VIRAL HEPATITIS A

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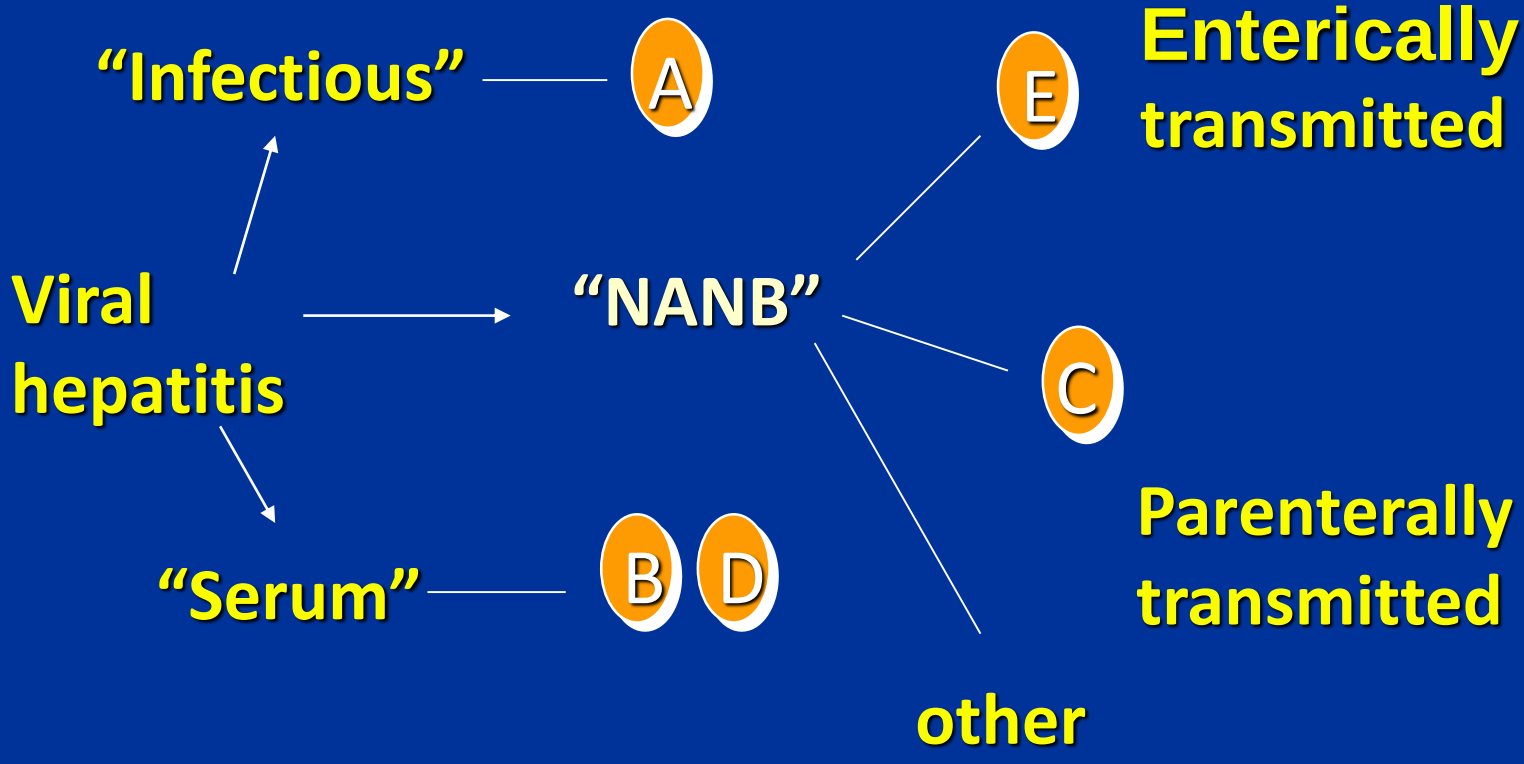
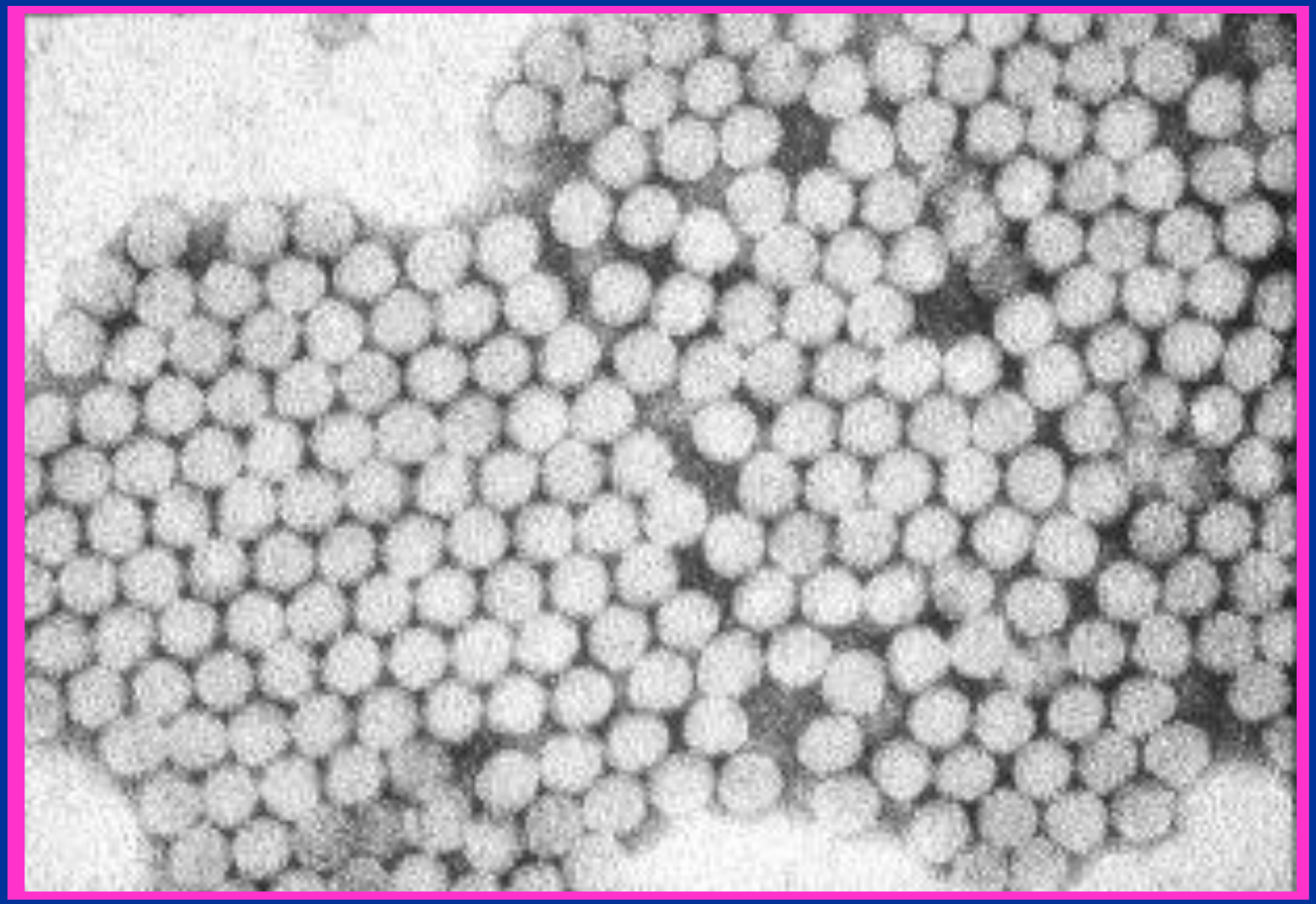
VIRAL HEPATITIS

HISTORICAL PERSPECTIVE



HEPATITIS A VIRUS



HEPATITIS A (Hepatitis A virus) - Case definition

Clinical Criteria

- Any person with a discrete onset of symptoms (e.g. fatigue, abdominal pain, loss of appetite, intermittent nausea and vomiting)
- AND
- At least one of the following three:
- — Fever
- — Jaundice
- — Elevated serum aminotransferase levels

Laboratory Criteria

- At least one of the following three:
- — Detection of hepatitis A virus nucleic acid in serum or stool
- — Hepatitis A virus specific antibody response
- — Detection of hepatitis A virus antigen in stool

Epidemiological Criteria

- At least one of the following four:
- — Human to human transmission
- — Exposure to a common source
- — Exposure to contaminated food/drinking water
- — Environmental exposure

Case Classification

- A. **Possible case** NA
- B. **Probable case**
- Any person meeting the clinical criteria and with an epidemiological link
- C. **Confirmed case**
- Any person meeting the clinical and the laboratory criteria

CDC

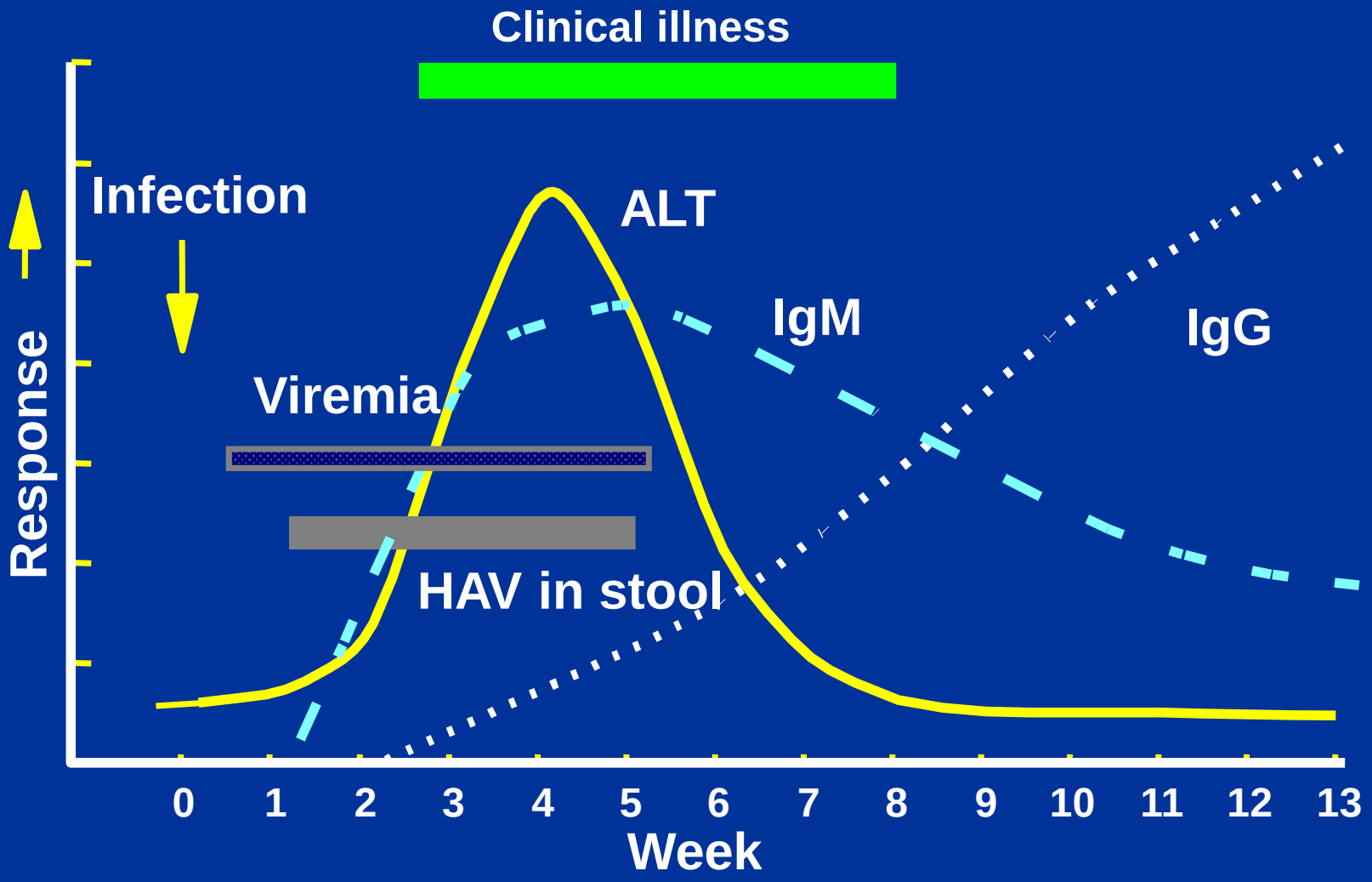
HEPATITIS A VIRUS

- RNA Picornavirus
  - Single serotype worldwide
  - Acute disease and asymptomatic infection
- No chronic infection
  - Protective antibodies develop in response to infection - confers lifelong immunity

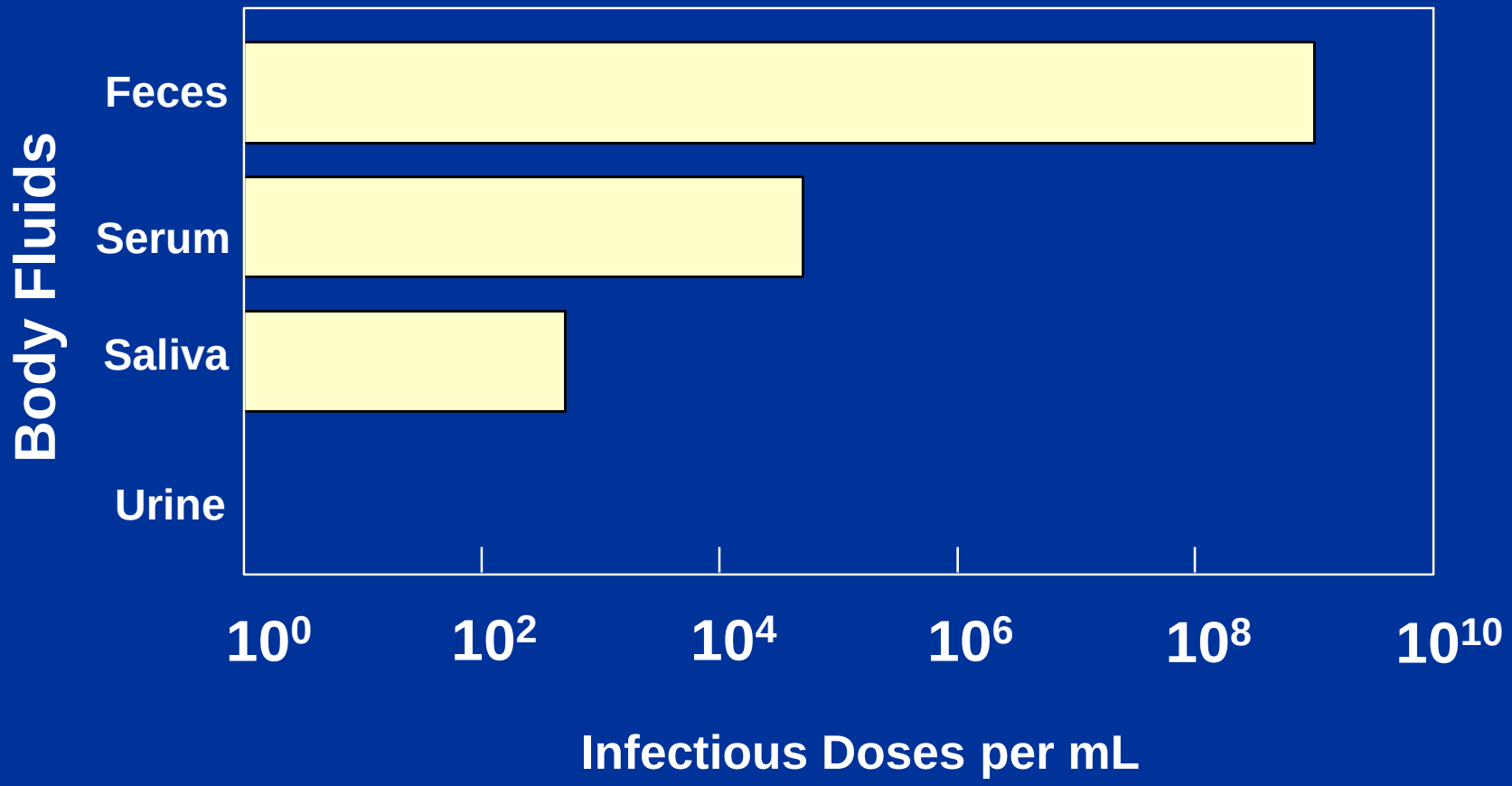
HEPATITIS A - CLINICAL FEATURES

- Jaundice by age group:
  - <6 yrs: <10%
  - 6-14 yrs: 40%-50%
  - >14 yrs: 70%-80%
- Rare complications: Fulminant hepatitis, Cholestatic hepatitis, Relapsing hepatitis
- Incubation period: Average 30 days, Range 15-50 days
- Chronic sequelae: None

EVENTS IN HEPATITIS A VIRUS INFECTION

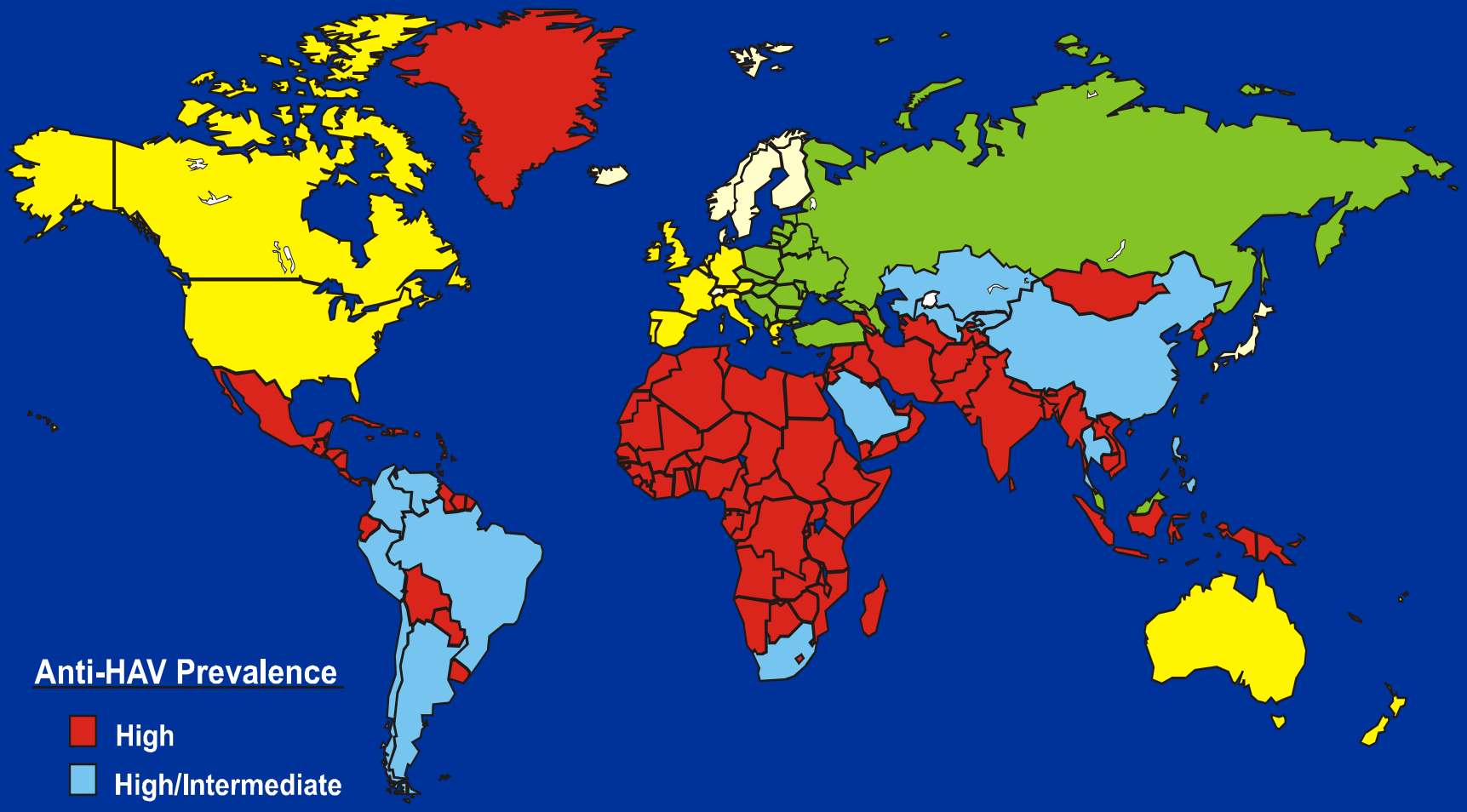


CONCENTRATION OF HEPATITIS A VIRUS IN VARIOUS BODY FLUIDS



Source: Viral Hepatitis and Liver Disease 1984;9-22
J Infect Dis 1989;160:887-890

GEOGRAPHIC DISTRIBUTION OF HEPATITIS A VIRUS INFECTION



CDC

ACUTE HEPATITIS A CASE DEFINITION FOR SURVEILLANCE

- **Clinical criteria**

  An acute illness with:
  - discrete onset of symptoms (e.g. fatigue, abdominal pain, loss of appetite, intermittent nausea, vomiting), **and**
  - jaundice or elevated serum aminotransferase levels

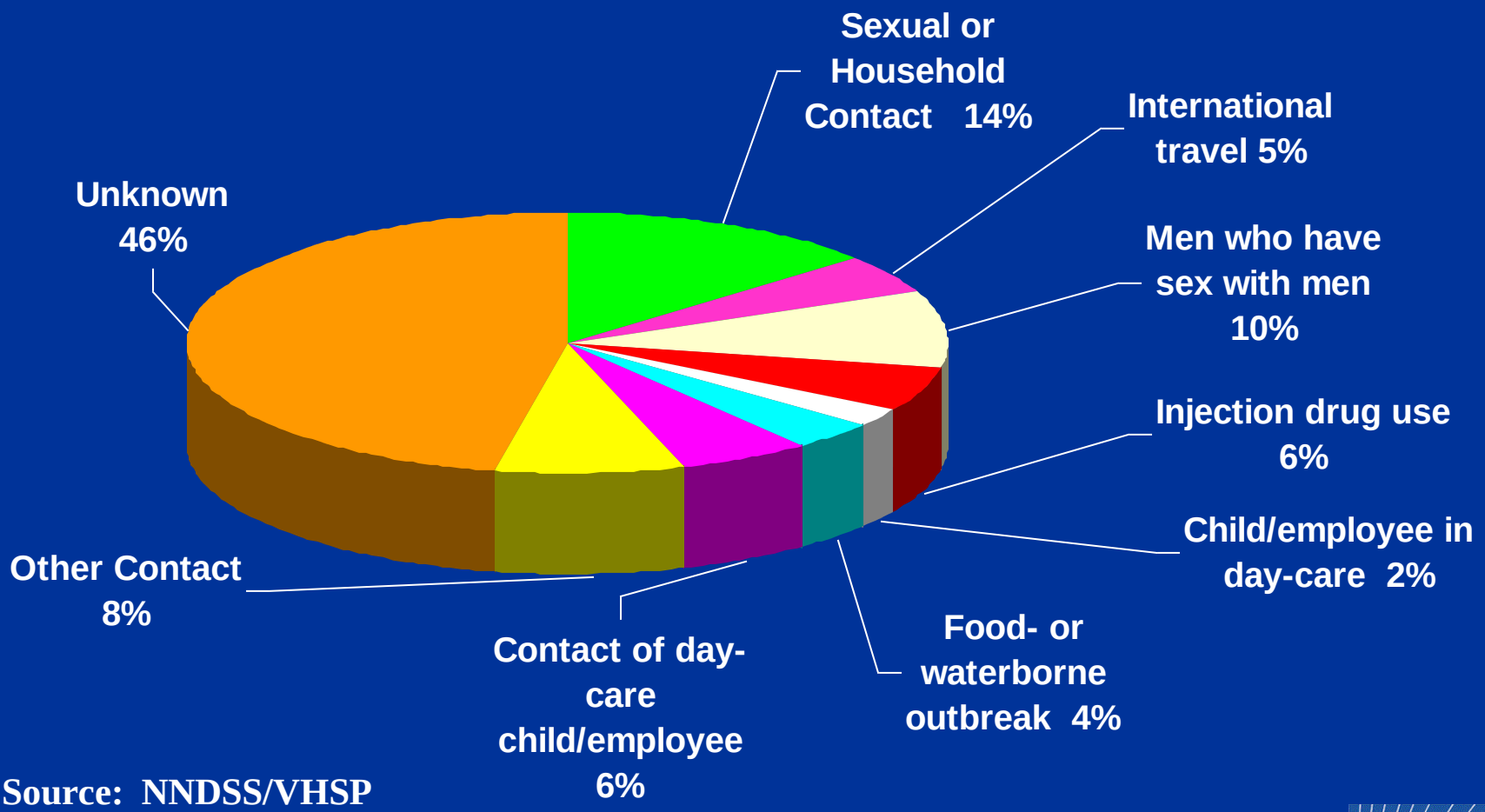
- **Laboratory criteria**
  - IgM antibody to hepatitis A virus (anti-HAV) positive

- **Case Classification**
  - Confirmed. A case that meets the clinical case definition and is laboratory confirmed or a case that meets the clinical case definition and occurs in a person who has an epidemiologic link with a person who has laboratory-confirmed hepatitis A (i.e., household or sexual contact with an infected person during the 15-50 days before the onset of symptoms).

HEPATITIS A VIRUS TRANSMISSION

- **Close personal contact (e.g., household contact, sex contact, child day-care centers)**
- **Contaminated food, water (e.g., infected food handlers)**
- **Blood exposure (rare) (e.g., injection drug use, rarely by transfusion)**

RISK FACTORS ASSOCIATED WITH REPORTED HEPATITIS A, 1990-2000, UNITED STATES



Source: NNDSS/VHSP

CDC

PREVENTING HEPATITIS A

- **Hygiene (e.g., hand washing)**
- **Sanitation (e.g., clean water sources)**
- **Hepatitis A vaccine (pre-exposure)**
- **Immune globulin (pre- and post-exposure)**

PREPARATION OF INACTIVATED HEPATITIS A VACCINES

- Cell culture adapted virus grown in human fibroblasts
- Purified product inactivated with formalin
- Adsorbed to aluminum hydroxide adjuvant

HEPATITIS A VACCINES

- **Highly immunogenic**
  - **97%-100% of children, adolescents, and adults have protective levels of antibody within 1 month of receiving first dose; essentially 100% have protective levels after second dose**
- **Highly efficacious**
  - **In published studies, 94%-100% of children protected against clinical hepatitis A after equivalent of one dose**

HEPATITIS A VACCINES

Recommended Dosages of Hepatitis A Vaccines

Schedule Vaccine	Age (yrs)	Dose	Volume (mL)	2-Dose (mos)
HAVRIX ® #	1-18	720 (EL.U.*)	0.5	0, 6-12
	>18	1,440	1.0	0, 6-12
VAQTA ® ##	1-18	25 (U**)	0.5	0, 6-18
	>18	50	1.0	0, 6-18

* EL.U. – Enzyme-linked immunosorbent assay (ELISA) units

** Units

has 2-phenoxyethanol as a preservative

has no preservative

CDC

SAFETY OF HEPATITIS A VACCINE

- Most common side effects
  - Soreness/tenderness at injection site - 50%
  - Headache - 15%
  - Malaise - 7%
- No severe adverse reactions attributed to vaccine
- Safety in pregnancy not determined – risk likely low
- Contraindications - severe adverse reaction to previous dose or allergy to a vaccine component
- No special precautions for immunocompromised persons

DURATION OF PROTECTION AFTER HEPATITIS A VACCINATION

- Persistence of antibody
  - At least 5-8 years among adults and children
- Efficacy
  - No cases in vaccinated children at 5-6 years of follow-up
- Mathematical models of antibody decline suggest protective antibody levels persist for at least 20 years
- Other mechanisms, such as cellular memory, may contribute

FACTORS ASSOCIATED WITH DECREASED IMMUNOGENICITY TO HEPATITIS A VACCINE

- Decreased antibody concentration:
  - Concurrent administration of IG
  - Presence of passively-transferred maternal antibody
  - Age
  - Chronic liver disease
- Decreased seroconversion rate:
  - HIV infection
    - May be related to degree of immunosuppression
  - Liver transplantation

USE OF HEPATITIS A VACCINE FOR INFANTS

- **Safe and immunogenic for infants without maternal antibody**
- **Presence of passively-acquired maternal antibody blunts immune response**
  - **all respond, but with lower final antibody concentrations**
- **Age by which maternal antibody disappears is unclear**
  - **still present in some infants at one year**
  - **probably gone in vast majority by 15 months**

COMBINED HEPATITIS A HEPATITIS B VACCINE

- **Approved by the FDA in United States for persons ≥18 years old**
- **Contains 720 EL.U. hepatitis A antigen and**

  20 µg. HBsAg
- **Vaccination schedule: 0,1,6 months**
- **Immunogenicity similar to single-antigen vaccines given separately**
- **Can be used in persons ≥ 18 years old who need vaccination against both hepatitis A and B**
- **Formulation for children available in many other countries**

PRE-VACCINATION TESTING

- **Considerations:**
  - **cost of vaccine**
  - **cost of serologic testing (including visit)**
  - **prevalence of infection**
  - **impact on compliance with vaccination**
- **Likely to be cost-effective for:**
  - **persons born in high endemic areas**
  - **Older U.S. born adults**
  - **Older adolescents and young adults in certain groups (e.g., Native Americans, Alaska Natives, Hispanics, IDUs)**

POST-VACCINATION TESTING

Not recommended:

- High response rate among vaccinees
- Commercially available assay not sensitive enough to detect lower (protective) levels of vaccine-induced antibody

HEPATITIS A PREVENTION IMMUNE GLOBULIN

- **Pre-exposure**
  - **travelers to intermediate and high HAV-endemic regions**
- **Post-exposure (within 14 days)**

  Routine
  - **household and other intimate contacts**

  Selected situations
  - **institutions (e.g., day-care centers)**
  - **common source exposure (e.g., food prepared by infected food handler)**

HEPATITIS A VACCINATION RECOMMENDATIONS: GUIDING PRINCIPLES

- **Need comprehensive strategy to reduce overall rates**
  - **Routine vaccination of children likely to be most effective**
- **Need creative approaches**
  - **Formulation not available that would allow integration into infant schedule**

ACIP RECOMMENDATIONS PERSONS AT INCREASED RISK OF INFECTION, 1996

- Men who have sex with men
- Illegal drug users
- International travelers
- Persons who have clotting factor disorders
- Persons with chronic liver disease