

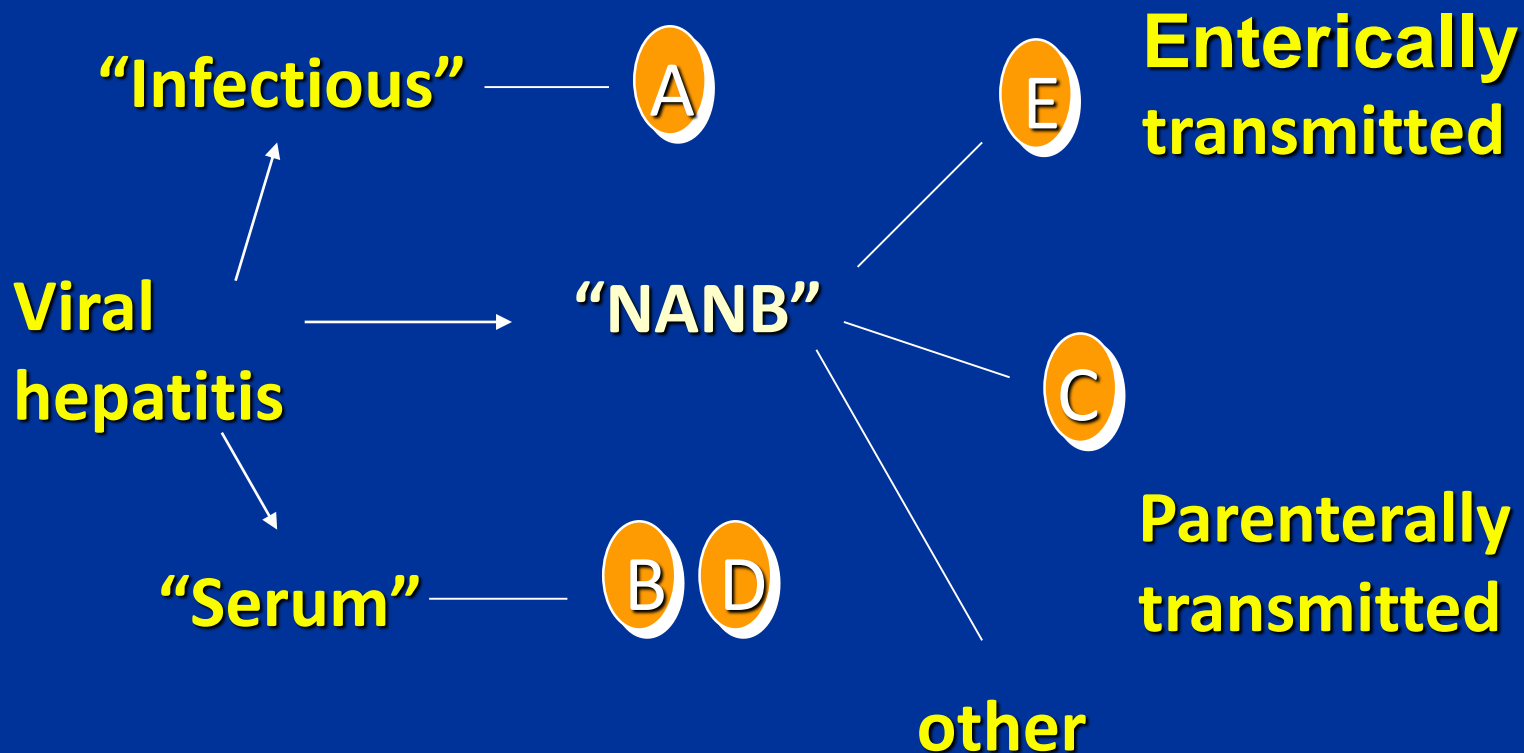
VIRAL HEPATITIS A

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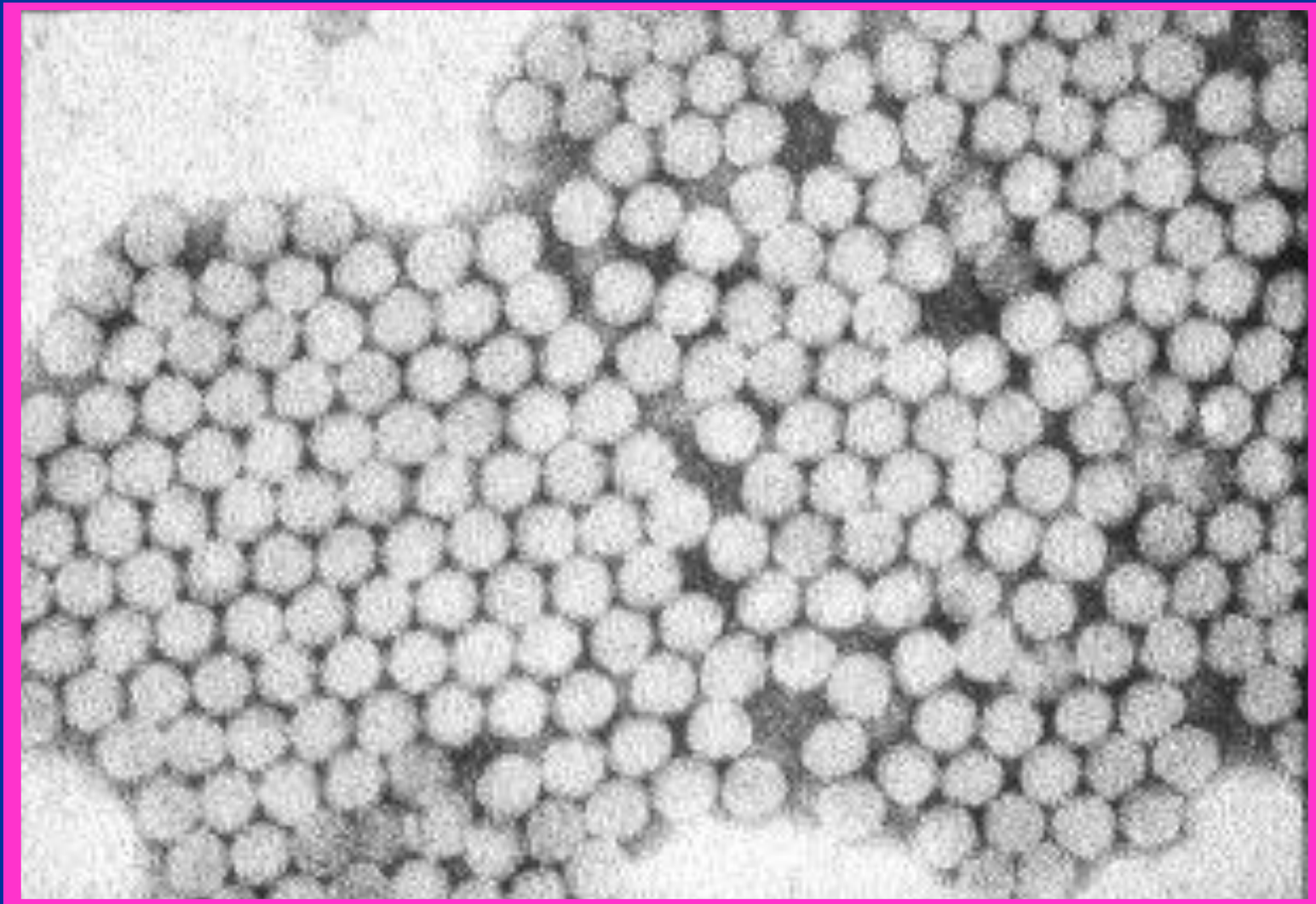


VIRAL HEPATITIS

HISTORICAL PERSPECTIVE



HEPATITIS A VIRUS



HEPATITIS A VIRUS

■ RNA Picornavirus

- Single serotype worldwide
- Acute disease and asymptomatic infection

■ No chronic infection

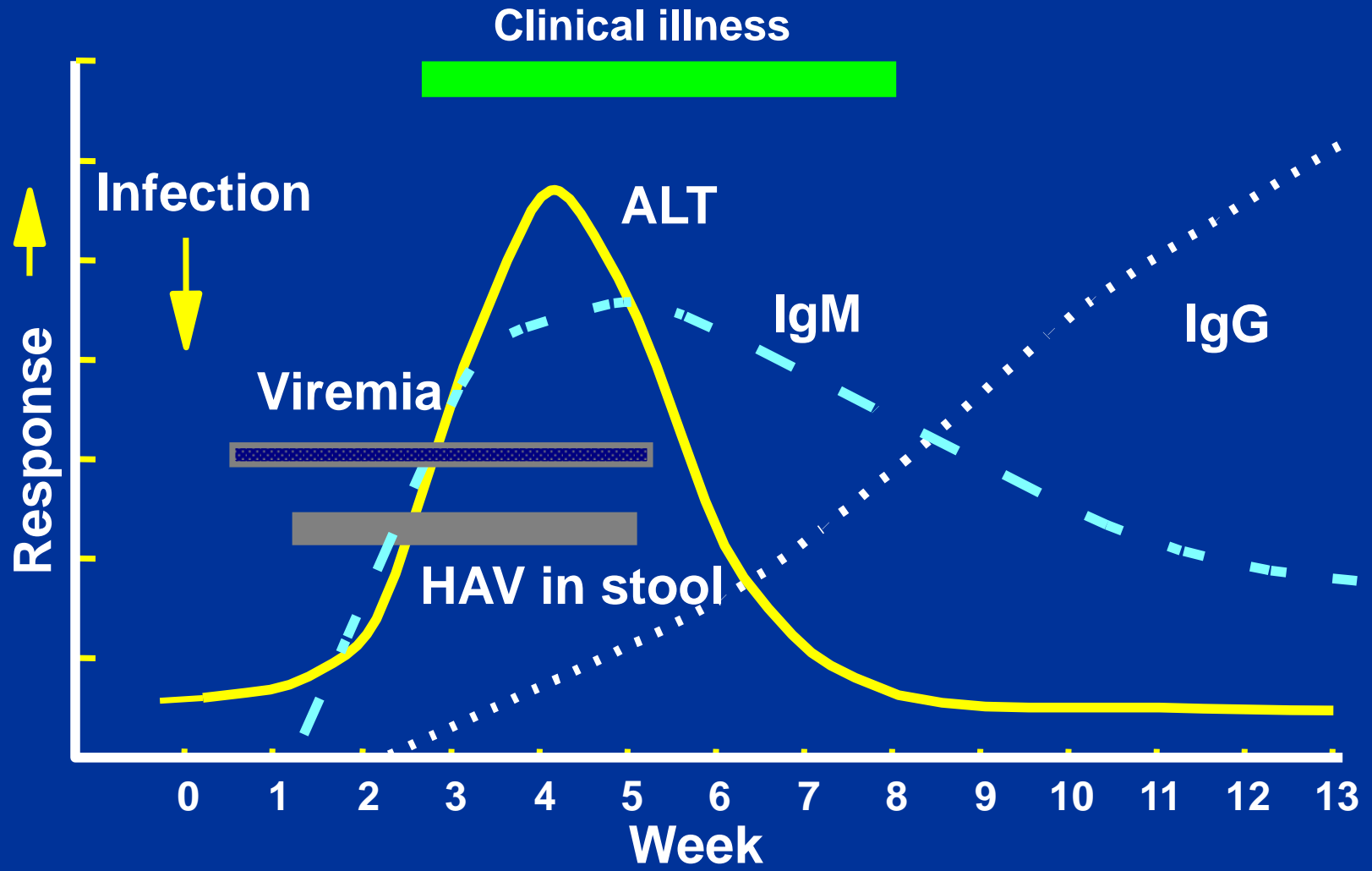
- Protective antibodies develop in response to infection - confers lifelong immunity

HEPATITIS A - CLINICAL FEATURES

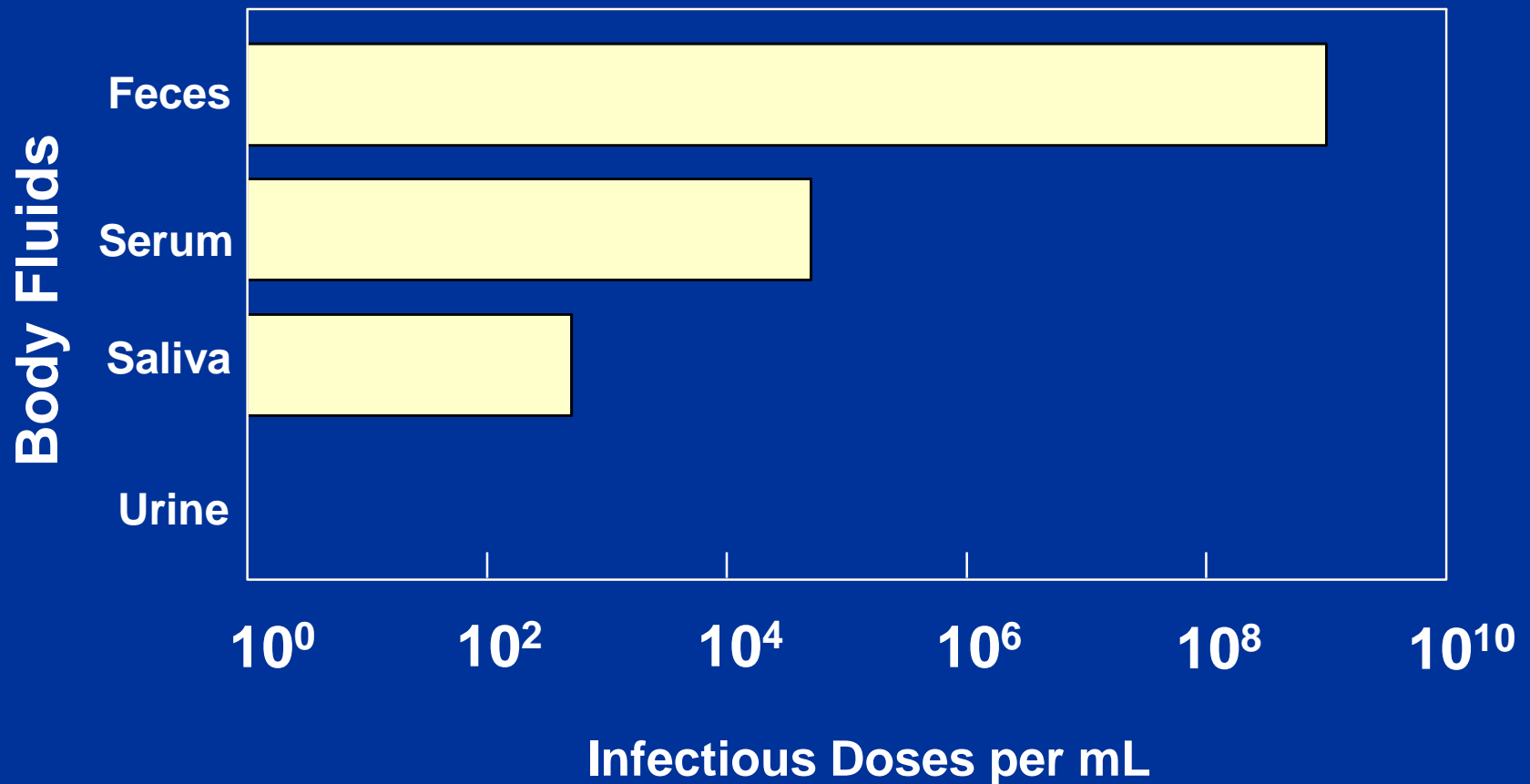
- Jaundice by age group:

<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

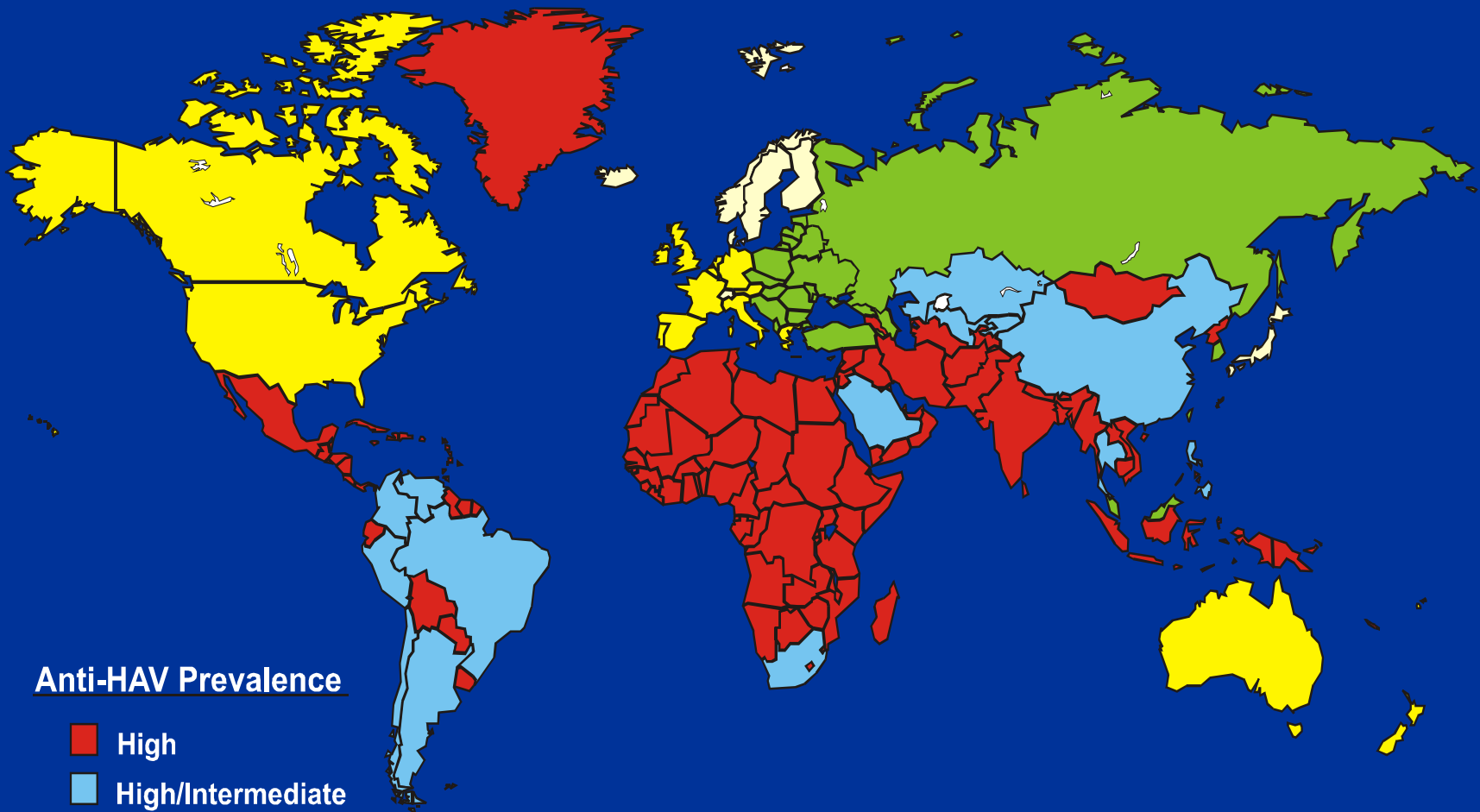


CONCENTRATION OF HEPATITIS A VIRUS IN VARIOUS BODY FLUIDS



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

GEOGRAPHIC DISTRIBUTION OF HEPATITIS A VIRUS INFECTION



Anti-HAV Prevalence

- High
- High/Intermediate
- Intermediate
- Low
- Very Low

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

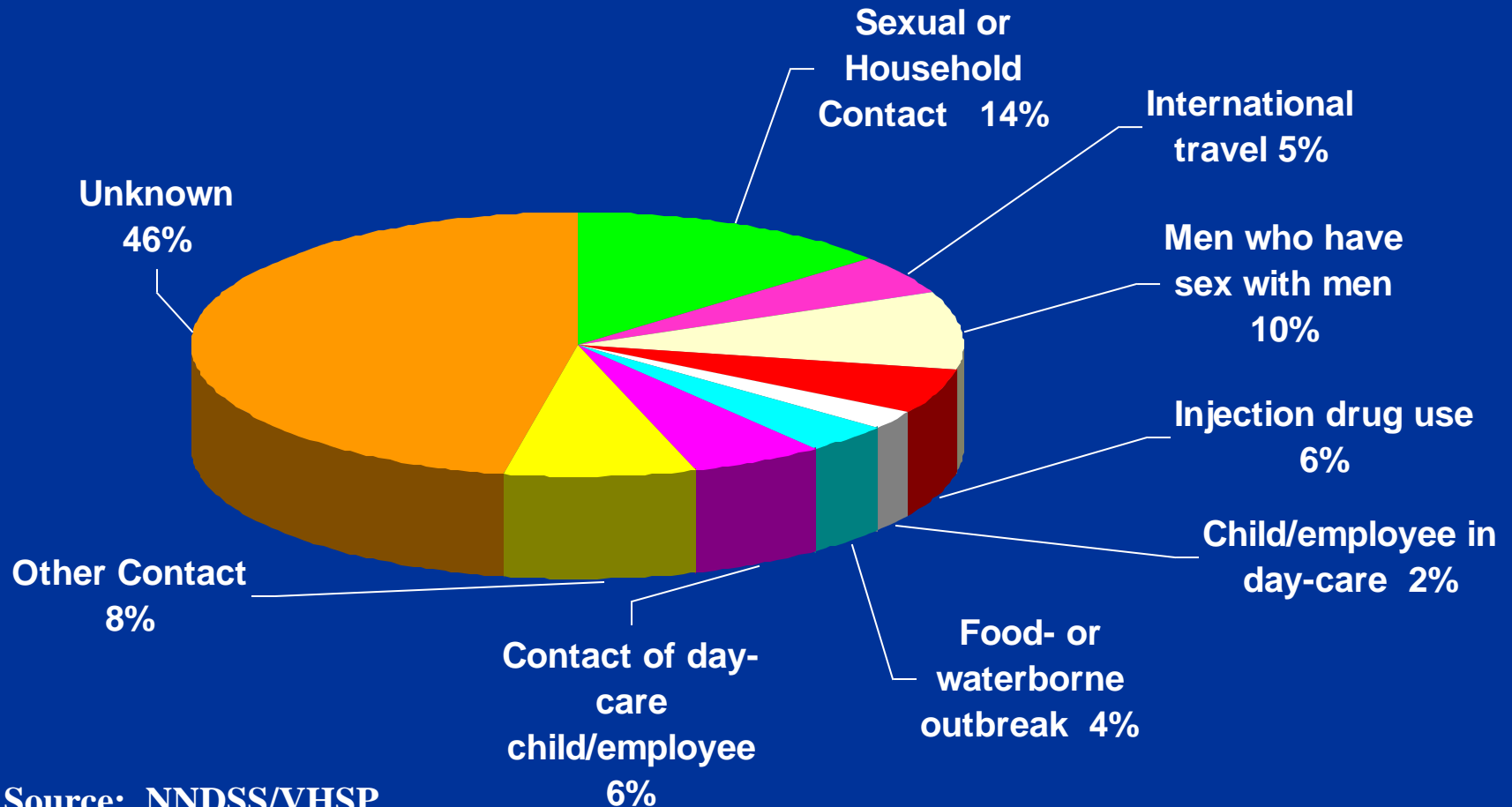
◆ **Case Classification**

- 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



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

<u>Schedule Vaccine</u>	<u>Age (yrs)</u>	<u>Dose</u>	<u>Volume (mL)</u>	<u>2-Dose (mos)</u>
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



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)**

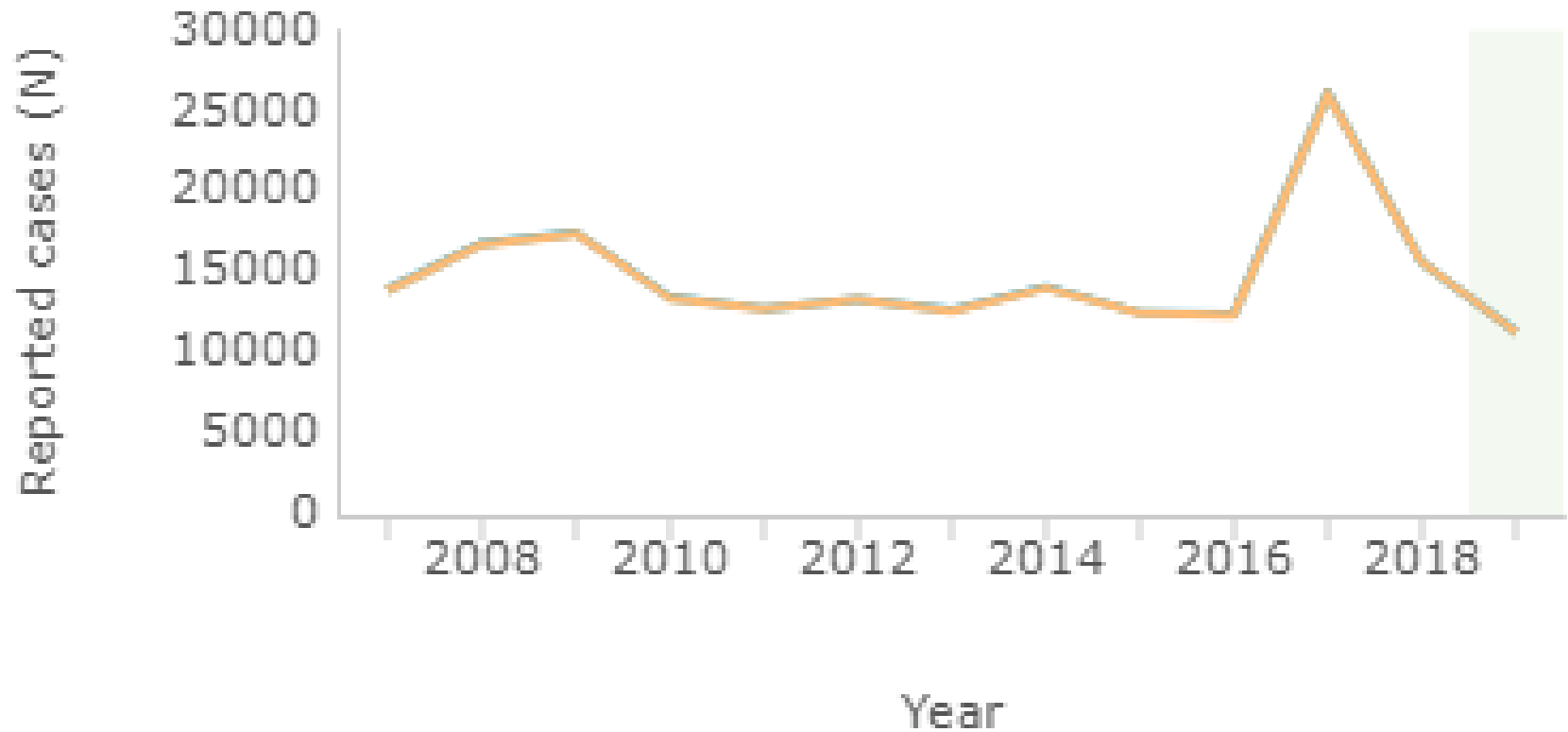
HEPATITIS A VACCINATION RECOMMENDATIONS: GUIDING PRINCIPLES

- **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**

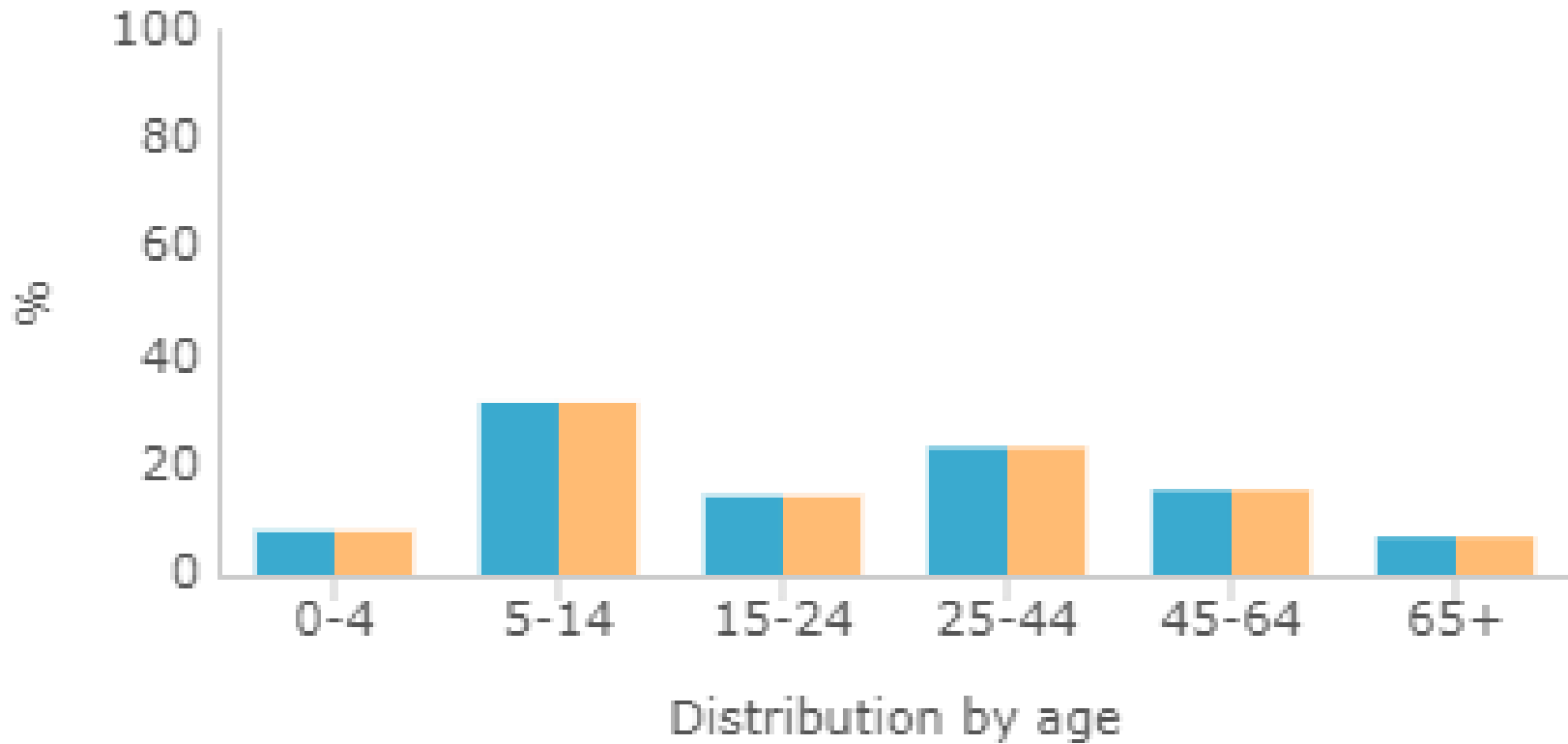
ACIP RECOMMENDATIONS PERSONS AT INCREASED RISK OF INFECTION, 1996

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

VHA



VHA



ACUTE HEPATITIS A Case definition

Clinical Criteria:

Any person with a discrete onset of symptoms (for example, 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

- Possible case NA
- Probable case Any person meeting the clinical criteria with an epidemiological link
- Confirmed case Any person meeting the clinical and the laboratory criteria

Note: If the national surveillance system is not capturing clinical symptoms, all laboratory-confirmed individuals should be reported as confirmed cases.

