Hepatitis Training Webinar
August 2nd, 2017

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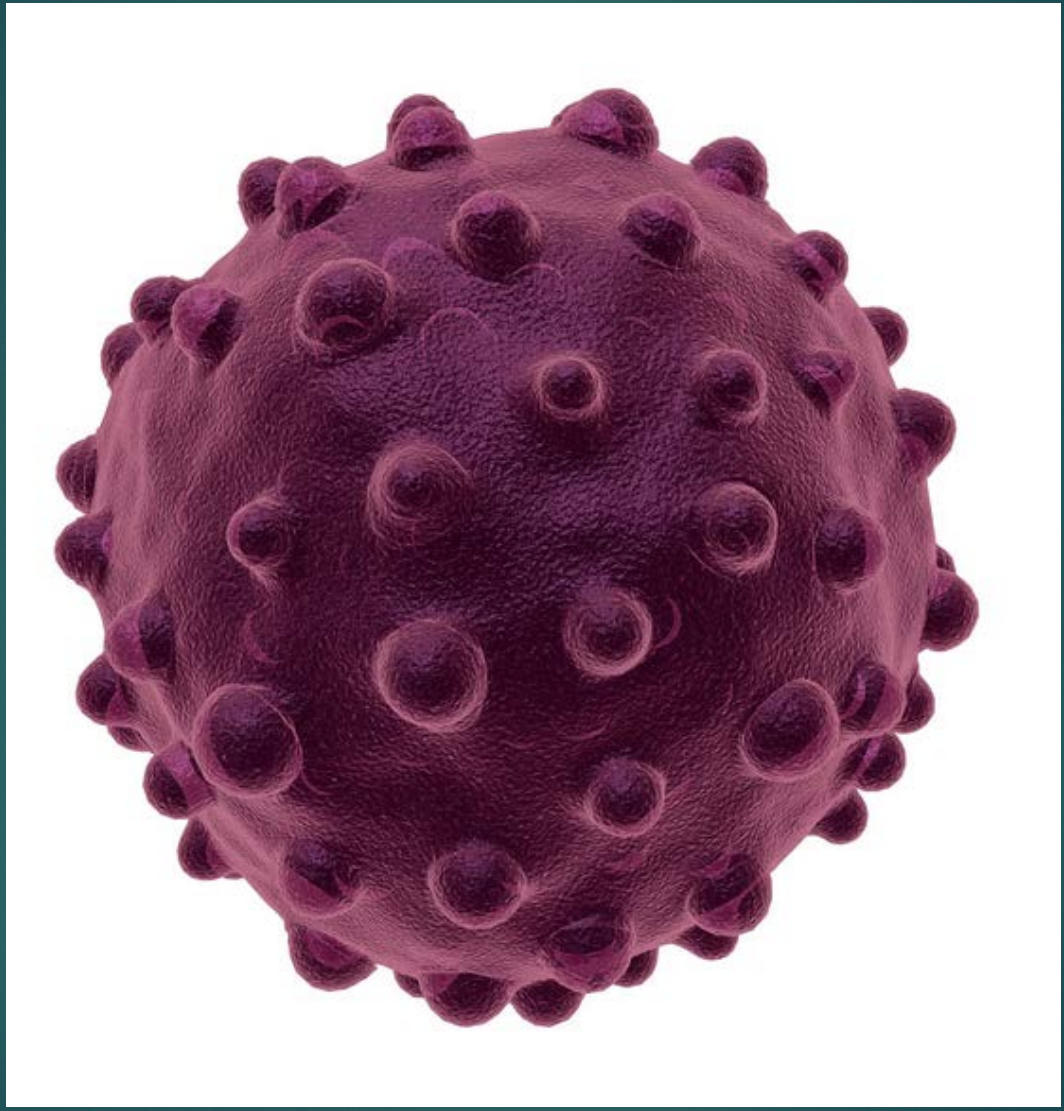
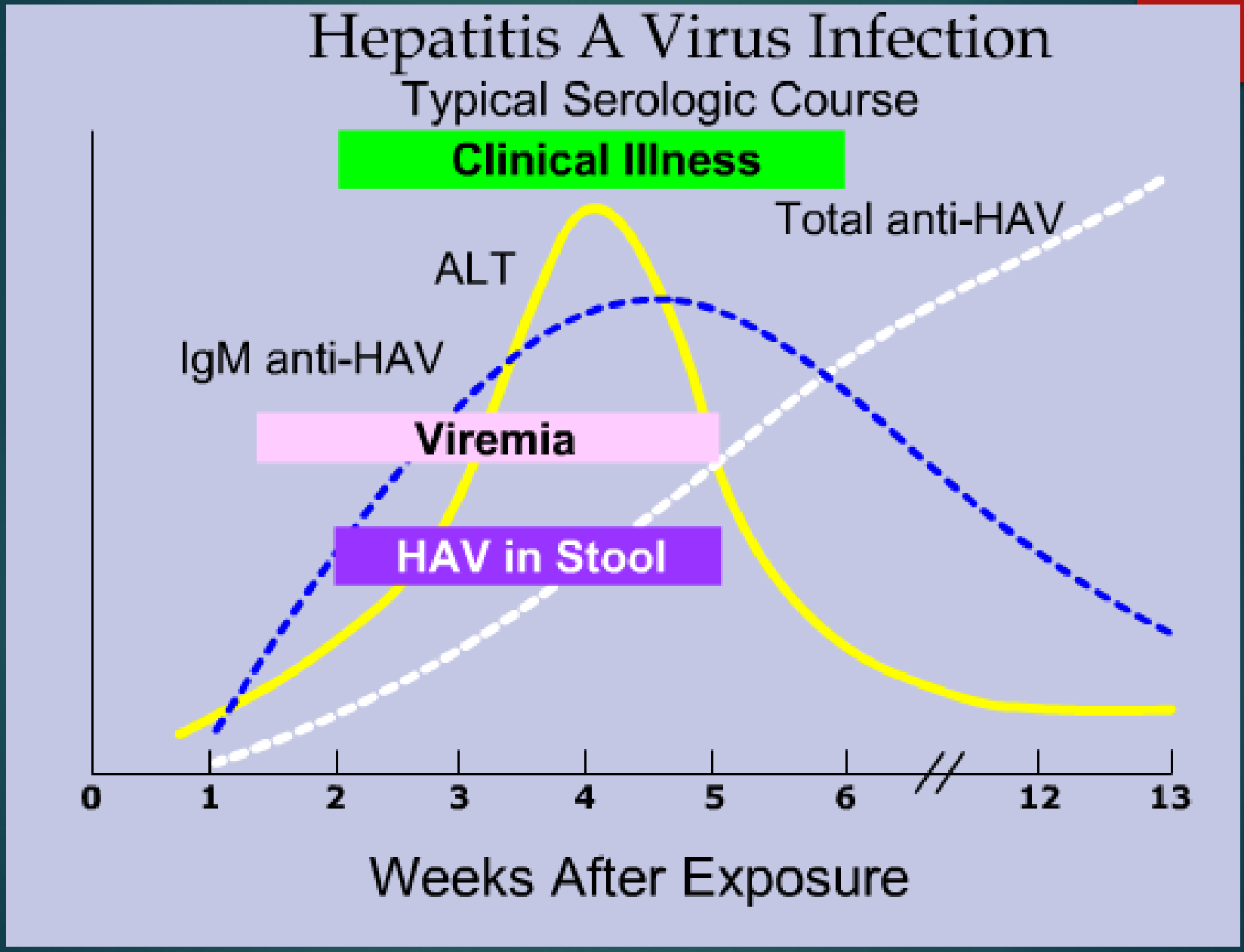
OREGON HEALTH AUTHORITY

Hepatitis A

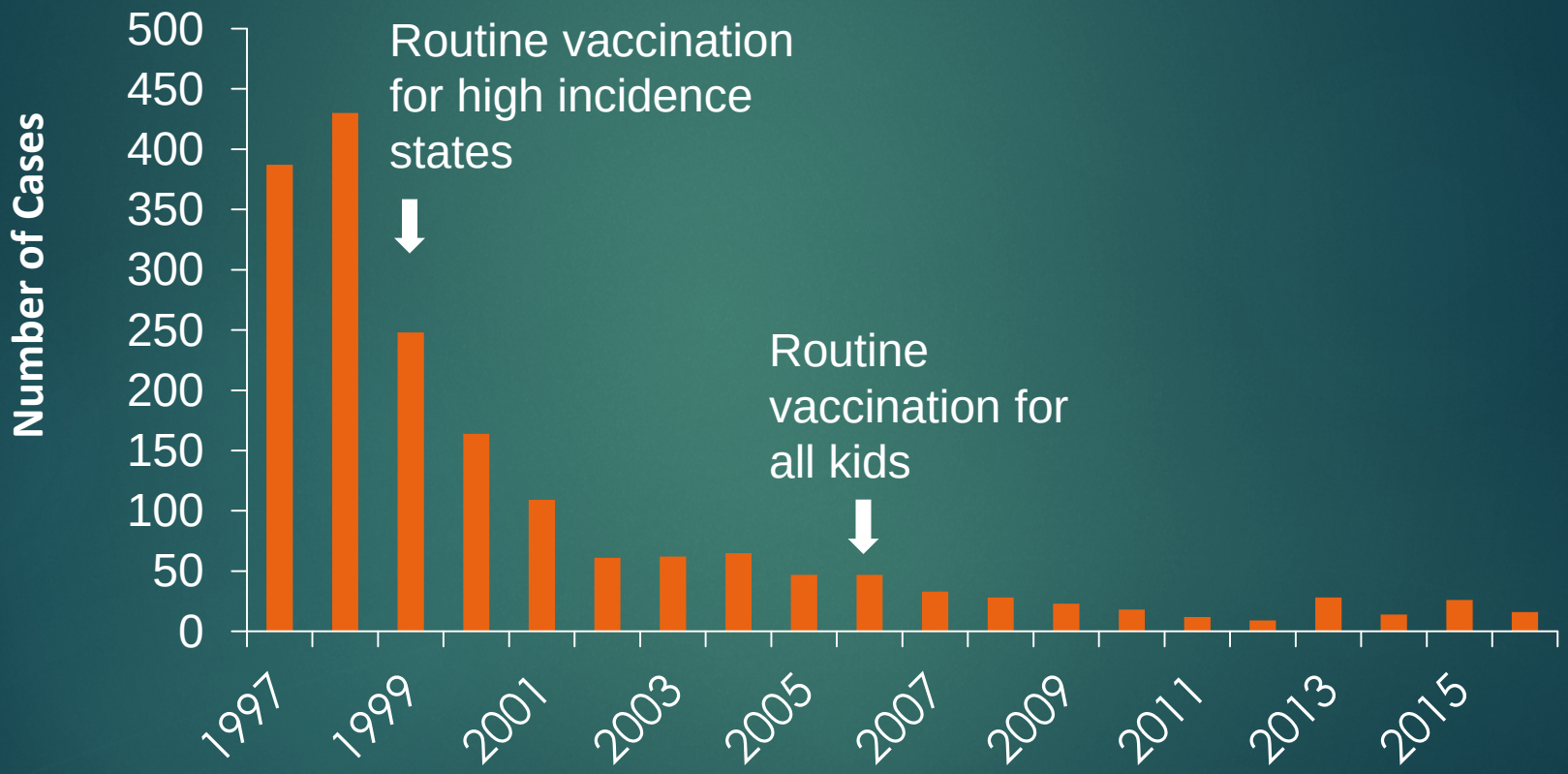


Hepatitis A - Serologies

- Anti-HAV, IgM: indicates acute infection.
- Anti-HAV, total (IgM and IgG): marker of past or present infection.
- ALT/AST: useful indicators of liver damage.

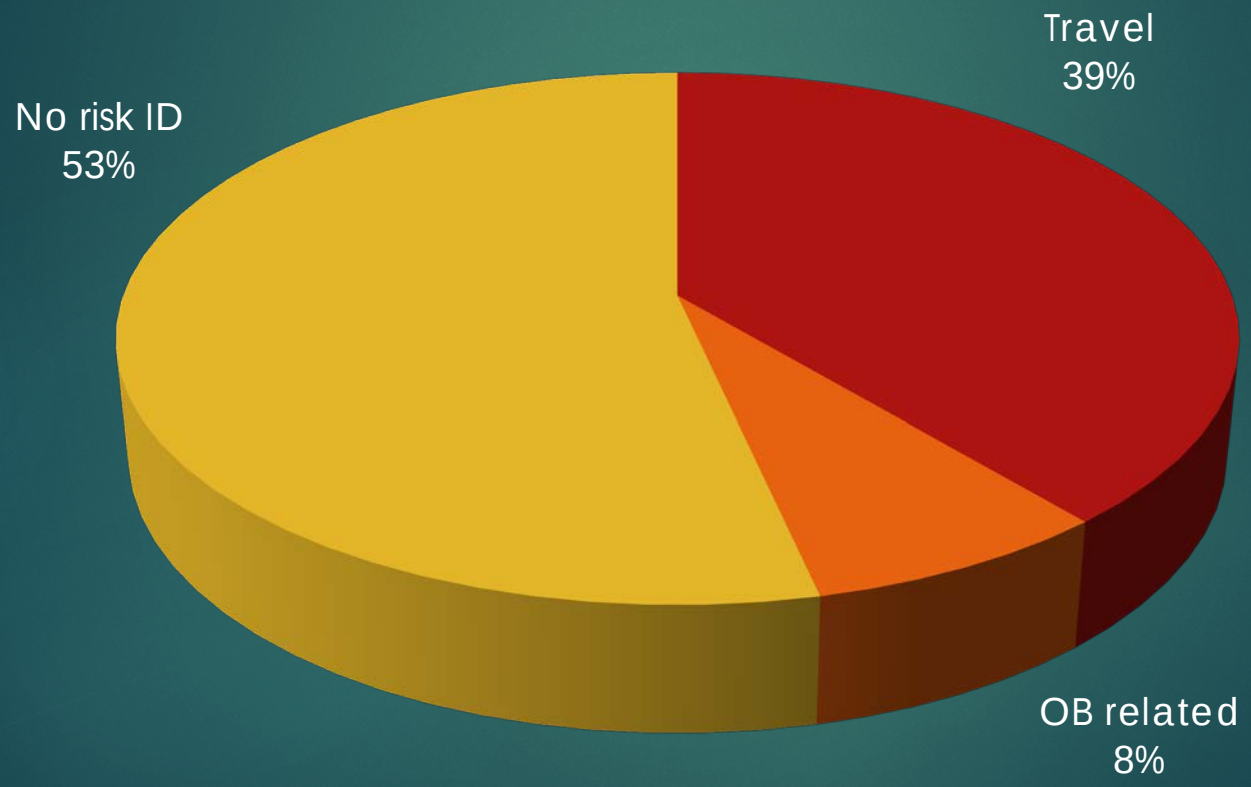

Hepatitis A Virus Infection
Typical Serologic Course
Clinical Illness
Total anti-HAV
ALT
IgM anti-HAV
Viremia
HAV in Stool
0
1
2
3
4
5
6
12
13
Weeks After Exposure

Number of Cases of HAV by Year, Oregon, 1997-2016

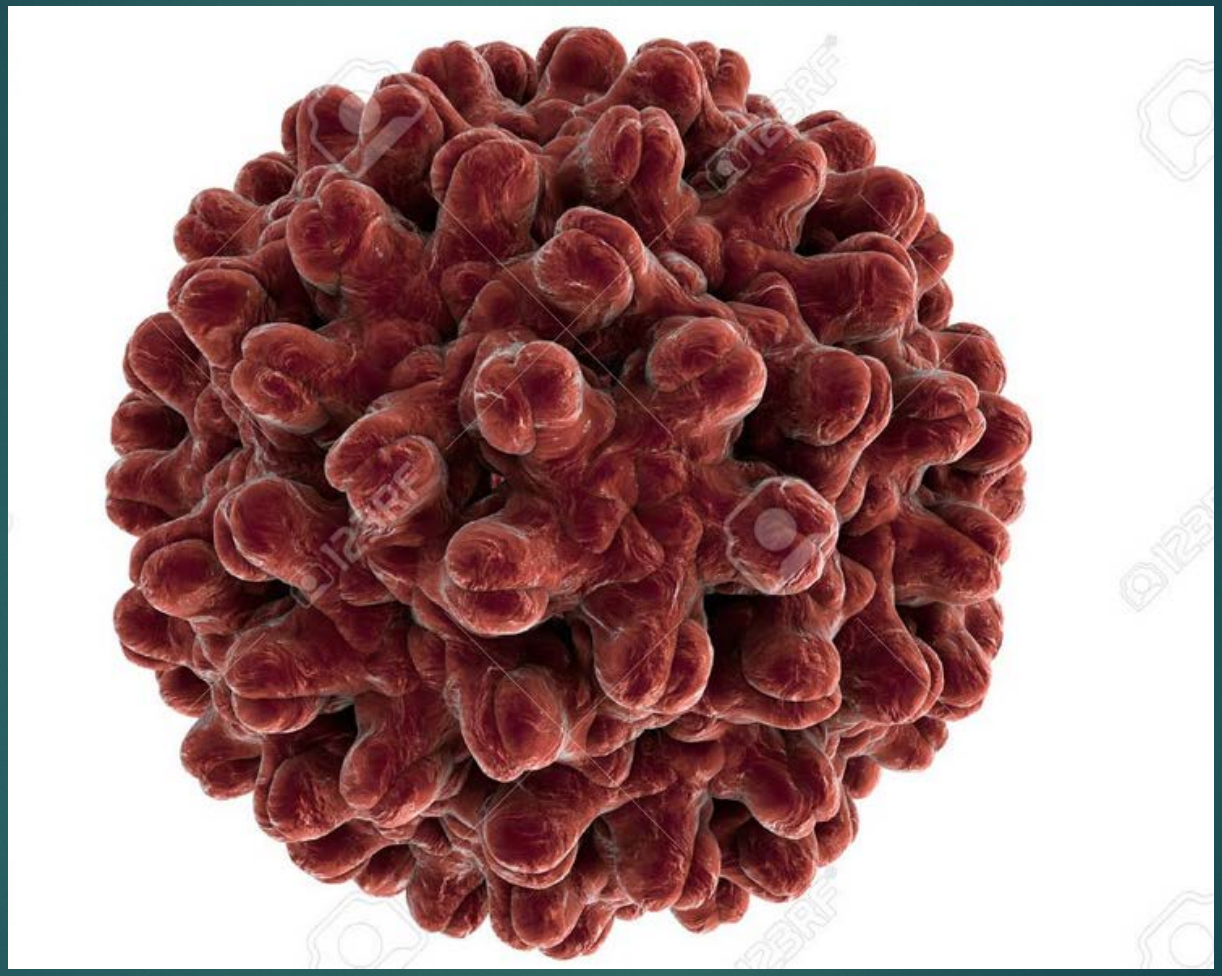


Oregon: Annual case counts < 100 since 2002; <50 since 2005
>99% reduction from pre-vaccine era

Reported Risk Factors (mutually exclusive) for Acute Hepatitis A, Oregon, 2016 (n=17)



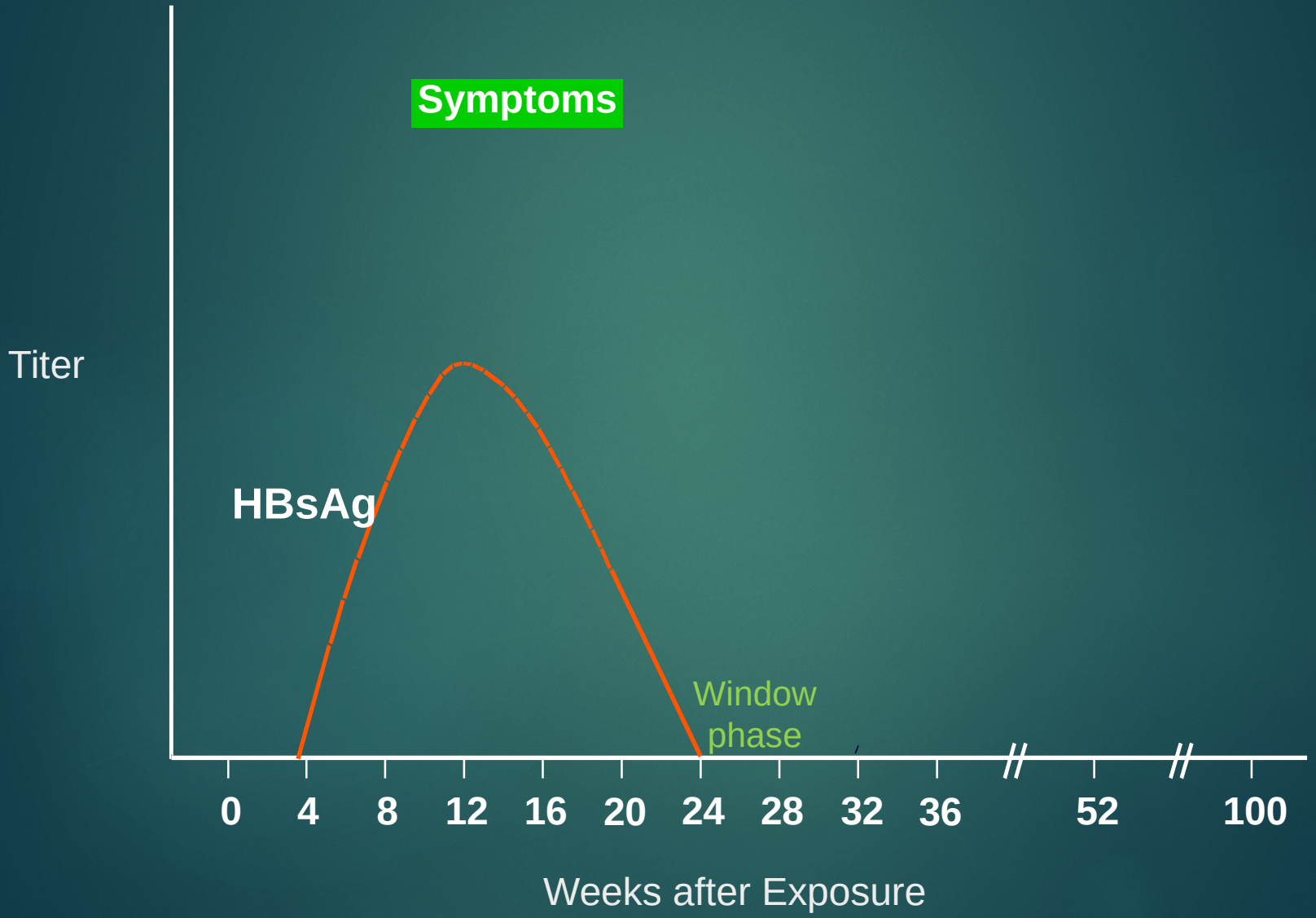
Hepatitis B



Surface Antigen (HBsAg)

- Protein found on the outer surface of the virus
- Marker of replicating virus, either acute or chronically infected
- Persists indefinitely in chronic infection
- Patient is infectious
- Transient HBsAg positivity has been reported for up to 18 days after vaccination

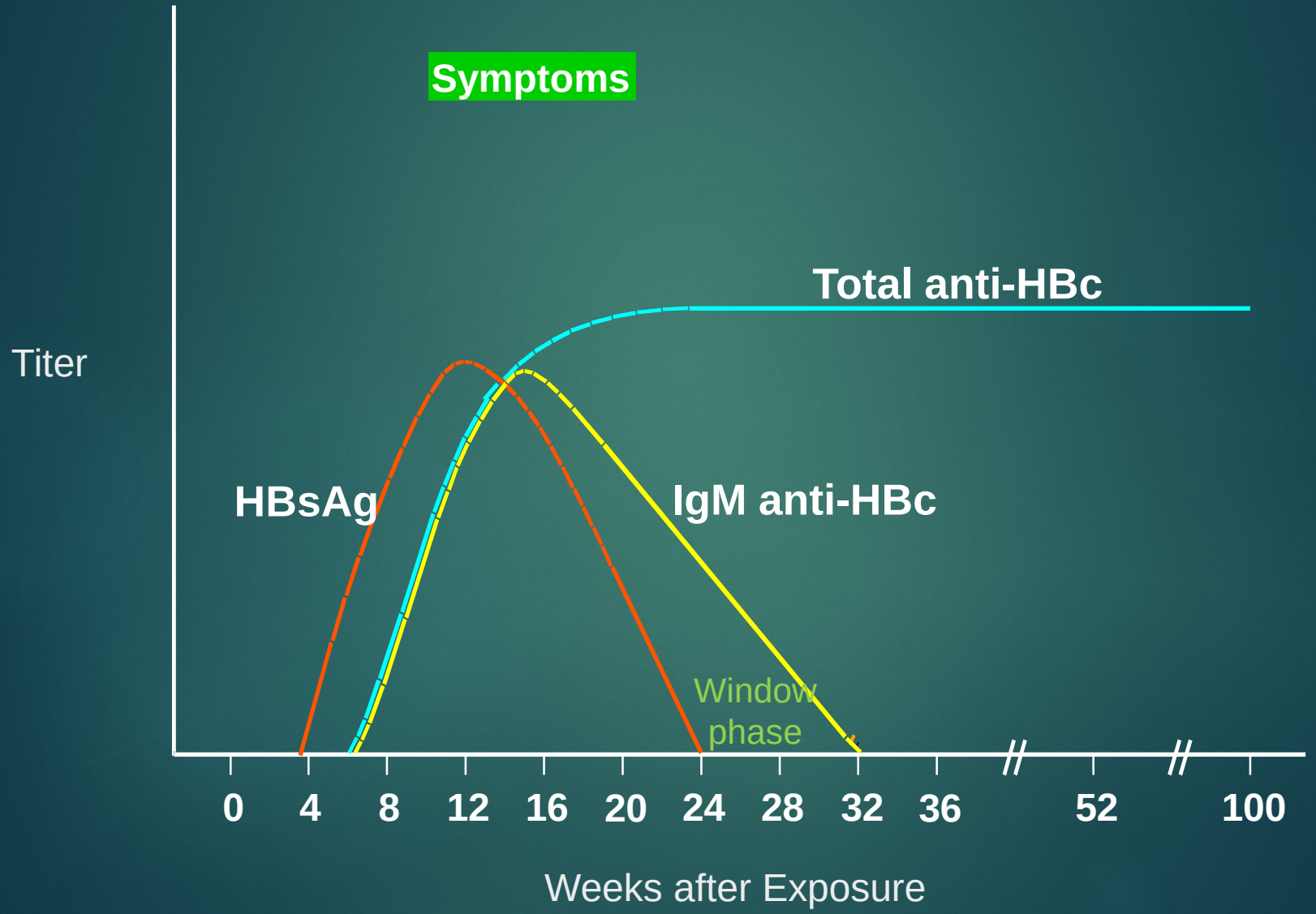
Acute HBV Infection with Recovery
Typical Serological Course



Core antibody (anti-HBc)

- IgM anti-HBc: indicative of infection in the recent past (<6 months). Best test for acute infection.
  - But no longer part of our acute case definition. Doh!
- Anti-HBc, total (IgG and IgM): marker of past or current infection.
  - Vaccination does not produce anti-HBc.
  - False positive tests can occur in up to 20% of persons tested

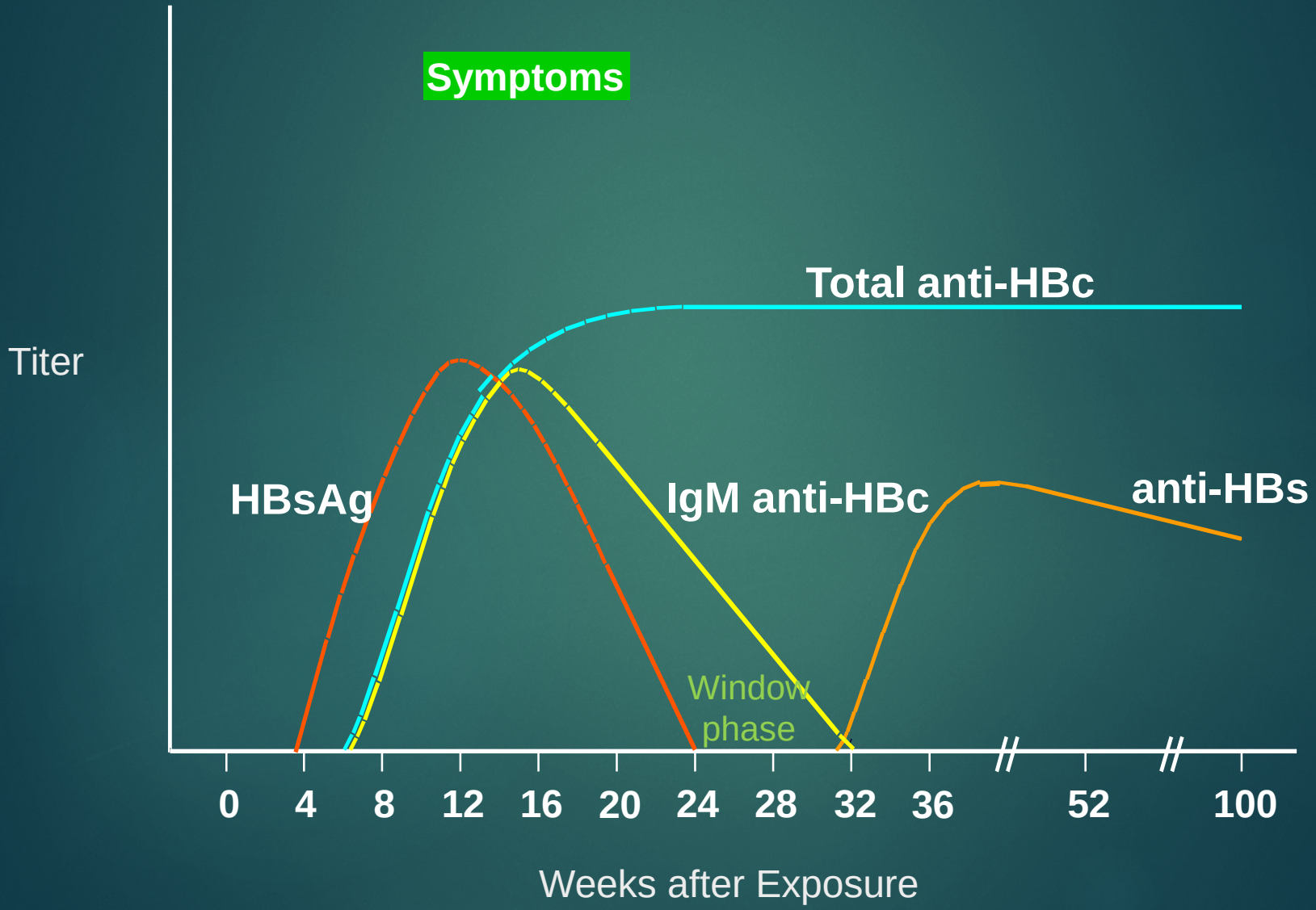
Acute HBV Infection with Recovery
Typical Serological Course



Surface Antibody (anti-HBs)

- Antibodies produced against HBsAg as the host recovers from infection
- Produced after either natural infection or immunization (lasts for months after HBIG)
- Indicates immunity

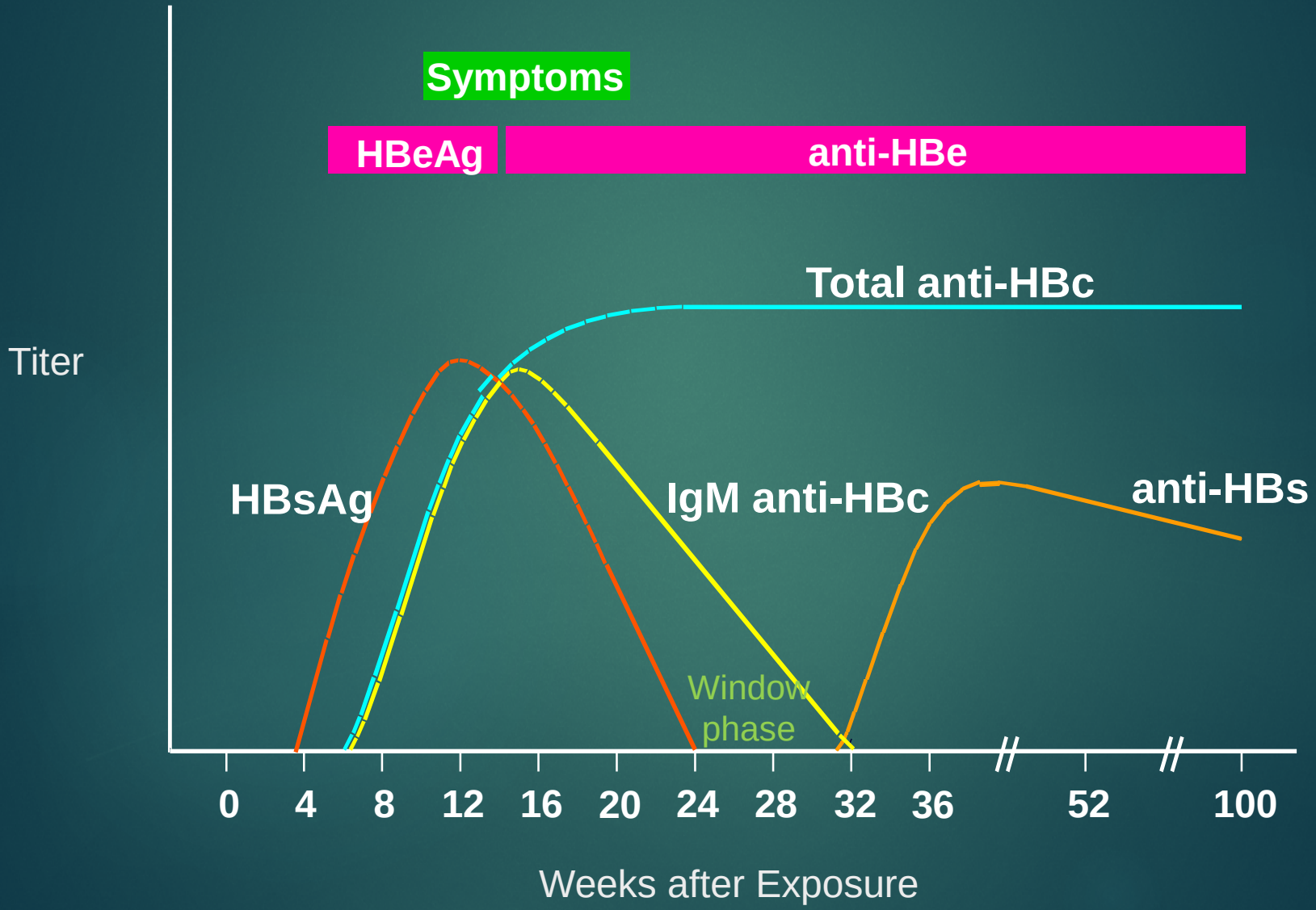
Acute HBV Infection with Recovery
Typical Serological Course



E Antigen (HBeAg) and Antibody (Anti-HBe)

- HBeAg:
  - Marker of high infectivity (4X more infectious)
- HBeAb/anti-HBe:
  - Indicates loss of HBeAg
  - Seroconversion from e antigen to e antibody is a predictor of long-term clearance of HBV

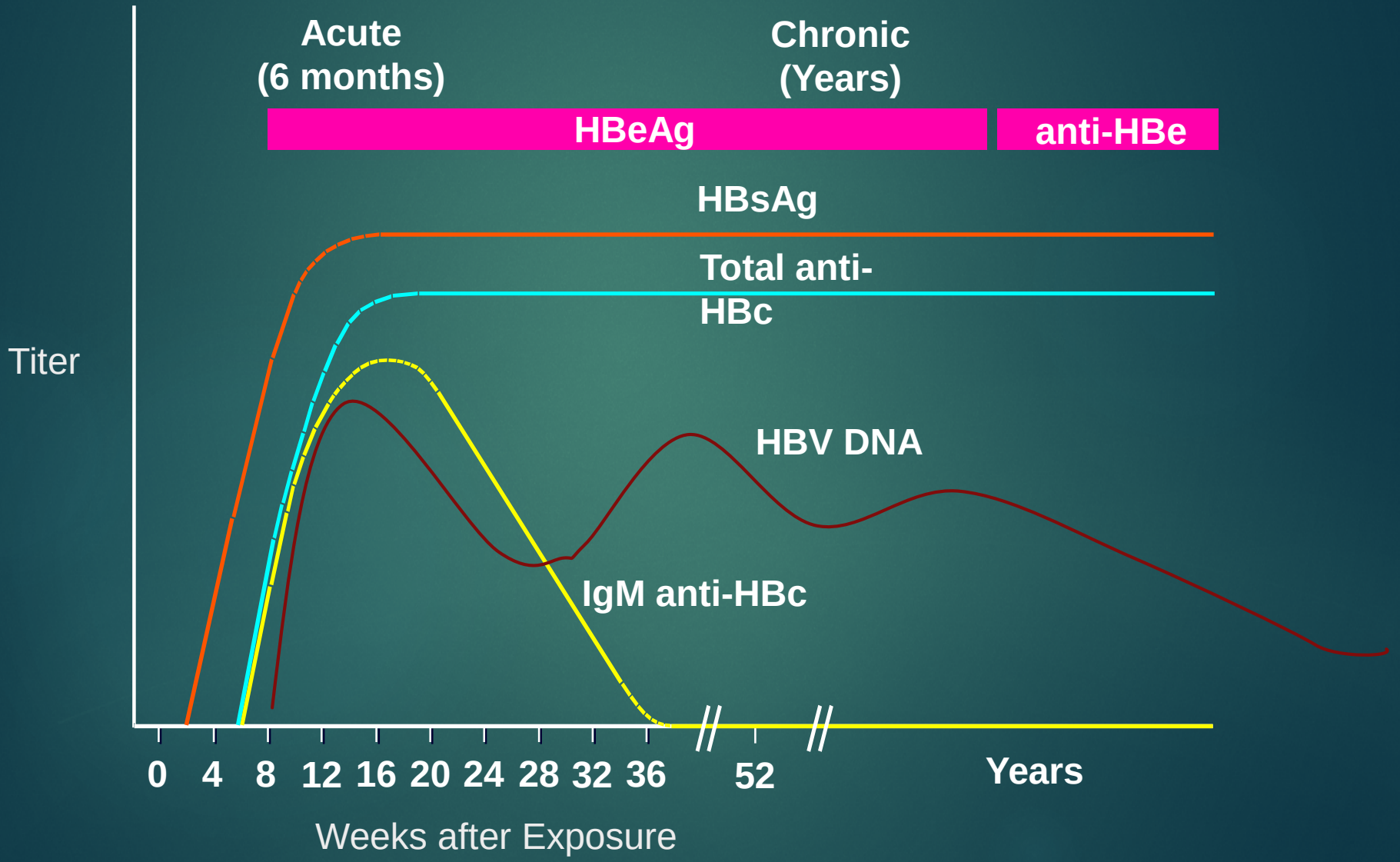
Acute HBV Infection with Recovery
Typical Serological Course



HBV DNA

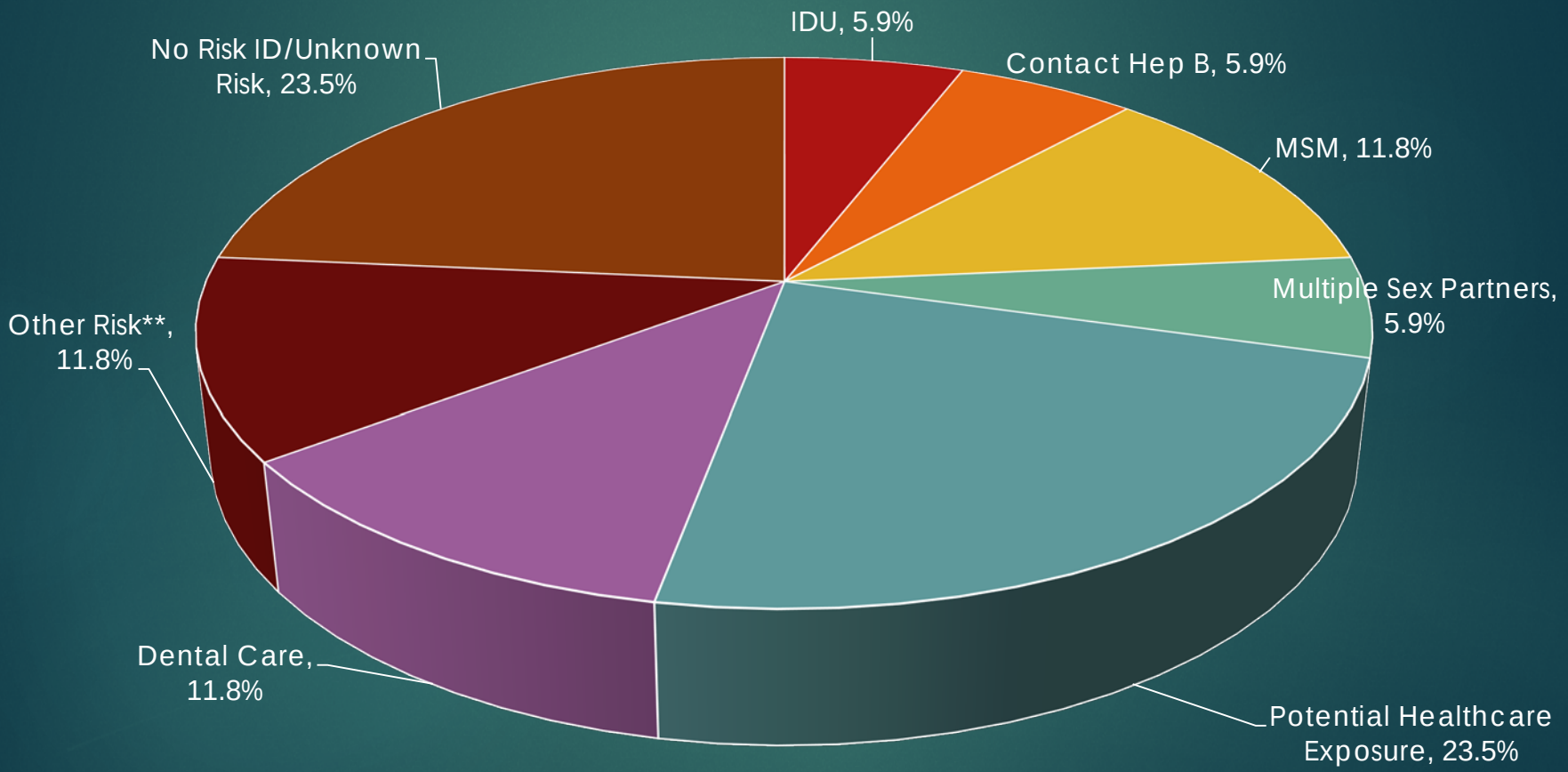
- Active replication of virus, patient infectious
- Testing is expensive, rarely obtained during acute infections
- Used to detect chronic infection, viral load may be used to decide whether to initiate treatment
- Detectable in ~50% of carriers. Can be present when HBsAg is undetectable

Chronic HBV Infection
Typical Serological Course



Cases of Acute HBV, Oregon, 2005-2016

Reported Risk Factors (mutually exclusive) for Acute Hepatitis B, Oregon, 2016



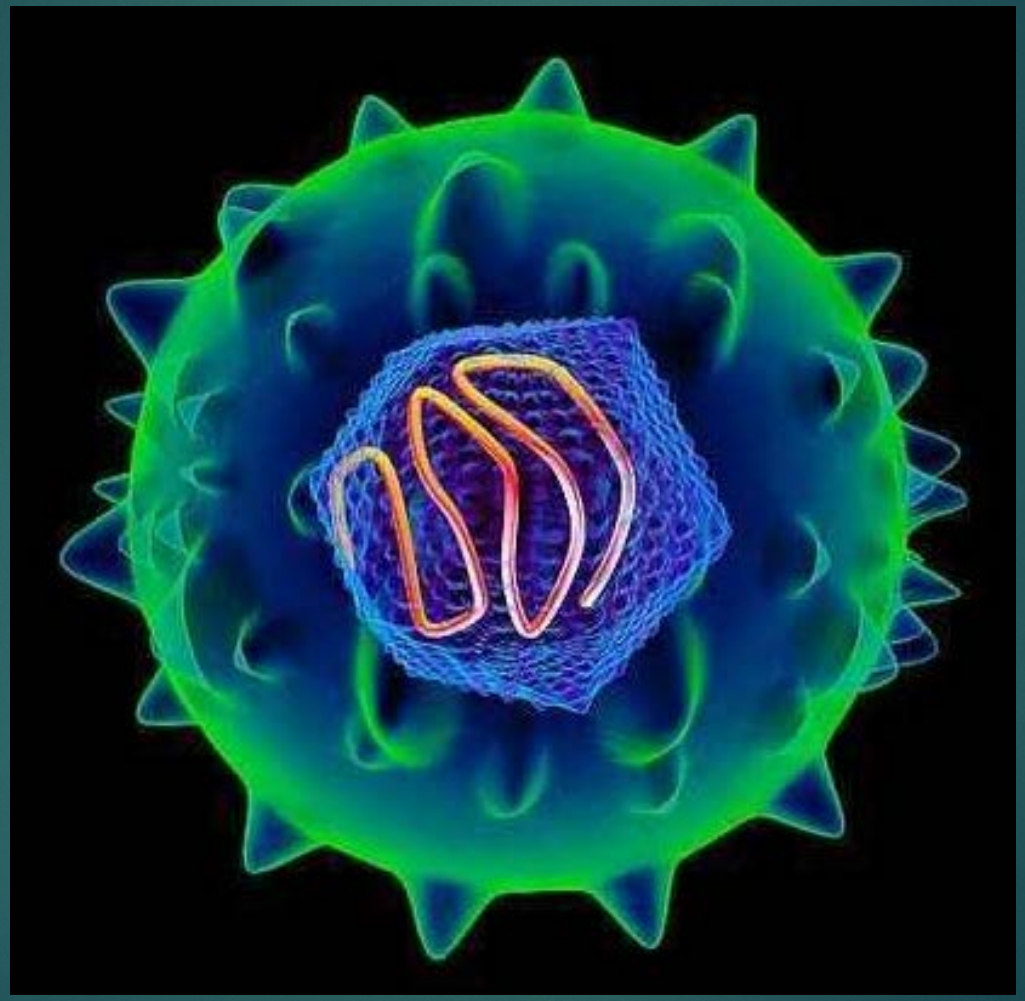
*infusions, transfusions, dialysis and surgery
**street drugs, needlestick, tattoo. piercing, other blood exposure

Cases of Chronic HBV Oregon, 2005-2016

Most common risk factors among chronic HBV Cases, Oregon, 2016 (n=313 interviewed)

Risk factor	No. (%)
Foreign born	189 (60%)
Multiple sex partners	110 (35)
Contact of a case	96 (31)
History of transfusion	34 (11)
Employed in a medical field	25 (8)
Ever STD	24 (8)
MSM	18 (6)

Hepatitis D



Hepatitis D - Serologies

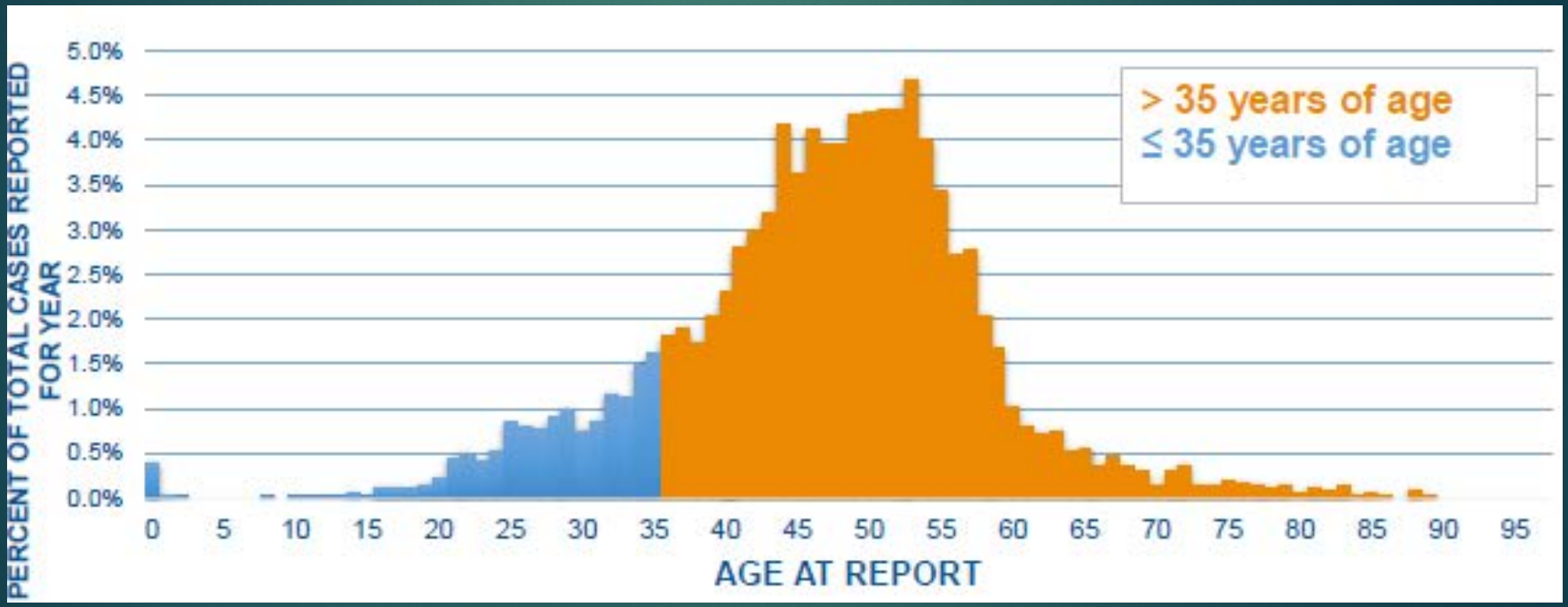
- anti-HDV IgM: indicative of ongoing replication
- Anti-HDV total (IgG and IgM): indicative of chronic or acute infection
- HDV PCR: most sensitive for detecting HDV viremia

Hepatitis C

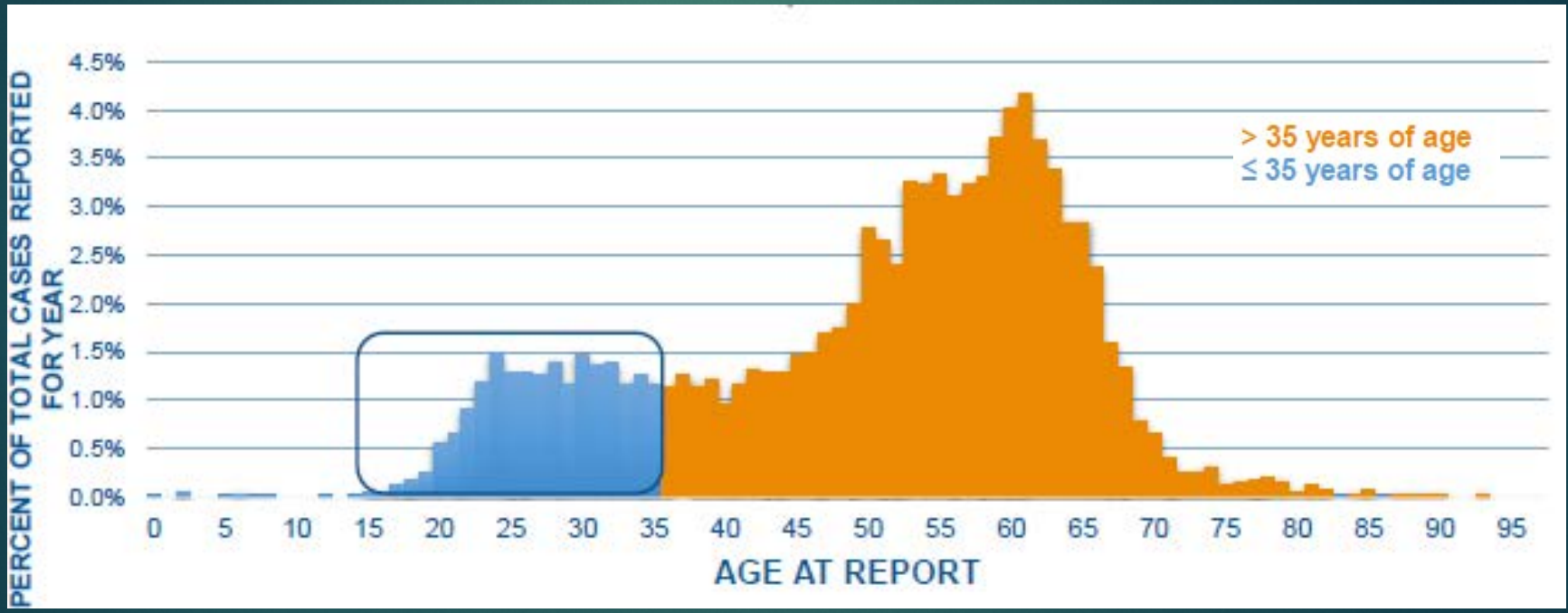
Hepatitis C - Serologies

- Anti-HCV EIA
  - Enzyme immunoassay to measure HCV antibody. Cannot be used to distinguish between recent and past infection.
  - Signal-to-cutoff ratio is used to determine the likelihood that a positive HCV EIA represents a true positive. It is calculated by dividing the optical density value of the sample.
  - Infants born to HCV+ mothers, can have detectible maternal antibodies for up to 18 months
- PCR
  - Polymerase chain reaction. Used to measure HCV RNA. There are both qualitative (more sensitive) and quantitative tests.
- Genotyping
  - 6 different genotypes. Genotype 1 is the most common in the US, accounting for 70-75% of infections.

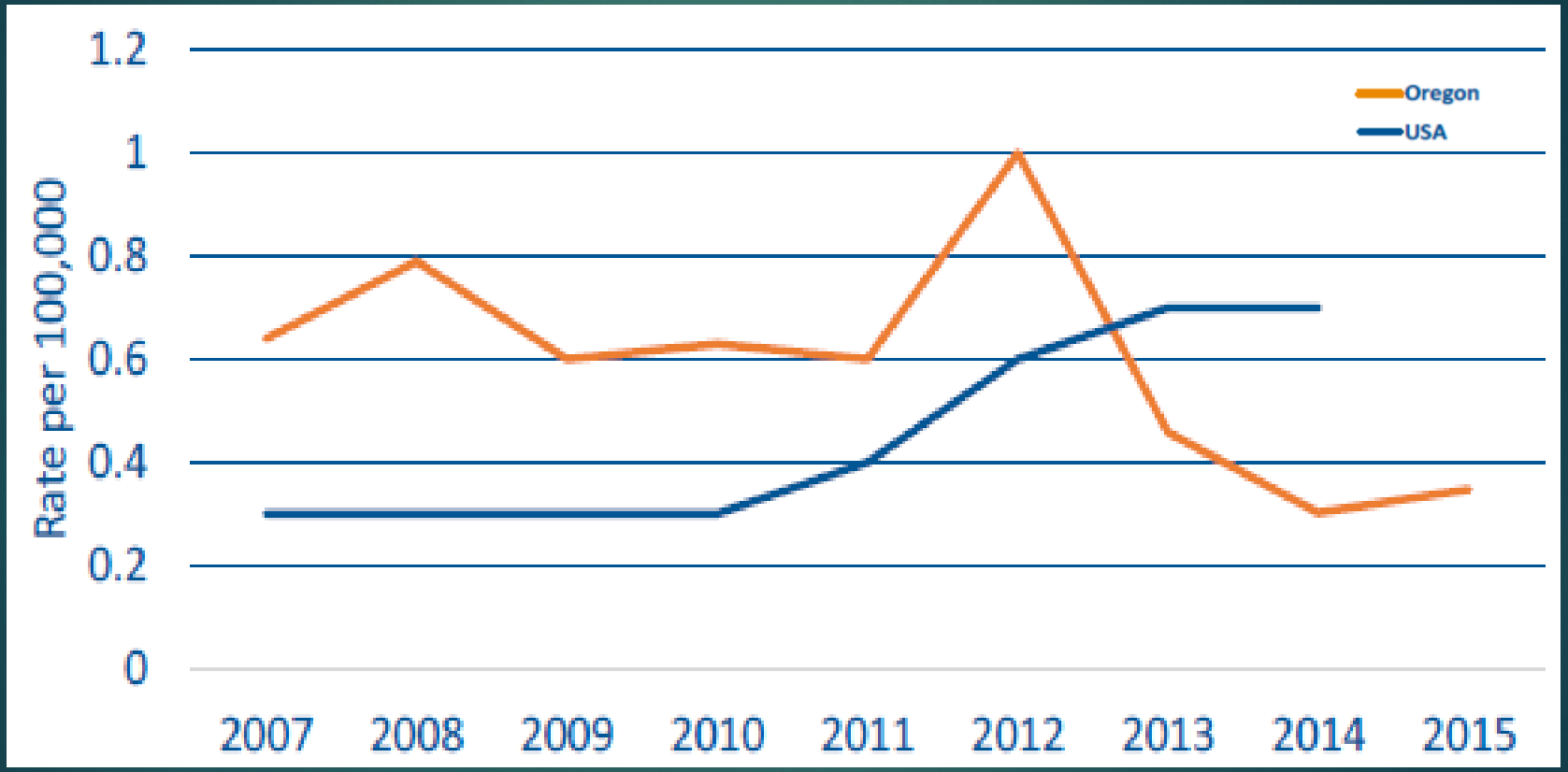
2006 Age Distribution of newly reported HCV cases, n=5,463



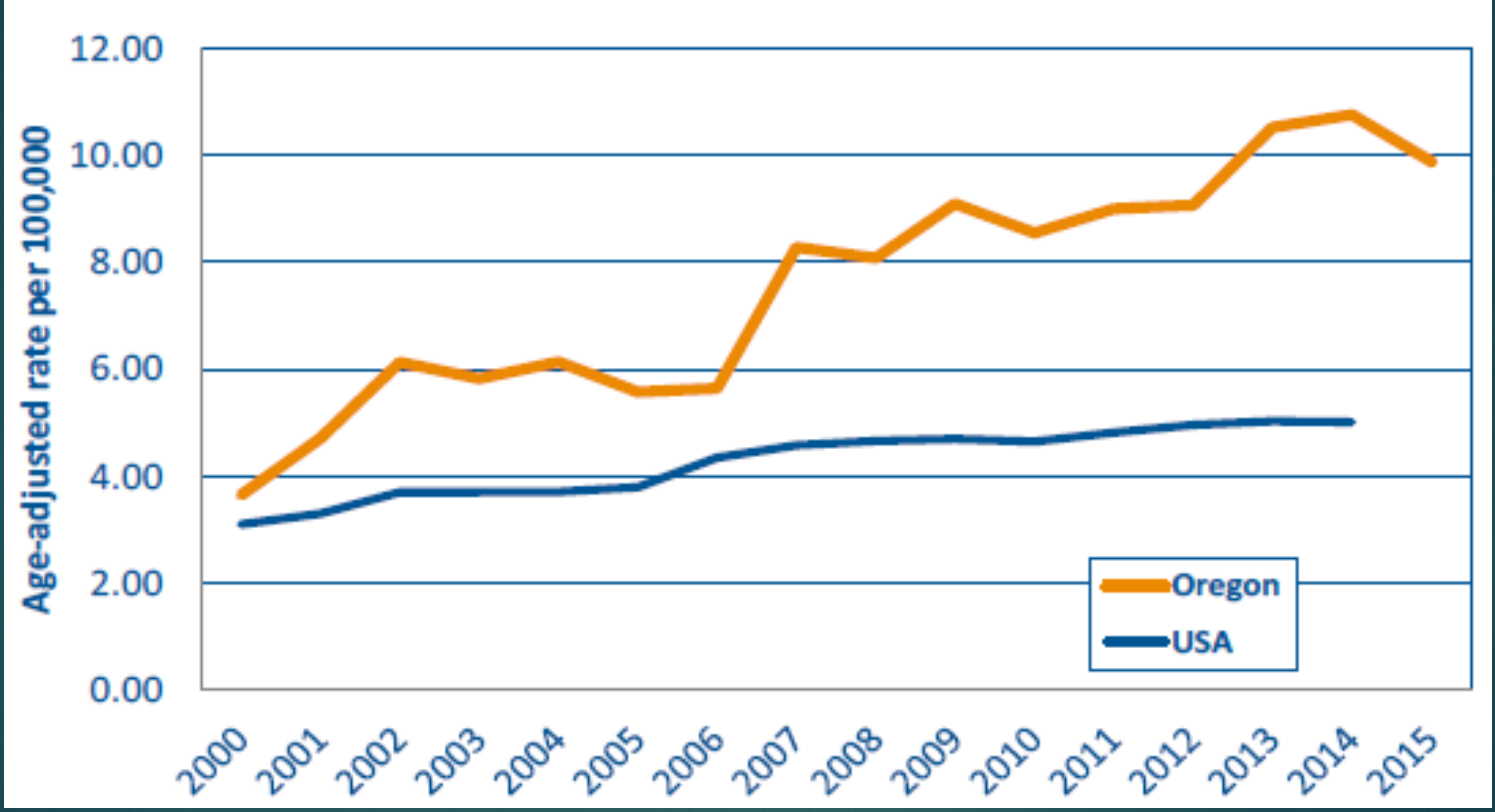
2015 Age Distribution of newly reported HCV cases, n=5,926



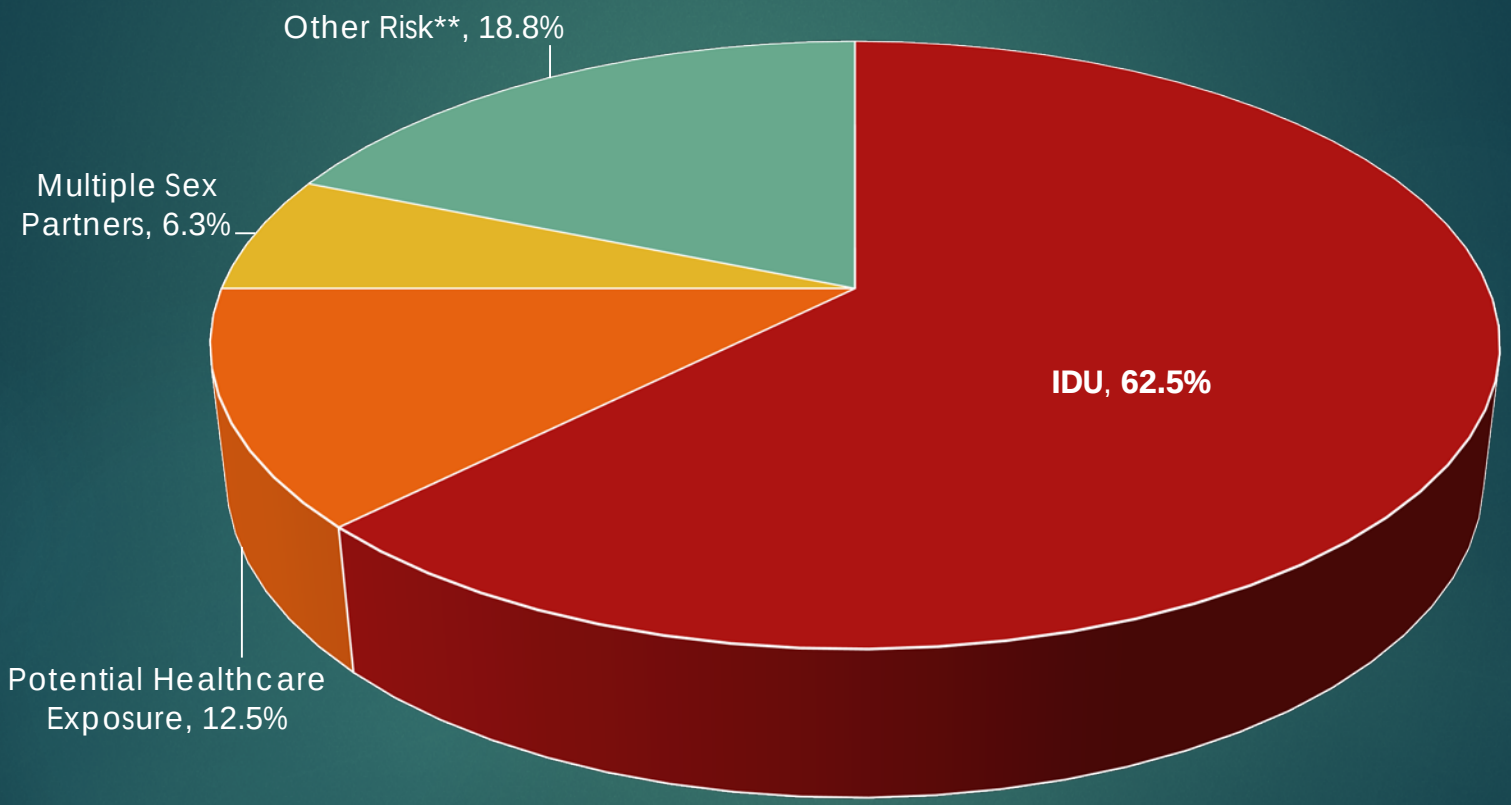
Acute Hepatitis C, Oregon and Nationally, 2007-2015



Hepatitis C Deaths in Oregon and Nationally, 2000-2015

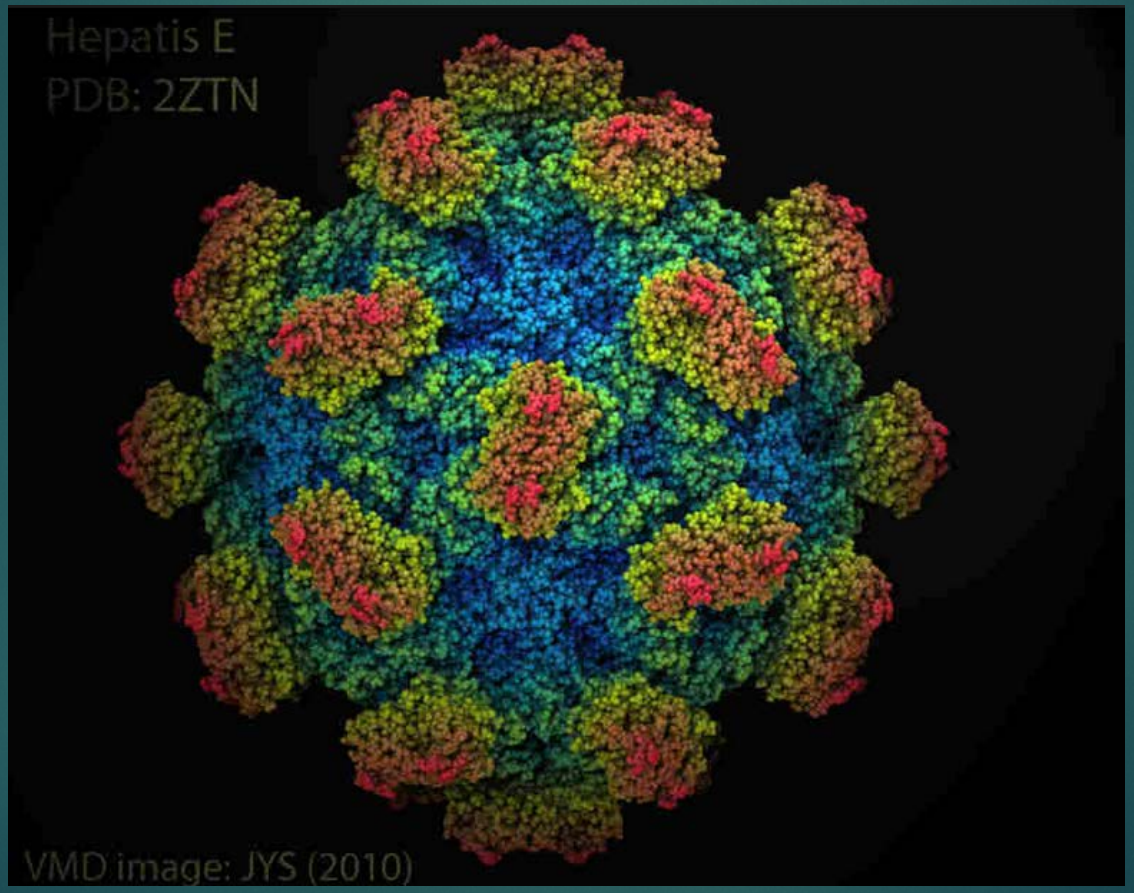


Reported Risk Factors (mutually exclusive) for Acute Hepatitis C, Oregon, 2016



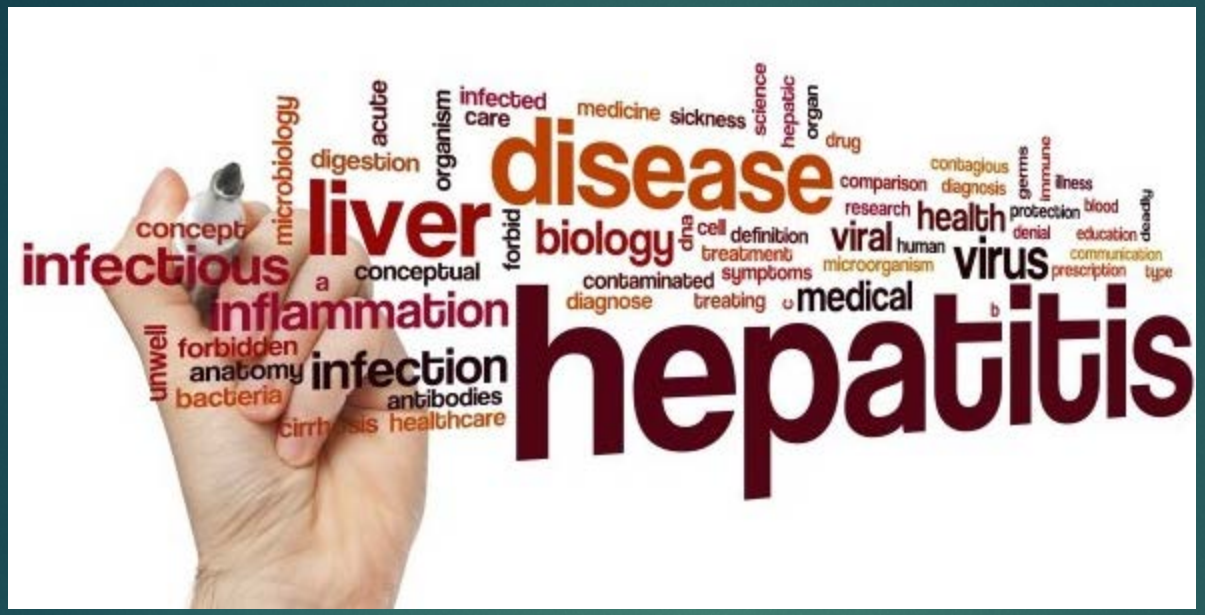
*Transfusion, infusions, dialysis and surgery
**street drugs, needlestick, tattoo, piercing, contact of a case, and other blood exposure

Hepatitis E



Serologies – Hepatitis E

- Anti-HEV, IgM: indicates acute infection.
- Anti-HEV, total (IgM and IgG): marker of past infection.
- HEV RNA: detectable by PCR in acute phase feces in ~50% of cases.



Case Studies

Hepatitis B

- 36 year old male IDU tested for hepatitis during follow up for cellulitis. Test results are as follows:
  - + anti-HCV
  - - total anti-HAV
  - - HBsAg
  - - anti-HBs
  - + total anti-HBc
  - - IgM anti-HBc
- The patient began injecting drugs at age 23. Does not recall ever having acute HBV infection and does not remember ever receiving HBV vaccine

Which one of the following most accurately describes the patient's HBV serology results?

A. A finding of isolated anti-HBc represents past infection with hepatitis B

B. The isolated anti-HBc test has a greater than 95% likelihood of representing a false positive result, and thus the patient should be considered negative for acute or prior HBV infection.

C. A finding of isolated anti-HBc most likely represents a weak response to hepatitis B vaccine, and the patient probably just doesn't remember that he's been vaccinated.

D. Persons with HIV and chronic HCV infection have the lowest prevalence of isolated anti-HBc because they generate enhanced levels of anti-HBs that remain elevated on a long-term basis.

Hepatitis B

- 27-year old woman presents to the urgent care clinic with new onset of nausea and jaundice
- For three years, she has experienced major problems with drug addiction and regularly injects meth
- She usually uses clean needles, but six weeks ago shared needles with a man she found out has HBV infection
- She has never received HBV vaccine
- Two years ago, she tested negative for hepatitis A, B, and C
- Physical examination is normal except for track marks on her arms and visible jaundice.
- Laboratory studies show elevated LFTs, and serology tests for hepatitis A, B, and C viruses are ordered

Which of the following serologic profiles would be most consistent with acute HBV infection?

Test	(a) Results	(b) Results	(c) Results	(d) Results
HBsAg	-	+	+	-
Anti-HBs	+	-	-	+
Total anti-HBc	+	-	+	-
HBeAg	-	-	+	-
Anti-HBe	+	+	-	-

Hepatitis C

- 27 year old female with a history of injection drug use gives birth at 37 weeks. Mom is tested for hepatitis C due to her history of IDU. She has no signs or symptoms of acute viral hepatitis. Results are:
  - +anti-HCV
  - + RNA PCR

How would you classify this case?

A. Confirmed, acute hepatitis C
B. Presumptive, acute hepatitis C
C. Confirmed, chronic hepatitis C
D. Presumptive, chronic hepatitis C
E. No case

Hepatitis C

- The infant is then tested and she is anti-HCV positive.
- What now?
  A. Create an acute case
  B. Create a presumptive chronic case
  C. Create a confirmed chronic case
  D. Create a suspect chronic case
  E. Call me and get the answer

Hepatitis B

- 40 year old male tested for HBV during his yearly physical
- Case is asymptomatic and LFTs are within normal limits
- Case was born in the United States but mother is from China
- Lab results show:
  - HBsAg Positive
  - Total anti-HBc Positive
- ELRs comes through under Hepatitis B (acute)

How should this case be classified?

A. Presumptive, acute hepatitis B
B. Confirmed, acute hepatitis B
C. Presumptive, chronic hepatitis B
D. Confirmed, chronic hepatitis B
E. No case

Hepatitis B ELRs

Test Info	Result	Disease Name	Disease Group	Done	
Hepatitis B virus	6.1	HepB (chronic)	Hepatitis	☐	Ignore
Ref lab test Pnl	<20	HepB (chronic)	Hepatitis	☐	Ignore
HEPATITIS BE ANTIBODY	Reactive (qualifier value)	HepB (chronic)	Hepatitis	☐	Ignore
Hepatitis B Surface Antibody	Reactive Reactive	HepB (chronic)	Hepatitis	☐	Ignore
Hepatitis B Surface Antibody	31.62	HepB (chronic)	Hepatitis	☐	Ignore
HEPATITIS B VIRUS DNA, QN,	>8.23	HepB (chronic)	Hepatitis	☐	Ignore
Hepatitis B DNA Quantitative	Detected Detected	HepB (chronic)	Hepatitis	☐	Ignore
Ref lab test Pnl	<20	HepB (chronic)	Hepatitis	☐	Ignore
HBV Real-Time PCR, Quant	30.0000	HepB (chronic)	Hepatitis	☐	Ignore
HBV Real-Time PCR, Quant	657000000.0000	HepB (chronic)	Hepatitis	☐	Ignore

- For chronic hepatitis B, cases should be positive for one or more:
  - Hepatitis B surface antigen
  - Hepatitis B e surface antigen
  - Hepatitis B DNA
- Results for IgM anti-HBc may not be reported if negative

Hepatitis B Lab Testing

- Some facilities report preliminary test results via ELR
- If you do not receive confirmatory results, please follow up as the confirmatory testing may have been negative
- Labs noted to report preliminary results:
  - Providence
  - Biomat Plasma
  - CSL Plasma
  - Talecris Plasma
  - Bloodworks NW

Perinatal Hepatitis B Prevention Program Overview

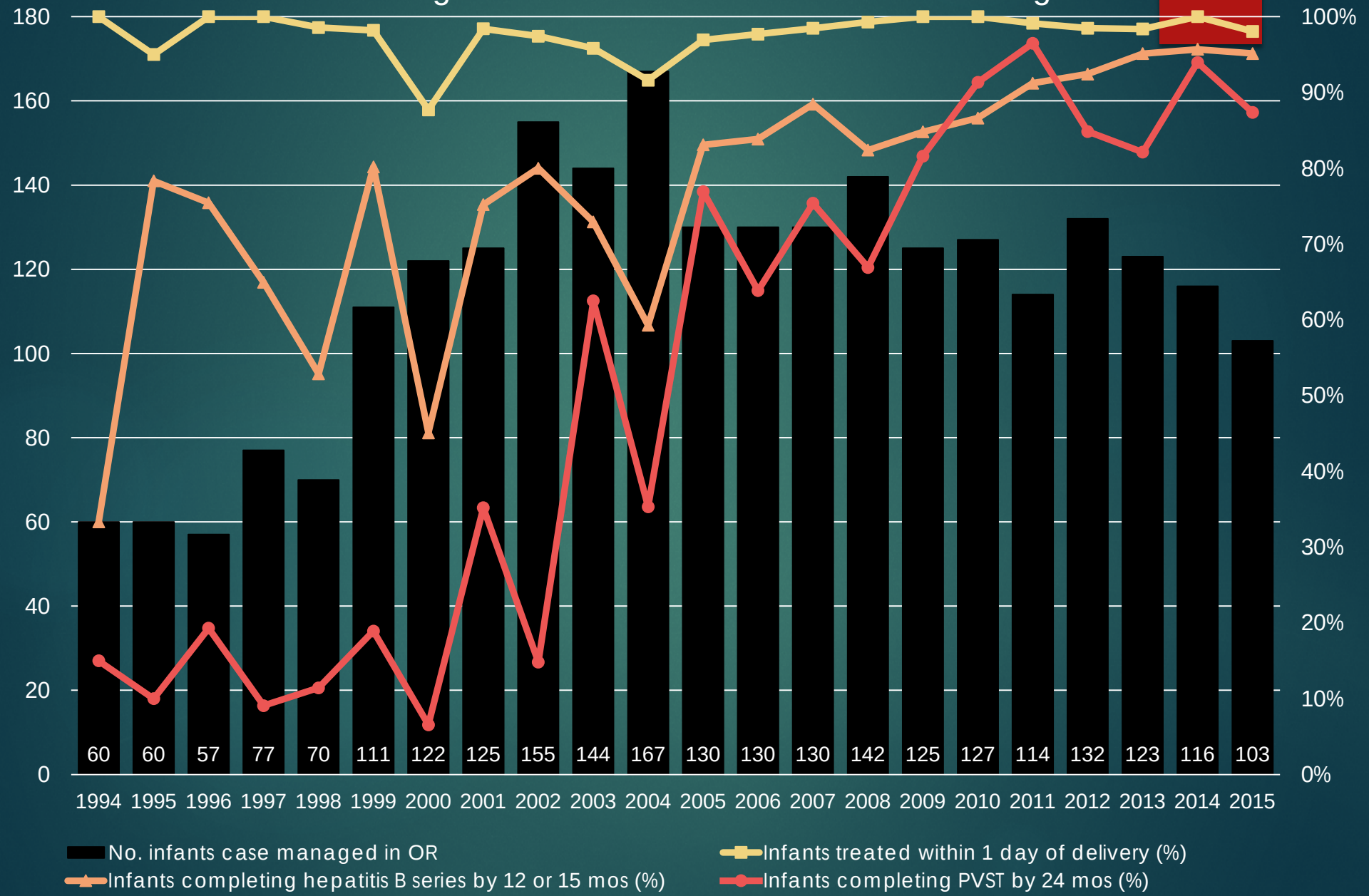
- Ensure all pregnant women are tested for hepatitis B with each pregnancy
  - In Orpheus this means checking pregnancy status when new labs received for all women of child bearing age [15-45]
  - Some ELRs now indicate if the results are from a prenatal panel (e.g. OB, prenatal)

- Infants born to HBV+ women receive proper preventative treatment (HBIG + vaccine) and testing
  - In Orpheus: add the infant as a contact and track each piece of case management

Updates

- Investigative Guidelines (April 2017)
  - Expanded case definitions to include HBeAg and HBV DNA
  - Added Probable case definition
    - HBV+ infant born to a mother with an unknown status
  - New recommendations for infants requiring a second vaccine series
  - Added a standard lost to follow-up definition
- Orpheus
  - Tracking pregnancies that end in miscarriage
  - Tracking pregnancies transferred out of state before delivery
    - Both in the pregnancy history box

Perinatal hepatitis B case management activities in Oregon, 1994-2015 birth cohorts. Shown is the number of infants enrolled in case management and the percent of those infants meeting the indicators of successful case management



Best Practices

- If you need to change an acute case to chronic, may need to copy down risks before changing the disease in Orpheus
- If new labs are received for an existing acute hepatitis case that suggest chronic infection, create a new chronic hepatitis case for the person
- When interviewing cases, please try to obtain information on contacts and country of birth
- Make sure to enter contacts on the contact tab
- Assess vaccination status by querying ALERT for cases and any contacts elicited

Best Practices con't

- If you have multiple serology results, it might be a good idea to create a manual lab so you can get an easy snap shot of all of the different results
- For old, out of state cases with a new ELR/Oregon residency:
  - Create a new case with the new lab; email the tech team to merge the OLD case to the NEW case
- While not required, LHDs are encouraged to determine reason for testing on chronic hep C cases for persons <30 years of age and to determine if there was a previous negative result (possible asymptomatic seroconverter)

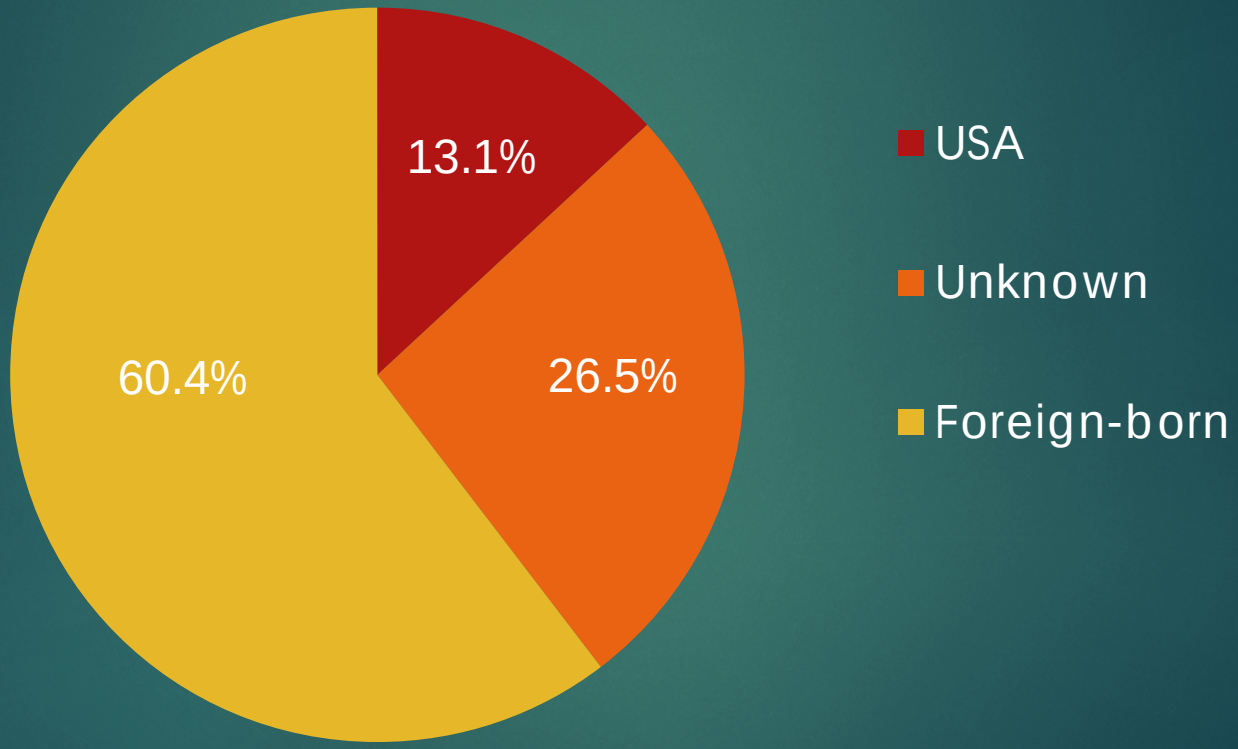
Best Practices con't

- To transfer a case between counties:
  - Add the new address to the Person Record (not on the Basic tab)
  - On the More tab, add the new county of residences and mark as 'current'
  - Notify the new county of residences so they can add a new Local Epi
- Check on pregnancy status for females of childbearing age
- The pregnancy field in the demographics section only needs to be answered when a case is first identified and interviewed.
- When an infant contact is created, connect it to the appropriate pregnancy from the Pregnancy History box on the Basic tab

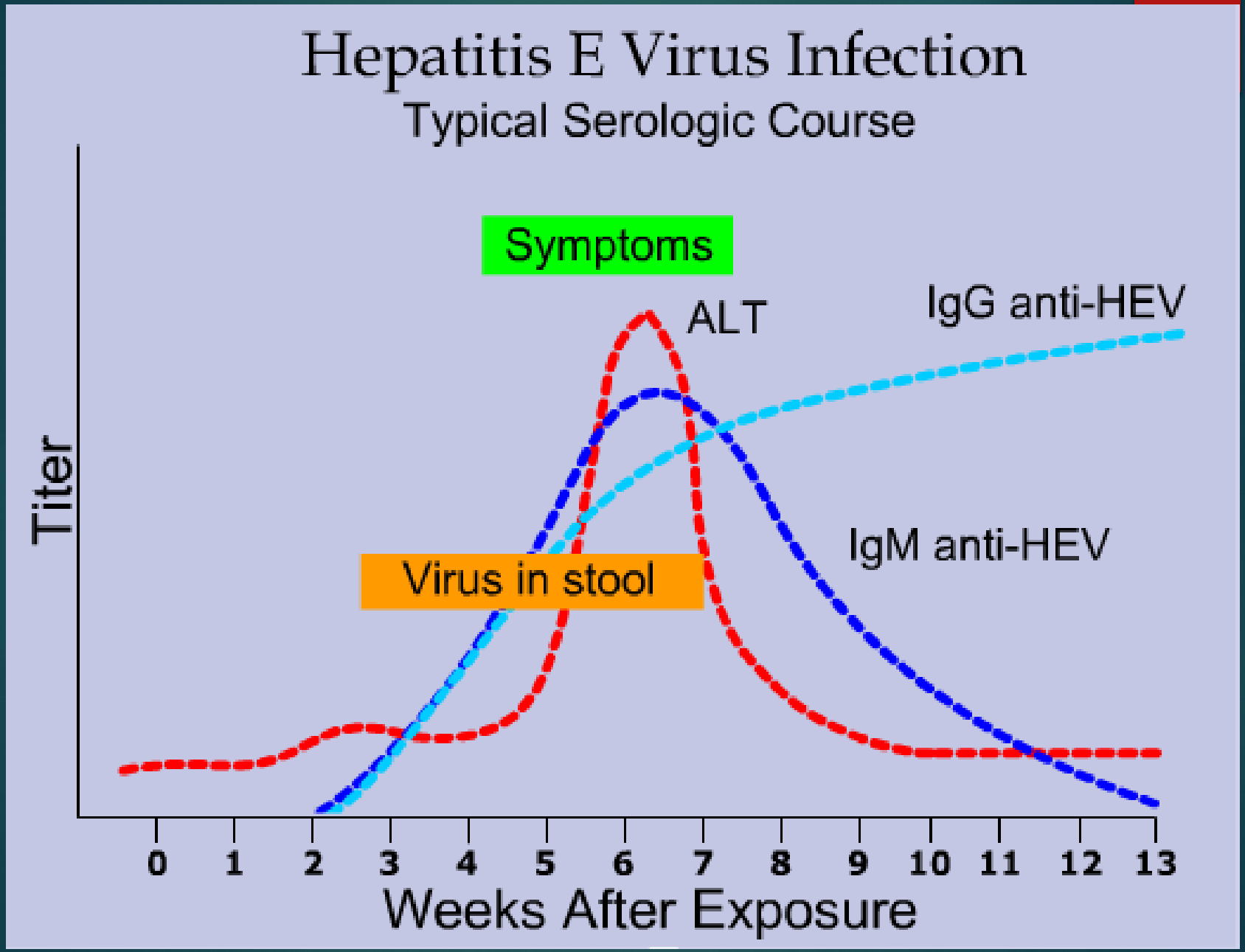

Fin

Questions?

Country of origin for interviewed HBV cases, Oregon 2016



n=313 interviewed


Hepatitis E Virus Infection
Typical Serologic Course
Symptoms
ALT
IgG anti-HEV
IgM anti-HEV
Virus in stool
Titer
0
1
2
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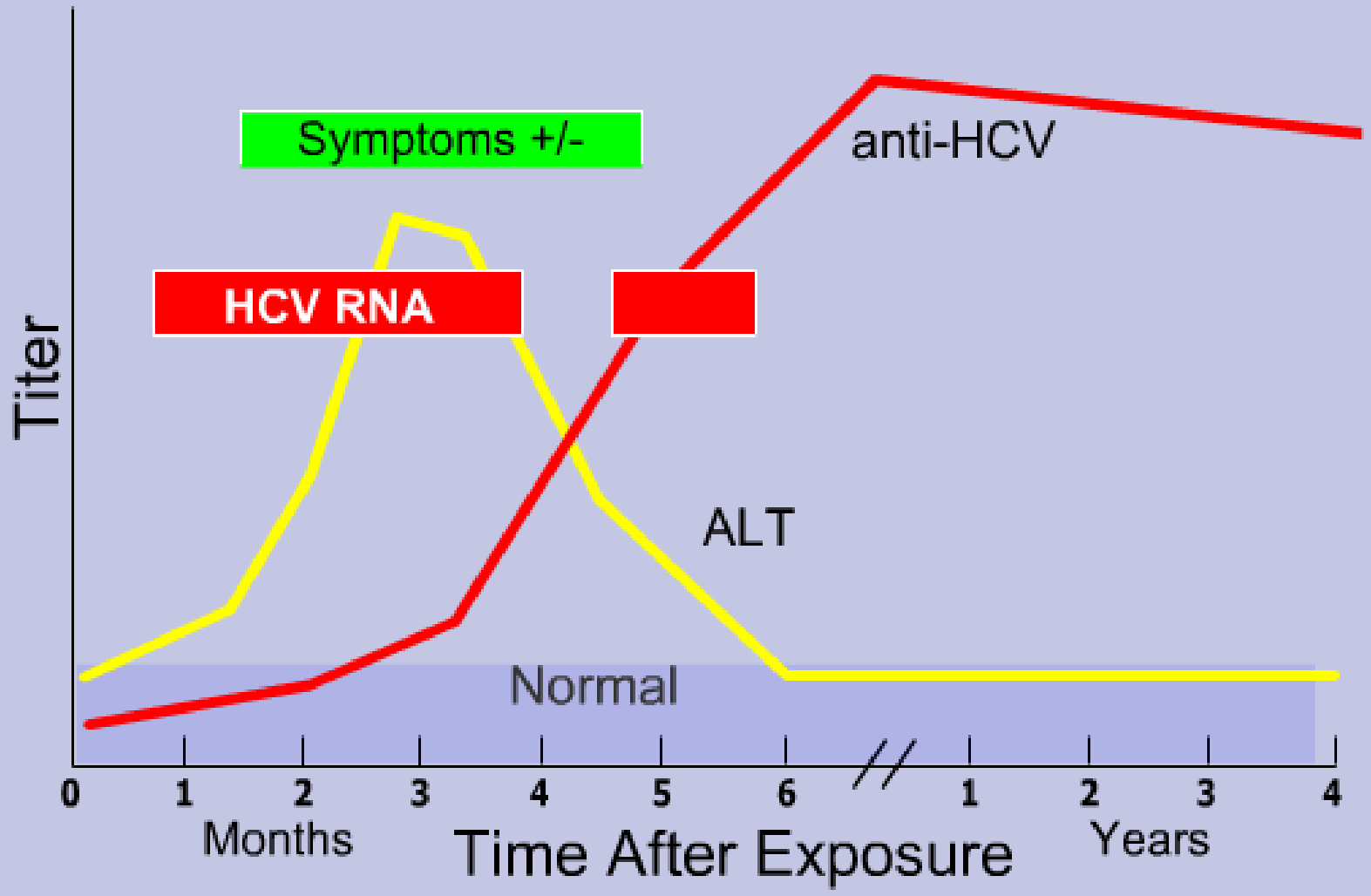
Weeks After Exposure

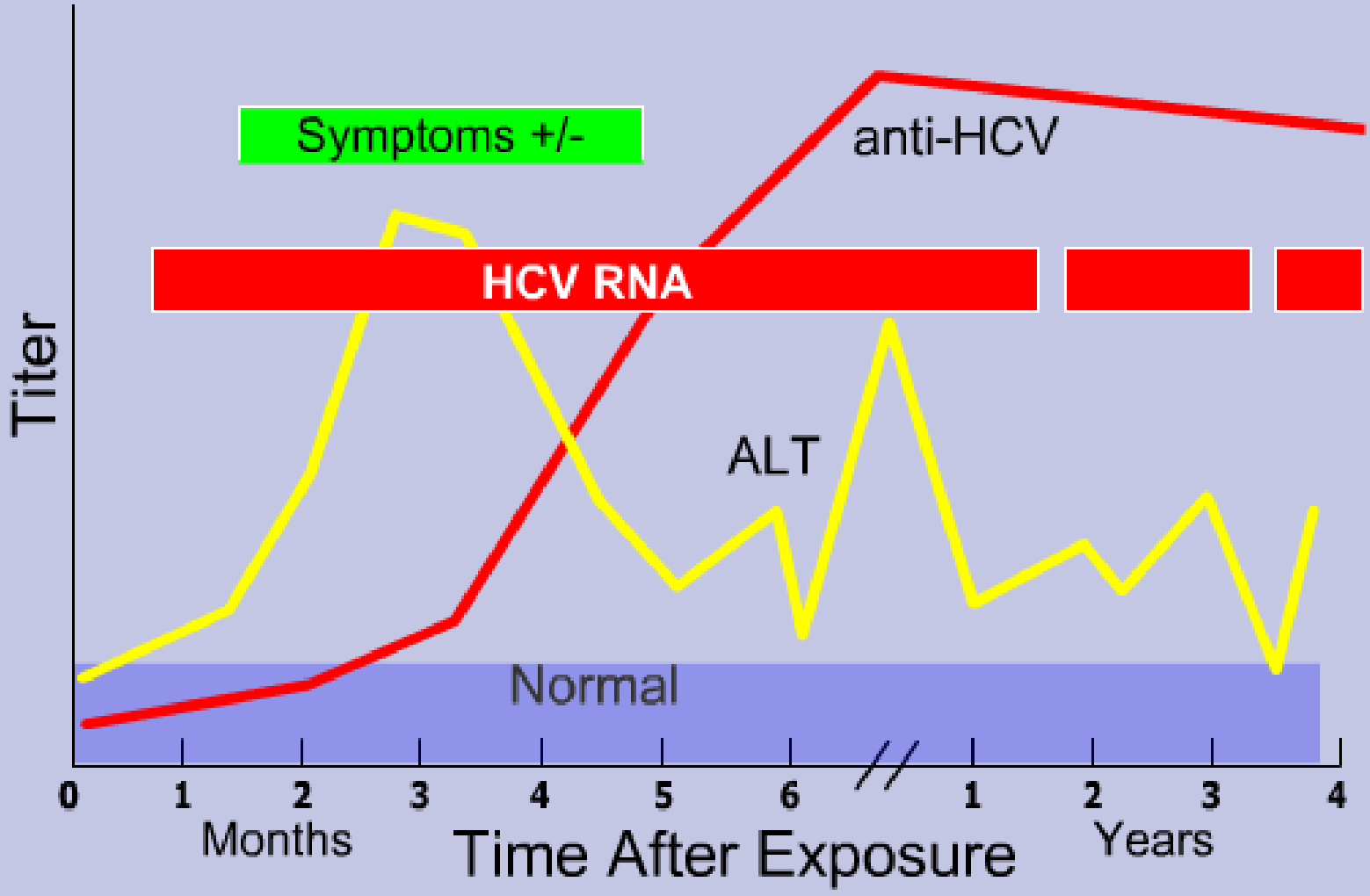
Acute HCV Infection with Recovery

Typical Serologic Course



Progression to Chronic HCV Infection

Typical Serologic Course



Risk of Fatal Outcome in Persons Who Develop Hepatitis C Infection

100

85%

Time

15%

Resolved
15

Chronic
85

20%

Cirrhosis
17

80%

Stable
68

25%

Mortality
4

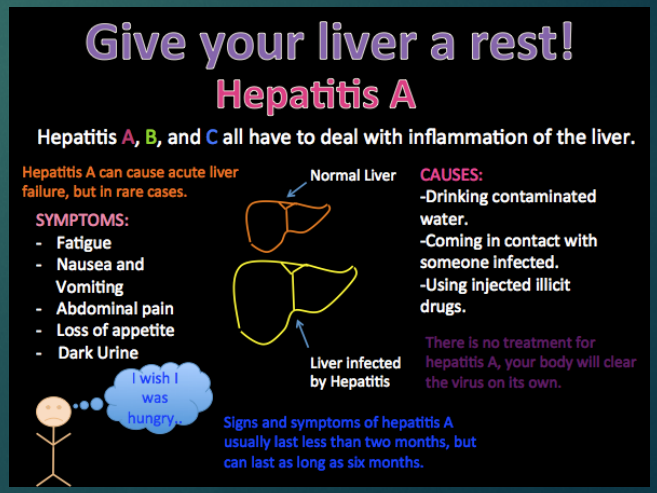
75%

Stable
13

Courtesy of Seeff, LB and Alter, HJ.

Hepatitis A – Clinical Features

- Incubation period — Average: 30 days; Range: 15-50 days
- Clinical illness (jaundice) — <6 yrs: <10%; 6-14 yrs: 40-50%; >14 yrs: 70-80%
- Complications — Fulminant hepatitis in <1%
- Chronic sequelae — None
- Transmission — Fecal-oral

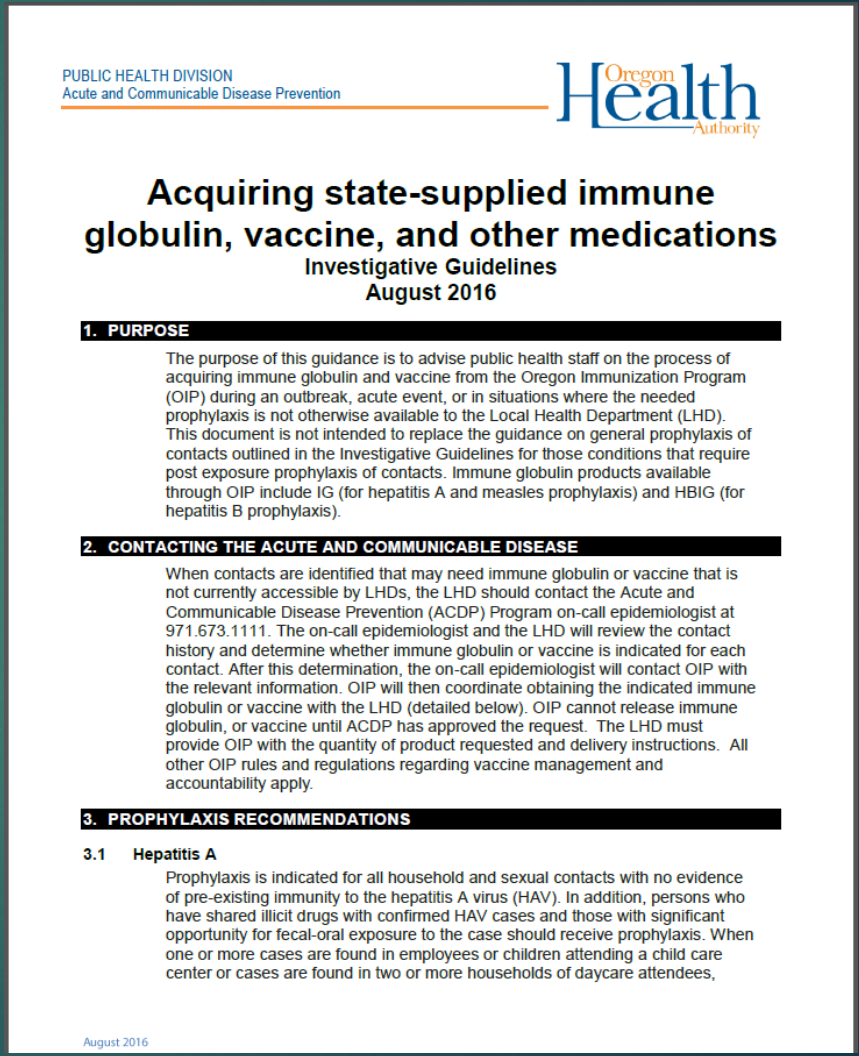


Post-exposure prophylaxis

- Vaccine (HAVRIX or VAQTA) is recommended as post exposure prophylaxis in health persons 12 months through 40 years of age
- Immune globulin (IG) is typically used for post-exposure prophylaxis persons who are either older than 40 years of age, children younger than 12 months of age, immunocompromised persons, and persons with chronic liver disease.
  - Might as well vaccinate at the same time

Requesting IG

- Contact ACDP Epi on-call for approval with the following information:
  - Number of contacts needing IG
  - Weight and age of each contact eligible for IG
  - Insurance status of each contact.
  - Calculated amount of IG needed
- IG is supplied in 2-mL and 10-mL vials
- IG dosage recommendation: 0.02 mL/kg; IM
- LHDs should bill insurance for IG if the contact has insurance



PUBLIC HEALTH DIVISION
Acute and Communicable Disease Prevention

Oregon Health Authority

Acquiring state-supplied immune globulin, vaccine, and other medications
Investigative Guidelines
August 2016

1. PURPOSE

The purpose of this guidance is to advise public health staff on the process of acquiring immune globulin and vaccine from the Oregon Immunization Program (OIP) during an outbreak, acute event, or in situations where the needed prophylaxis is not otherwise available to the Local Health Department (LHD). This document is not intended to replace the guidance on general prophylaxis of contacts outlined in the Investigative Guidelines for those conditions that require post exposure prophylaxis of contacts. Immune globulin products available through OIP include IG (for hepatitis A and measles prophylaxis) and HBIG (for hepatitis B prophylaxis).

2. CONTACTING THE ACUTE AND COMMUNICABLE DISEASE

When contacts are identified that may need immune globulin or vaccine that is not currently accessible by LHDs, the LHD should contact the Acute and Communicable Disease Prevention (ACDP) Program on-call epidemiologist at 971.673.1111. The on-call epidemiologist and the LHD will review the contact history and determine whether immune globulin or vaccine is indicated for each contact. After this determination, the on-call epidemiologist will contact OIP with the relevant information. OIP will then coordinate obtaining the indicated immune globulin or vaccine with the LHD (detailed below). OIP cannot release immune globulin, or vaccine until ACDP has approved the request. The LHD must provide OIP with the quantity of product requested and delivery instructions. All other OIP rules and regulations regarding vaccine management and accountability apply.

3. PROPHYLAXIS RECOMMENDATIONS

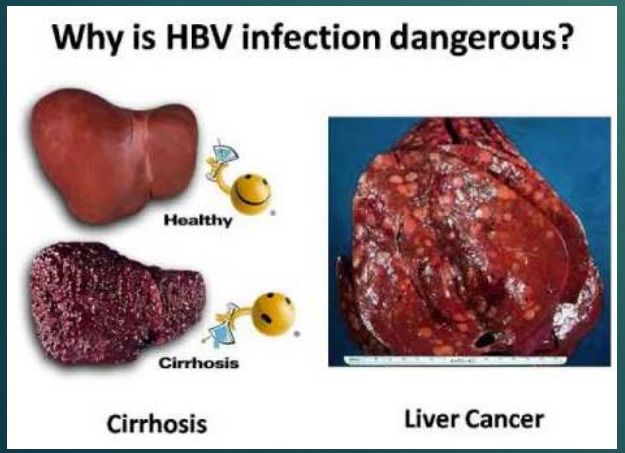
3.1 Hepatitis A

Prophylaxis is indicated for all household and sexual contacts with no evidence of pre-existing immunity to the hepatitis A virus (HAV). In addition, persons who have shared illicit drugs with confirmed HAV cases and those with significant opportunity for fecal-oral exposure to the case should receive prophylaxis. When one or more cases are found in employees or children attending a child care center or cases are found in two or more households of daycare attendees,

August 2016

Hepatitis B – Clinical Features

Incubation period	Average: 60-90 days Range: 45-180 days
Clinical illness (jaundice)	Mild to severe
Complications	Fulminant hepatitis in <1%, cirrhosis, HCC
Chronic infection	10-90% (varies inversely with age)
Transmission	Blood, percutaneous and permucosal contact, close personal contact, perinatal.



Concentration of Hepatitis B Virus in Various Body Fluids

High	Moderate	Low/Not Detectable
blood	semen	urine
open wounds	vaginal fluid	feces
	saliva	sweat
		tears
		breast milk

Post-exposure Prophylaxis for Occupational Exposure to HBV

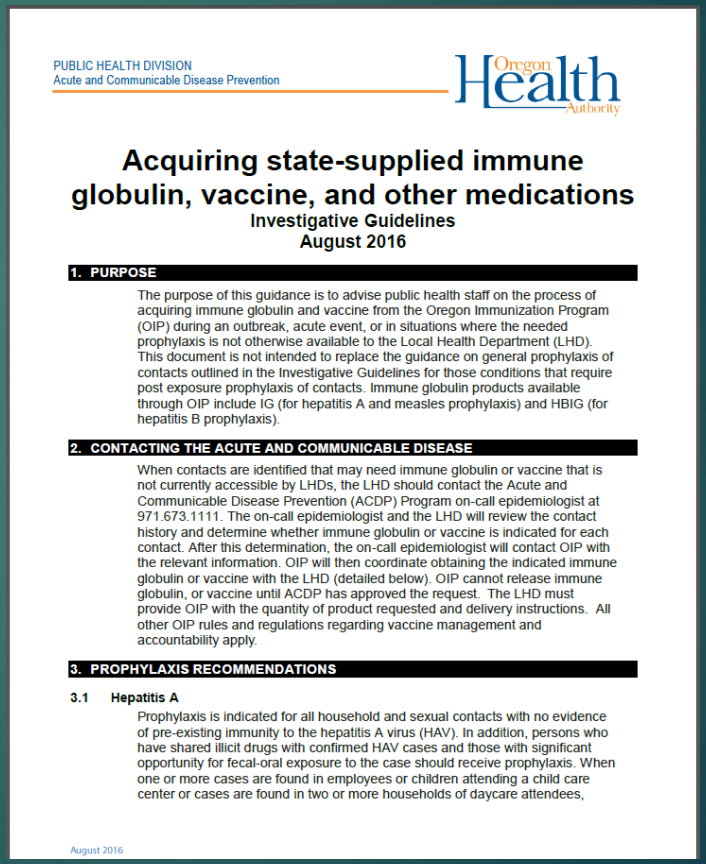
Vaccination and antibody response status of exposed workers	Treatment		
	Source HBsAg positive	Source HBsAg negative	Source unknown or not available for testing
Unvaccinated	Hepatitis B immune globulin (HBIG) x 1 (0.06/mL/kg IM) and initiate HB vaccine series	Initiate HB vaccine series	Initiate HB vaccine series
Previously Vaccinated			
Known responder[§]	No treatment	No treatment	No treatment
Known nonresponder**	HBIG x 1 and initiate revaccination or HBIG x 2[¶]	No treatment	If known high risk source, treat as if source were HBsAg positive
Response unknown	Test exposed person for anti-HBs 1. If adequate, no treatment is necessary 2. If inadequate, administer HBIG x 1 and vaccine booster	No treatment	Test exposed person for anti-HBs 1. If adequate, no treatment is necessary 2. If inadequate, administer vaccine booster and recheck titer in 1-2 months

Post-exposure Prophylaxis for Non-Occupational Exposure to HBV

Exposure	Treatment	
	Unvaccinated person†	Previously vaccinated person§
Percutaneous (e.g., bite or needlestick) or mucosal exposure to HBsAg-positive blood or body fluids	Administer hepatitis B vaccine series and hepatitis B immune globulin (HBIG). HBIG dose is 0.06 mL/kg intramuscularly	Administer hepatitis B vaccine booster dose
Sex or needle-sharing contact of an HBsAg-positive person		
Victim of sexual assault/abuse by a perpetrator who is HBsAg-positive		
Victim of sexual assault/abuse by a perpetrator with unknown HBsAg status	Administer hepatitis B vaccine series	No treatment
Percutaneous (e.g., bite or needlestick) or mucosal exposure to potentially infectious blood or body fluids from a source with unknown HBsAg status	**Administer hepatitis B vaccine series**	**No treatment**
Sex or needle-sharing contact of a person with unknown HBsAg status		
Victim of sexual assault/abuse by a perpetrator with unknown HBsAg status		

Requesting HBIG

- Contact ACDP Epi on-call for approval with the following information:
  - Number of contacts needing HBIG
  - Weight and age of each contact eligible for HBIG
  - Insurance status of each contact.
- HBIG is supplied in 5-mL vials. HBIG costs >$600 per 5-mL vial, and OHA has a very limited supply.
- HBIG dosage recommendations
  - Adults: 0.06 mL/kg; IM
  - Infants <12 months: 0.5 mL single dose
- LHDs should bill insurance for IG if the contact has insurance



PUBLIC HEALTH DIVISION
Acute and Communicable Disease Prevention

Oregon Health Authority

Acquiring state-supplied immune globulin, vaccine, and other medications

Investigative Guidelines
August 2016

1. PURPOSE

The purpose of this guidance is to advise public health staff on the process of acquiring immune globulin and vaccine from the Oregon Immunization Program (OIP) during an outbreak, acute event, or in situations where the needed prophylaxis is not otherwise available to the Local Health Department (LHD). This document is not intended to replace the guidance on general prophylaxis of contacts outlined in the Investigative Guidelines for those conditions that require post exposure prophylaxis of contacts. Immune globulin products available through OIP include IG (for hepatitis A and measles prophylaxis) and HBIG (for hepatitis B prophylaxis).

2. CONTACTING THE ACUTE AND COMMUNICABLE DISEASE

When contacts are identified that may need immune globulin or vaccine that is not currently accessible by LHDs, the LHD should contact the Acute and Communicable Disease Prevention (ACDP) Program on-call epidemiologist at 971.673.1111. The on-call epidemiologist and the LHD will review the contact history and determine whether immune globulin or vaccine is indicated for each contact. After this determination, the on-call epidemiologist will contact OIP with the relevant information. OIP will then coordinate obtaining the indicated immune globulin or vaccine with the LHD (detailed below). OIP cannot release immune globulin, or vaccine until ACDP has approved the request. The LHD must provide OIP with the quantity of product requested and delivery instructions. All other OIP rules and regulations regarding vaccine management and accountability apply.

3. PROPHYLAXIS RECOMMENDATIONS

3.1 Hepatitis A

Prophylaxis is indicated for all household and sexual contacts with no evidence of pre-existing immunity to the hepatitis A virus (HAV). In addition, persons who have shared illicit drugs with confirmed HAV cases and those with significant opportunity for fecal-oral exposure to the case should receive prophylaxis. When one or more cases are found in employees or children attending a child care center or cases are found in two or more households of daycare attendees,

Hepatitis B Serologies

Hepatitis D – Clinical Features

Incubation period	2-8 weeks
Clinical illness (jaundice)	Mild to severe. Abrupt onset.
Chronic sequelae	Superinfection in persons with chronic HBV
Complications	Children with acute coinfection have higher likelihood of developing chronic infection
Transmission	Similar to HBV
Prevention	HBV vaccination

Hepatitis C – Clinical Features

Incubation period	Average: 6-9 weeks Range: 2 weeks – 6 months
Clinical illness (jaundice)	Mild (20-30%)
Chronic sequelae	75-85%
Complications	Cirrhosis, hepatocellular CA
Transmission	Blood
Post-exposure prophy/ vaccine	None
Treatment	>90% cured

How it's *Not* Spread

- Not spread by sneezing, hugging, coughing, food or water, sharing eating utensils or drinking glasses, or casual contact
- People should not be excluded from work, school, play, child-care or other settings on the basis of their HCV infection

Hepatitis E – Clinical Features

Incubation period	Average: 26-42 days Range: 15-64 days
Clinical illness (jaundice)	Similar to HAV
Complications	20% case-fatality in pregnant women (3rd trimester)
Chronic sequelae	Chronic disease among immunocompromised
Transmission	Fecal-oral
Vaccine	Yes, but only in China
Prophylaxis	IG has not been effective

Hepatitis A

- 39 year old female with + anti-HAV IgM reported to LHD
- Has signs and symptoms consistent with hepatitis A and elevated LFTs
- Two household contacts identified
  - 8 year old son; vaccination status is unknown
  - 45 year old spouse; never vaccinated

Prophy - who should get it and how?

- Which contact should receive IG?
  A. Son
  B. Spouse
  C. Both
  D. Neither

- Where do I call to get IG?
  A. ACDP – ask for Tasha
  B. ACDP – ask for Ann Thomas
  C. ACDP – ask for the Epi on-call
  D. Immi – ask for Tila
  E. Immi – ask for Paul Cieslak

What information does ACDP need with the IG request?

A. Age
B. Height
C. Weight
D. Insurance status
E. Amount IG needed
F. Name of PCP
G. A, C, D, and E
H. A, B, D, E, and F
I. All of the above

Fun Fact

- The weapon I fence with is?
  - Broadsword
  - Foil
  - Epee
  - Sabre