat HCV infection**
- **Hepatitis A and B screening and vaccine**

Hepatitis C Treatment: Objectives

- **Viral eradication**
  - Persistent undetectable plasma HCV-RNA 24 weeks post treatment
- **Histologic and clinical outcomes**
  - Delay fibrosis and progression to cirrhosis
  - Prevent hepatic decompensation and hepatocellular carcinoma

3 – Tertiary Prevention:

Medical Evaluation and Management for Chronic HCV Infection

- Assess for biochemical evidence of CLD
- Assess for severity of disease and possible treatment, according to current practice guidelines
  - 40-50% sustained response to antiviral combination therapy (peg interferon, ribavirin)
  - Vaccinate against hepatitis A
- Counsel to reduce further harm to liver
  - Limit or abstain from alcohol

Warning Signs of Advanced Fibrosis

- AST > ALT
- Thrombocytopenia
- Leukopenia
- Hypoalbuminemia
- Reversed albumin to globulin ratio
- Elevated prothrombin time

Hepatitis C Treatment: Objectives

- **Viral eradication**
  - **Persistent undetectable plasma HCV-RNA 24 weeks post treatment**
- **Histologic and clinical outcomes**
  - **Delay fibrosis and progression to cirrhosis**
  - **Prevent hepatic decompensation and hepatocellular carcinoma**

Pre-Treatment Laboratory Evaluation

- **Tests for Monitoring Therapy**
  - CBC with differential, platelets, renal function, glucose, TSH
- **Diagnostic Tests**
  - ALT, AST, Anti HCV Antibody (EIA), Genotype, Quantitative HCV RNA assay
- **Liver Function Tests**
  - Bilirubin, Albumin, PTT, PT (INR)

Patient Selection Criteria for Treatment of Chronic Hepatitis C With Interferon Alfa-2b Plus Ribavirin

- ≥ 18 years of age
- HCV EIA and RNA positive
- Liver biopsy consistent with diagnosis of chronic hepatitis (*not required*)
- No active autoimmune disease
- No hepatic encephalopathy, variceal bleeding, ascites, or other clinical signs of decompensation
- Exceptions to all of the above

Labs – The Basics

- **Tests for Monitoring Therapy**
  - **CBC with diff, platelets, renal function, glucose, TSH**
- **Diagnostic Tests**
  - **ALT & AST, Anti HCV Antibody (EIA), Genotype, Quantitative HCV RNA assay (PCR more sensitive than bDNA)**
- **Liver Function Tests**
  - **Bilirubin, Albumin, PTT, PT (INR)**

Liver Transplantation and Hepatitis C

- Patients with decompensated liver disease should be considered
- Recurrence of HCV infection $\geq$ 90% in liver grafts
- Level of viremia increases dramatically with post-transplant immunosuppression
- Patient and graft survival rates are good in short term
- HIV + patients routinely excluded

Hepatitis C Treatment Options

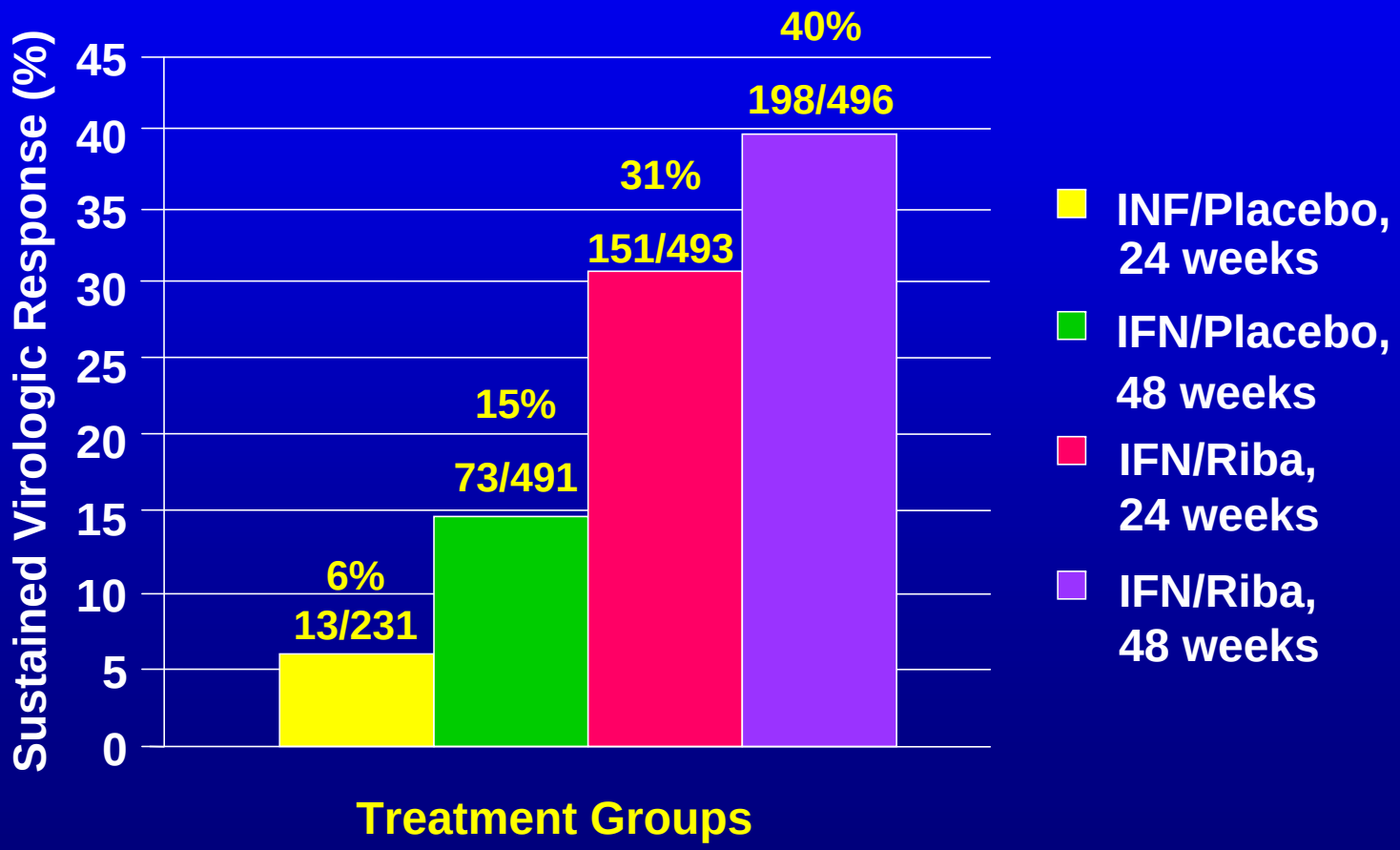
Current Options

- **Interferon alfa monotherapy**
  - **Interferon alfa-2b**
  - **Interferon alfa-2a**
  - **Interferon alfacon-1**
  - **Pegylated interferon alfa-2b**
- **Interferon alfa-2b plus ribavirin**

Under Investigation

- **Pegylated Interferon alfa-2a monotherapy**
- **Pegylated Interferon alfa-2b plus ribavirin**
- **Pegylated Interferon alfa-2a plus ribavirin**

IFN Alfa-2b and Ribavirin Therapy In Previously Untreated Patients



Hepatitis C Treatment Options

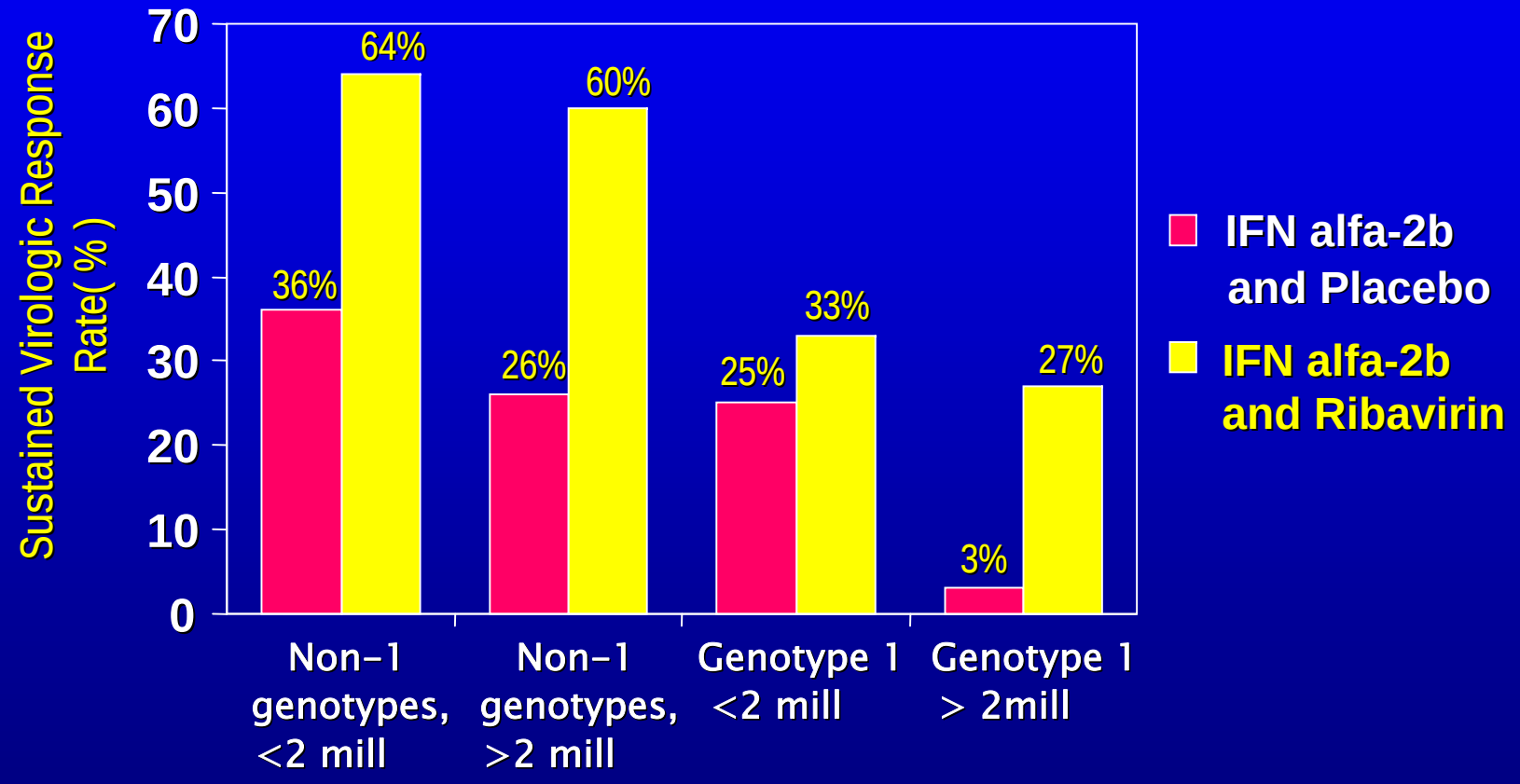
Monotherapy

- Interferon alfa-2a; Interferon alfa-2b; Interferon alfacon-1
- Pegylated interferon alfa-2a and alfa-2b

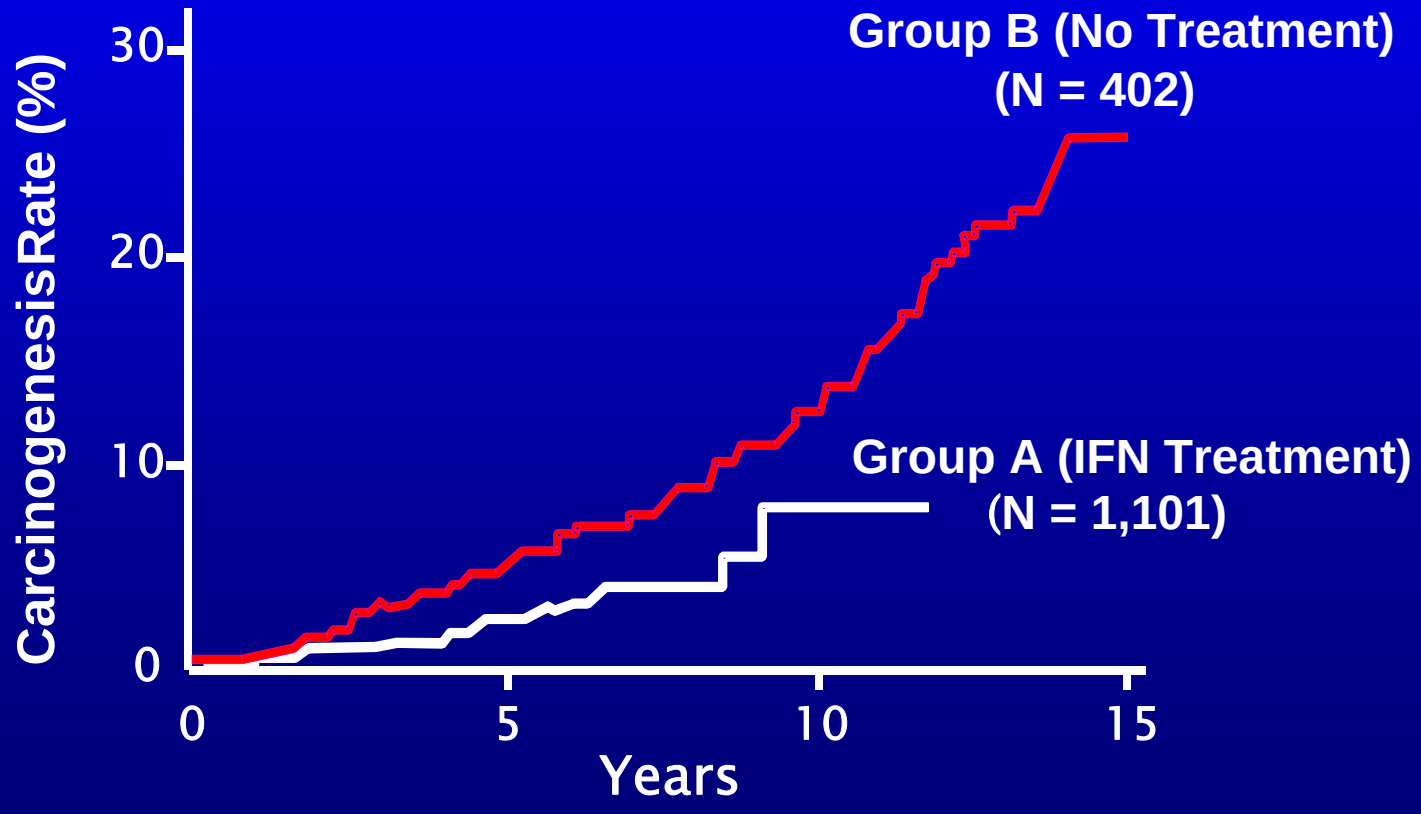
Combination Therapy

- Interferon alfa-2b plus ribavirin
- Pegylated Interferon alfa-2a plus ribavirin
- Pegylated Interferon alfa-2b plus ribavirin

IFN Alfa-2b and Ribavirin in Previously Untreated Patients: Effect of Viral Load + Genotype



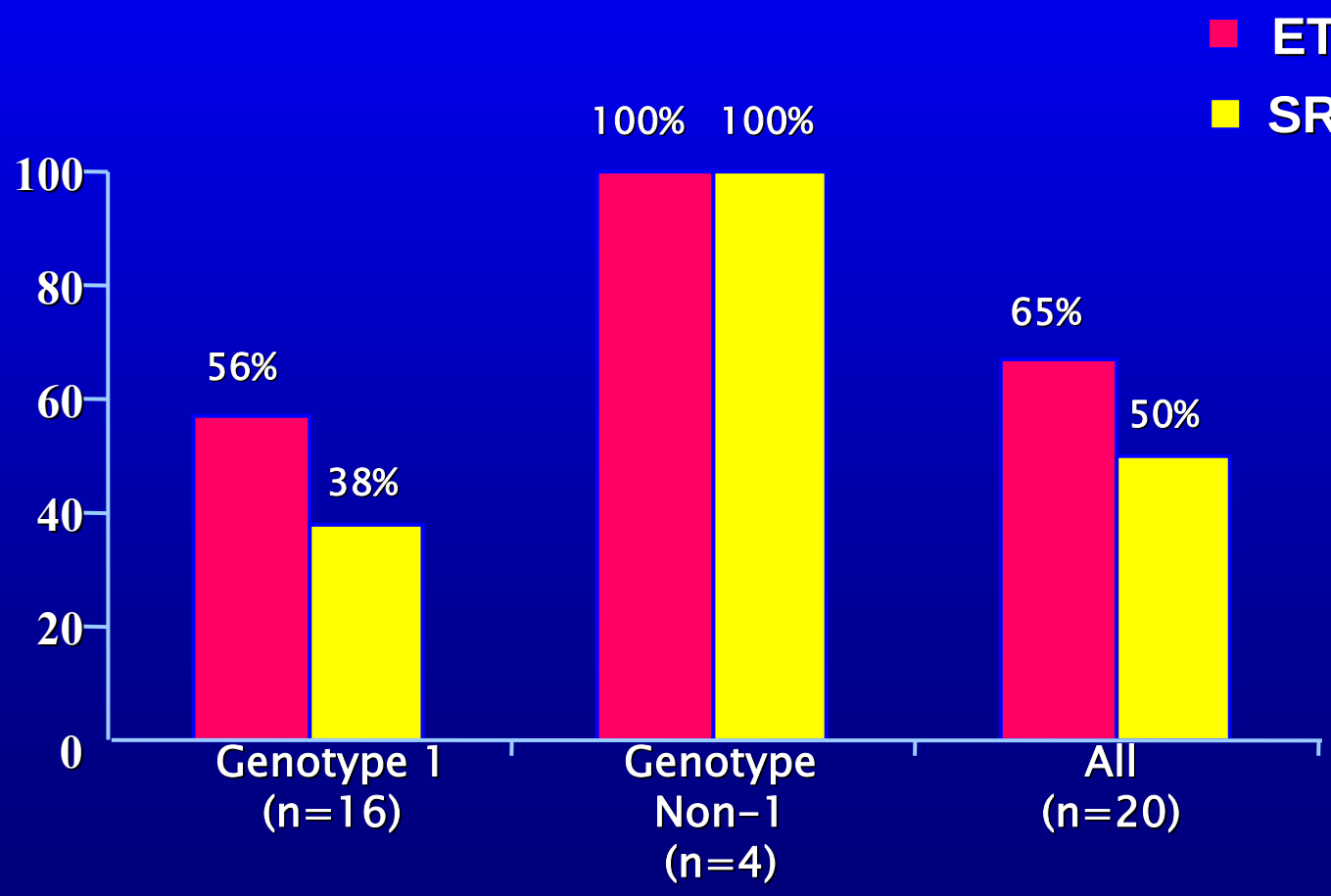
Effects of Interferon on Hepatocellular Carcinoma



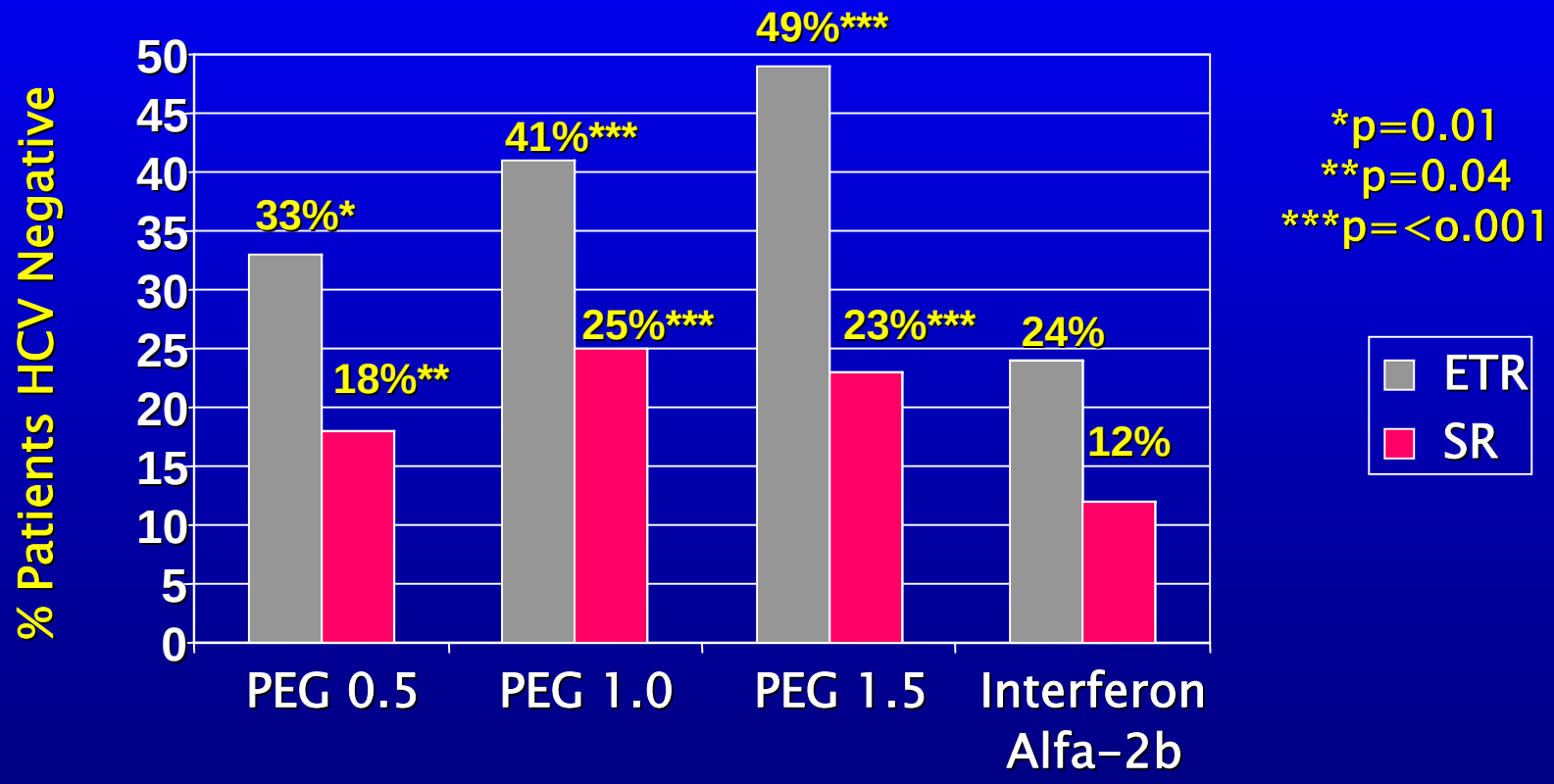
Why Pegylate Proteins?

- Improve efficacy and the therapeutic index
- Maintain therapeutic concentrations
  - Optimize absorption
  - Optimize distribution
  - Reduce rate of clearance
  - Decrease proteolysis
- Decrease immunogenicity

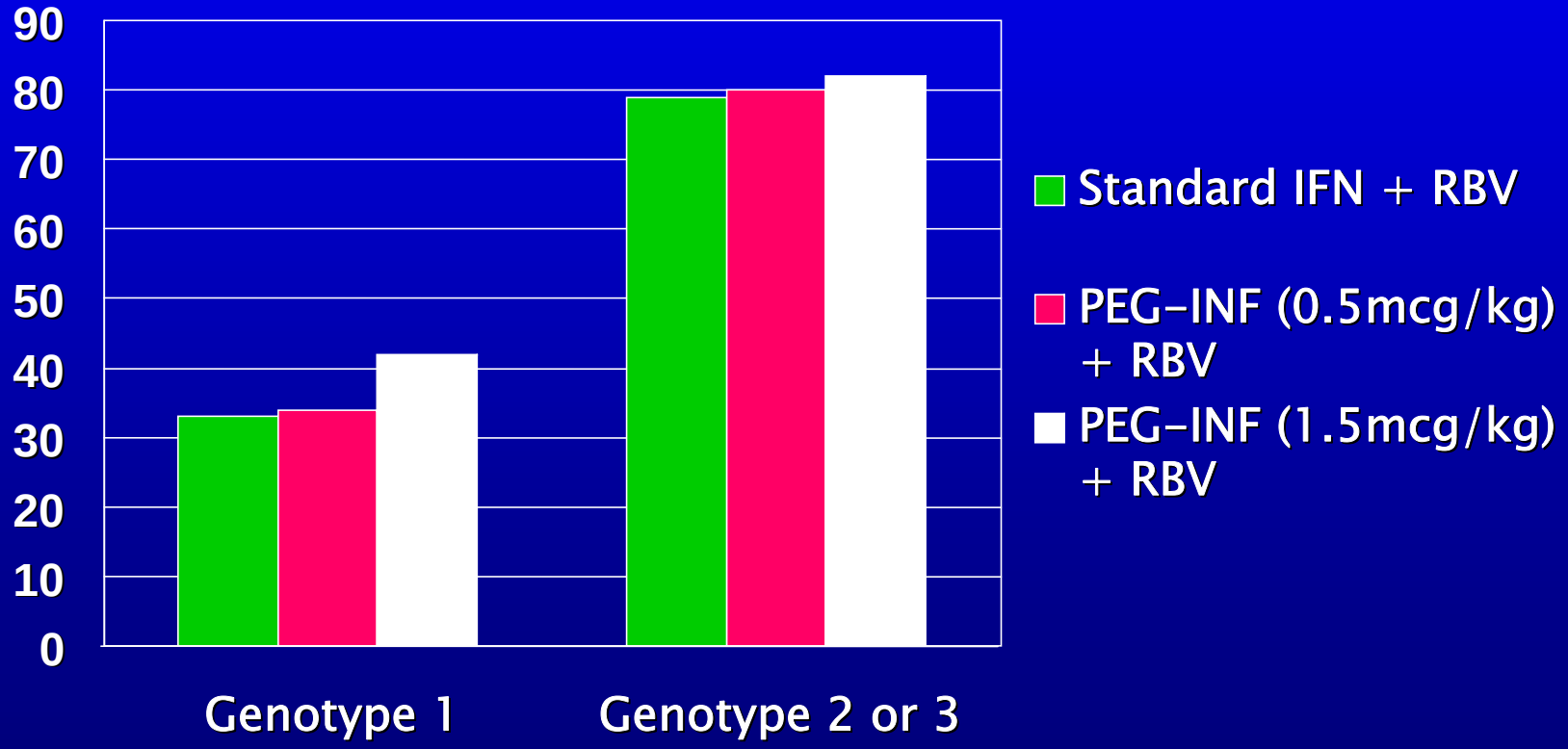
Peg-Interferon Alfa-2a + Ribavirin Virologic Response by Genotype



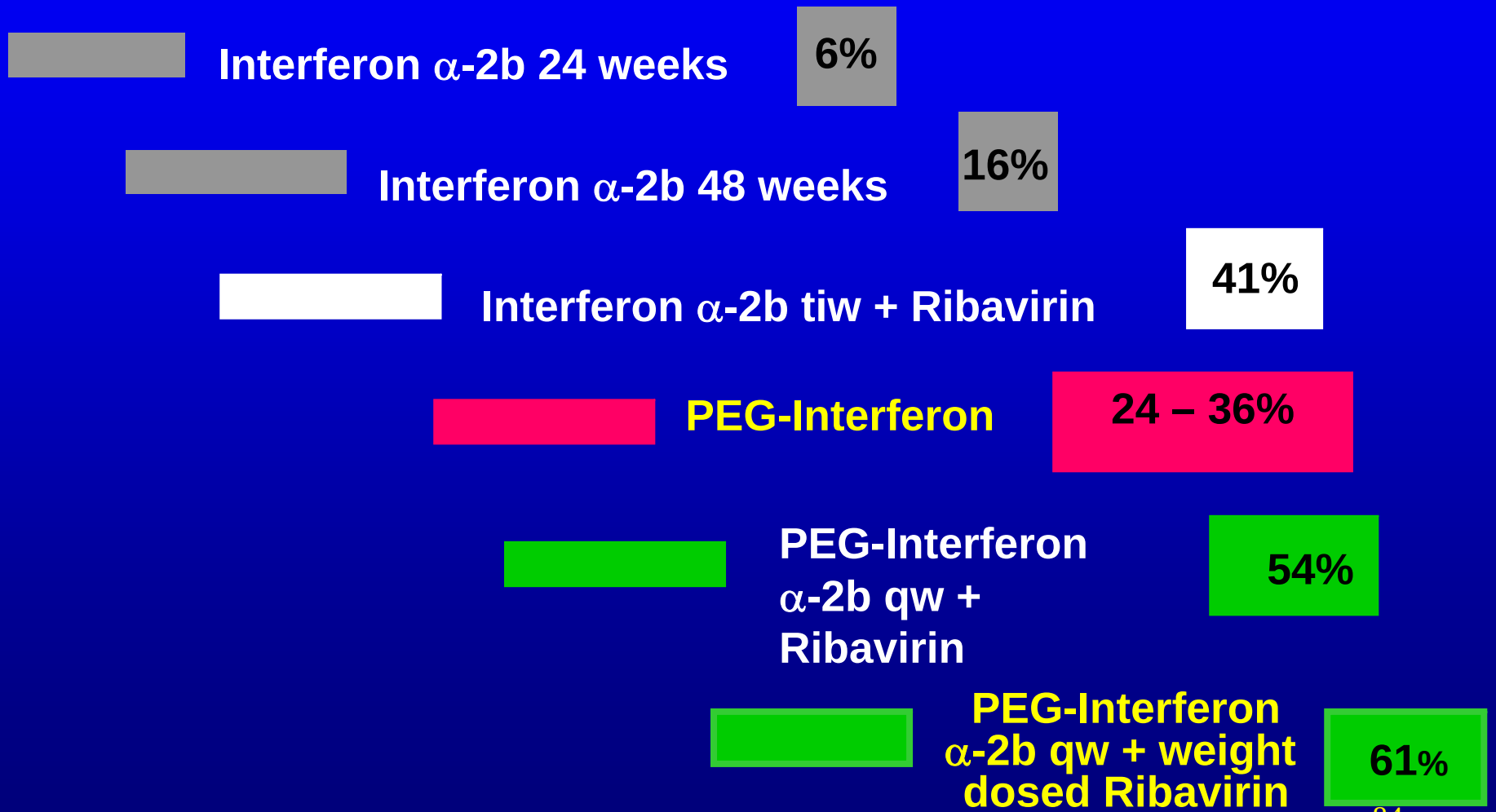
Sustained Response with PEG Interferon Alfa-2b—dose finding



Peg-interferon Alfa-2b + Ribavirin Virologic Response by Genotype (N = 1530)

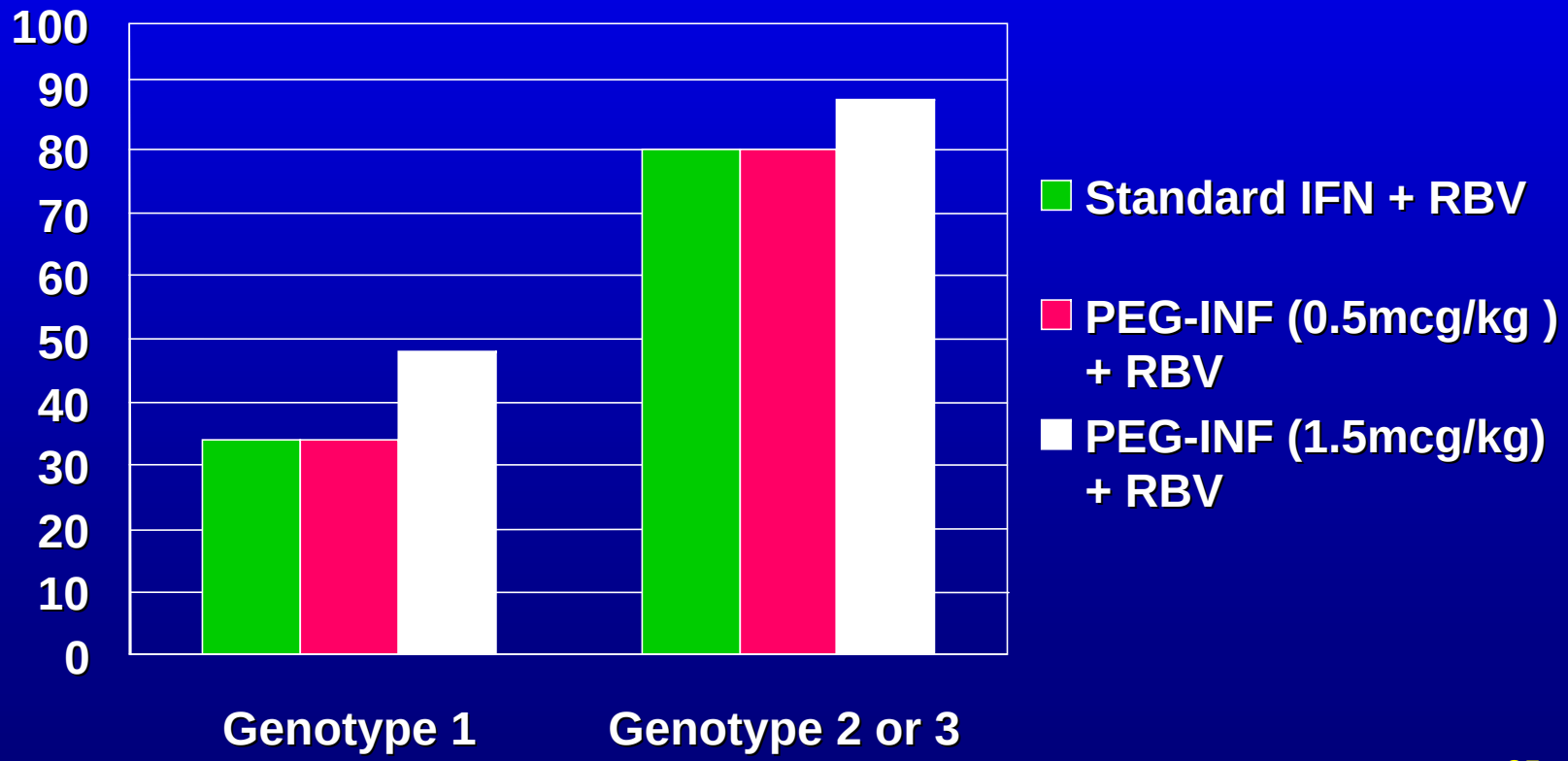


The Evolution Efficacy With Interferon Based Therapy Over the Last 10 Years



Peg-interferon Alfa-2b + Ribavirin Virology Response by Genotype

RBV Dose > 10.6 mg/kg



Side Effects of Interferon Alfa

- Insomnia
- Mood dysfunction→ depression
- Flu-like symptoms
- Rash and pruritus
- Anorexia
- Neutropenia
- Thrombocytopenia
- Thyroid dysfunction

Management of Thrombocytopenia

- **Dose Reduction**
  - **< 50,000/mm^3 – decrease 50%**
  - **< 25,000/mm^3 - stop**
- **Interleukin-11 (IL-11; oprelvekin)**
  - **Oncology dose, 25–50 mcg/kg SC daily**
  - **Platelet increase ~ 5–9 days**
- **Recombinant TPO - antibody formation**

Pharmacologic Management of Thrombocytopenia

- IL-11 - use in HCV therapy – very limited
  - Risk of IL-11 significant
  - Benefit – decrease bleeding? Unknown
- When should IL-11 be used?
  - Rarely – consider cirrhotic pt with high probability of SVR
  - Observe platelets > 50,000/mm^3
  - Dose Reduce PEG < 50,000/mm^3
  - Stop < 25,000/mm^3 or bleed

Interferon Alfa: Psychiatric Issues

- Assess mental health stability prior to therapy → predicts intensity of symptoms during therapy
- Provide counseling and support
- Administer antidepressants as needed
- Observe carefully while on therapy
- Consider support groups

Side Effects of Ribavirin

- Hemolytic anemia
- Teratogenicity
- Cough and dyspnea
- Rash and pruritus
- Insomnia
- Anorexia

Ribavirin and Pregnancy

- Confirm negative pregnancy test before
- initiating therapy due to teratogenicity
- Counsel all patients (male and female)
- about risks and to use birth control
- If pregnancy occurs in patient or
- partner, stop therapy and call
- 1/800-727-7064

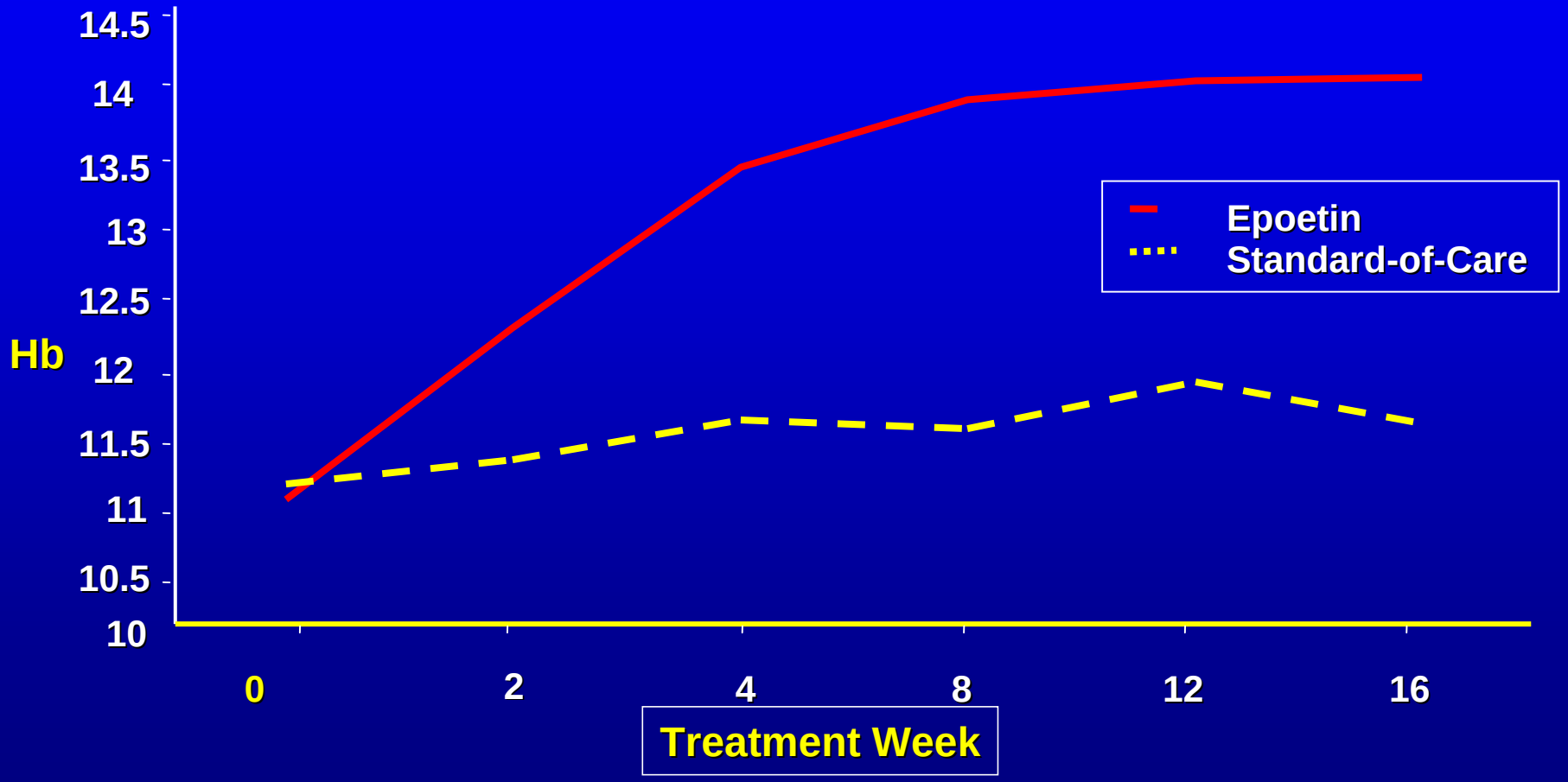
Management of Neutropenia

- **Neutropenia**
  - **Reduce interferon dose for ANC< 750**
  - **Consider GCSF 300 mcg sq TIW; titrate to maintain ANC ≥750**

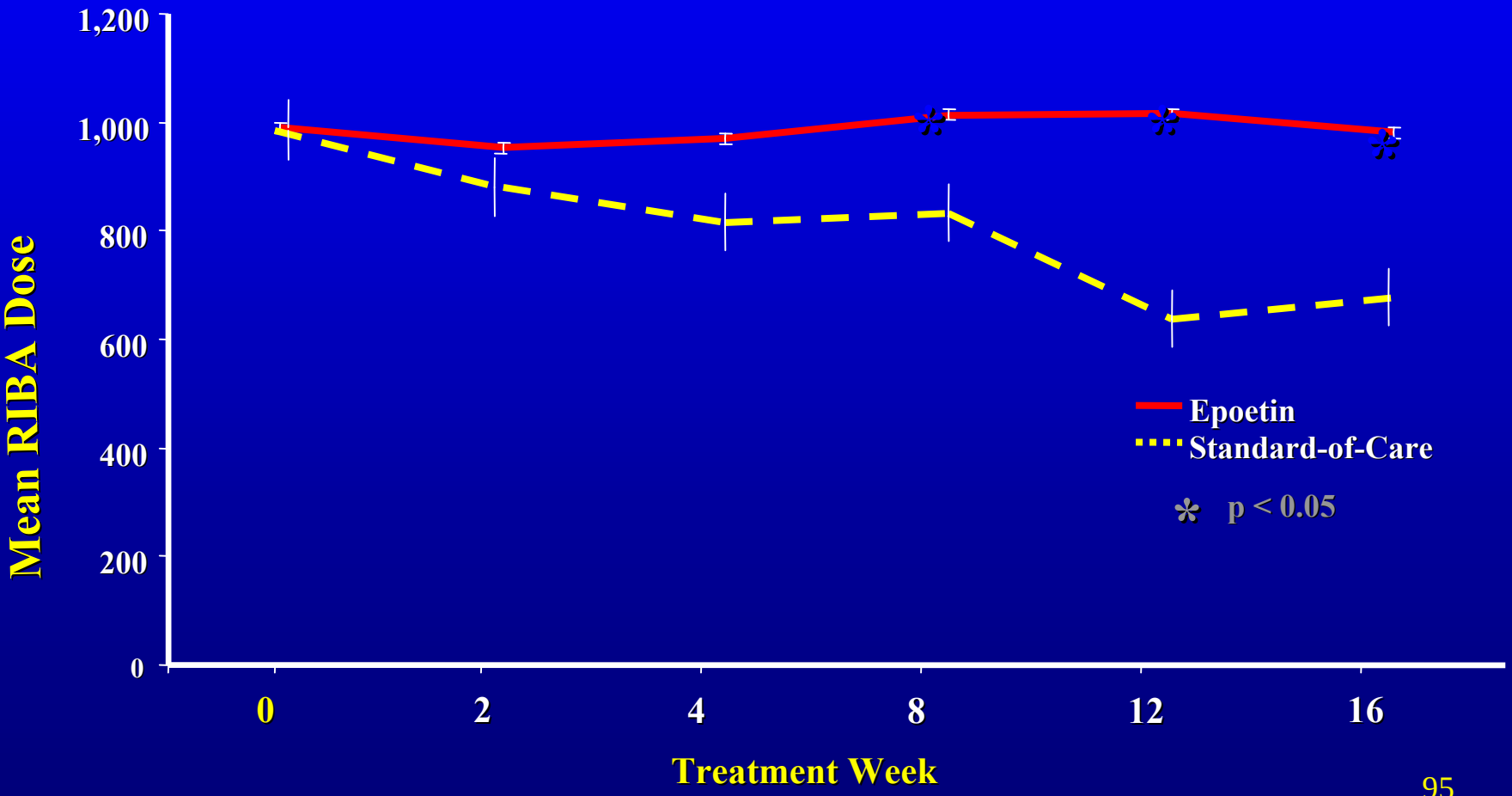
Management of Anemia

- **Anemia**
  - **Reduce ribavirin for Hgb < 10 g/dL**
  - **Consider epoetin alfa 40,000U sq weekly**
  - **Obtain CBC pretreatment, at week 2, at week 4, then more frequently if indicated**
- **Cardiac function**
  - **Anemia may exacerbate symptoms of coronary disease and/or deteriorate cardiac function**
  - **Recommend stress test for patients > 50 y/o**

Effect of epoetin Alfa on Hemoglobin in Anemic Patients on IFN Alfa +RBV



Effect of epoetin Alfa on Ribavirin Dosing in Patients on IFN Alfa +RBV



Guidelines for Dose Modification/Discontinuation of Ribavirin

Laboratory Values	Reduce Only RBV Dose to 600 mg/ day if:	Discontinue RBV if:
Hemoglobin in patients with no cardiac disease	<10 g/dL	<8.5 g/dL
Hemoglobin in patients with history of stable cardiac disease	≥2 g/dL decrease in hemoglobin during any 4 week period treatment	<12 g/dL despite 4 weeks at reduced dose

HCV Counseling

- **Prevent transmission to others**
  - **Direct exposure to blood**
  - **Perinatal exposure**
  - **Sexual exposure**
- **Refer to support group**

Sources :

1) *East Mediterr Health J. 2000 Mar-May;6(2-3):372-7.Zali MR, Mayumi M, Raoufi M, Nowroozi A.*
2) *J Med Virol. 2004 Oct;74(2):246-52.Samimi-Rad K, Nategh R, Malekzadeh R, Norder H, Magnius L.*
3) *CDC Internet site, 2004*
4) *WHO Internet site, 2004*
5) *Hepatitis resource network*
6) *Hatami H. Malekzadeh R. Emerging Hepatitis C, In : Emerging and reemerging infectious diseases and employee health, 1th ed. 2004.*

اپیدمیولوژی بالینی و کنترل بیماری‌های عفونی

آدرس اسلایدها و کتب الکترونیک در سایت‌های اینترنتی :

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