Viral Hepatitis in Reproductive Health

Yaoundé
26 Novembre 2007
GFMER

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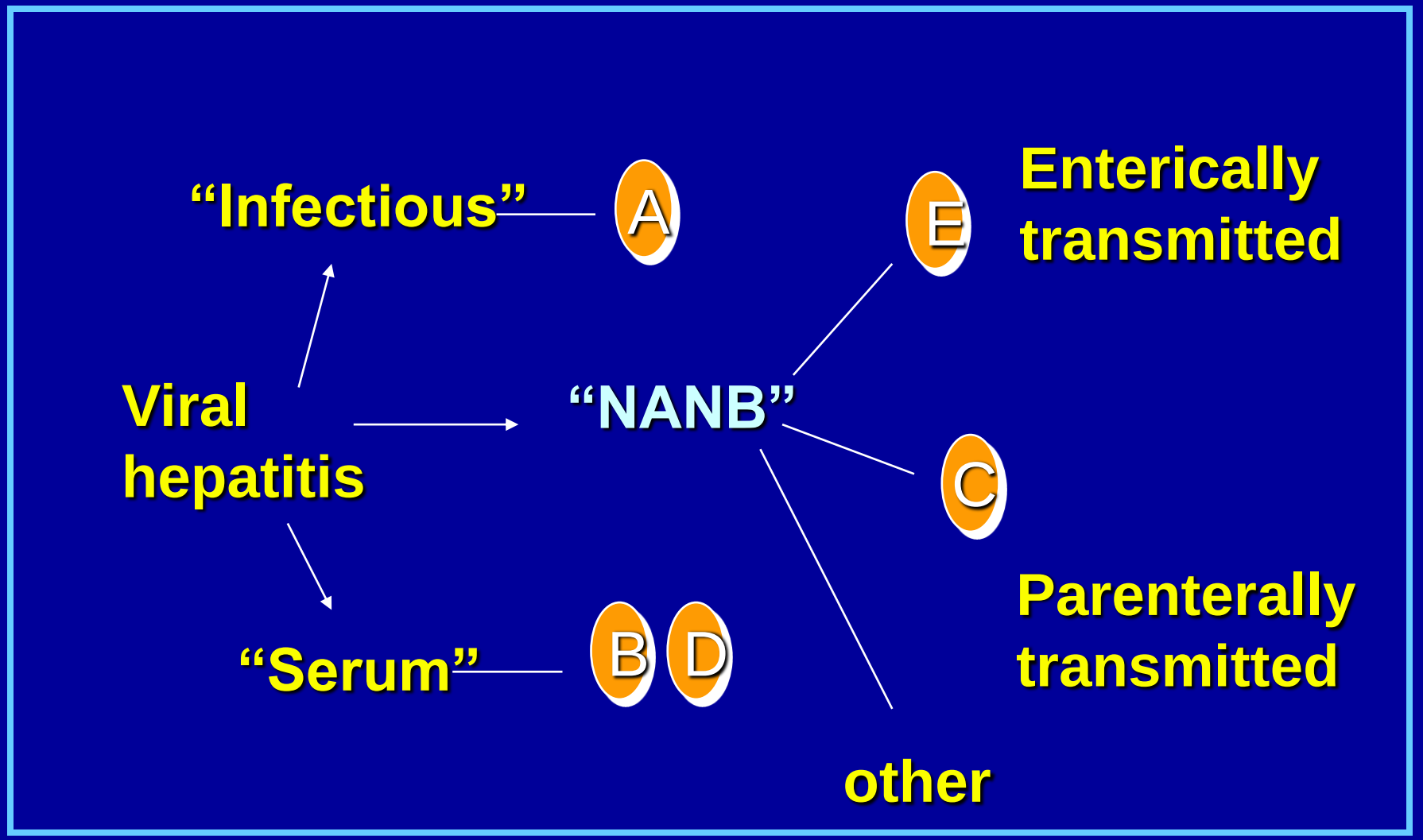
Geneva - Switzerland

- Epidemiologie de l’hépatite B
- Epidemiologie de l’hépatite C
- Traitement des hépatites B et C
- Vaccins des hépatites virales
- Hépatites virales et grossesse

Hépatites virales – perspective historique



CDC

Epidemiologie des hépatites virales

Porteurs chroniques dans le monde

VHB	400’000’000
VHC	250’000’000

Les hépatites virales

Types of Viral Hepatitis

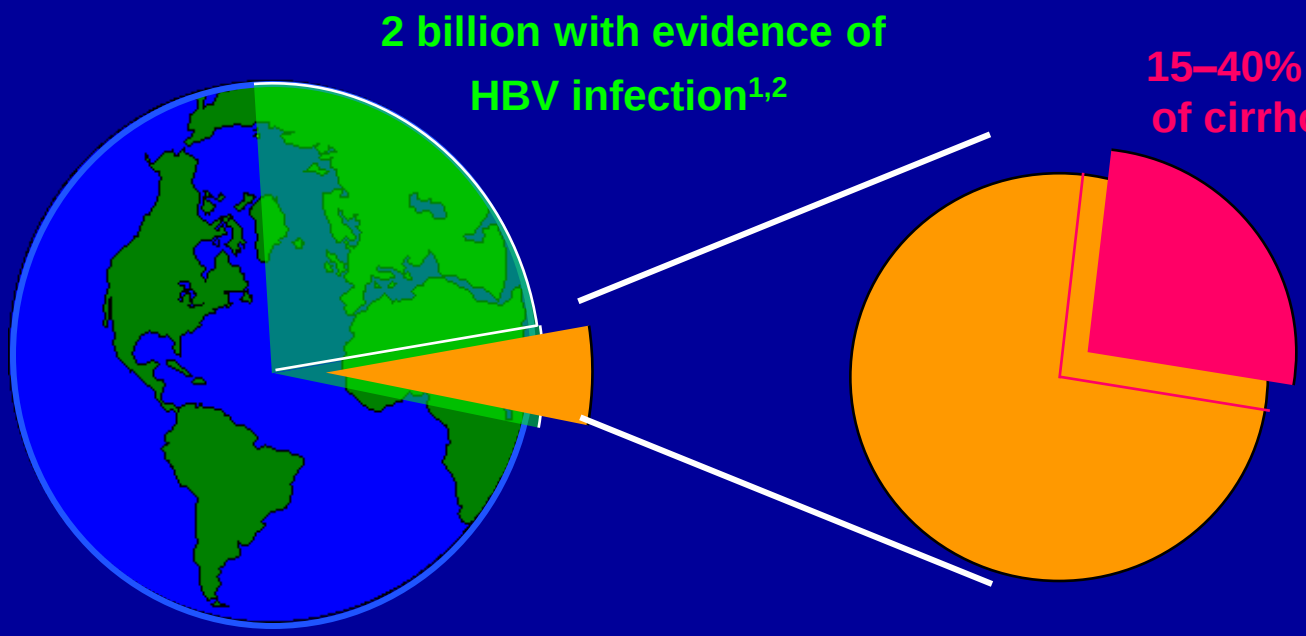
	A	B	C	D	E
Source of virus	feces	blood	blood	blood	feces
Route of transmission	fecal-oral	percutaneous permucosal	percutaneous permucosal	percutaneous permucosal	fecal-oral
Chronic infection	no	yes	yes	yes	no
Prevention	pre-exposure immunization	pre/post-exposure immunization	blood donor screening; risk behavior modification	pre/post-exposure immunization	ensure safe drinking water

CDC

A B C des hépatites virales

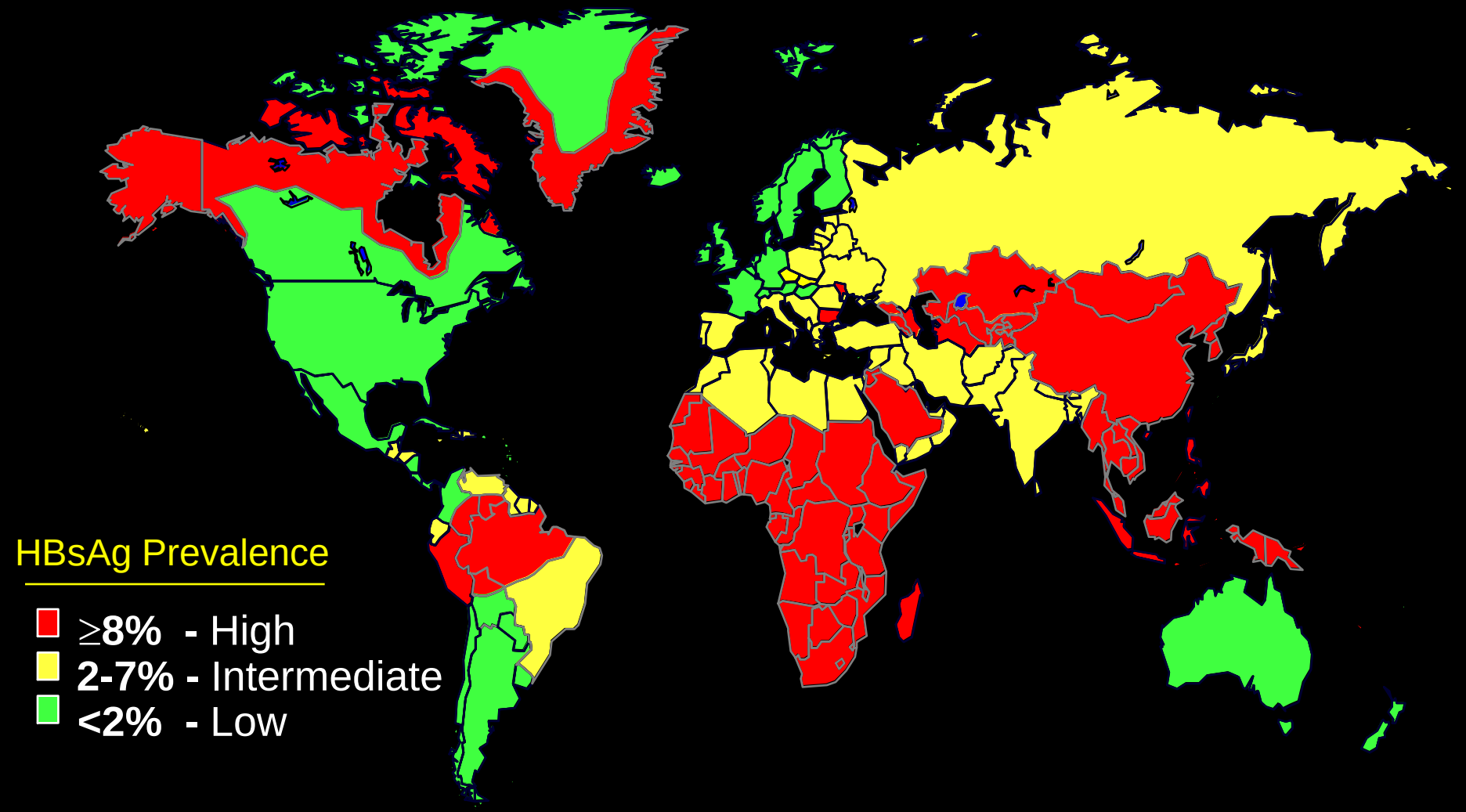
- **A**
  - **féco-orale** (hygiène, eau, aliments)
  - **vaccin**
- **B**
  - **sang** (mère-enfant, injections)
  - **sexe** (100x plus contagieux que VIH)
  - **vaccin**
- **C**
  - **sang** (injections, soins de santé)
  - **pas de vaccin**

Global impact of hepatitis B



1. World Health Organisation Fact Sheet/204. Hepatitis B. Geneva: World Health Organisation; 2000. (WHO Fact Sheets, available at www.who.int Accessed July 26 2005); 2. Lee WM. Hepatitis B virus infection. N Engl J Med 1997;337(24):1733-45.; 3. Lok AS. Chronic hepatitis B. *N Engl J Med* 2002; 346:1682–1683.; 4. Conjeevaram HS, Lok AS. Management of chronic hepatitis B. J Hepatol 2003; 38:S90–S103.

Geographic Distribution of Chronic HBV Infection



CDC

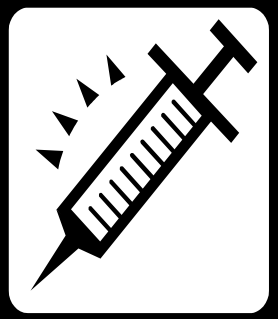
Prévalences globales de l'hépatite B

- Elevée (>8%)
  45% de la population globale
  – infections tôt dans l'enfance fréquentes
- Intermédiaire (2%-7%)
  43% de la population globale
  – infections à tous les âges
- Basse (<2%)
  12% de la population globale
  – Majorité des infections à l'âge adulte

CDC

HBV Modes of Transmission

- Sexual
- Parenteral
- Perinatal



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Concentration du VHB dans les liquides corporels

Elevée	Modérée	Basse/non détectable
sang	semen	urine
serum	fluide vaginal	selles
exudats	salive	sueur
		larmes
		lait maternel

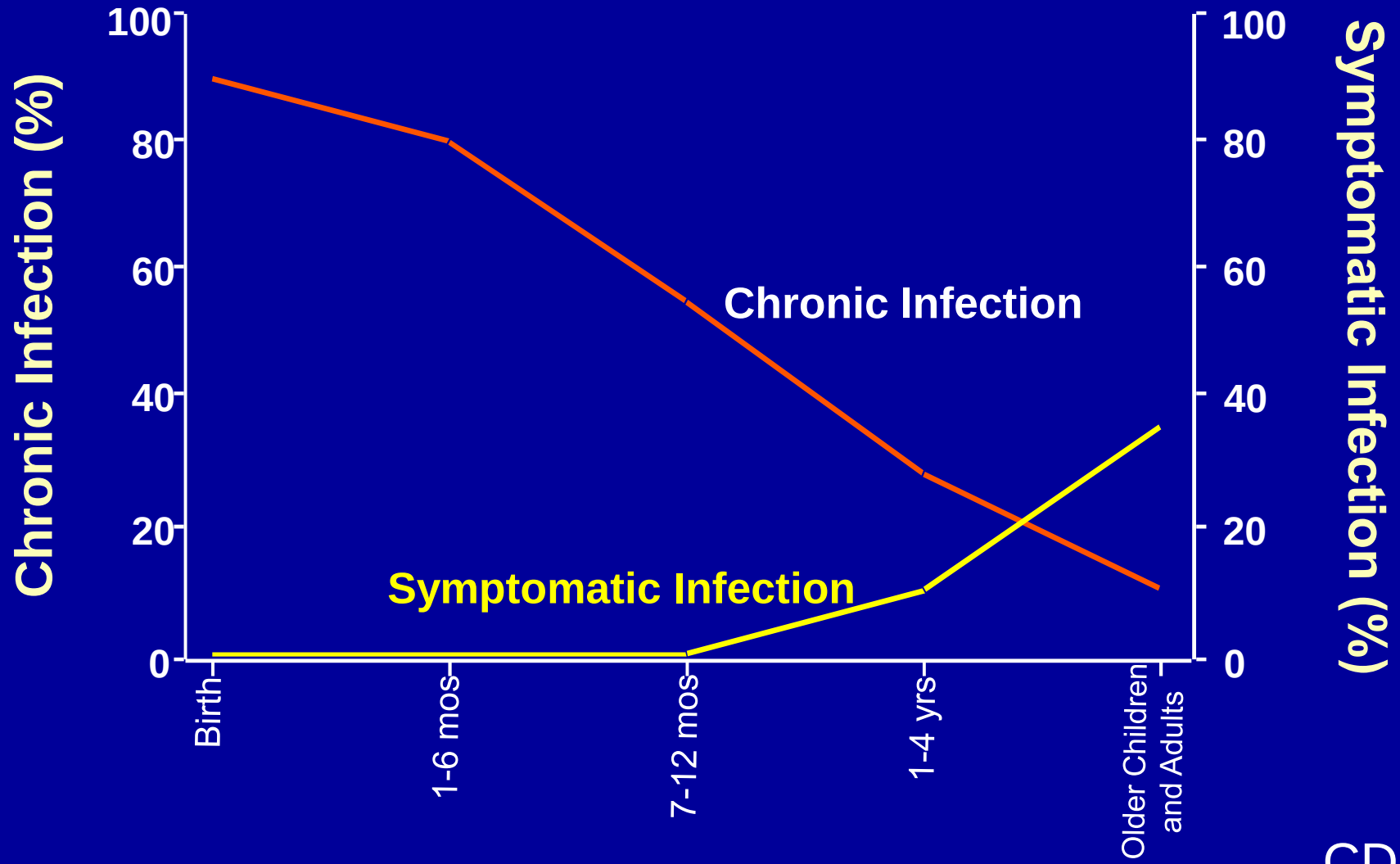
CDC

Hépatite B – Clinique

- **Incubation :** moyenne 60-90 jours
- **Maladie clinique:** (jaunisse) si <5 ans : <10%
si >5 ans : 30%-50%
- **Mortalité aigue:** 0.5% - 1%
- **Infection chronique :** <5 ans : 30%-90%
>5 ans : 2%-10%
- **Mortalité précoce de maladie chronique du foie:** 15% - 25%

CDC

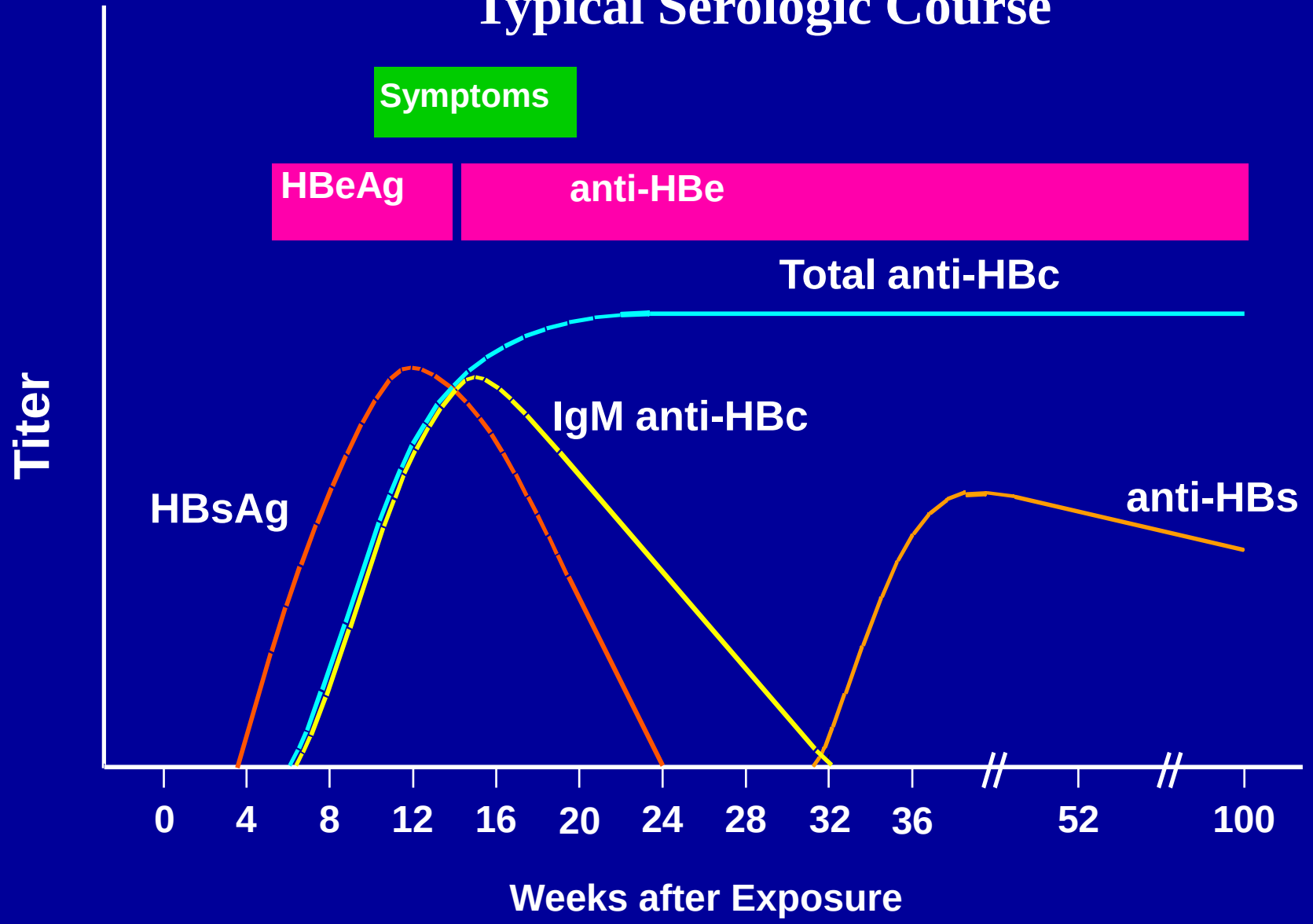
Outcome of Hepatitis B Virus Infection
by Age at Infection



CDC

Acute Hepatitis B Virus Infection with Recovery

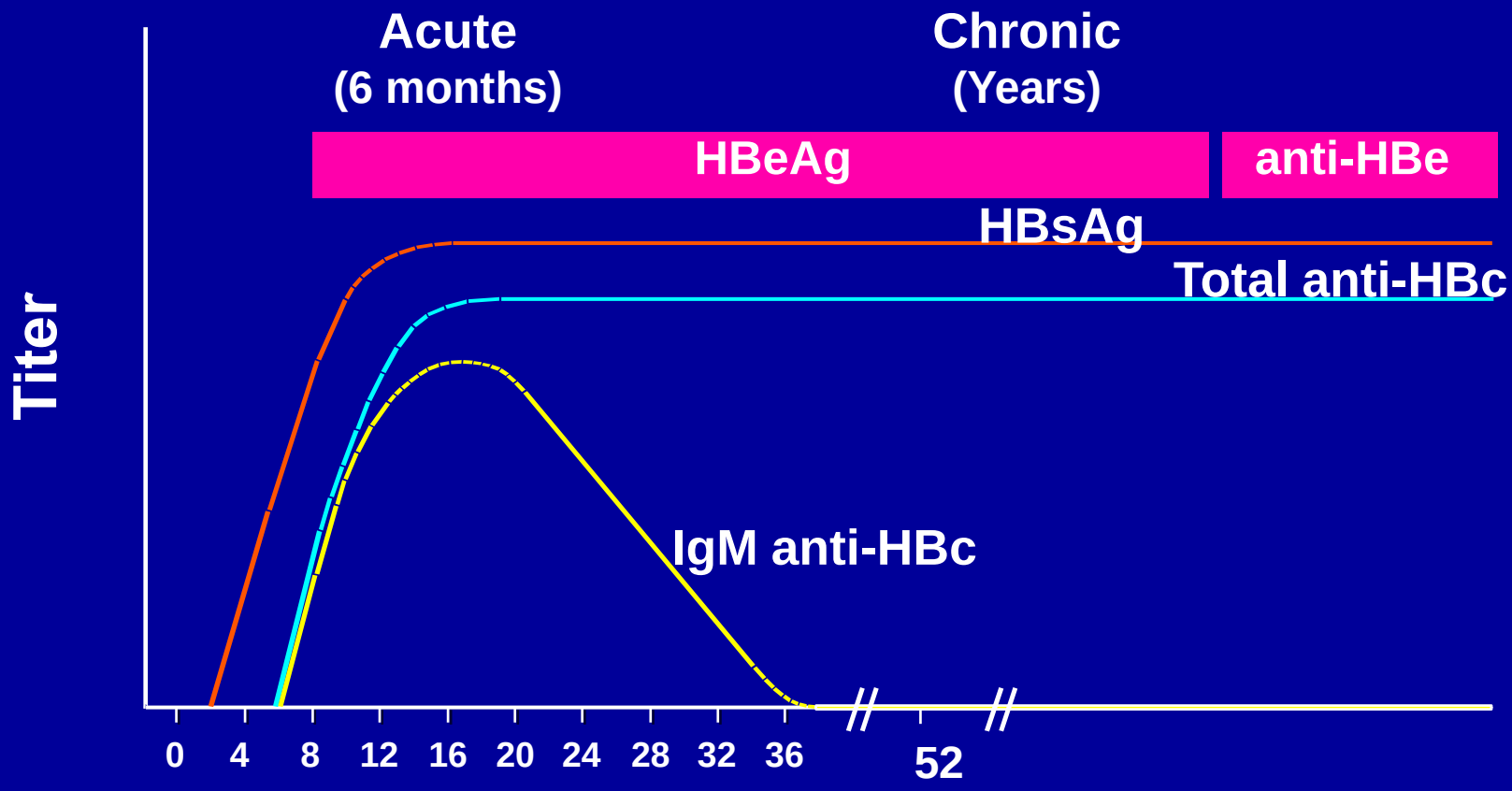
Typical Serologic Course



CDC

Progression to Chronic Hepatitis B Virus Infection

Typical Serologic Course

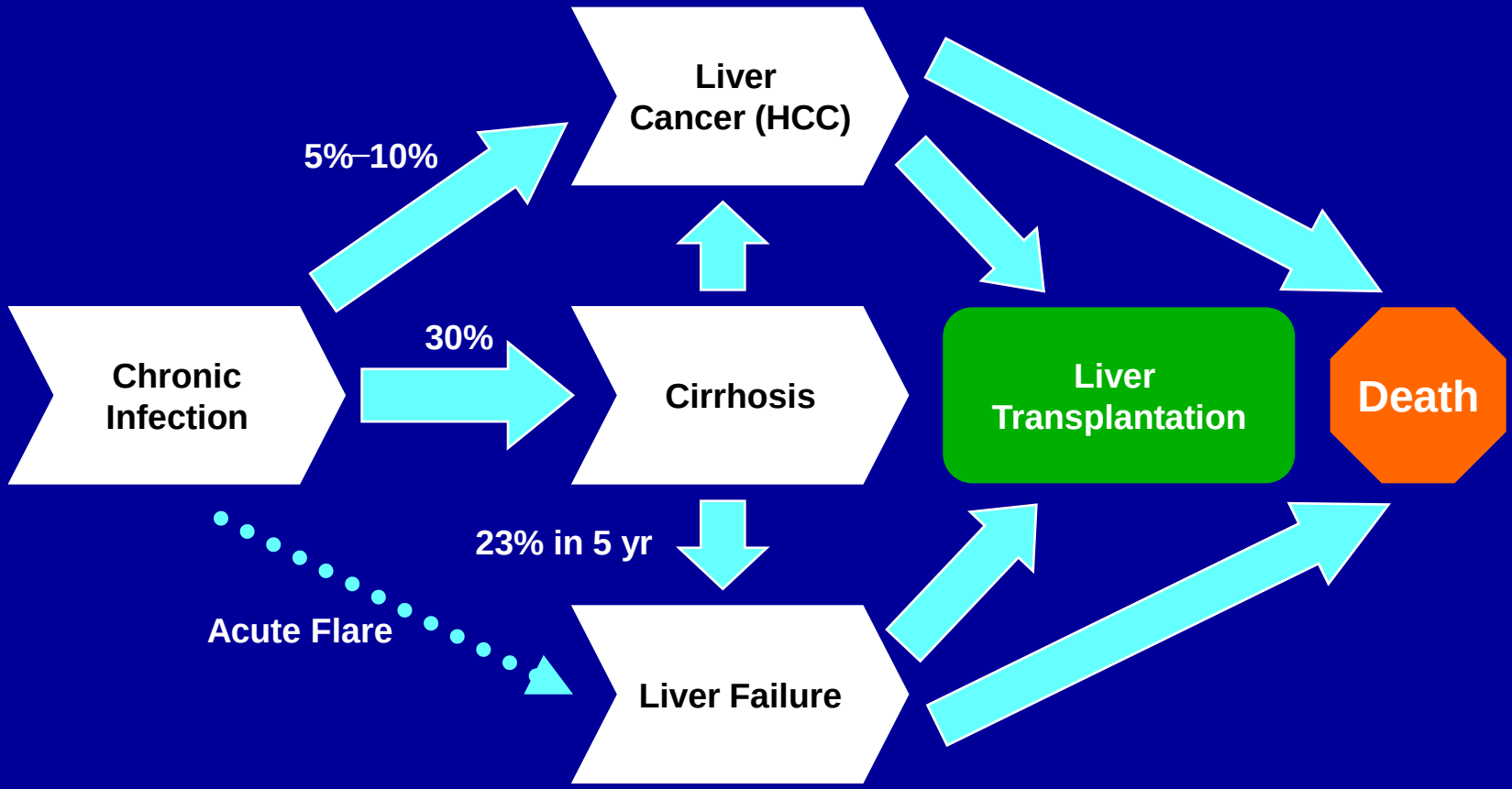


CDC

Phases de l'infection hépatite B

- immunotolérance
  - virus est non pathogène pour la cellule hépatique
  - peut durer de nombreuses années
- immunoélimination
  - hépatite active, ALT élevée, fibrose, cirrhose
  - hépatite chronique HBeAg positive
- porteur inactif HBsAg
  - virémie basse, HBeAg négatif
- réactivation
  - mutation virale, HBeAg négatif

Chronic Hepatitis B Disease Progression



Torresi J *et al*. *Gastroenterol* 2000;**118**:S83–S103
Fattovich G *et al*. *Hepatol* 1995;**21**:77–82
Perrillo RP *et al*. *Hepatol* 2001;**33**:424–432

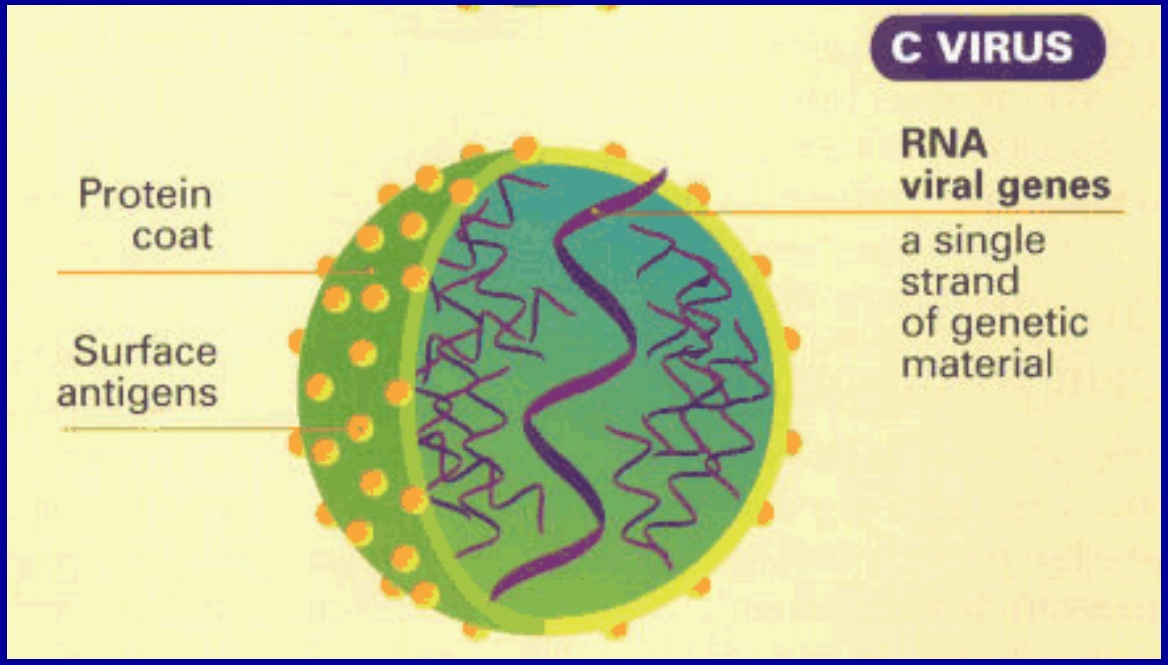
Hepatitis C

Virus, Prevalence, Natural History, Acute & Chronic Hepatitis C

List of Contents

The Hepatitis C Virus

Virus Hépatite C



- appartient à la famille des *flaviridae*
- possède une capside avec les antigènes E1, E2, un core, et un *ARN à simple filament* (génome)
- a 6 génotypes principaux (G1 à G6) divisés en sous-types (a, b,...)

Figure: http://www.battlinghepc.com/virus.html

Prevalence of Chronic Hepatitis C (2002)

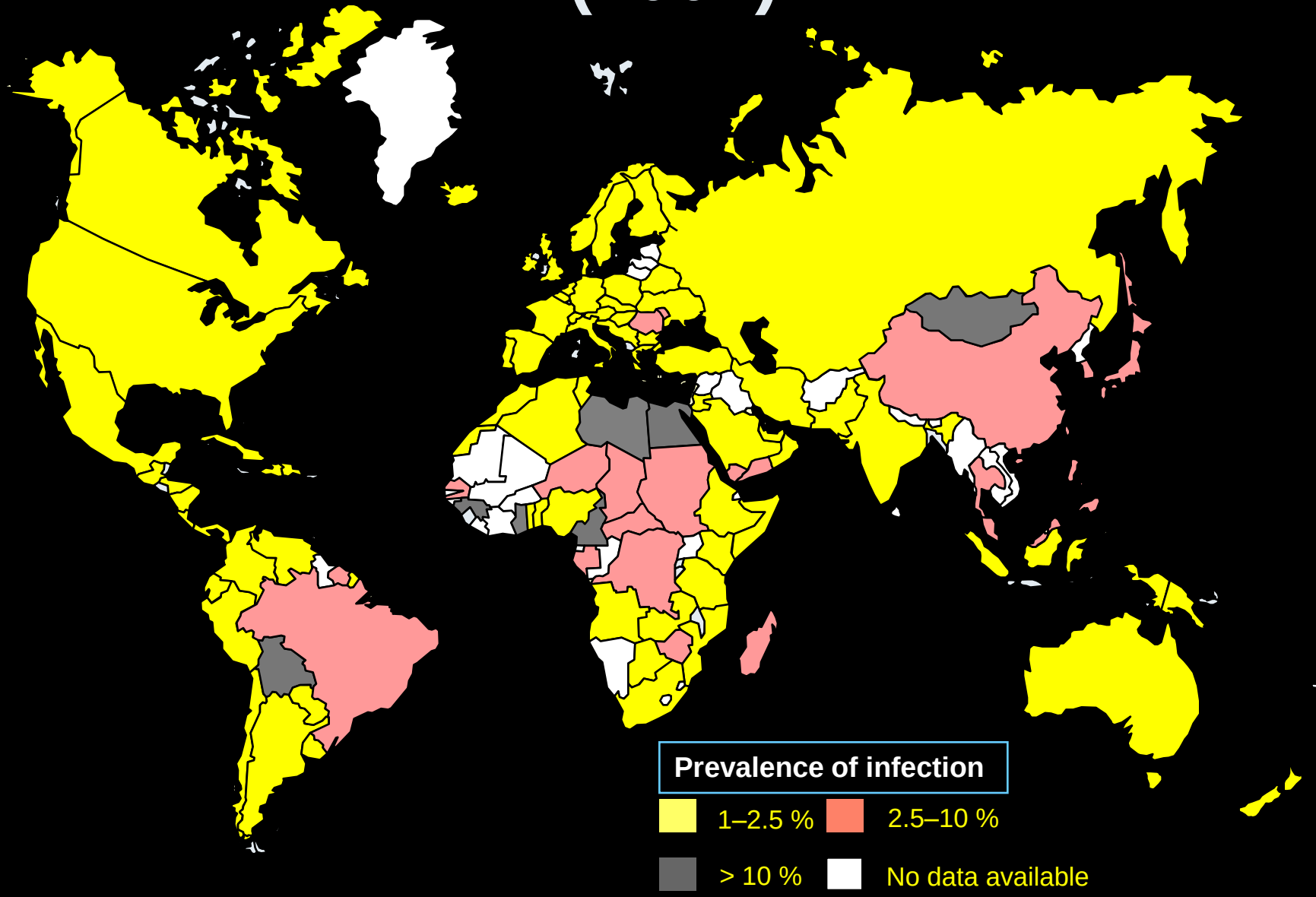


Figure: http://www.who.int/

HCV Genotypes and Subtypes

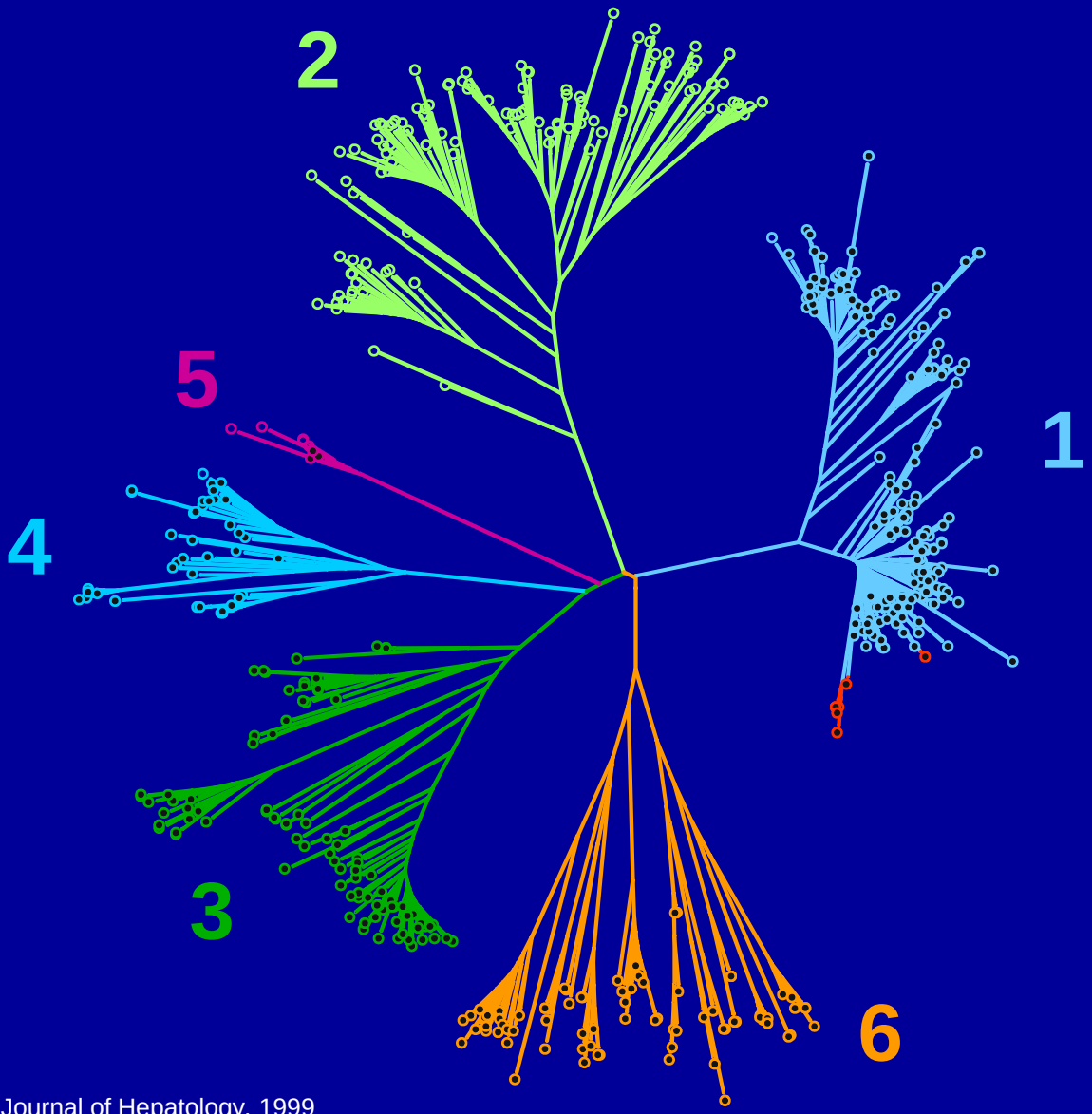
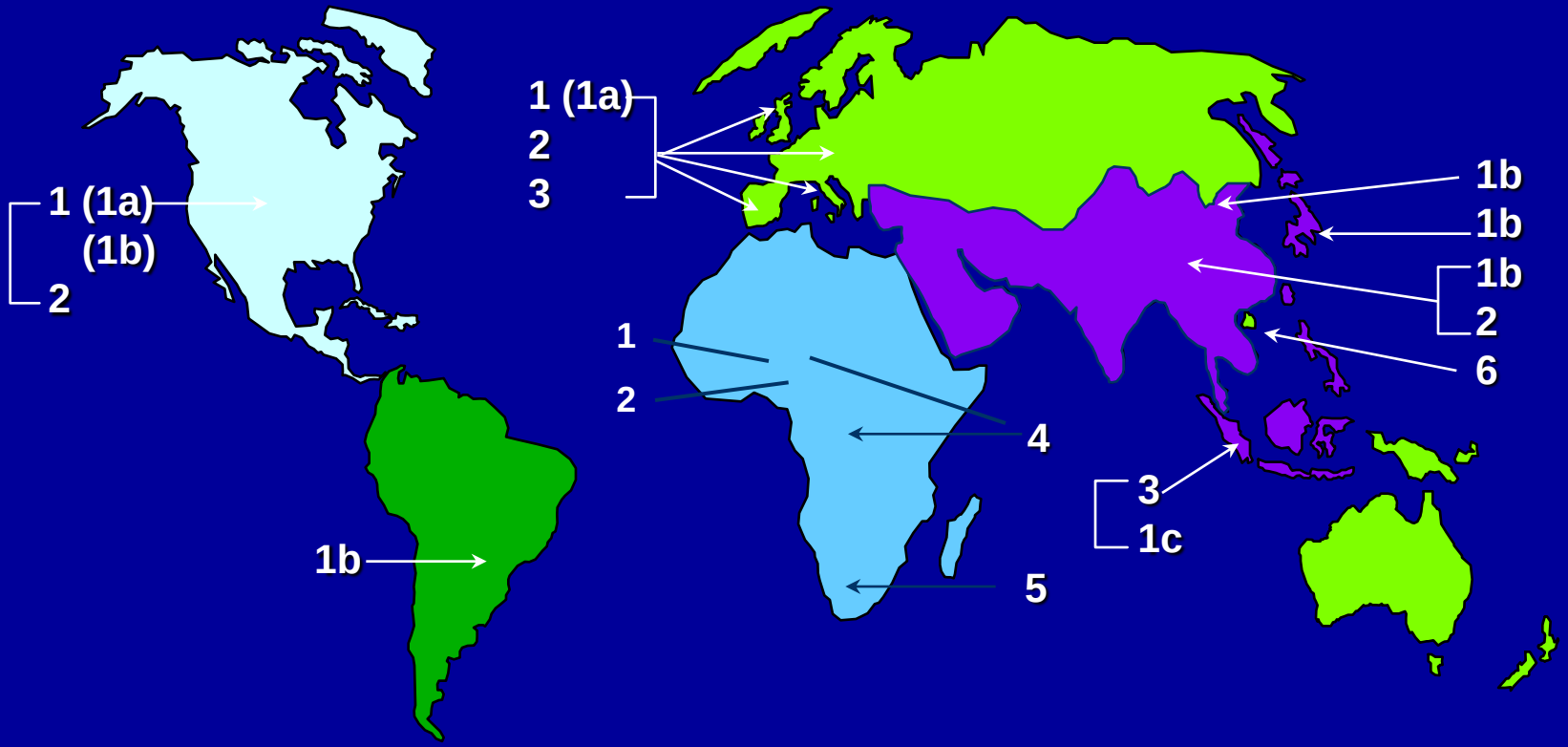


Figure: Simmonds P, Journal of Hepatology, 1999

Distribution of HCV Genotypes

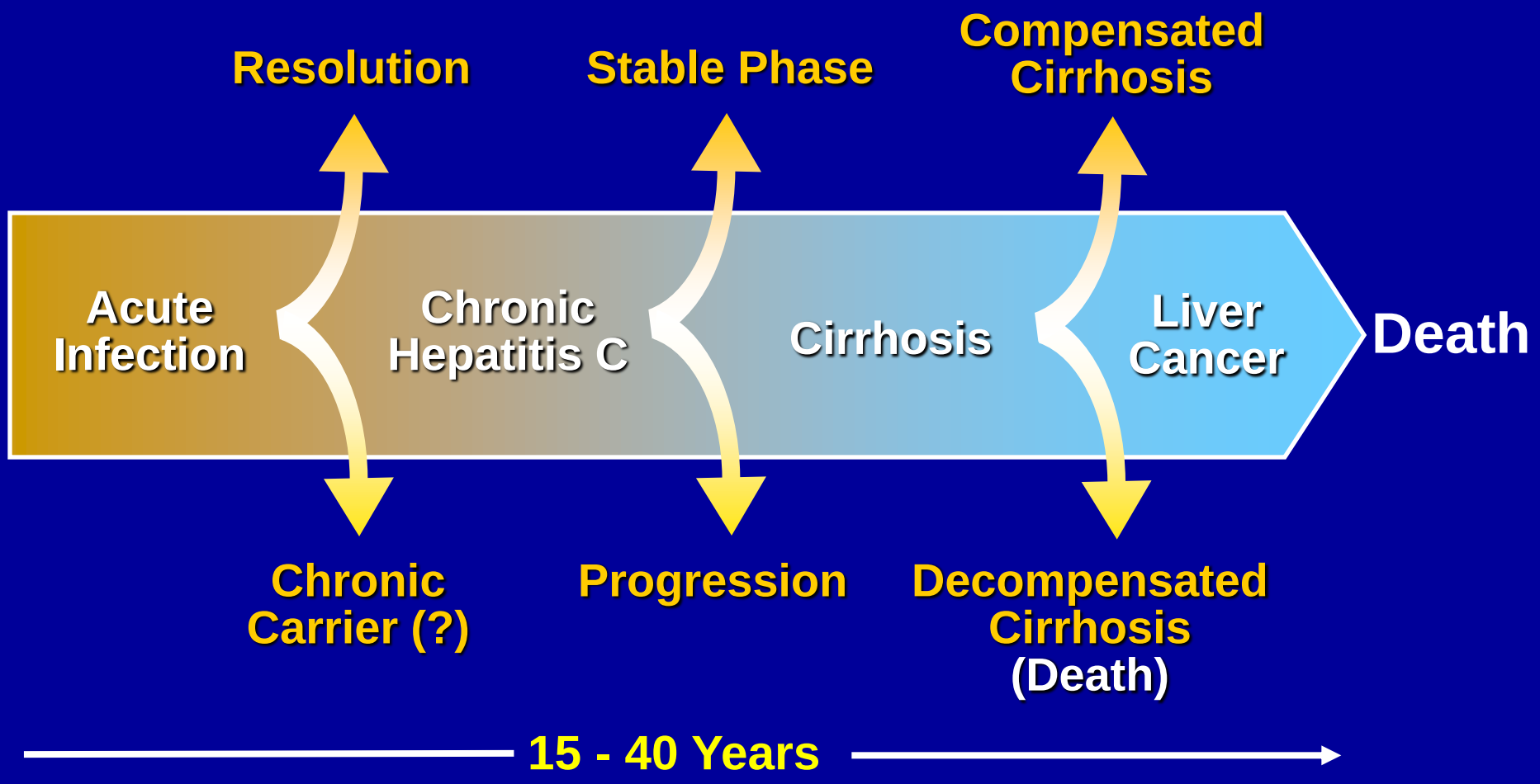


Hépatite C

- Cause principale de la cirrhose hépatique
- 250’000’000 de cas dans le monde
- > 200’000 décès/ an
  - nombre croissant de décès dans les 10-20 prochaines années
  - coûts médicaux exponentiels
- Risque accru de cancer hépatocellulaire

CDC. MMWR. 1998; 47
NIH Consensus Hepatitis C, 2002

Natural History of chronic hepatitis C



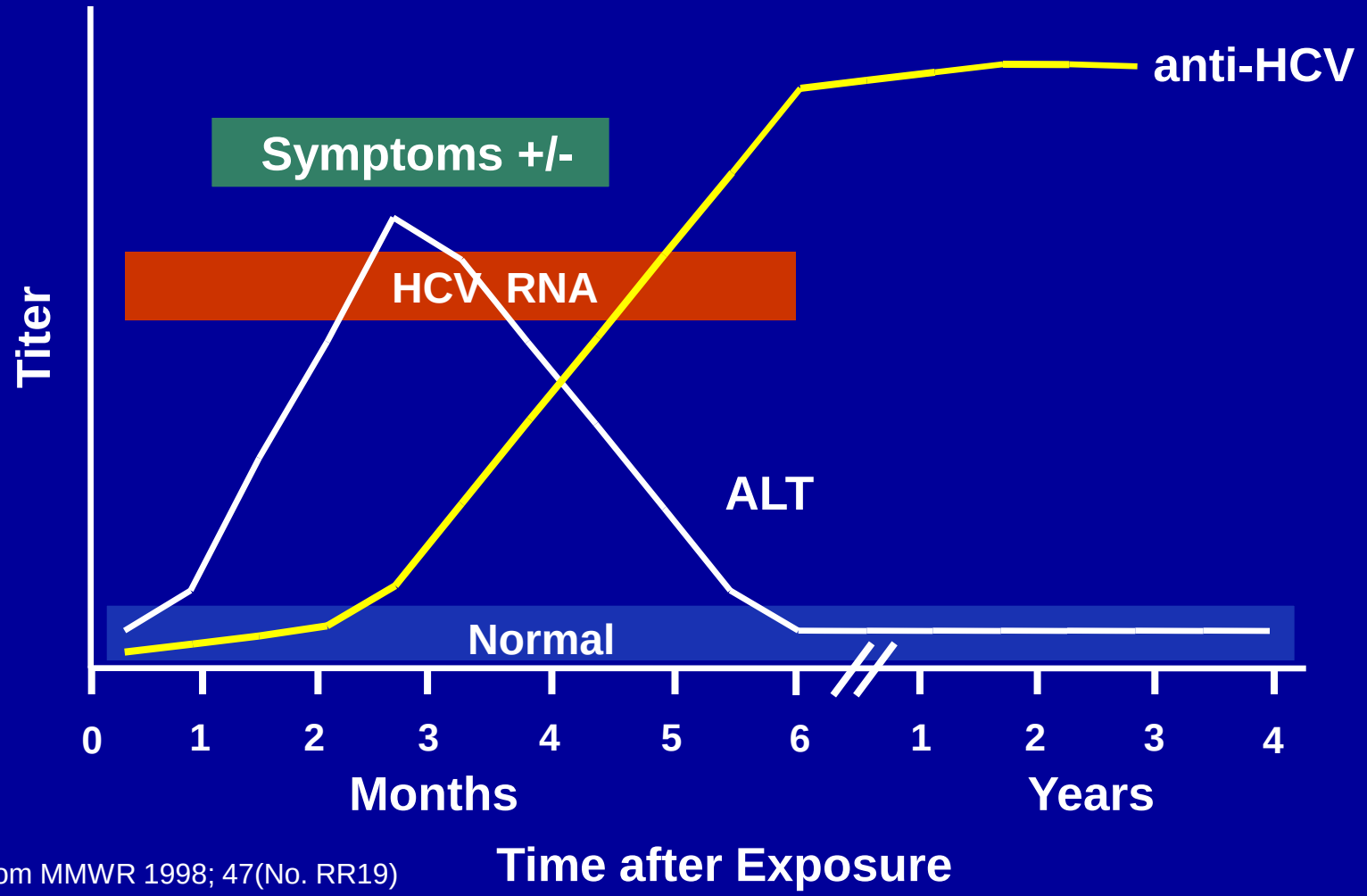
Infection avec le VHC

Incubation		**2-26 semaines (moyenne 6-7 sem)**
Maladie aigue (jaunisse)		**moins de 20%**
Infection chronique	**Fonction de l'âge**	**60%-85%**
Hépatite chronique		**10%-70%**
Cirrhose		**<5%-20%**
Mortalité de la maladie chronique du foie		**1%-5%**

Source (CDC, 2003): http://www.cdc.gov/ncidod/diseases/hepatitis/slideset/index.htm

Serologic Pattern of Acute HCV Infection

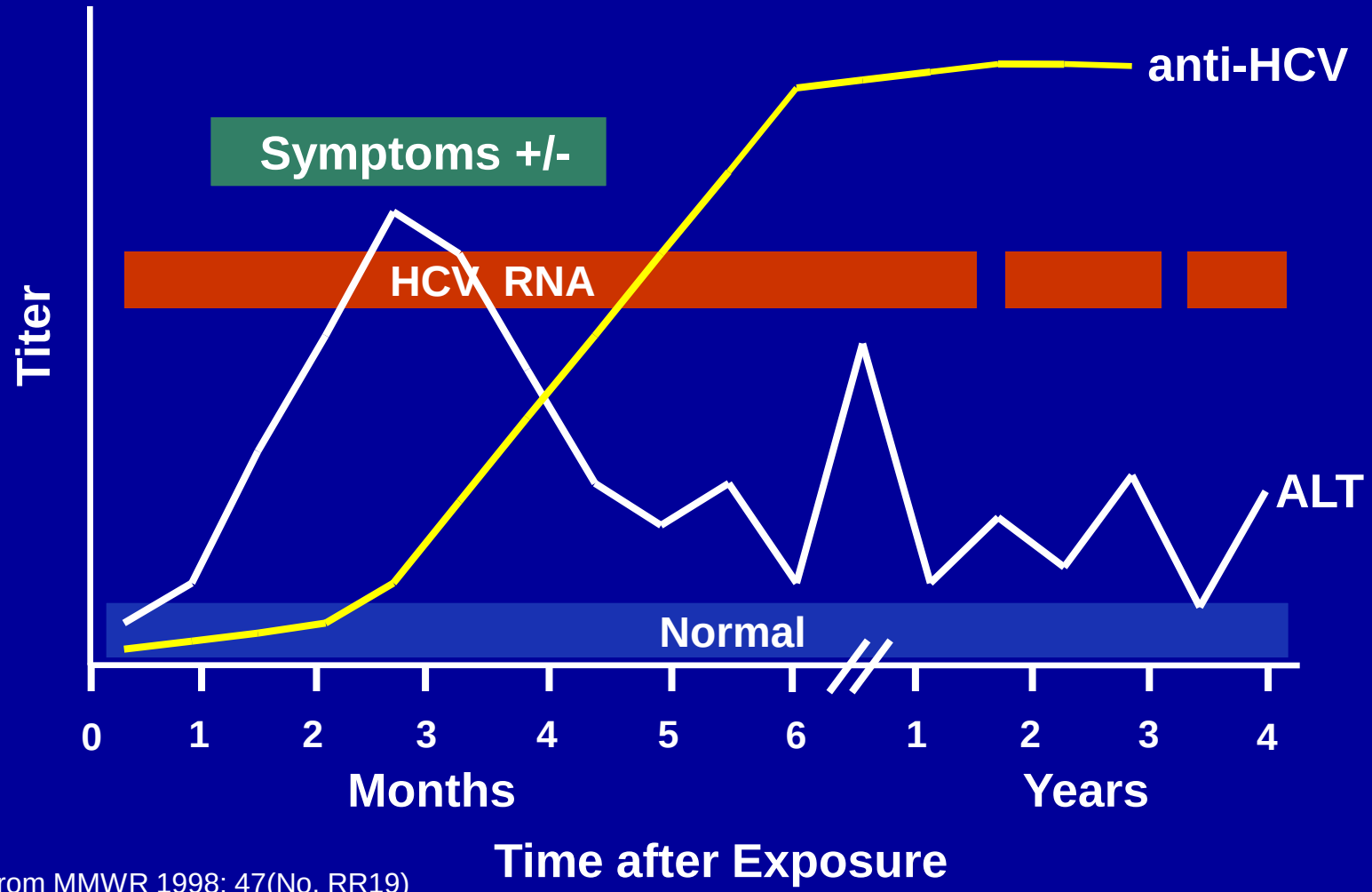
with Recovery



Adapted from MMWR 1998; 47(No. RR19)

Serologic Pattern of Acute HCV Infection

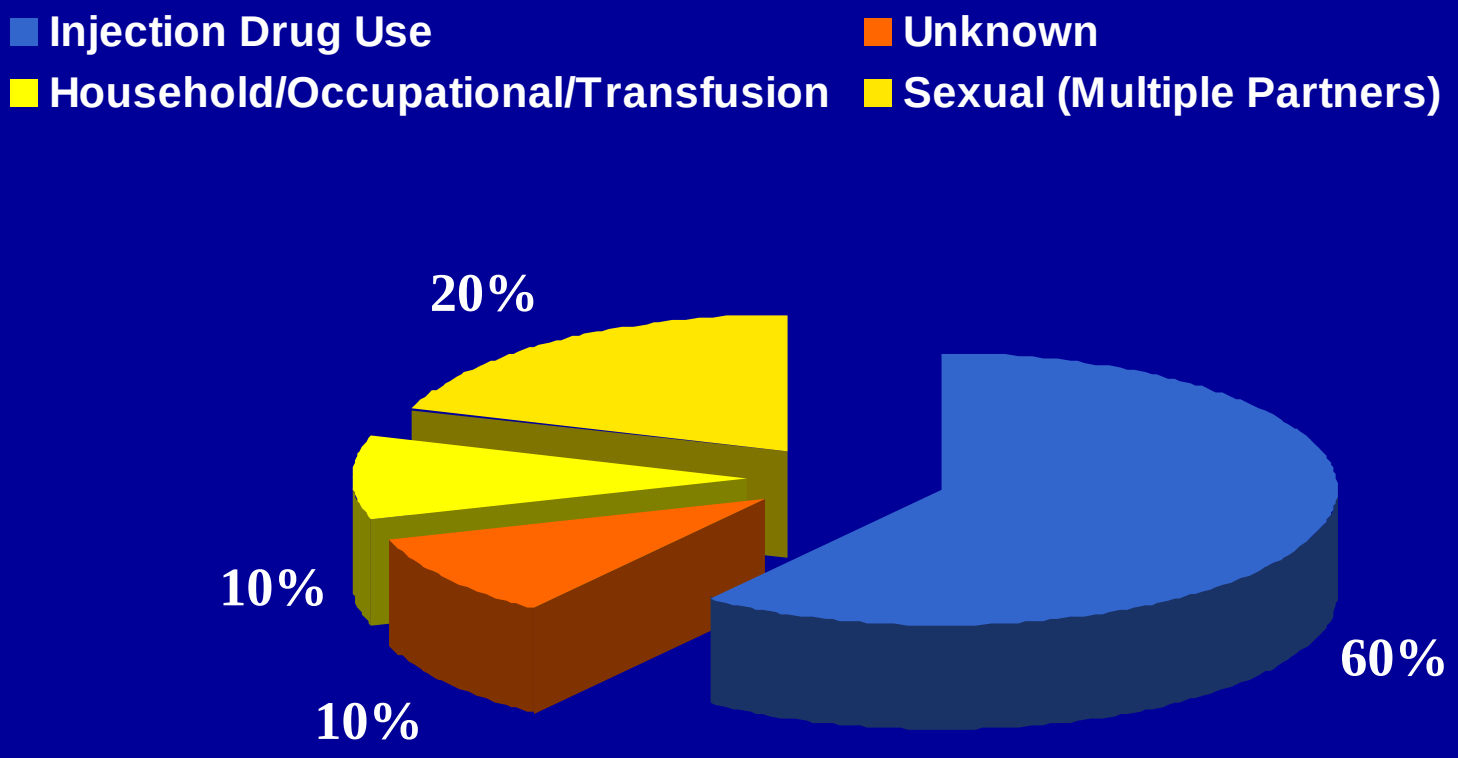
with Progression to Chronic Infection



Adapted from MMWR 1998; 47(No. RR19)

Risk Factors for Acute Hepatitis C

United States, 1991-1995



Alter MT. Hepatology, 1997

Review of Hepatitis C in Africa

Country	Group	n	HCV +	RNA +	G1	G2	G4	Reference
Burkina Faso	pregnant women	547	3.3%	27%	40	60		J MedVirol 2005
Ivory Coast	pregnant women	1000	1%	80%	50	50		J MedVirol 2004
Ghana	blood donors	4984	1.3%	47%	13	87		J Virology 2003
Nigeria	HIV +	146	8.2%		75	25		J ClinVirol 2004
Cameroon	Bantus	409	17%	68%	8	16	76	J MedVirol 2003
Cameroon	pregnant women	1494	1.9%	75%	24	38	38	J MedVirol 2003
Cameroon	pregnant women	5008	1.8%	76%	28	26	45	AJ TropMed 2005

Complications des hépatites virales

Cirrhose

progression lente sur 30 – 40 ans

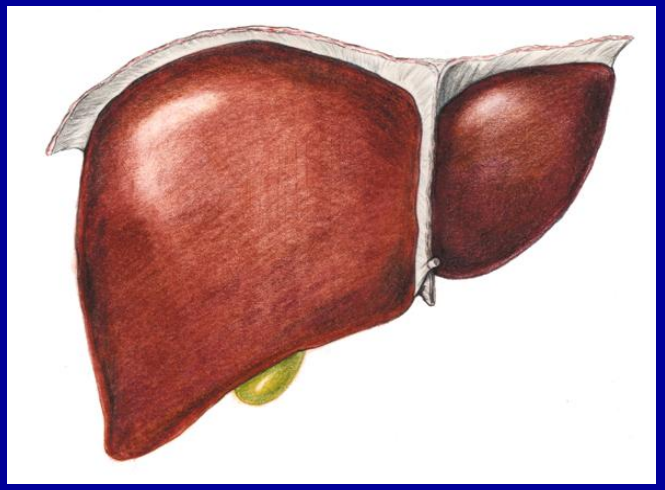
CHC (carcinome hépatocellulaire)

- pays à prédominance HVC (Europe, USA, Japon)
- pays à prédominance HVB (Afrique, Asie, Brésil)
- autres carcinogènes:

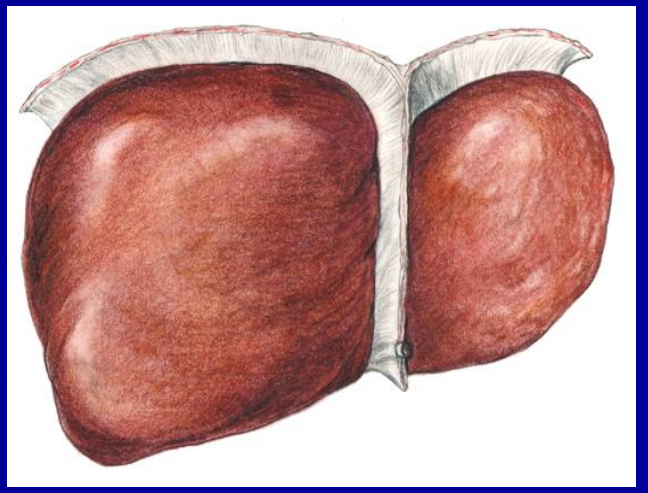
  alcool par stress oxydatif et fibrogénèse

  aflatoxine (Aspergillus flavus) (Afrique, Chine)

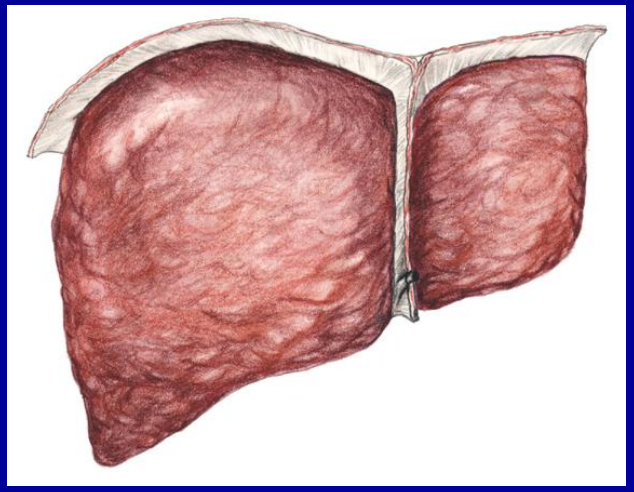
Foie normal



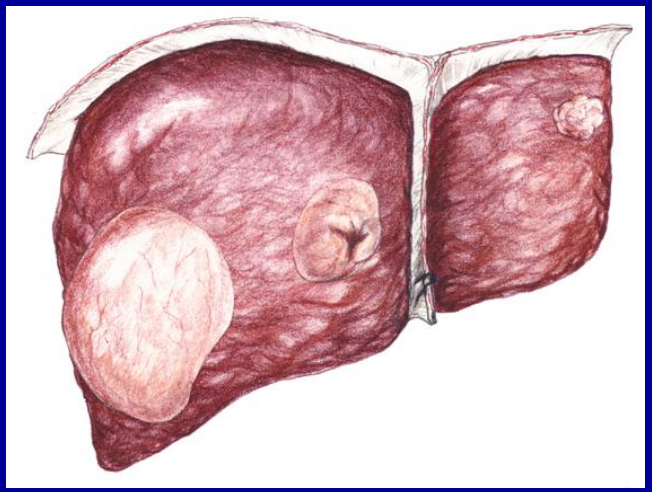
Fibrose hépatique



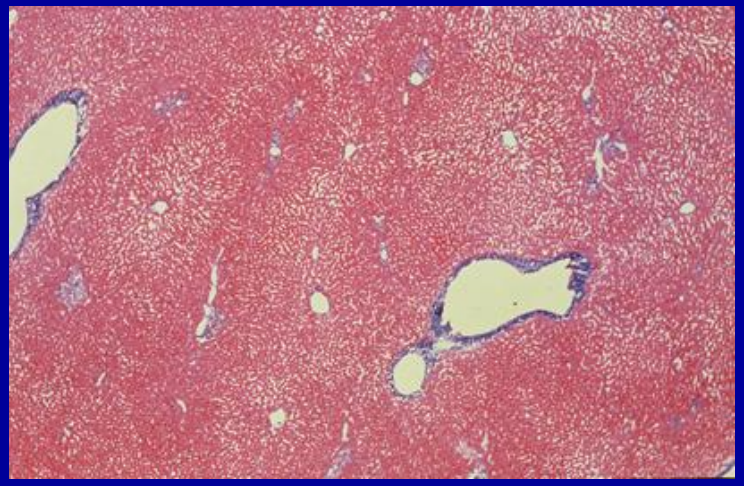
Cirrhose



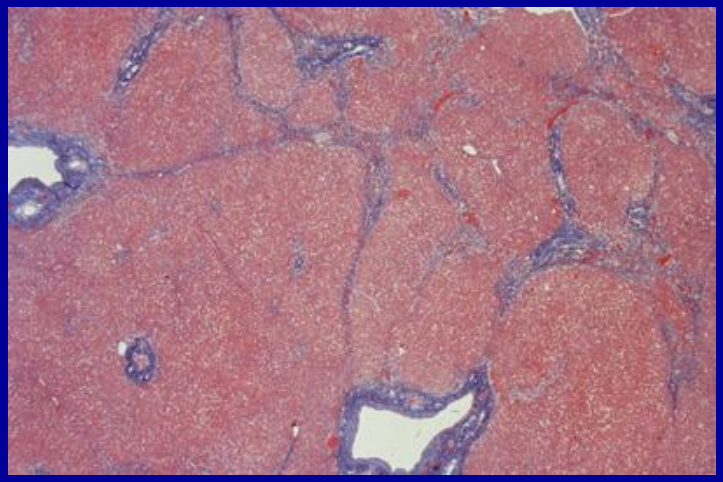
Cancer du foie



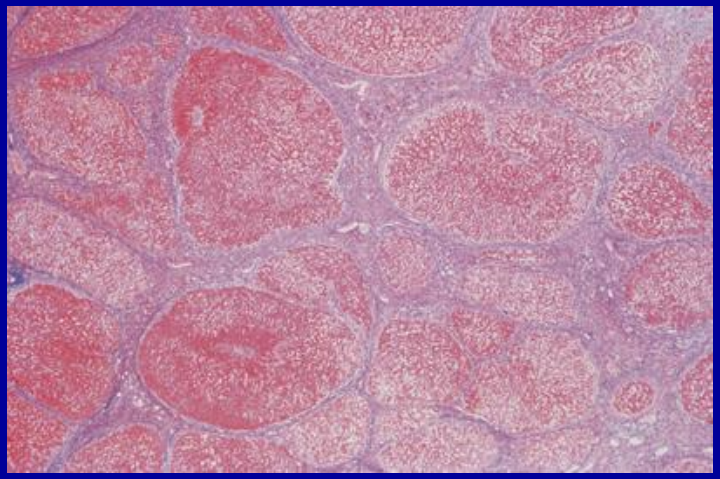
Foie normal



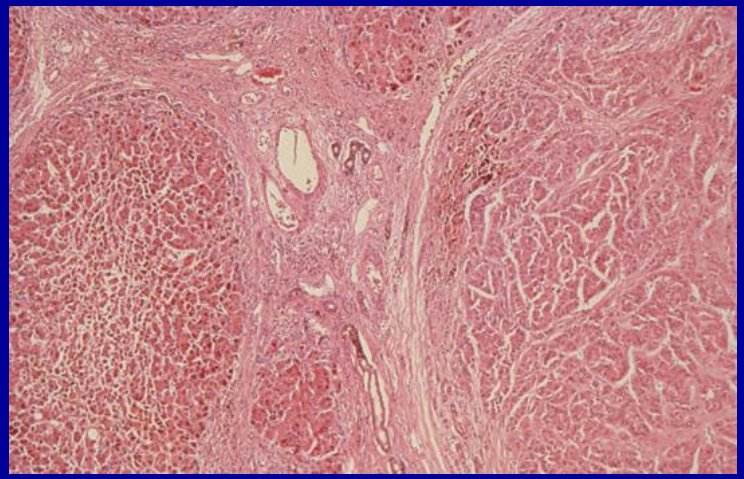
Fibrose hépatique



Cirrhose



Cancer du foie



Global Epidemiology of Hepatocellular Carcinoma

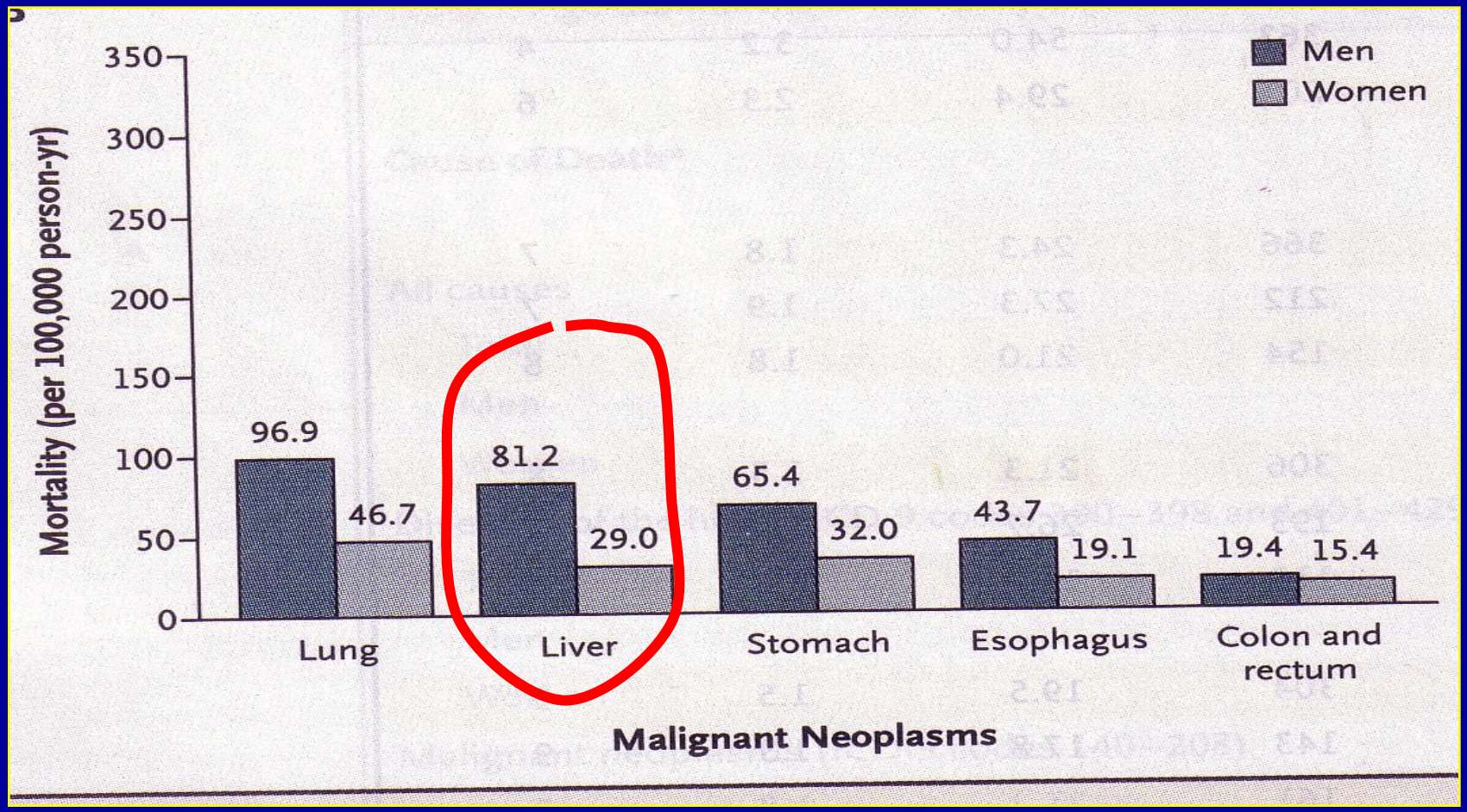
- 320,000-400,000 deaths are related to HCC/year
- Great variability according to geographic region
  - Hong Kong: 29 deaths / 100’000 population annually
  - Japan: 19 deaths / 100’000 population annually
  - France: 9 deaths / 100’000 population annually
  - Germany: 4 deaths / 100’000 population annually
  - North America: 2 deaths / 100’000 population annual

Higuchi et al., Jpn J Inf Dis, 2002

N Engl J Med September 15, 2005

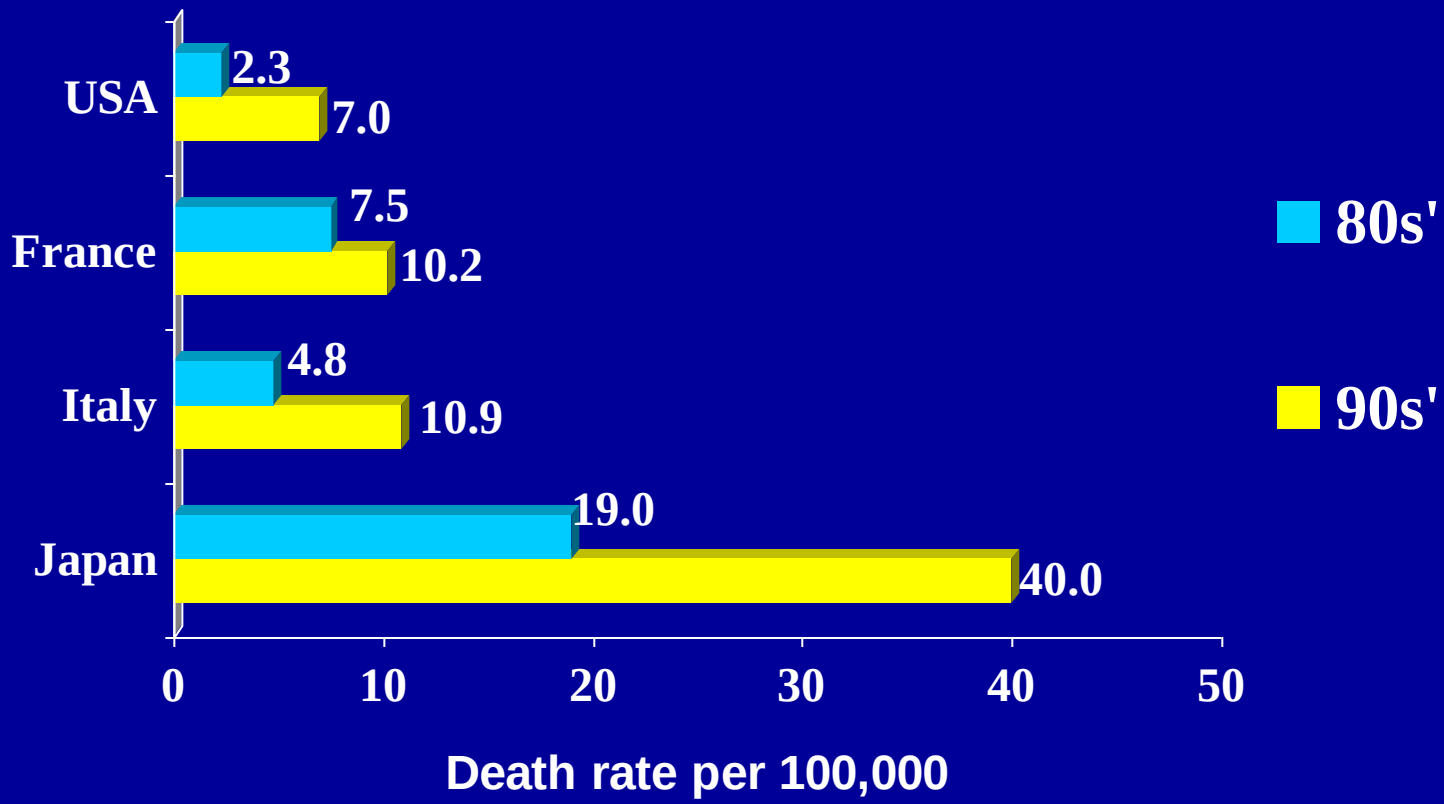
Major Causes of Death among Men and Women in China

Jiang He, M.D., Ph.D., Dongfeng Gu, M.D., Xigui Wu,et al



Hepatocellular Carcinoma : Incidence Time Trends

(Age-adjusted rates of death for HCC per 100,000 of population)



H. El Serag, A. Mason, NEJM, 1999
Higuchi et al., Jpn J Inf Dis, 2002

High Viral Load Predicts Poor Outcomes

- Large, long-term, prospective cohort studies have linked high viral load with poor outcomes

1. Haimen City Cohort
   Chen G, et al. Am J Gastroenterol. 2006;101:1797
2. Fox Chase Cancer Center Cohort Study
   Evans AA, et al. AASLD 2004. Abstract 144.
3. R.E.V.E.A.L Study Group
   Chen CJ, et al. JAMA. 2006;295:65-73.
   Iloeje UH, et al. Gastroenterology. 2006;130:678

Haimen City Cohort: Viral Load and Mortality From Liver Disease

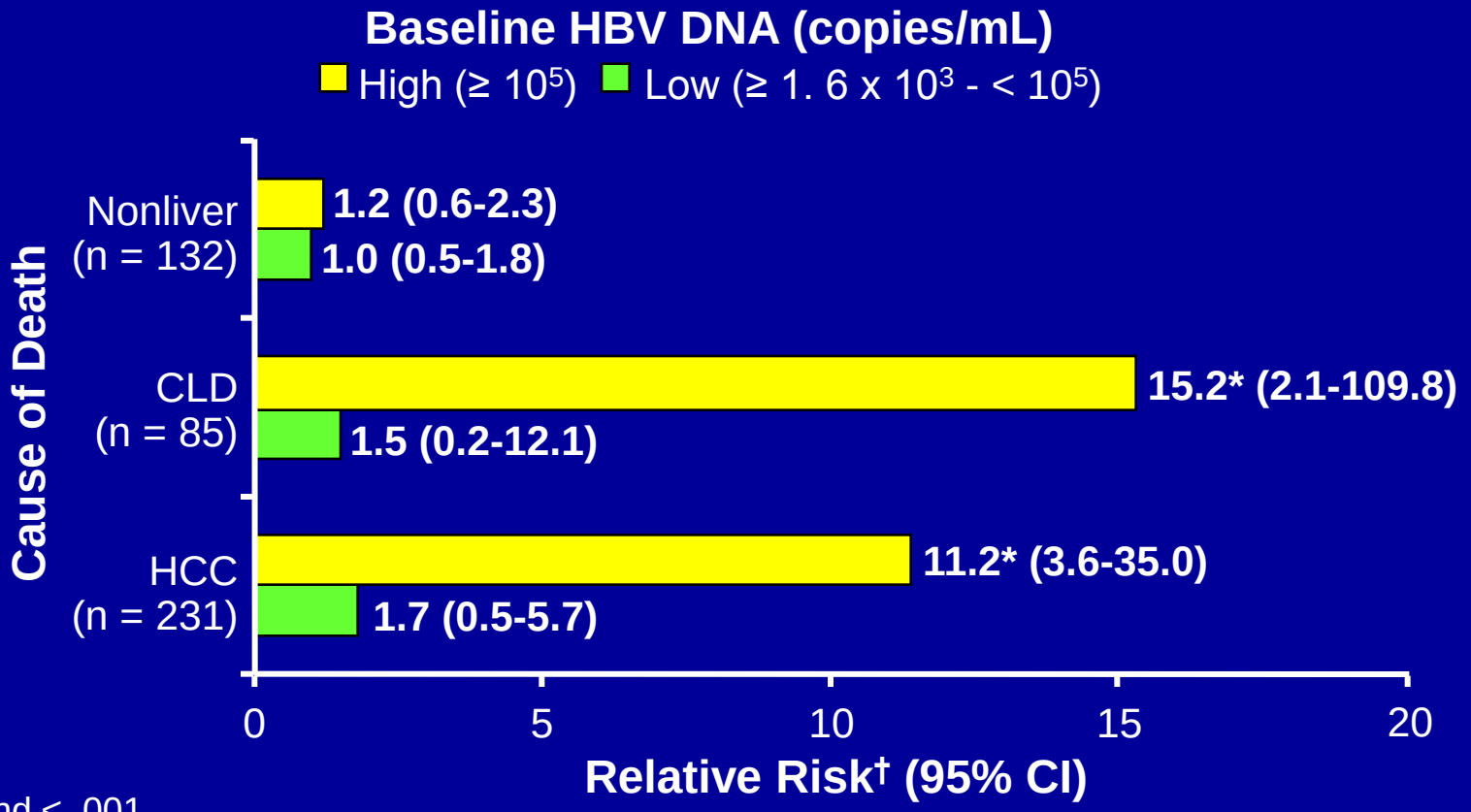
- 10-year prospective cohort study in Haimen City
- Permanent cohort of 83,794 subjects established 1992-1993
- 2354 subjects included in HBV mortality analysis
  - Serum HBV DNA tested on baseline samples
  - Mortality information from death certificate records
  - 448 deaths (231 HCC, 85 CLD, and 132 nonliver deaths)

CLD, chronic liver disease

HCC, hepatocellular carcinoma

Chen G, et al. Am J Gastroenterol. 2006;101:1797-1803.

Haimen City: Increased RR of HCC and CLD Mortality With High Viral Load



*P trend < .001

†Reference HBV DNA: < 1.6 x 10^3 copies/mL, adjusted for age and sex

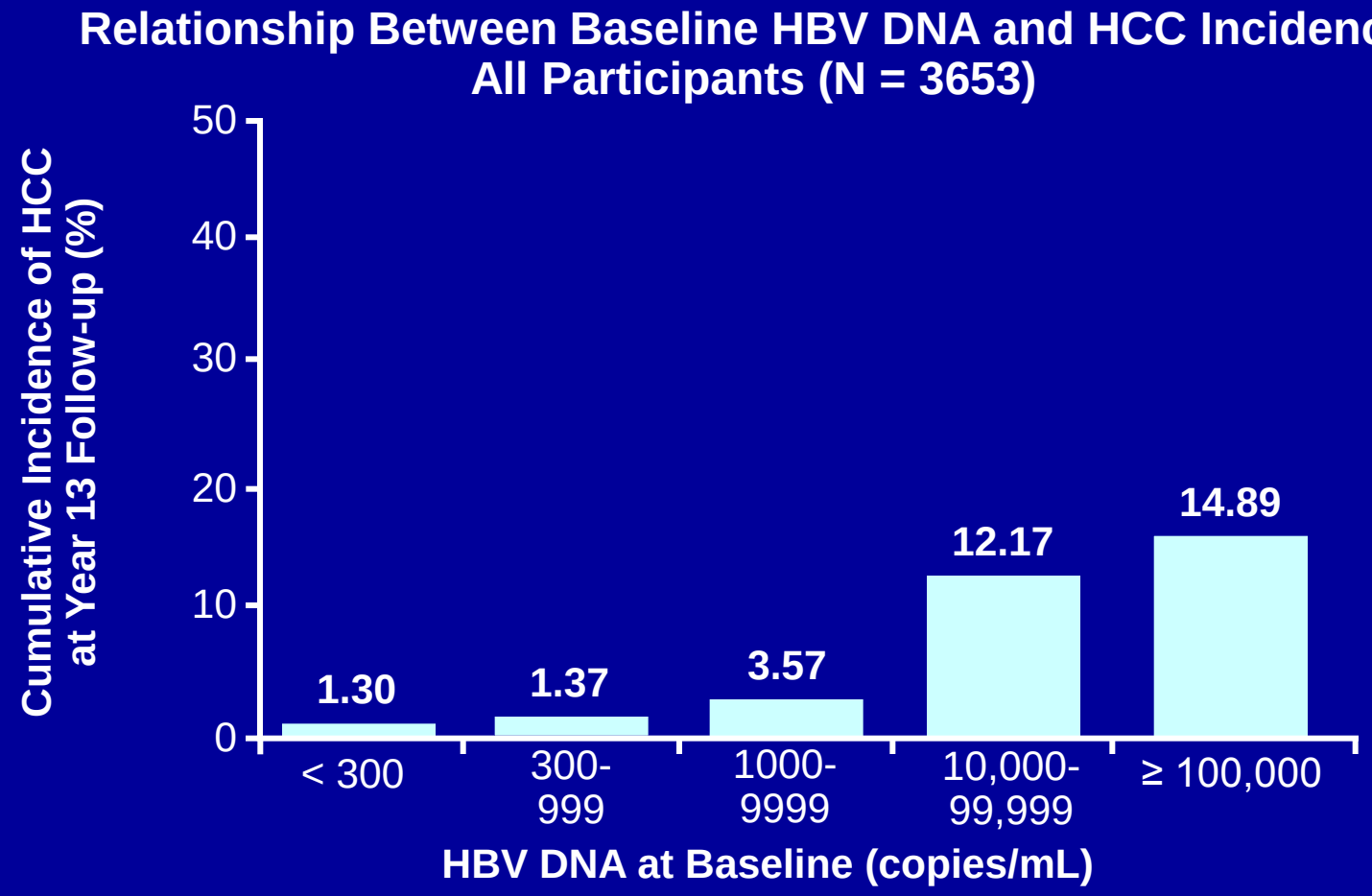
Chen G, et al. Am J Gastroenterol. 2006;101:1797-1803.

Haimen City Cohort: Conclusions

- Elevated baseline HBV DNA is
  - Associated with increased mortality from HCC and CLD
  - Useful prognostic tool
- Intervention for HBV DNA reduction should be explored

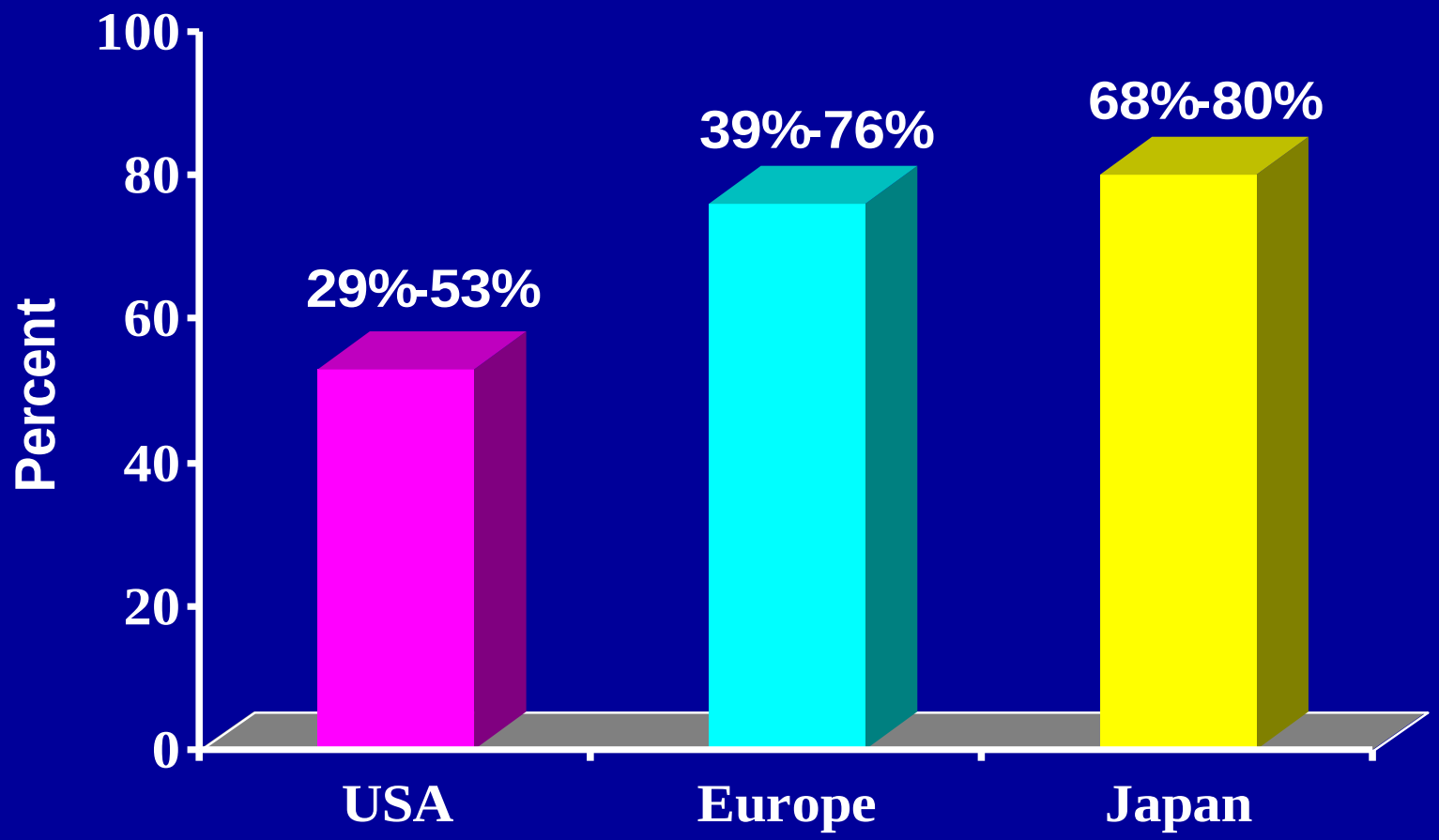
Chen G, et al. Am J Gastroenterol. 2006;101:1797-1803.

REVEAL: High HBV DNA Associated With Increased HCC Incidence



Chen CJ, et al. JAMA. 2006;295:65-73.

Prevalence of HCV Positivity in HCC



H. El Serag and A. Mason, NEJM, 1999
Yoshizawa et al. Oncology 2002;62 Suppl 1:8-17
Yao F et al., Curr Treat Options Oncol 2001 Dec;2(6):473-83

Conclusions

- Les hépatites B et C représentent un problème de santé publique dans de nombreux pays
- La transmission est sexuelle, parentérale et périnatale
- L'hépatite B peut être prévenue par le vaccin
- La cirrhose et le cancer du foie vont augmenter
- Des progrès thérapeutiques mais à coût élevé

Unsafe injections, needle-stick injuries cause 33 percent of hepatitis B infections worldwide, WHO says.

China's Xinhua (10/24/07) reports, "the World Health Organization (WHO) began an expert meeting to explore strategies aimed at promoting the use of safer needles." WHO said that "unsafe injections and needle stick injuries together cause 33 percent of new Hepatitis B infections and 2 million new cases of Hepatitis C in the world each year."

AHN (10/24/07) adds, "Six billion injections are given globally with syringes or needles that are reused without sterilization. This represents 40 percent of all injections given in developing countries; in some countries, the proportion is as high as 70 percent of injections."