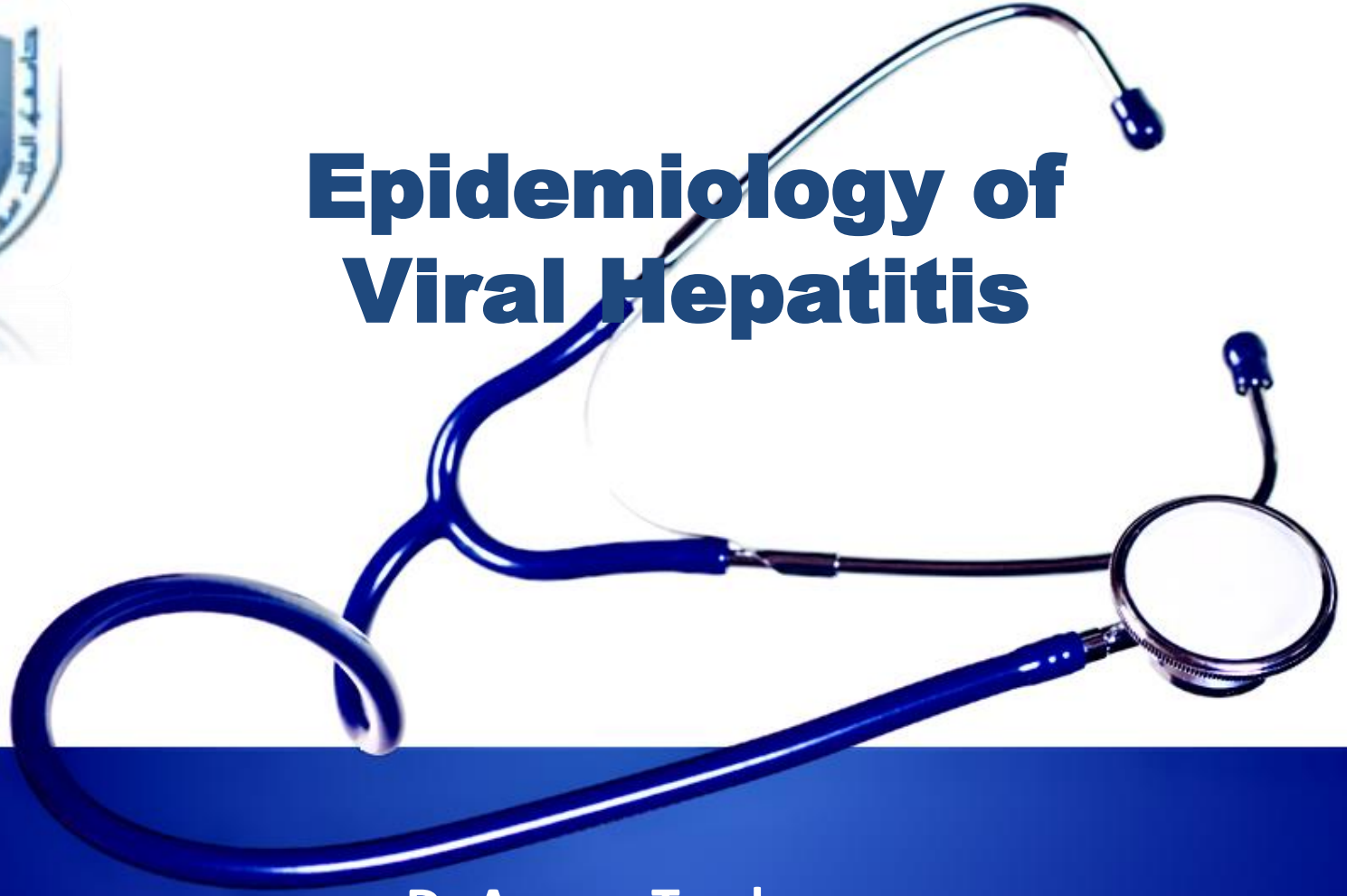
Epidemiology of Viral Hepatitis



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Objectives

At the end of the lecture students should be able:

- Understand Classification of viral hepatitis.
- Recognize the magnitude of viral hepatitis infections.
- Understand modes of transmission of different serotypes.
- Understand measures of prevention and control of different serotypes of viral hepatitis.

What is hepatitis?

- Hepatitis is an inflammation of the liver.
- The condition can be self-limiting or can progress to fibrosis (scarring), cirrhosis or liver cancer.
- Hepatitis viruses are the most common cause of hepatitis
- Other infections, toxic substances (e.g. alcohol, certain drugs), and autoimmune diseases can also cause hepatitis.
- There are 5 main hepatitis viruses: types A, B, C, D and E.
- Types B and C lead to chronic disease in hundreds of millions of people and, together, are the most common cause of liver cirrhosis and cancer.

Hepatitis

1. Viral hepatitis is a major global health problem and needs an urgent response.

- There were approximately 350 million people living with chronic hepatitis at the end of 2015.
- Globally, an estimated 257 million people were living with hepatitis B (HBV) infection, and 71 million people were living with hepatitis C (HCV) infection in 2015.

2. Very few of those infected accessed testing and treatment, especially in low- and middle-income countries.

- By the end of 2015, only 9% of HBV-infected people and 20% of HCV-infected people had been tested and diagnosed. Of those diagnosed with HBV infection, 8% (or 1.7 million people) were on treatment, while 7% of those diagnosed with HCV infection (or 1.1 million people) had started treatment in 2015.
- The global targets for 2030 are: 90% of people with HBV and HCV infections tested and 80% of eligible patients are reached with treatment.

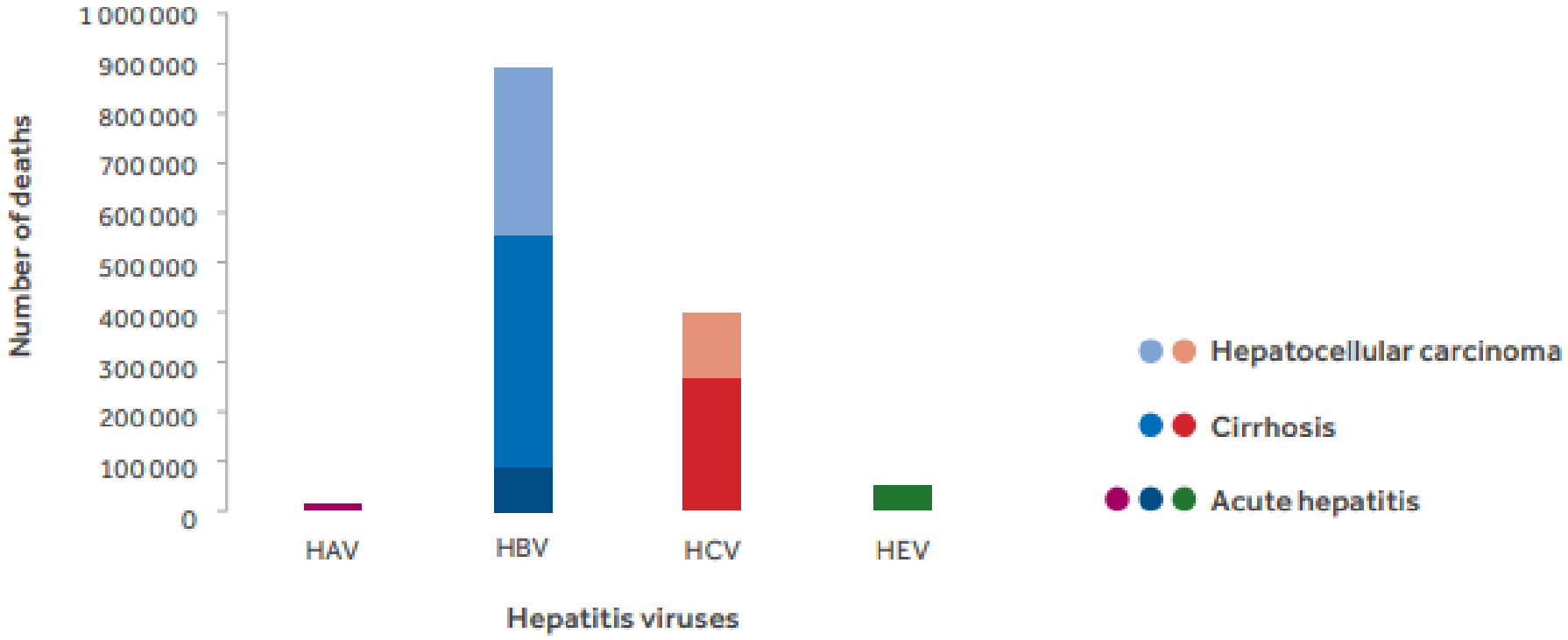
Hepatitis

3. Viral hepatitis caused 1.34 million deaths in 2015 - comparable with TB deaths and exceeding deaths from HIV. Hepatitis deaths are increasing.

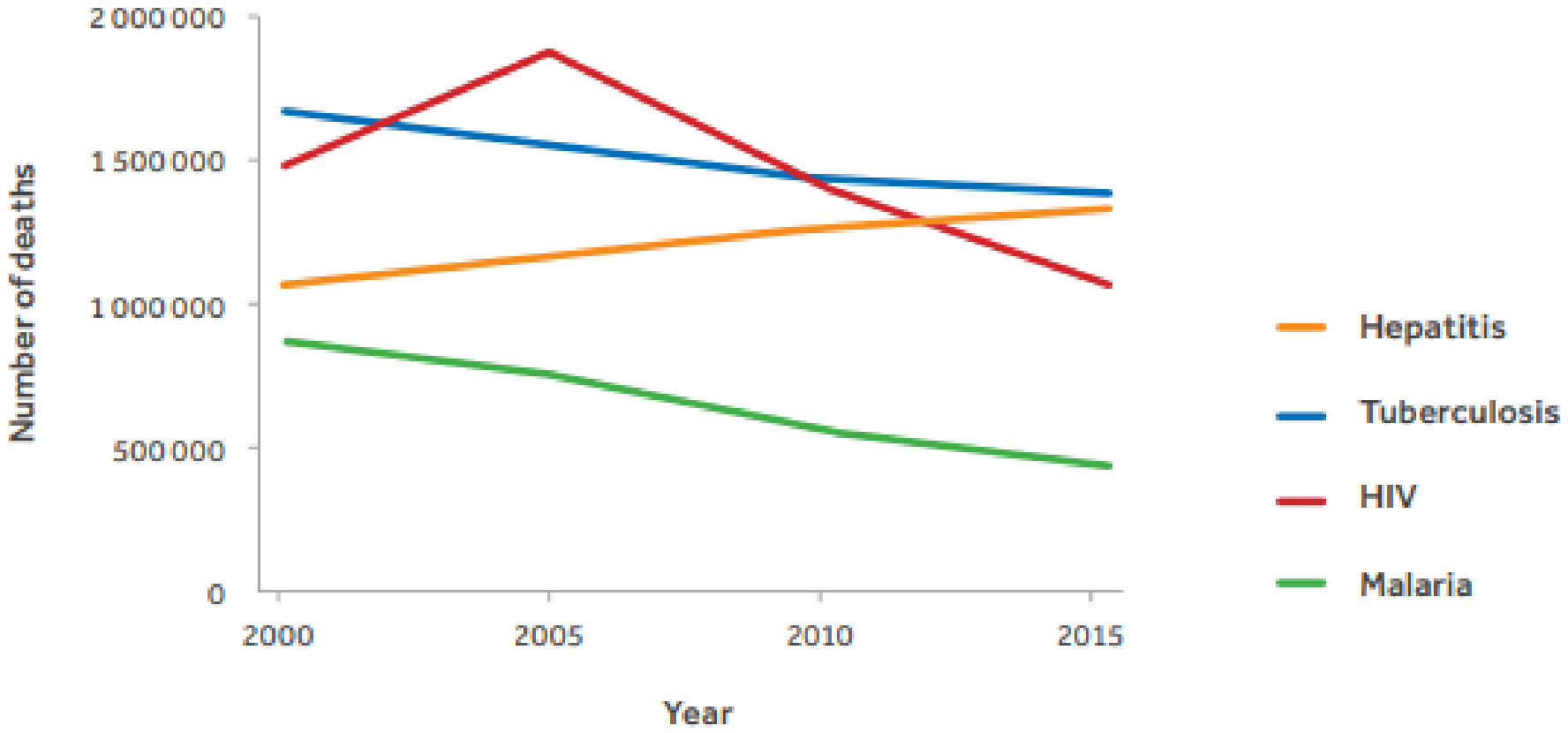
4. New hepatitis infections continue to occur, mostly hepatitis C.

- The number of children under five living with chronic HBV infection was reduced to 1.3% in 2015 (from 4.7% before vaccines were introduced).
- Hepatitis B vaccine is preventing approximately 4.5 million infections per year in children.
- However, 1.75 million adults were newly infected with HCV in 2015, largely due to injecting drug use and due to unsafe injections in health care settings in certain countries.

Deaths from viral hepatitis, by virus and type of sequelae, 2015

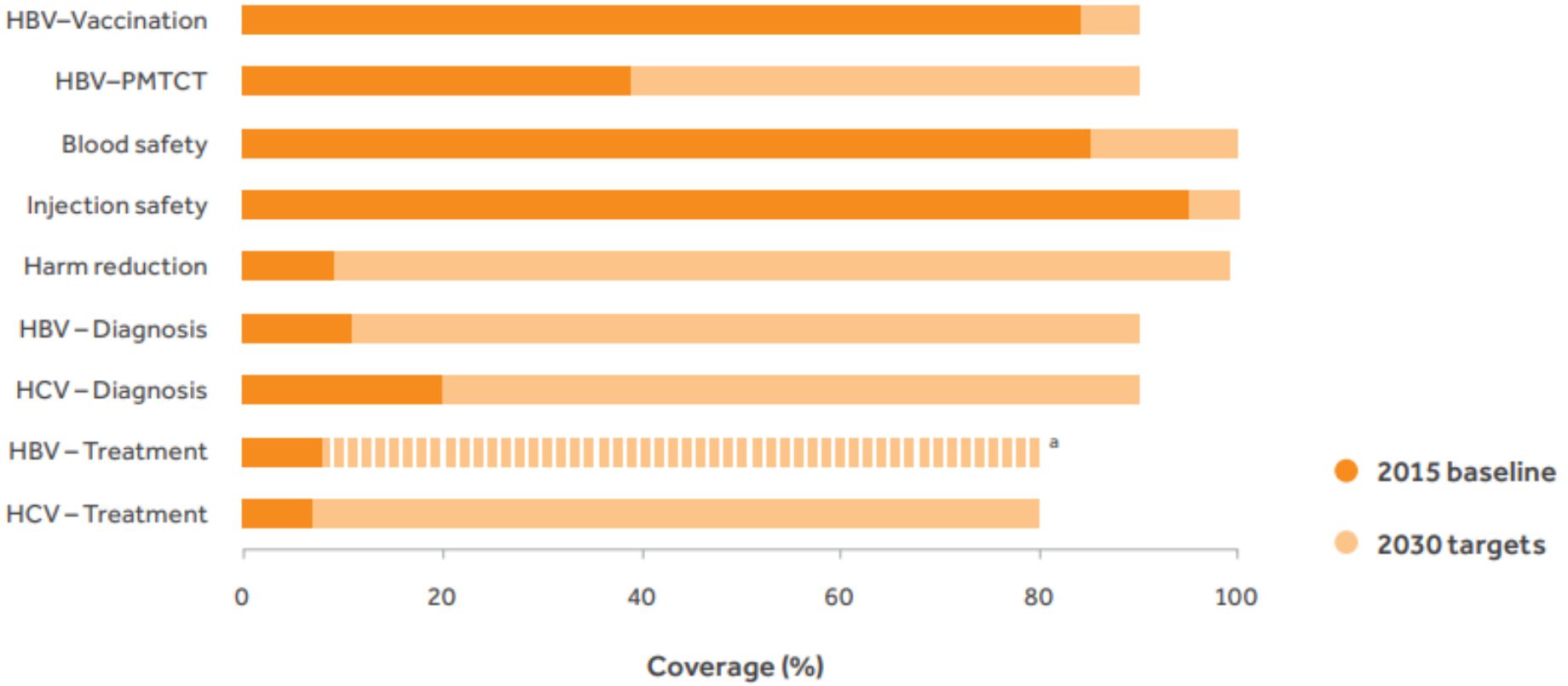


Global annual mortality from hepatitis, HIV, tuberculosis and malaria, 2000–2015



Source: WHO global health estimates (Global Health Estimates 2015: deaths by cause, age, sex, by country and by region, 2000-2015. Geneva: World Health Organization; 2016.)

Global Health Sector Strategy on viral hepatitis: 2015 baseline towards the 2030 targets

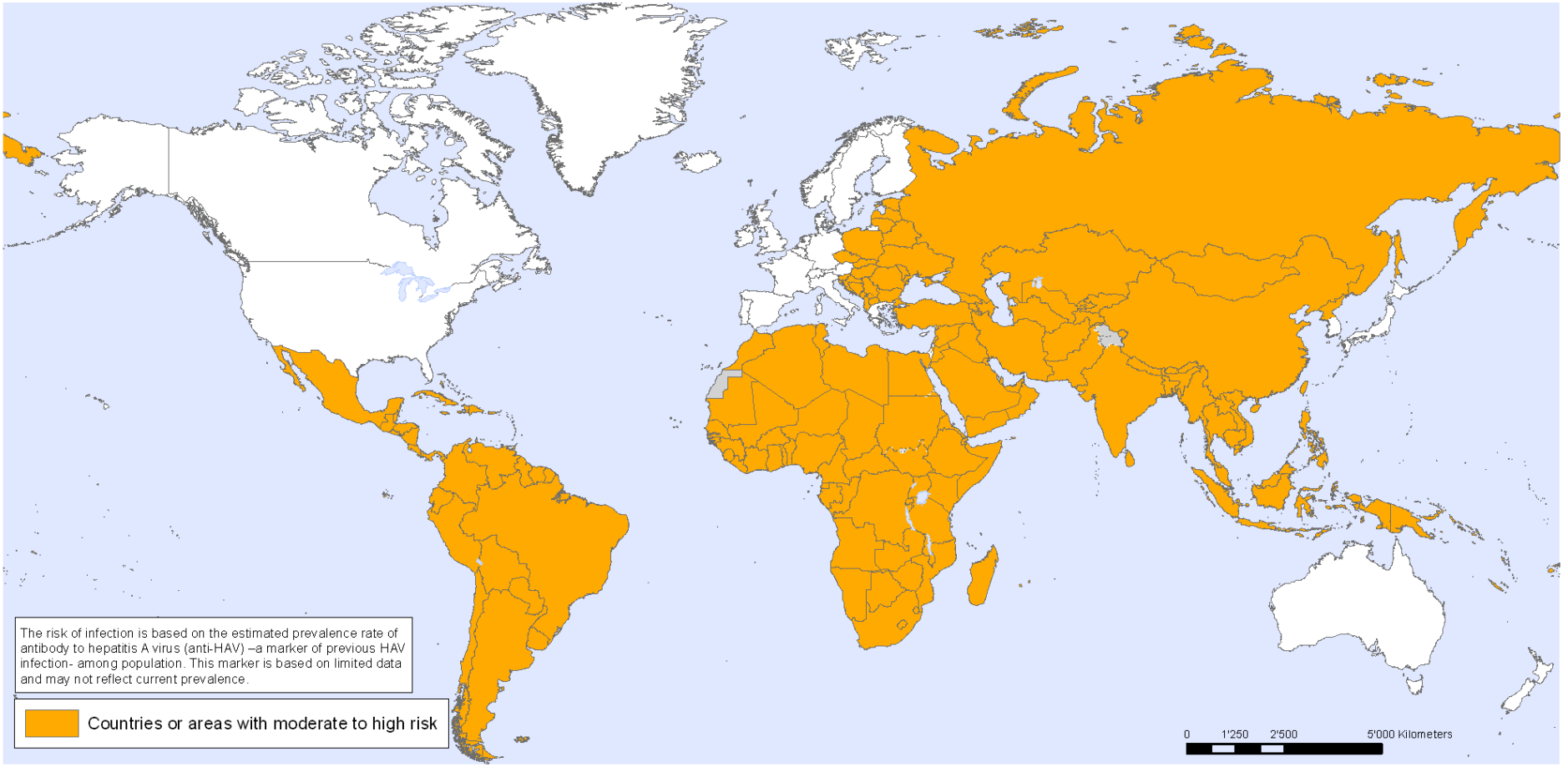


[a] Measurement of progress on HBV treatment target currently limited by the absence of data on the proportion of persons eligible and the absence of a functional cure

Hepatitis A

- Hepatitis A is a viral liver disease that can cause mild to severe illness.
- The hepatitis A virus (HAV) is transmitted through ingestion of contaminated food and water or through direct contact with an infectious person.
- Almost everyone recovers fully from hepatitis A with a lifelong immunity. However, a very small proportion of people infected with hepatitis A could die from fulminant hepatitis.
- The risk of hepatitis A infection is associated with a lack of safe water, and poor sanitation and hygiene (such as dirty hands).
- Epidemics can be explosive and cause substantial economic loss.
- A safe and effective vaccine is available to prevent hepatitis A.
- Safe water supply, food safety, improved sanitation, hand washing and the hepatitis A vaccine are the most effective ways to combat the disease.

Hepatitis A, countries or areas at risk



The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

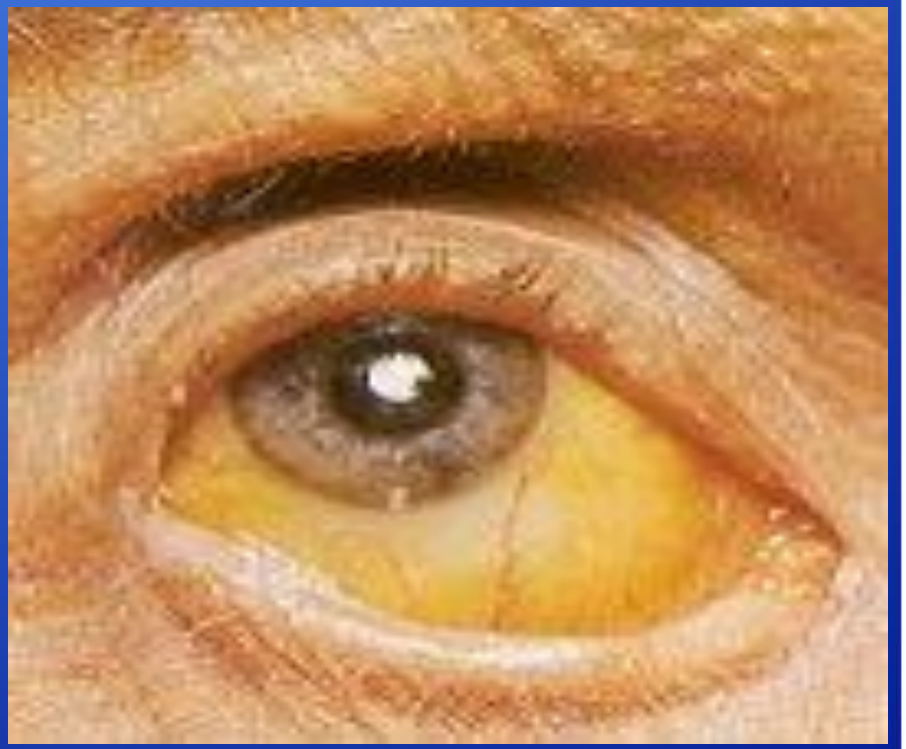
Data Source: World Health Organization.
Jacobsen KH, Wiersma ST. Hepatitis A virus seroprevalence by age and world region, 1990 and 2005. Vaccine 2010 Sep;28(41):6653-7
Map Production: Public Health Information and Geographic Information Systems (GIS)
World Health Organization

World Health Organization

Hepatitis A

Clinical presentation:

- Abrupt onset.
- Fever
- Malaise
- Anorexia
- Abdominal discomfort
- Jaundice



Hepatitis A

- More than **90% are asymptomatic**
- Seroprevalence **increases with age.**
- At age 15, 95% are seropositive.
- Case fatality rate (CFR)= 0.3%.
- If age > 40 years CFR=2%.
- **Studies in KSA:**

1997	25%	
1999	25%	Taif
	10-82%	Jazan (1-12 years)

Chain of infection

- **Agent**: RNA virus
- **Reservior** : Human (Clinical & subclinical cases)
- **Incubation period**: 15-45 days (median one month).

Chain of infection

- **Period of communicability** : Last two weeks of I.P. + one week of illness.

- **Modes of transmission**:

  Fecal-oral route.

  Common source outbreaks.

  Blood transfusion (rare).

Prevention and Control

- **Good sanitation & personal hygiene**.

  "Careful hand washing"

- Day- Care centers

  Hand washing after every diaper change and before eating.

- **Shellfish**

  heat 85-90C 4 minutes.

  steam 90 seconds.

Prevention and Control

- Inactivated **hepatitis A vaccine**
- Schedule 2 doses after 6 months interval.
- Intramuscularly.
- Protection after one month.
- Lasting immunity at least 10 years.

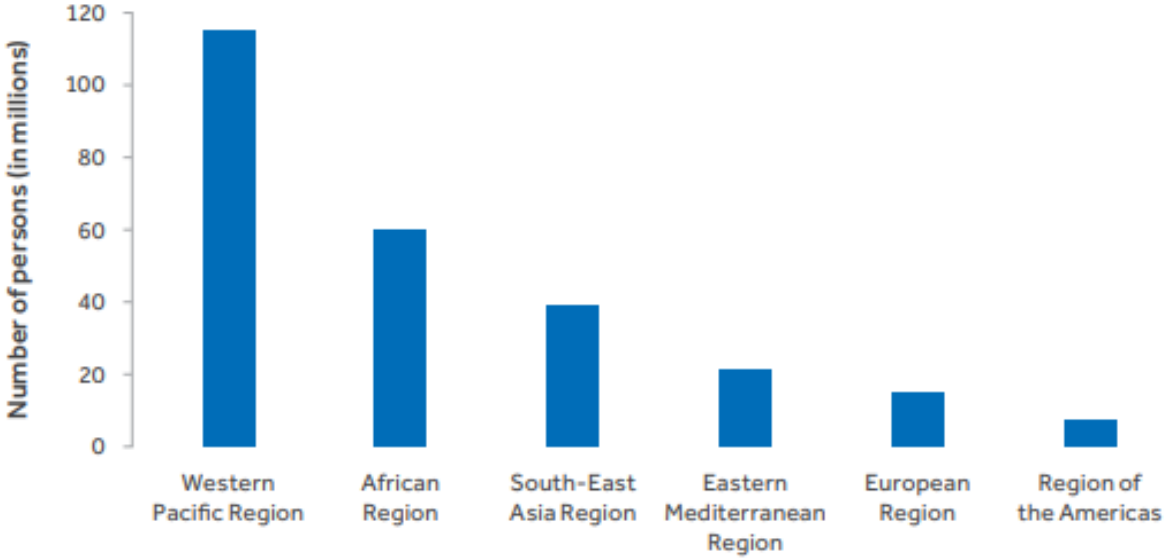
Hepatitis A patient:

- **Enteric precaution** for the Period of communicability

Hepatitis B

- Hepatitis B is a viral infection that attacks the liver and can cause both acute and chronic disease.
- The virus is transmitted through contact with the blood or other body fluids of an infected person.
- An estimated 257 million people are living with hepatitis B virus infection (defined as hepatitis B surface antigen positive).
- In 2015, hepatitis B resulted in 887 000 deaths, mostly from complications (including cirrhosis and hepatocellular carcinoma).
- Hepatitis B is an important occupational hazard for health workers.
- However, it can be prevented by currently available safe and effective vaccine.

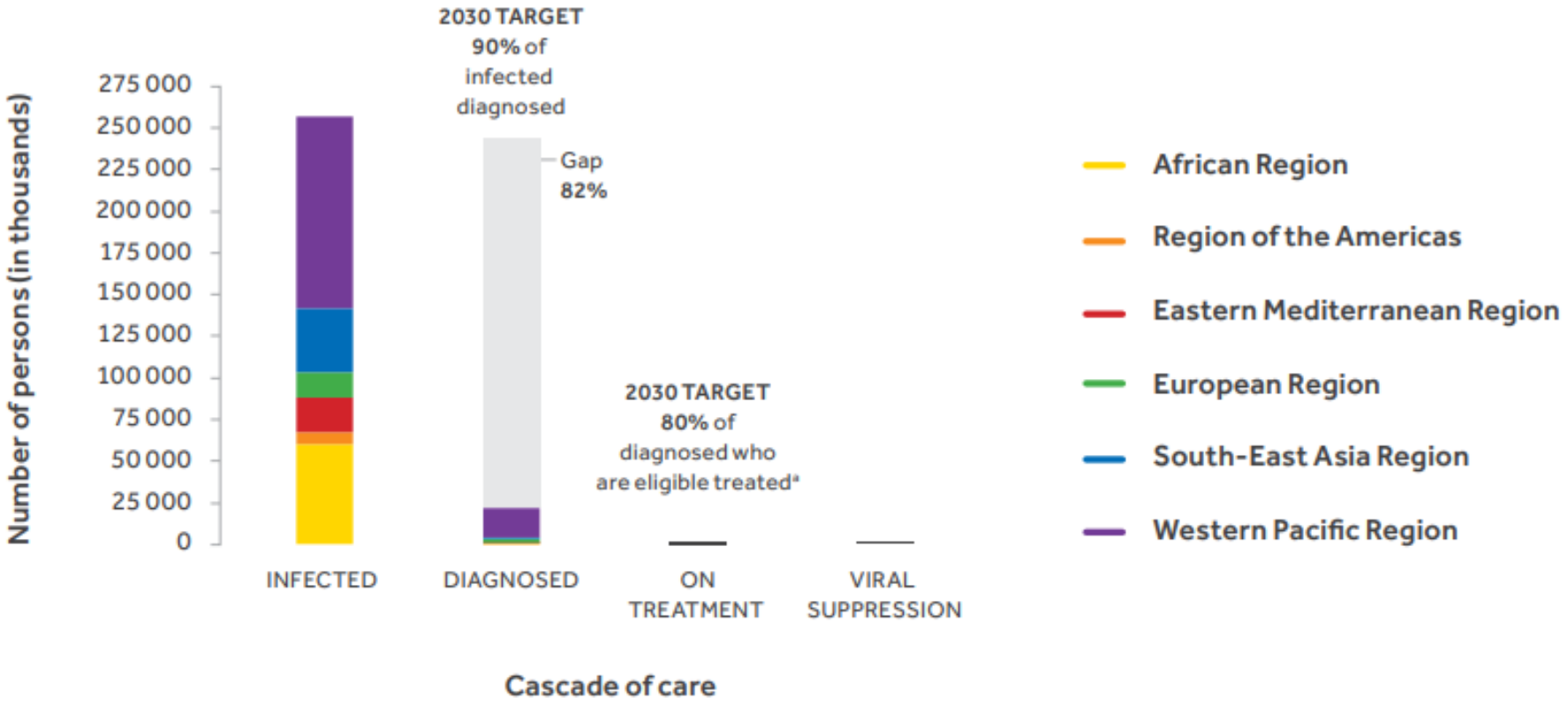
Prevalence of HBV infection (HBsAg) in the general population by WHO region 2015:



	Estimates of the prevalence of HBV infection (%)			Estimated number of persons living with HBV (millions)		
		Uncertainty interval (95%)			Uncertainty interval (95%)	
WHO region	**Best**	**Lower**	**Higher**	**Best**	**Lower**	**Higher**
African Region	6.1	4.6	8.5	60	45	84
Region of the Americas	0.7	0.4	1.6	7[a]	4	16
Eastern Mediterranean Region	3.3	2.6	4.3	21	17	28
European Region	1.6	1.2	2.6	15	11	23
South-East Asia Region	2.0	1.5	4.0	39	29	77
Western Pacific Region	6.2	5.1	7.6	115	93	140
Total	**3.5**	**2.7**	**5.0**	**257**	**199**	**368**

Source: WHO, work conducted by the London School of Hygiene & Tropical Medicine (LSHTM). *See* Annex 2.

Cascade of care for HBV infection, by WHO region, 2015: effective treatment is underused in most regions



Source: WHO estimates, conducted by the Center for Disease Analysis. *See* Annex 2.

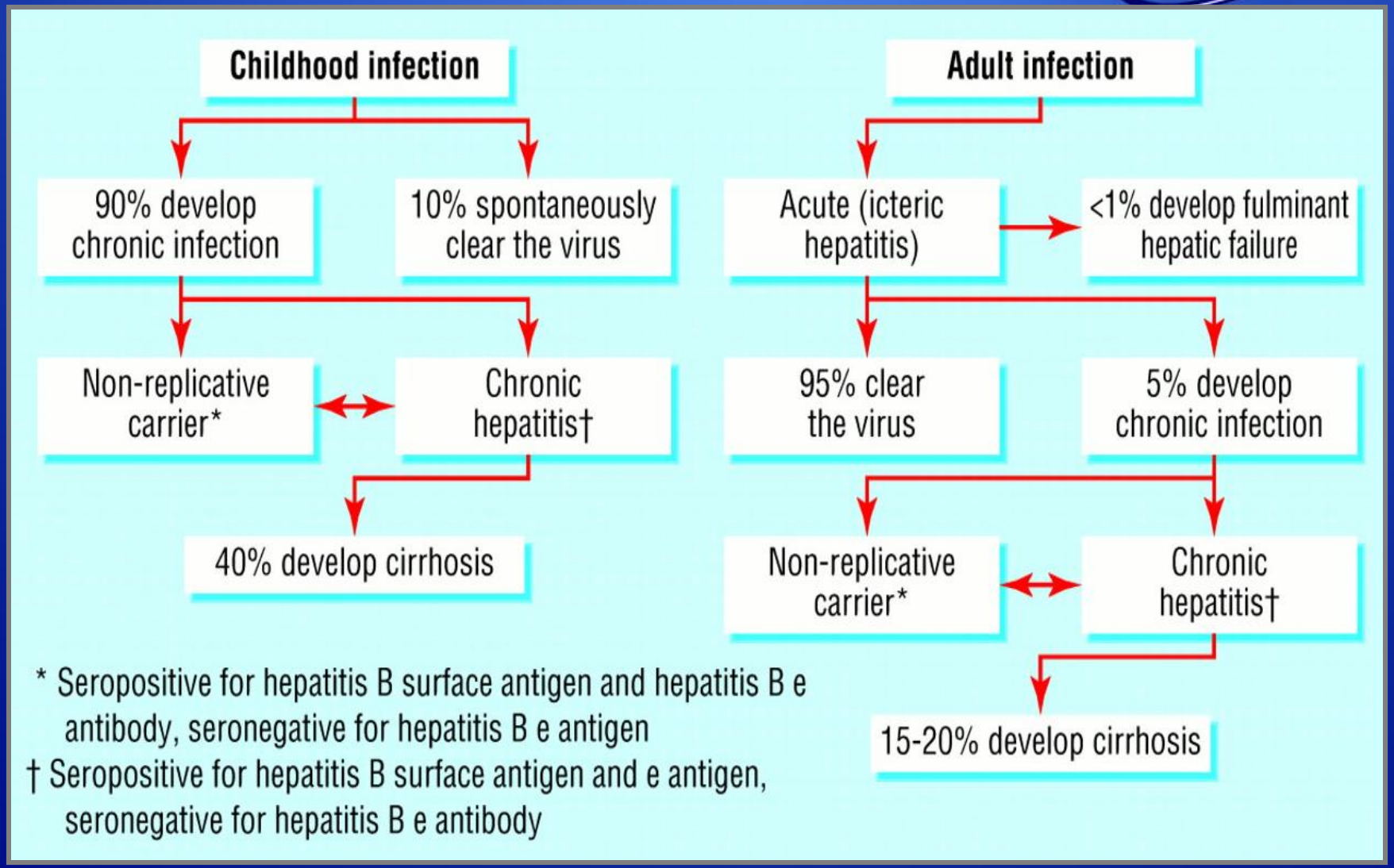
[a] As the proportion of persons eligible for treatment among those diagnosed is unknown, the treatment gap cannot be calculated.

Hepatitis B

Clinical presentation:

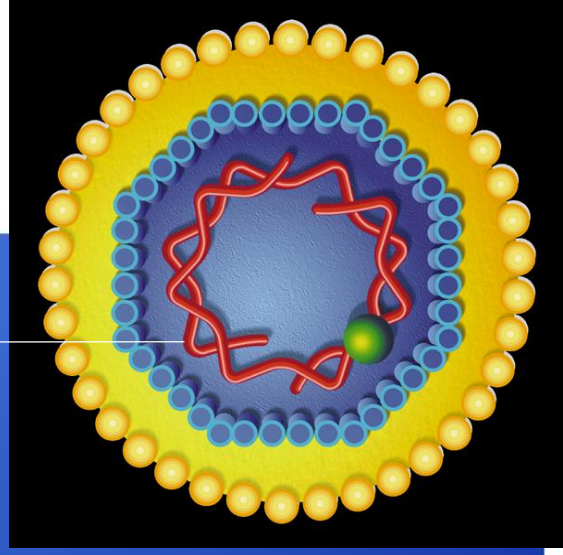
- Insidious onset.
- Anorexia.
- Abdominal discomfort.
- Nausea.
- Vomiting.
- Arthralgia.
- Jaundice.

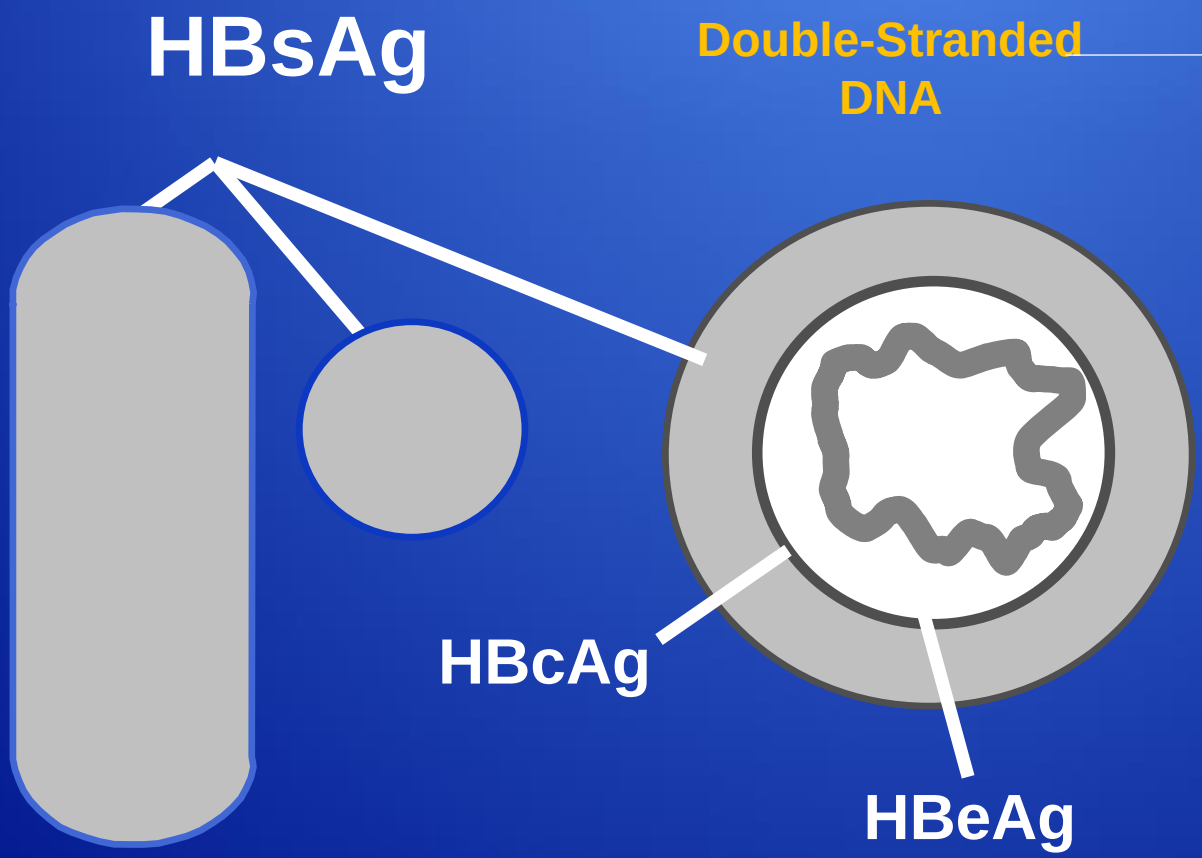
Natural History



Gow, BMJ 2001

Hepatitis B Virus





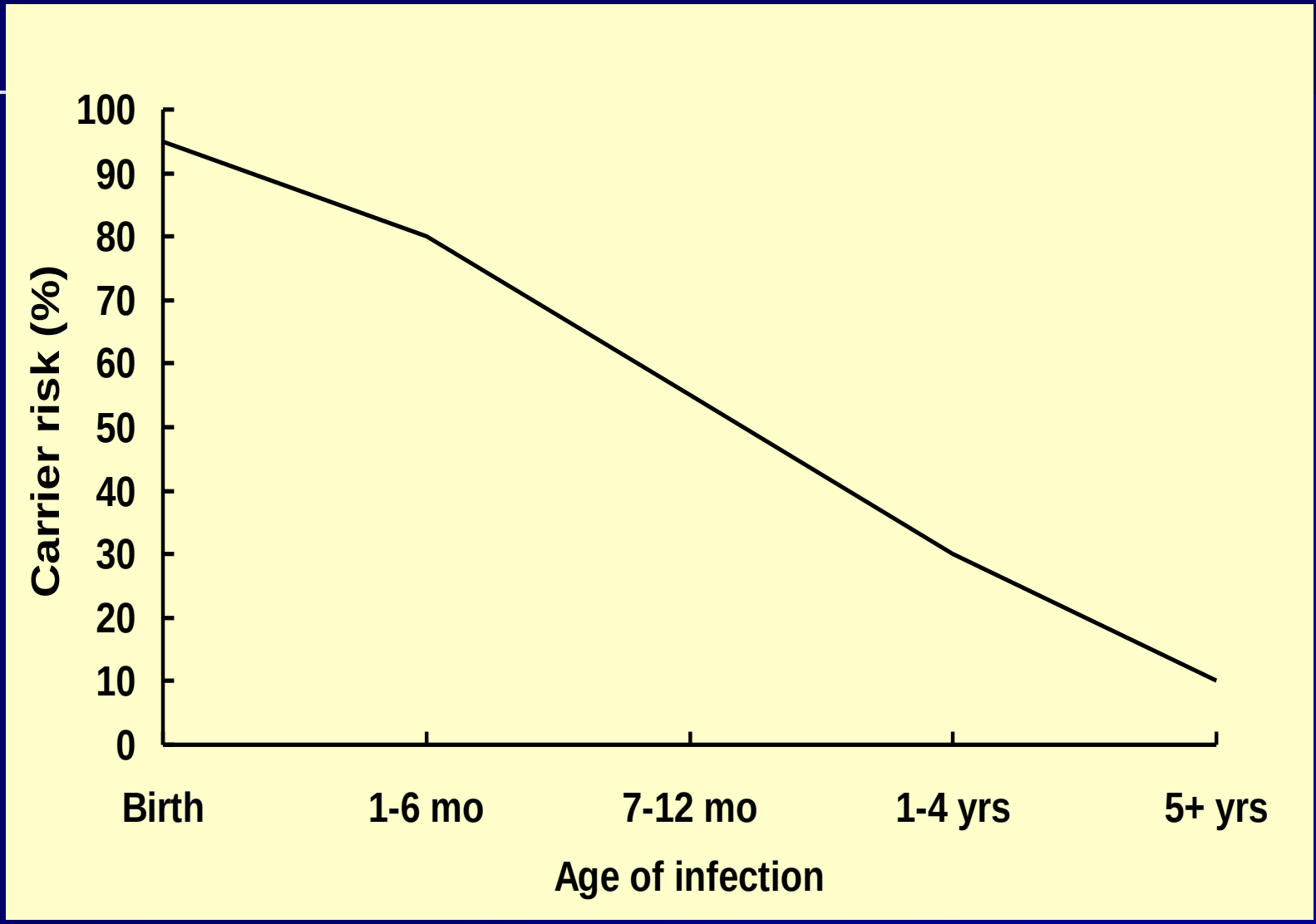
- The presence of HBsAg indicates active infection or chronic carrier.
- Antibody to HBsAg, from either disease or vaccine, indicates immunity.

Chain of infection

- **Agent**: Double strand DNA.

  Serotypes adw, ayw, adr, ayr.
- **Reservior**: Human (case + carrier).
- **I.P.** 2-3 months.
- **P.C.** One week of I.P. + illness period + carriage.
- **Carriage depends on age at infection;**
  - <5 yrs, 30%-90% chronicity
  - >5 yrs, 2%-10% chronicity

Risk of Chronic HBV Carriage by Age of Infection



Concentration of Hepatitis B Virus in Various Body Fluids

High	Moderate	Low/Not Detectable
blood	semen	urine
serum	vaginal fluid	feces
wound exudates	saliva	sweat
		tears
		breastmilk

CDC
Centers for Disease Control and Prevention

Hepatitis B Virus
Modes of Transmission

- Parenteral
- Sexual
- Perinatal

Modes of transmission:

- Percutaneous and permucosal exposure to:
  - infective body fluids
  - Blood transfusion
  - Organs transplants
  - Sharing needles
  - Haemodialysis
  - Needlestick
  - Tattooing
  - Razors & toothbrushes.

Modes of transmission:

- **Sexual transmission.**
- **Perinatal transmission** especially when HBs Ag carrier mothers are also HBe Ag positive.

Prevention and control

- **Hepatitis B Vaccine**

Subunit recombinant HBs Ag IM in the deltoid region.

3 dose series, typical schedule 0, 1, 6 months - no maximum time between doses (no need to repeat missed doses or restart)

- Wide scale **immunization of infants** (revise compulsory vaccination schedule).
- **Immunization of high risk persons**.

Haemodialysis patients.

Bleeding disorders.

Susceptible households.

Health care personnel.

Prevention and control

- **Blood banks:**

Avoid donors from risky groups.

Education & history taking.

Testing for HBs Ag.

- **Discourage:**

Tattooing, Drug abuse,

Extramarital sexual relations.

- **Needle stick**

Single dose of HBIG (24 hours).

Vaccine series.

Prevention and control

- **Sexual exposure**
  - Single dose of HBIG (14 days) and
  - Vaccination.

- **Infants to HBsAg +ve mothers.**
  - 0.5 ml HBIG (IM).
  - First dose of the vaccine.
  - 2nd & 3rd doses at 1 & 6 months later.

- **Health care personnel.**

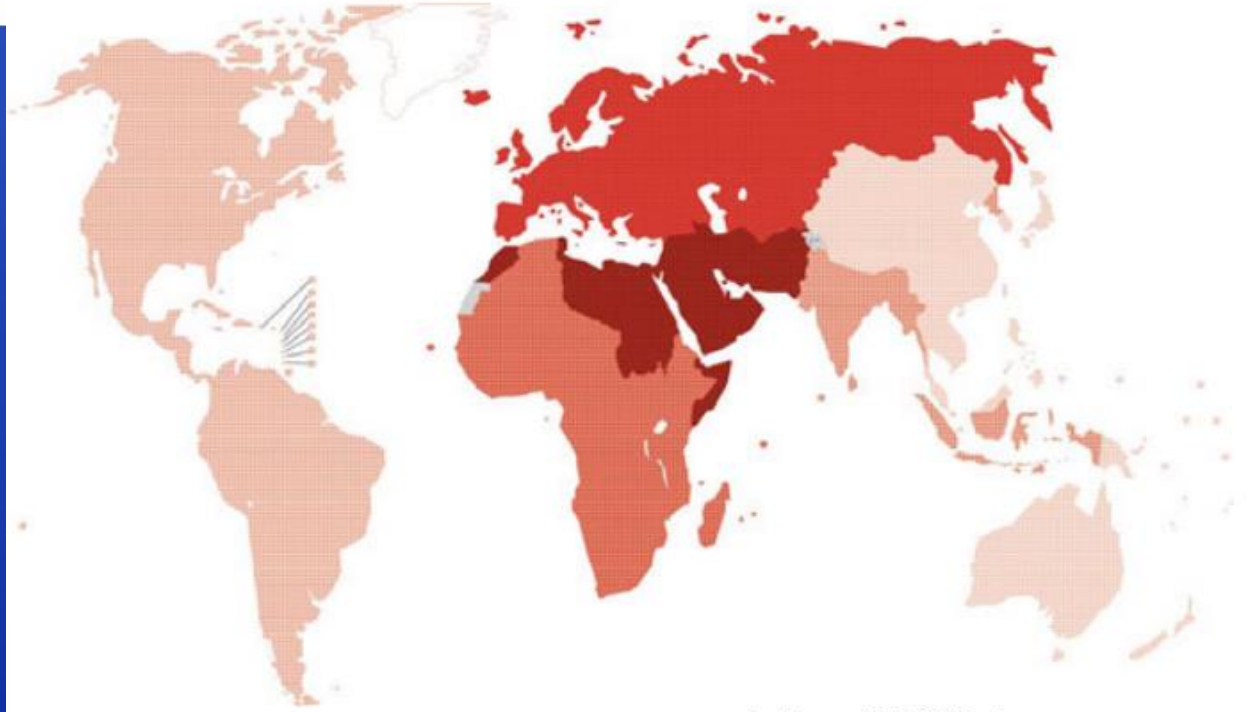
  Universal precautions

Hepatitis C

Hepatitis C

- Hepatitis C virus can cause both acute and chronic hepatitis, ranging in severity from a mild illness lasting a few weeks to a serious, lifelong illness.
- The hepatitis C virus is a bloodborne virus and the most common modes of infection are through exposure to small quantities of blood. This may happen through injection drug use, unsafe injection practices, unsafe health care, and the transfusion of unscreened blood and blood products.
- Globally, an estimated 71 million people have chronic hepatitis C infection.
- A significant number of those who are chronically infected will develop cirrhosis or liver cancer.
- Approximately 399 000 people die each year from hepatitis C, mostly from cirrhosis and hepatocellular carcinoma.
- Antiviral medicines can cure more than 95% of persons with hepatitis C infection,but access to diagnosis and treatment is low.
- There is currently no vaccine for hepatitis C; however research in this area is ongoing.

Incidence of HCV infection in the general population, by WHO region, 2015:



		Incidence of HCV infection			
		Incidence rate (per 100 000)		Total number (000)	
WHO region	Map key	Best estimate	Uncertainty interval	Best estimate	Uncertainty interval
African Region		31.0	22.5–54.4	309	222–544
Region of the Americas		6.4	5.9–7.0	63	59–69
Eastern Mediterranean Region		62.5	55.6–65.2	409	363–426
European Region		61.8	50.3–66.0	565	460–603
South-East Asia Region		14.8	12.5–26.9	287	243–524
Western Pacific Region		6.0	5.6–6.6	111	104–124
Global		**23.7**	**21.3–28.7**	**1 751**	**1 572–2 120**

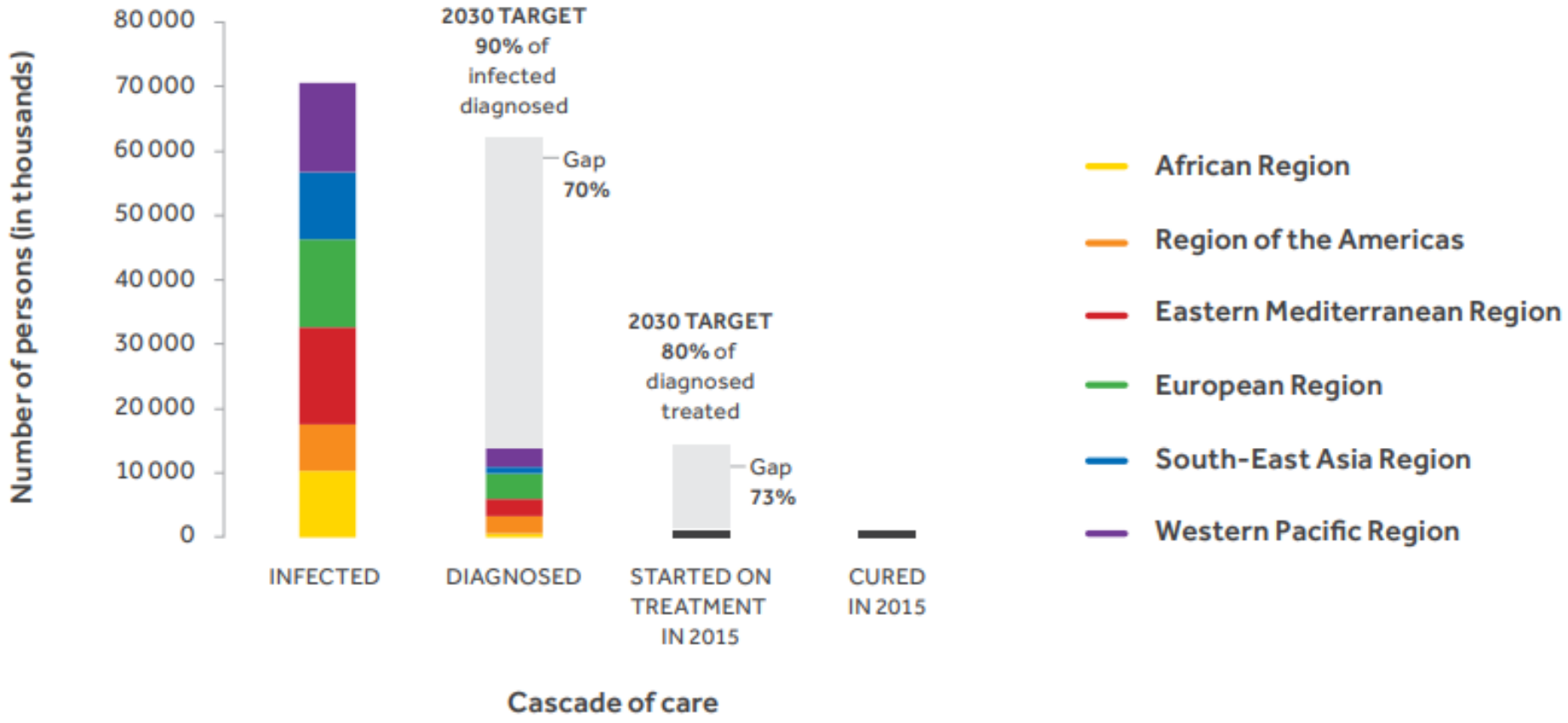
Source: WHO, work conducted by the Center for Disease Analysis. *See* Annex 2.

Prevalence of HCV infection (HCV RNA positive) in the general population, by WHO region, 2015

	Estimates of the prevalence of HCV infection (%)			Estimated number of persons living with HCV (millions)		
		Uncertainty interval			Uncertainty interval	
WHO region	**Best**	**Lower**	**Higher**	**Best**	**Lower**	**Higher**
African Region	1.0	0.7	1.6	11	7	16
Region of the Americas	0.7	0.6	0.8	7	6	8
Eastern Mediterranean Region	2.3	1.9	2.4	15	13	15
European Region	1.5	1.2	1.5	14	11	14
South-East Asia Region	0.5	0.4	0.9	10	8	18
Western Pacific Region	0.7	0.6	0.8	14	10	15
Total	**1.0**	**0.8**	**1.1**	**71**	**62**	**79**

Source: WHO, work conducted by the Center for Disease Analysis. *See* Annex 2.

Cascade of care for HCV infection, by WHO region, 2015



Source: WHO estimates, conducted by the Center for Disease Analysis. *See* Annex 2.

AGE SPECIFIC PREVALENCE OF ANTIBODY TO HCV/ANTI-HCV AMONG HEALTHY SAUDIS

Age Group (years)	Community Based Study		
	No. tested	Anti-HCV Pos. (%)	Location
1 – 10	1214	0.6	Central Province
	490	0.0	Eastern Province
	677	0.4	North-Western Province
	1096	0.9	South-Western Province
	1019	1,9	Southern Province
10 – 19	504	6 (1.2)	Gizan
20 – 29	361	4 (1.1)	Gizan
30 - 39	290	6 (2.1)	Gizan
40 – 49	183	6 (3.3)	Gizan
> 50	144	5 (3.5)	Gizan
Total	1482	27 (1.8)	Gizan

Al-Faleh et al, Hepatology Vol. 14(2), 1991

PREVALENCE OF ANTIBODY TO HCV TO SAUDI HIGH RISK GROUPS

High Risk Group	No. Tested	No. Pos.	%	Location
Hemophiliacs	28	22	78.6	KKUH, Riyadh
Thalassaemia and sickle cell disease	78	26	33.3	KKUH, Riyadh
β-thalassaemia major	20	14	70.0	KKUH, Riyadh*
Sickle cell anaemia	55	10	18.2	KKUH, Riyadh*
Patients with sexually transmitted diseases	220	35	15.9	KKUH, Riyadh*

2nd-generation anti-HCV tests and confirmation were only done in this study.

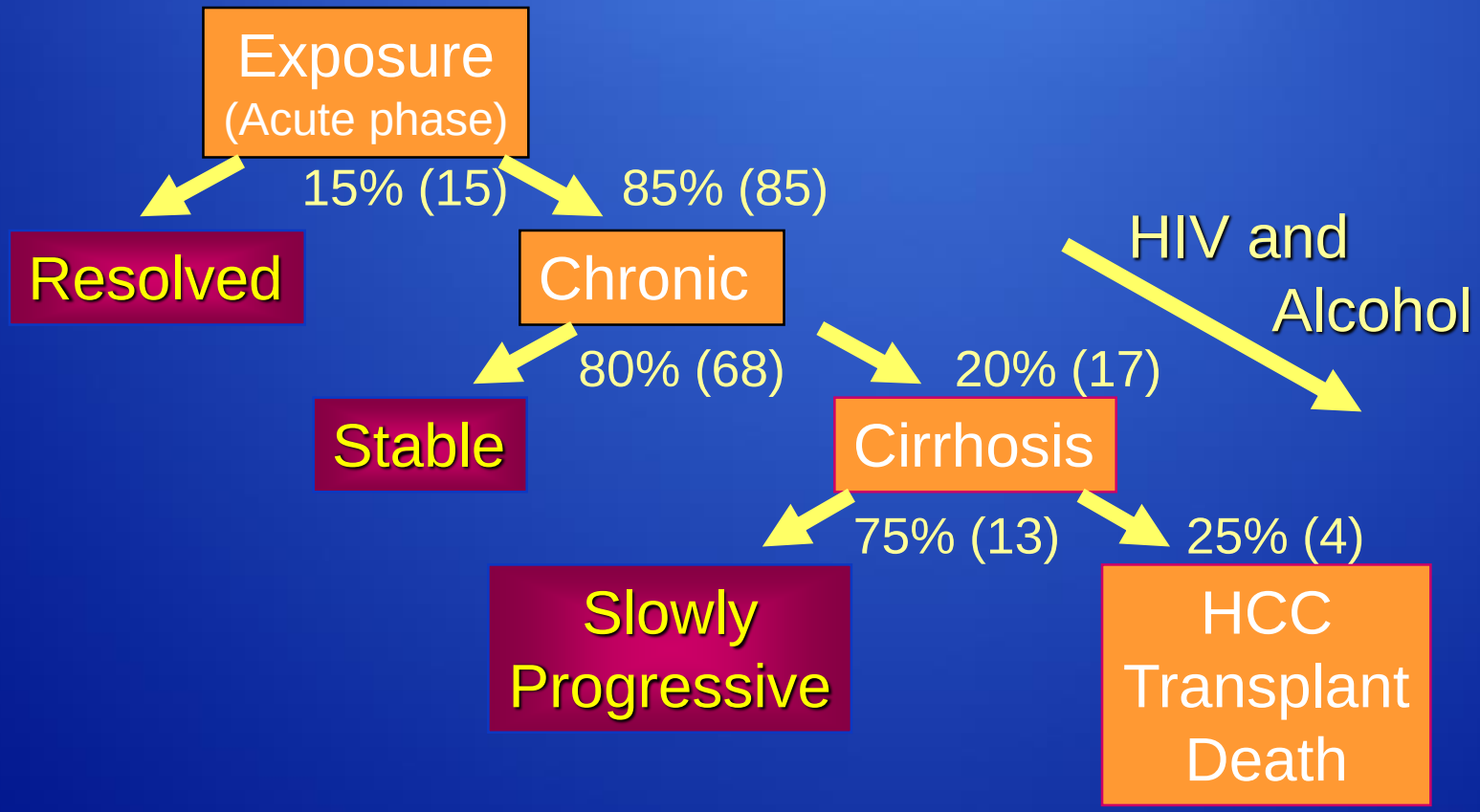
ANTI-HCV IN HAEMODYLYSIS PATIENTS IN SAUDI POPULATION

Author	No. of Persons	Type of Test	%
Fakunle et al	895	ELISA I	53.7
Al-Mugeriren et al	20 Children	ELISA I	45.0
Ayoola et al	74	ELISA I	41.9
Huraib et al	22 HD Centre 1147 Persons	ELISA II	68.8

Hepatitis C Virus Genotypes

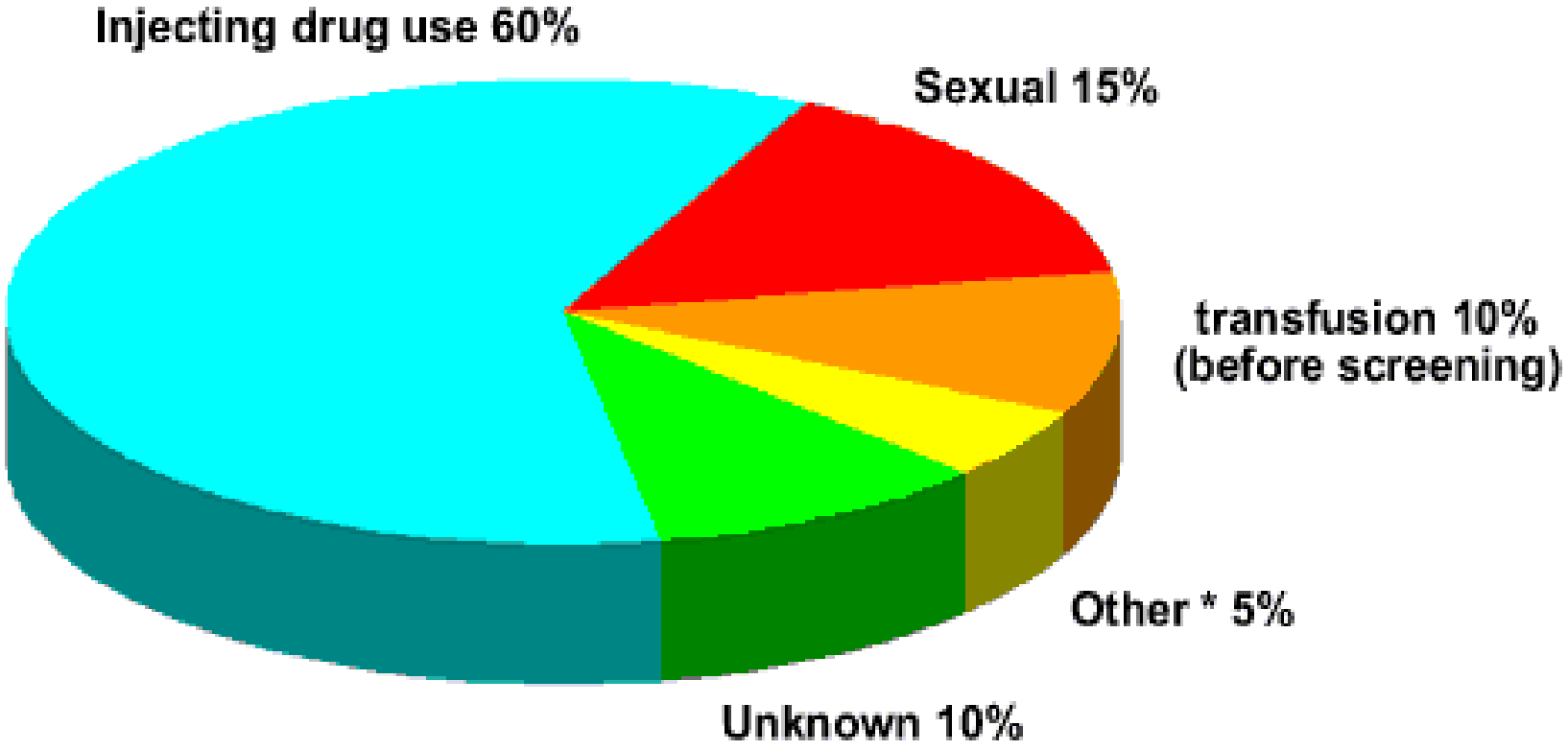
- 11 (6 major) with many subtypes and quasispecies
- The predominate genotype in Saudi is Genotype 4 (62.9%)
- Europe & America Genotype 1→ 75 (24.8) %
- Genotype 2 = 10.8 (7.4) % } → severe disease
- Genotype 3 = 5.8 (5.9) %
- Genotype 1 & 4 → Poor response to therapy

Natural History of HCV Infection



MJ Semin Liver Dis 1995; 15:
Management of Hepatitis C NIH Consensus Statement 1997; March 24-26:15(3).

Sources of Infection for Persons with Hepatitis C

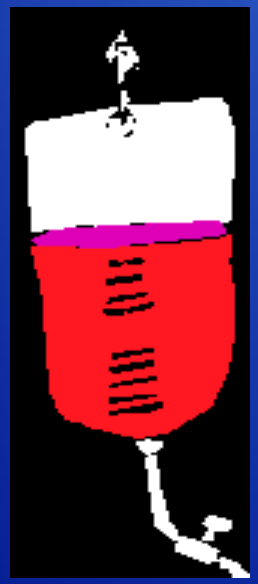


*Nosocomial: Health-care work; Perinatal

Source: Centers for Disease Control and Prevention

Important HCV Transmission Modes

Blood transfusion

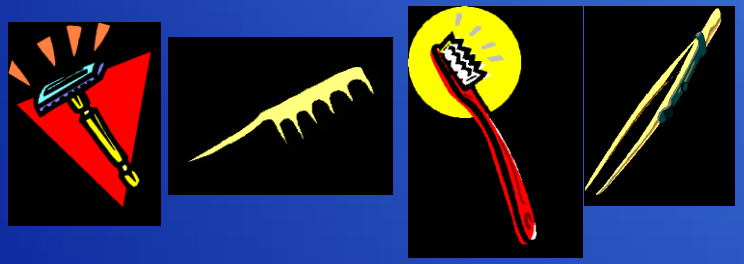


1:100,000 in US

IV drug abuse

80% infected in first year

Un-common HCV Transmission Modes



Household transmission

?

Needle stick injury

3%

Vertical transmission mother - Child

1-5%

Other Transmission Issues

- HCV not spread by kissing, hugging, sneezing, coughing, food or water, sharing eating utensils or drinking glasses, or casual contact
- Do not exclude from work, school, play, child-care or other settings based on HCV infection status

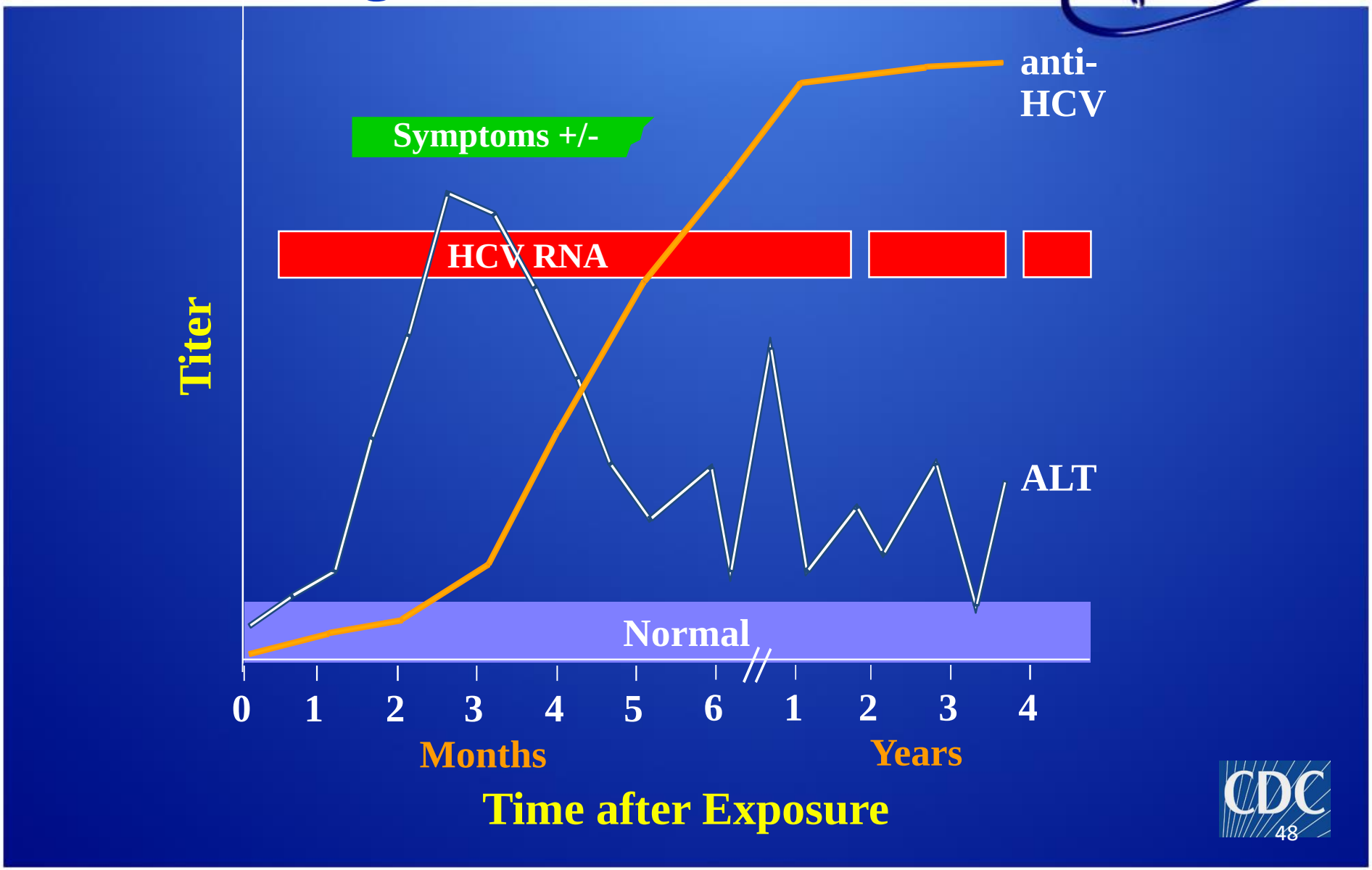
Features of Hepatitis C Virus Infection

Incubation period		Average 6-7 weeks Range 2-26 weeks
Acute illness (jaundice)		Mild (≤20%)
Case fatality rate		Low
Chronic infection	Age-related	60%-85%
Chronic hepatitis	Age-related	10%-70%
Cirrhosis	Age-related	<5%-20%
Mortality from CLD		1%-5%

Chronic Hepatitis C
Factors Promoting Progression or Severity

- Increased alcohol intake
- Age > 40 years at time of infection
- HIV co-infection
- Other
  - Male gender
  - Chronic HBV co-infection

Serologic Pattern of Acute HCV Infection with Progression to Chronic Infection



Perinatal Transmission of HCV

- Transmission only from women HCV-RNA positive at delivery
  - Average rate of infection 6%
  - Higher (17%) if woman co-infected with HIV
  - Role of viral titer unclear
- No association with
  - Delivery method
  - Breastfeeding
- Infected infants do well
  - Severe hepatitis is rare

Sexual Transmission of HCV

- Case-control, cross sectional studies
  - Infected partner, multiple partners, early sex, non-use of condoms, other STDs, sex with trauma, **Partner studies**
  - Low prevalence (1.5%) among long-term partners
    - infections might be due to common percutaneous exposures (e.g., drug use), BUT
  - Male to female transmission more efficient
    - more indicative of sexual transmission

Household Transmission of HCV

- Rare but not absent
- Could occur through percutaneous/mucosal exposures to blood
  - Contaminated equipment used for home therapies
    - IV therapy, injections
  - Theoretically through sharing of contaminated personal articles (razors, toothbrushes)

Public Health Service Guidelines for Anti-HCV-Positive Persons

Anti-HCV-positive persons should:

- Be considered potentially infectious
- Keep cuts and skin lesions covered
- Be informed of the potential for sexual transmission
- Be informed of the potential for perinatal transmission
  - no evidence to advise against pregnancy or breastfeeding

Anti-HCV-positive persons should not:

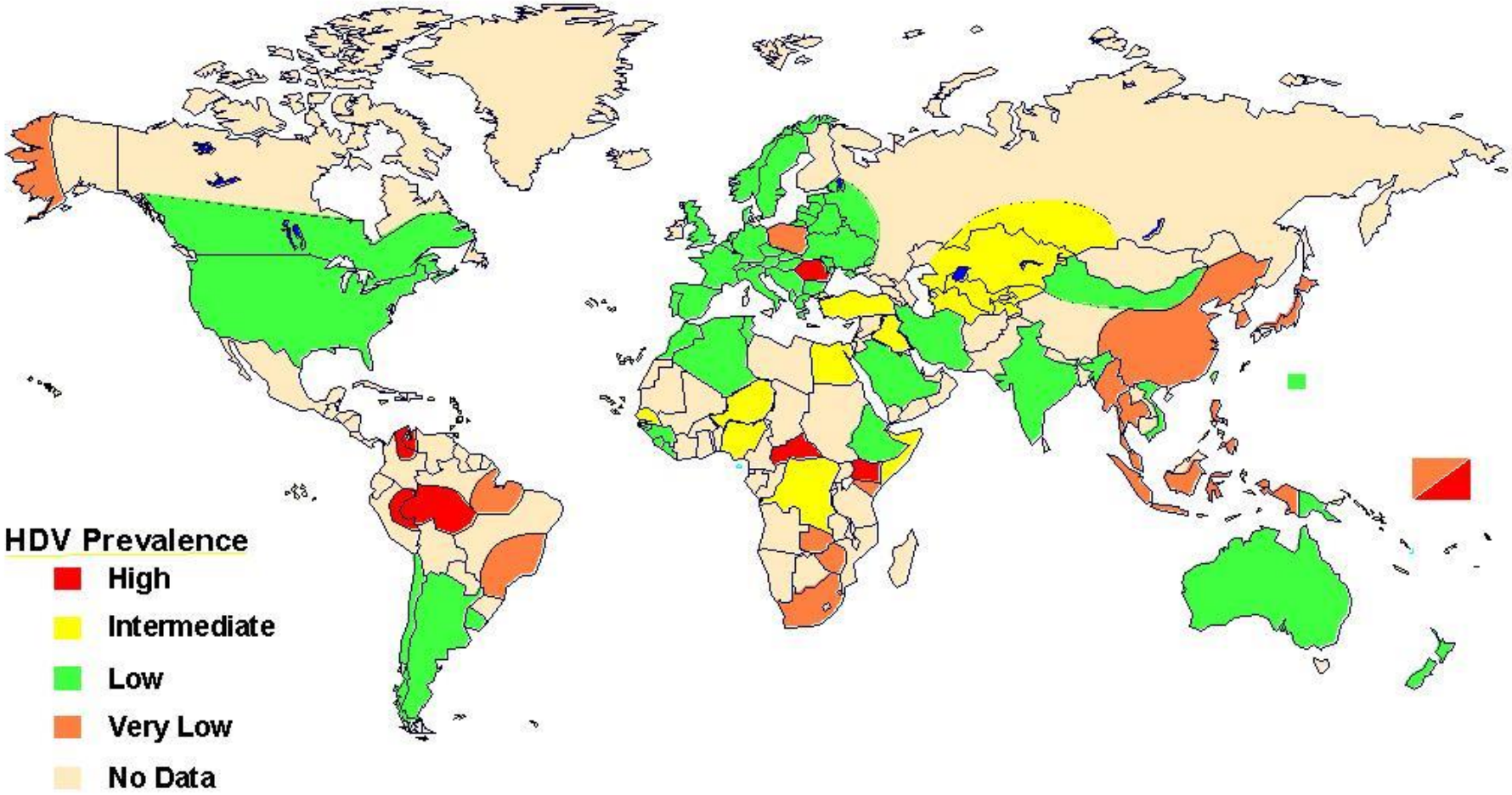
- Donate blood, organs, tissue, or semen
- Share household articles (e.g., toothbrushes, razors)

Hepatitis D

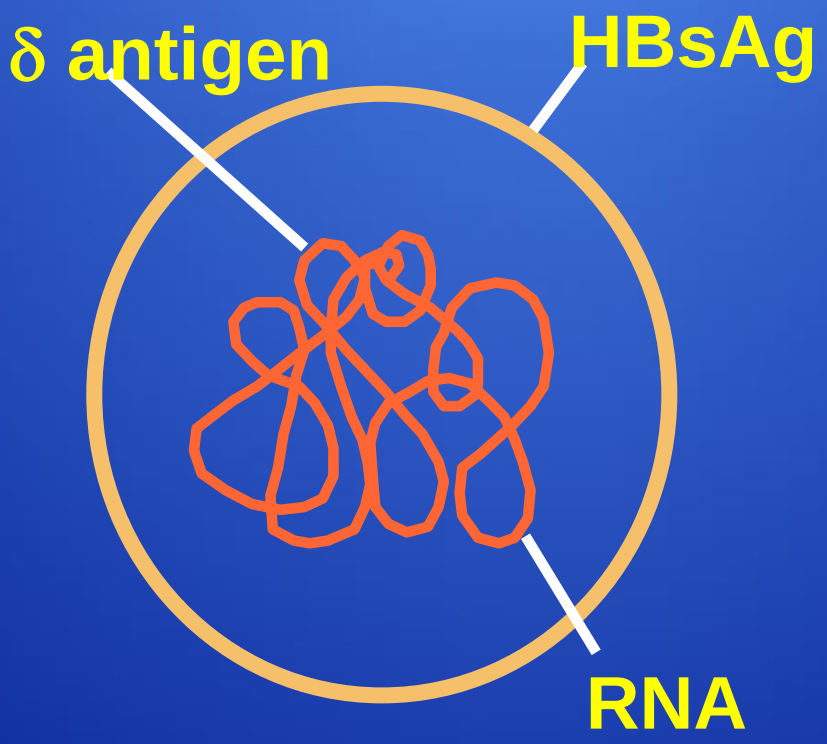
Hepatitis D

- Hepatitis D virus (HDV) requires hepatitis B virus (HBV) for its replication. HDV infection occurs only simultaneously or as super-infection with HBV.
- The virus is transmitted through contact with the blood or other body fluids of an infected person.
- Vertical transmission from mother to child is rare.
- At least 5% of people with chronic HBV infection are co-infected with HDV, resulting in a total of 15 – 20 million persons infected with HDV worldwide.
- Worldwide, the overall number of HDV infection has decreased since 1980s. This trend is mainly due to a successful global HBV vaccination programme.
- HDV-HBV co-infection is considered the most severe form of chronic viral hepatitis due to more rapid progression towards liver-related death and hepatocellular carcinoma.
- Currently, treatment success rates are generally low.
- Hepatitis D infection can be prevented by hepatitis B immunization.

Geographic Distribution of HDV Infection



Hepatitis D (Delta) Virus



HDV is a defective single-stranded RNA virus (delta Ag)

It requires HBV for synthesis of envelope protein composed of HBsAg

Hepatitis D - Clinical Features

- **Coinfection with HBV**
  - severe acute disease
  - low risk of chronic infection
- **Superinfection on top of chronic HBV**
  - usually develop chronic HDV infection
  - high risk of severe chronic liver disease

Hepatitis D Virus
Modes of Transmission

- Percutanous exposures
  - injecting drug use
- Permucosal exposures
  - sex contact

Hepatitis D - Prevention

- HBV-HDV Coinfection
  - Pre or postexposure prophylaxis to prevent HBV infection (HBIG and/or Hepatitis B vaccine)
- HBV-HDV Superinfection
  - Education to reduce risk behaviors among persons with chronic HBV infection

Hepatitis E

Hepatitis E

- **Hepatitis E is a liver disease caused by infection with a virus known as hepatitis E virus (HEV).**
- **Every year, there are an estimated 20 million HEV infections worldwide, leading to an estimated 3.3 million symptomatic cases of hepatitis E.**
- **WHO estimates that hepatitis E caused approximately 44 000 deaths in 2015 (accounting for 3.3% of the mortality due to viral hepatitis).**
- **The virus is transmitted via the faecal-oral route, principally via contaminated water.**
- **Hepatitis E is found worldwide, but the prevalence is highest in East and South Asia.**
- **A vaccine to prevent hepatitis E virus infection has been developed and is licensed in China, but is not yet available elsewhere.**

Hepatitis E - Clinical Features

- Incubation period: Average 40 days
Range 15-60 days
- Case-fatality rate: Overall, 1%-3%
Pregnant women, 15%-25%
- Illness severity: Increased with age
- Chronic sequelae: None identified

Hepatitis E - Epidemiologic Features

- Most outbreaks associated with fecally contaminated drinking water
- Minimal person-to-person transmission

Geographic Distribution of Hepatitis E

Outbreaks or Confirmed Infection in >25% of Sporadic Non-ABC Hepatitis

Viral Hepatitis - Overview

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

CDC
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References

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