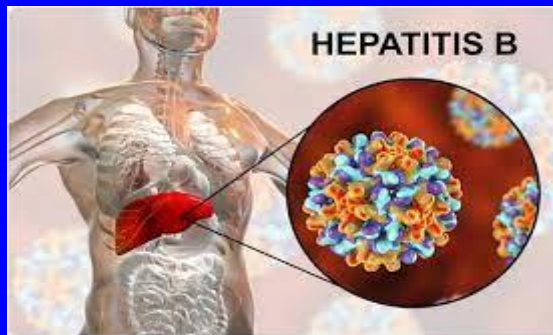




IN THE NAME OF GOD

Occupational Liver Diseases



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CLASSIFICATION OF OCCUPATIONAL LIVER DISEASES

- Chemically Induced Liver Disorders
- Inflammatory Liver Disorders
- Disorders Induced By Physical Agents
- Malignant Liver Diseases



Mechanisms of Toxicity

Category of Agent	Incidence	Experimental Reproducibility	Dose Dependent	Example
Intrinsic toxin				
Direct	High	Yes	Yes	Carbon tetrachloride
Indirect				
Cytotoxic	High	Yes	Yes	Dimethylnitrosamine
Cholestatic	High	Yes	Yes	Methylenedianiline
Host idiosyncrasy				
Hypersensitivity	Low	No	No	Phenytoin
Metabolic abnormality	Low	No	No	Isoniazid

MAJOR HUMAN HEPATOTOXINS

○ Solvents

Carbon Tetrachloride And Other chlorinated Solvent

Dimethylformamide

Toluene

Other Solvents

Mixed Solvent

Halothane And Other Anesthetic Solvents

○ Pesticides (And Related Halogenated Hydrocarbons)

○ Metals

Arsenic

Lead



EVALUATION OF LIVER DISEASE

- **Clinical History**

 - medical history

 - occupational history

 - exposure history

- **Physical Examination**

- **Laboratory Evaluation**

 - serum marker of hepatobiliary disease

 - ALT-AST-AP-*

 - biochemical tests of liver function

 - test of hepatic metabolism*

 - test of hepatic synthetic function*

- **Anatomic Tests**

- **Liver Biopsy**



Inflammatory Liver Disorders

Agent	Occupation
Hepatitis A virus	Nursery and kindergarten staff Sewer workers
Hepatitis B and C viruses	Health care workers with blood and body fluid contact
Cytomegalovirus	Pediatric health care workers
Coxiella burnetii	Animal care workers Farm workers Slaughterhouse workers
Leptospira icterohaemorrhagiae	Sewer worker Farm workers

MEDICAL SURVEILLANCE

- Surveillance Strategies
- Screening Tests

Clinical Management Of
Abnormal Liver Function Tests



What is occupational cancer?

Occupational cancer is cancer that is caused wholly or partly by exposure to a carcinogen at work.



Liver Cancer



Vinyl chloride, angiosarcoma of the liver
hydraulic cleaner from an open vinyl
chloride reactor, 1974

Chemical Carcinogenesis in humans

Target organs	Agents	Industry	Tumour type
Lung	Asbestos, Arsenic, Mustard gas, nickel, PAH (poly aromatic hydrocarbons), Tobacco smoke	Shipyard & Insulation workers, Smelting of copper, zinc, lead, Mustard gas production w. Nickel mining, refining, plating; Coke oven workers, Aluminum reduction workers, Environment with active smoker	Squamous, large cell and small cc, adenocarcinoma
Pleura	Asbestos		Mesothelioma
Oral cavity	Tobacco smoke, alcohol beverage, Nickel	Boot & shoe productions. Furniture manufacture, Alcohol productions	Squamous cell carcinoma
GI	Smoked, salted, pickled food, Tobacco, alcohol	Rubber Industry	adenocarcinoma Squamous CC
Liver	Aflatoxin, vinyl chloride, tobacco, alcohol, thorium dioxide		Hepatocellular C, Hemangiosarcoma



Chemical Carcinogenesis in humans

Kidney	Tobacco Smoke, phenacetin		Renal cell Carcinoma
Bladder	Tobacco, phenacetin benzidine	Magneta manufacture, auramine manufacture	Transitional cell carcinoma
Prostate	Cadmium		Adenocarcinom
Skin	Arsenic, benzopyrene, coal, mineral oil, cyclosporin A,PUVA	Coal gasification coke production.	SCC,BCC
Bone marrow	Benzene, tobacco, Ethylene oxide, Anti-neoplastic agents cyclosporin A	Rubber workers	Leukemia, Lymphoma



Type of Cancer	Related to Occupational Exposure Estimated % (USA)
Lung	6.3-13%
Bladder	3-19%
Mesothelioma	?
Leukemia	0.8-2.8%
Laryngeal	1-20% (men)
Skin Cancer (non-melanoma)	1.5-6% (men)
Sinonasal and nasopharyngeal	31-43% (men)
Kidney	0-2.3%
Liver	0.4-1.1 (vinyl chloride only; men)



Carcinogens

- Carcinogens cause the majority of fatal occupational diseases in the World
- Every year, occupational exposure to carcinogens
- **Many cases of occupational cancer are preventable**



Bloodborne Pathogens

“Bloodborne Pathogens” means pathogenic microorganisms that are present in human blood and can cause disease in humans.

Example:

hepatitis B virus (HBV)

hepatitis C virus (HCV)

human immunodeficiency virus (HIV).

■

Bloodborne Infection among Healthcare Workers

- 3 million healthcare workers exposed to bloodborne pathogens each year
- > 90% of infections occur in developing countries
- Many percent of HBV by needlestick injuries



Blood Borne Pathogens



- **Human immunodeficiency virus (HIV)**
- **Hepatitis B virus (HBV)**
- **Hepatitis C virus (HCV)**



Risk of Blood-borne Pathogen Transmission

- The risk of transmission of bloodborne pathogen from an infected patient to a HCW by a needlestick injury:
 - 30% for hepatitis B
 - 3% for hepatitis C
 - 0.3% for HIV



SOME WORKERS WHO ARE AT RISK

- ✓ Physicians
- ✓ Nurses
- ✓ Emergency Room Personnel
- ✓ Housekeeping Personnel
- ✓ Laundry Workers
- ✓ Laboratory Personnel
- ✓ Blood Bank Personnel
- ✓ Medical Examiners
- ✓ Dentists and Dental Workers
- ✓ Paramedics
- ✓ Emergency Medical Technicians
- ✓ Medical Waste Handlers
- ✓ Home Healthcare Workers
- ✓ Employees assigned to first-aid response duties by their employer
- ✓ Other workers assigned duties putting them at risk of occupational exposure



HOW DOES EXPOSURE OCCUR?

- ✓ Needlesticks (most common)

- 800,000 needlestick injuries occur each year in the U.S.

- ✓ Cuts from other contaminated sharps (scalpels, broken glass, etc.)

- ✓ Contaminated blood contact with the eyes, mucous membranes of the mouth or nose, or broken (cut or abraded) skin

Hepatitis B & C

	Hepatitis B	Hepatitis C
Virus	DNA	RNA
Spread	Blood, sexual	Blood
Presentation	Fever, malaise, anorexia, nausea, arthralgia, jaundice, RUQ pain	Usually asymptomatic early on
Investigation	See below. Biopsy	Anti-HCV, HCV DNA. Biopsy.
% Chronic	5-10%	85%
Treatment	Supportive. Chronic: antivirals (nucleoside analogues). Transplant	Nucleoside analogues, protease inhibitors (anti-retroviral). Liver transplant

HBV DNA = infectious

HBsAg = currently infected

Anti-HBs + Anti-HBc = past infection

Anti-HBs alone = vaccinated

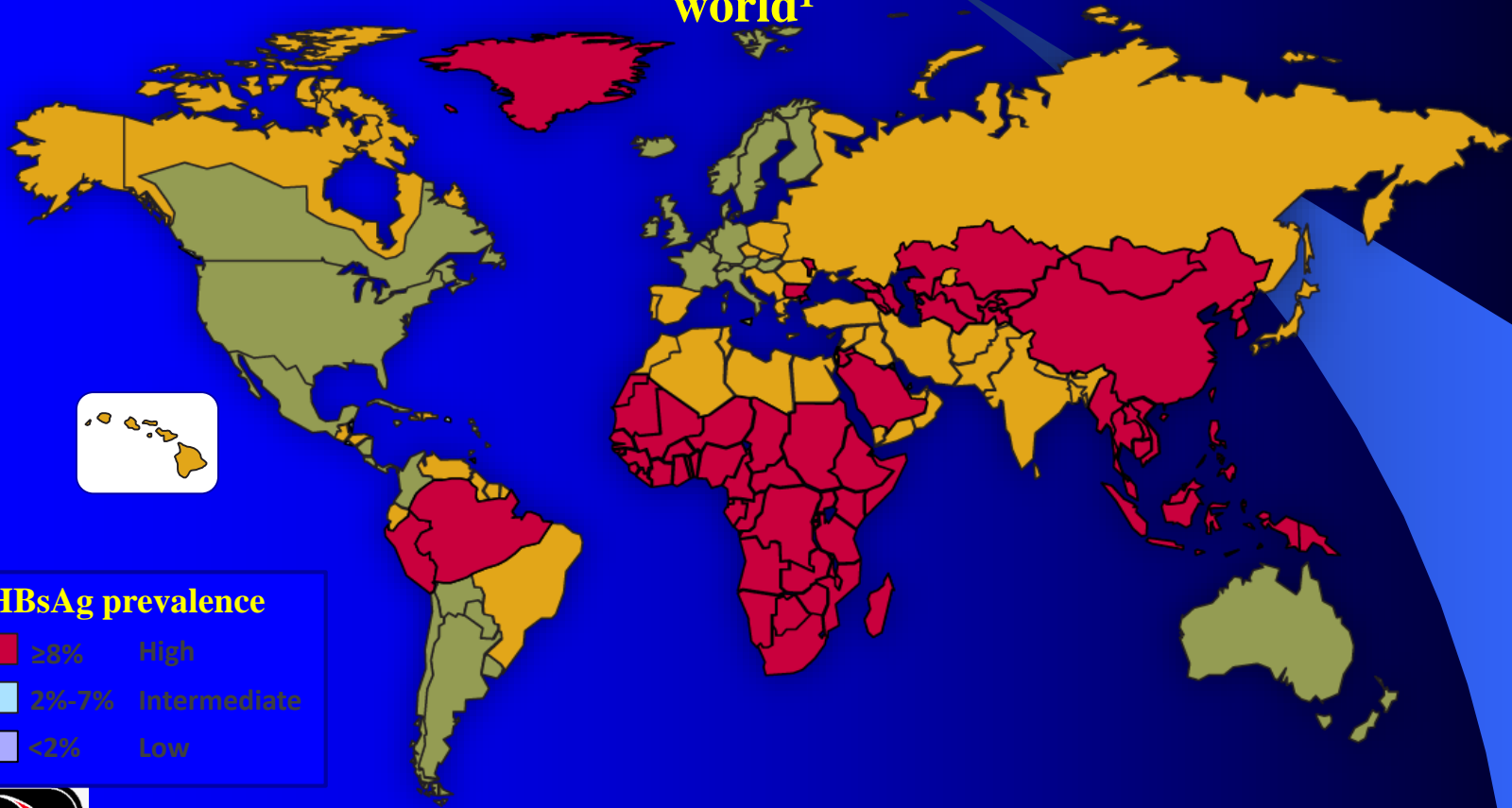


Hepatitis B



Chronic Hepatitis B Is a Global Health Problem

HBV infection is the most common chronic viral infection in the world¹



Virology of HBV Infection

- HBV is a partially double-stranded DNA virus which primarily infects liver cells¹
- Liver inflammation and fibrosis/cirrhosis are consequences of host's immune response¹
- The virus can evade the immune system during early phases of infection
 - Therefore, acute infections are primarily asymptomatic¹

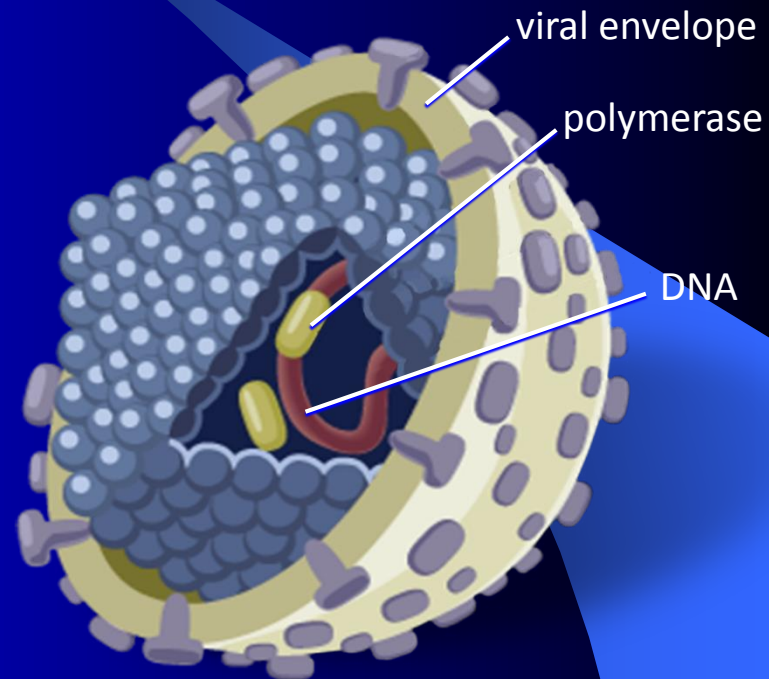
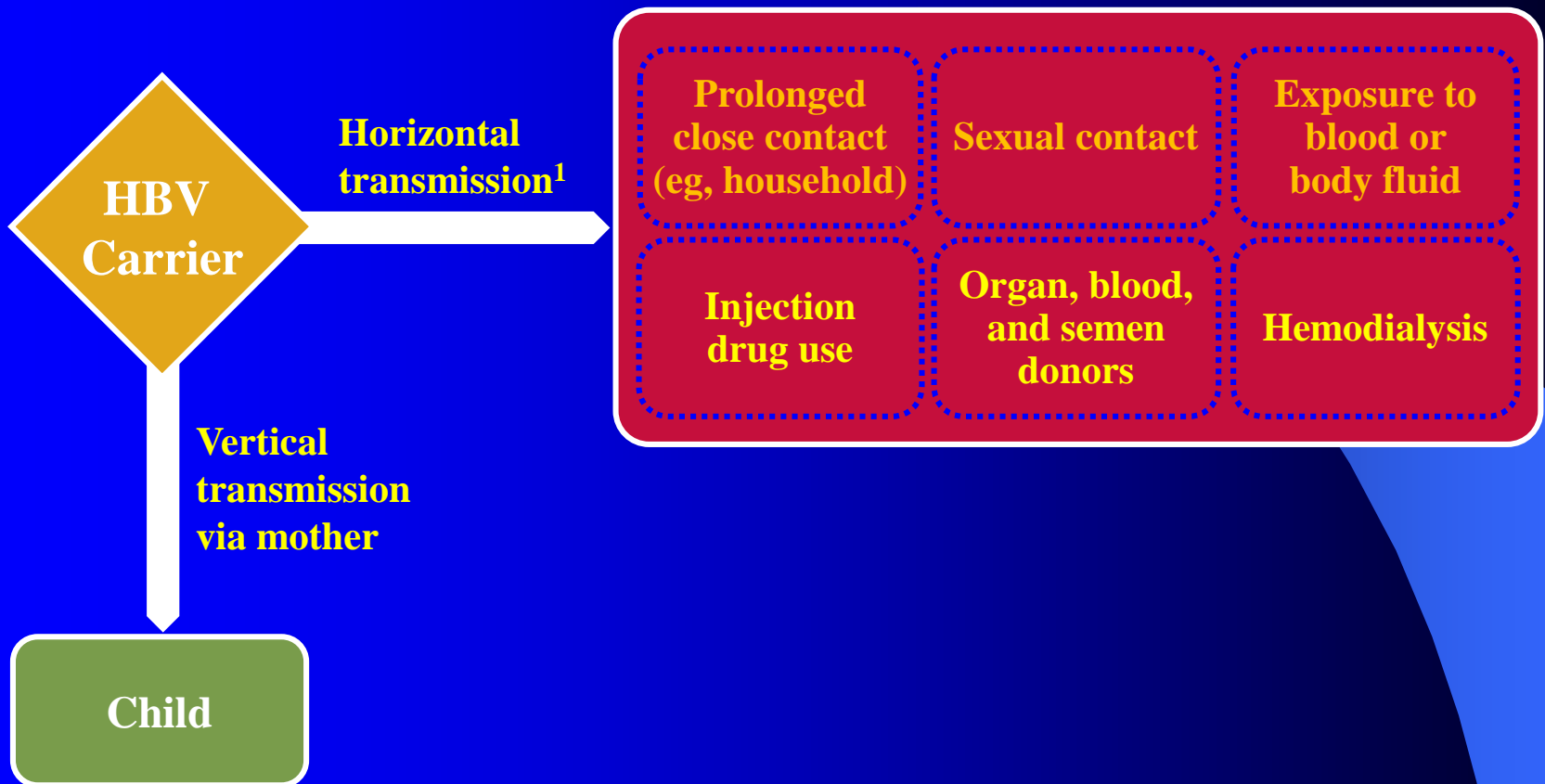


Figure adapted from Toronto Centre for Liver Disease. Hepatitis B. www.torontoliver.ca/hepatitis-b/.



cccDNA=covalently closed circular DNA.

Routes of HBV Transmission



HBsAg=hepatitis B e antigen.

Blood Borne Pathogens

● HBV

- virus that causes hepatitis B
- incubation period 45 to 180 days
- person is infectious if test for antigen (HBsAG) is positive
- unvaccinated persons are susceptible
 - vaccination is recommended for persons with occupational exposure



Blood Borne Pathogens

- **HBV**

- **risk of transmission**

- **needlestick: 22-31%**
if source is HBeAG +
 - **needlestick: 1-6%**
if source is HBeAG -
 - **direct or indirect contact with non-intact skin or mucous membranes is an important source of occupational exposure**



Progression and Complications of CHB

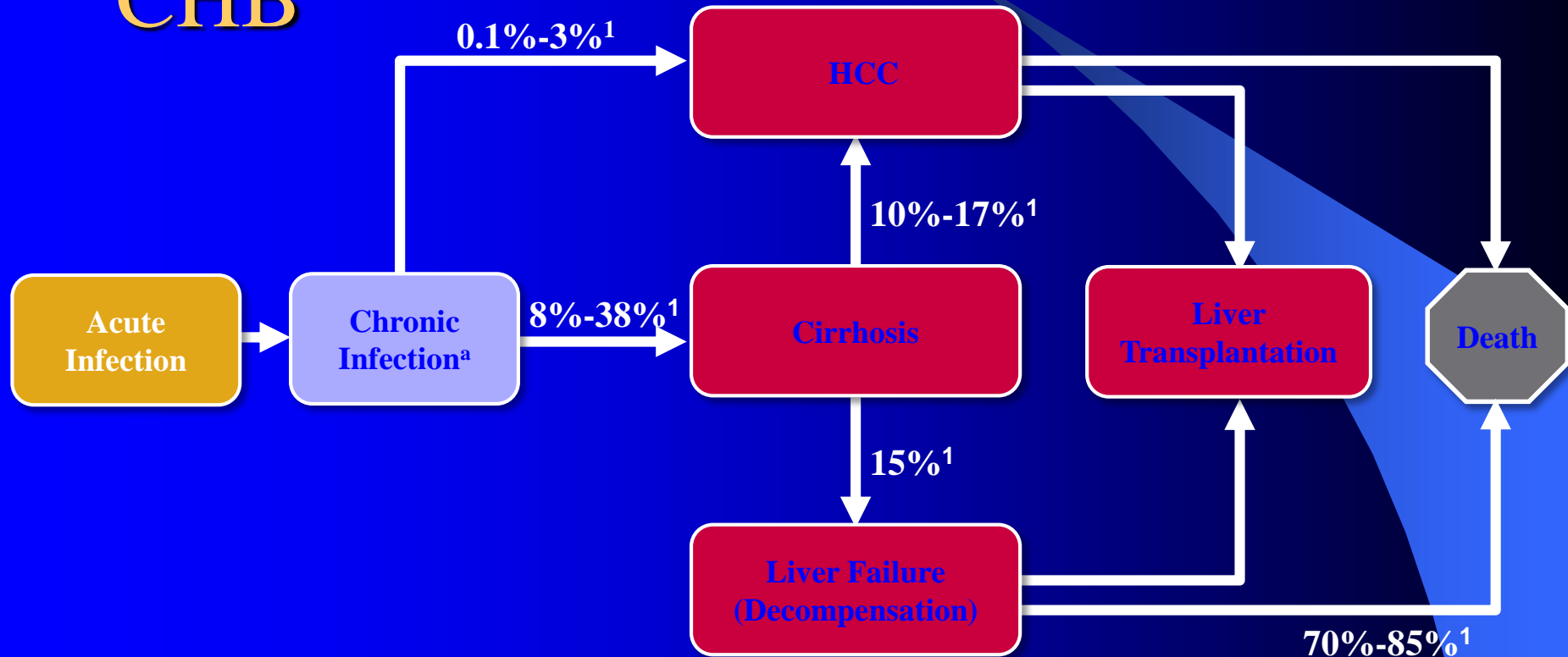


Figure adapted from Fattovich G, et al. In: Marcellin P, (ed.) *Management of Patients With Viral Hepatitis*. Paris: APMAHV; 2004.



^aChronic infection is defined as the persistence of positive test results for hepatitis B surface antigen or HBV DNA for at least 6 months.²

Percentages are 5-year cumulative incidence rates.

HCC=hepatocellular carcinoma.

1. Fattovich G, et al. *J Hepatol*. 2008;48:335-352; 2. CDC. *Morb Mortal Wkly Rep*. 2008;57:1-20.

Serologic Markers of HBV

HBsAg



- Hallmark of infection¹
- Major tool for screening and diagnosis of CHB² (if present ≥ 6 months³)

Anti-HBs



- Antibody to HBsAg⁴
- Marker of immunity to HBV⁴
- Only detectable marker of successful immunization⁴

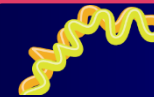
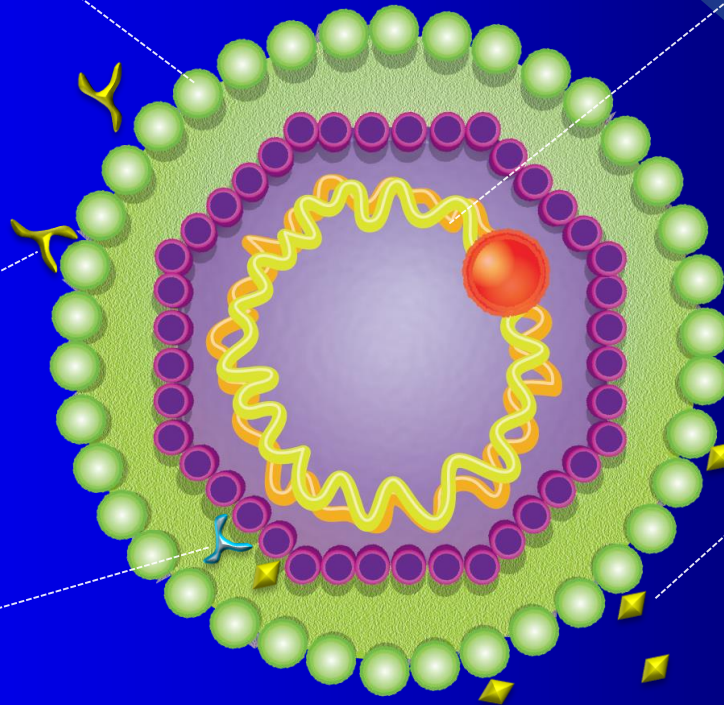
Anti-HBc



- Antibody to HBV core antigen⁴
- Marker of prior exposure⁴
- Anti-HBc is a marker of recent infection⁴



Hepatitis B Virus



HBV DNA

- Measure of viral load; indicates ongoing viral replication¹
- Correlates with infectivity⁴ and risk of major liver disease²



HBeAg

- Marker of risk of transmission of infection⁴

anti-HBs=antibody to HBsAg; anti-HBc=antibody to hepatitis B core antigen; IgM=immunoglobulin M.

1. Trepo C, et al. *Lancet*. 2014;384:2053-2063. 2. Niederau C. *World J Gastroenterol*. 2014;20:11595-11617. 3. CDC. *Morb Mortal Wkly Rep*. 2008;57:1-20;

4. Kao JH. *Expert Rev Gastroenterol Hepatol*. 2008;2:553-562.

HBV Infection Can Be Prevented

Screen for HBV Infection

Involves simple blood tests for serologic markers of infection¹

Identify CHB-infected patients^{1,2}

- Counsel to prevent transmission of infection to others
- Provide appropriate medical management

Identify unprotected patients for HBV vaccination^{1,2}

- Hepatitis B vaccination is the most effective measure to help prevent HBV infection and its consequences³
- It is important to screen for HBV infection before vaccination¹



HBV Screening Tests

Screening tests for virologic markers of HBV infection include HBsAg, anti-HBs, and anti-HBc^{1,2}

HBsAg	Anti-HBs	Anti-HBc ^a	Interpretation	Recommended Follow-up
+	—	+	Acute or chronic infection ^b	Contact patient for evaluation and further testing
—	+	+	Patient has immunity from previous infection	Follow up as appropriate ^{c,d}
—	+	—	Patient has immunity from vaccination	No further action required
—	—	—	Patient is at-risk for HBV infection	Vaccinate

^aAnti-HBc refers to total anti-HBc.²

^bPatients who are acutely infected if HBsAg+ for ≥6 months.³

^cPatients who are anti-HBc positive should be monitored closely during and after the administration of cytotoxic chemotherapy for signs of HBV reactivation.³

^dPatients with cirrhosis may need to be monitored for hepatocellular carcinoma per the AASLD guidelines.⁴



HBV Vaccination

Populations recommended for HBV vaccination by the CDC¹

- All newborns^a
- All unvaccinated children and adolescents through 18 years of age
- All unvaccinated adults at risk for infection and those requesting protection from HBV infection

• Primary vaccination consists of 3 intramuscular doses given at 0, 1, and 6 months²

- A full 3-dose vaccine series is associated with immunity in >90% of healthy adults²



^aInfants born to HBsAg-positive mothers should also receive hepatitis B immune globulin ≤ 12 hours of birth.³

1. CDC. Vaccination and Immunizations: Hepatitis B In-Short. <http://www.cdc.gov/vaccines/hcp/vis/vis-statements/hep-b.html>. February 2, 2012. Accessed March 25, 2015;

2. CDC. *Morb Mortal Wkly Rep*. 2006;55:1-33; 3. CDC. *Morb Mortal Wkly Rep*. 2005;54:1-33.

Blood Borne Pathogens

- HCV

- virus that causes hepatitis C
- incubation period 6 to 9 weeks
- most persons are infectious for life
- all are susceptible



Blood Borne Pathogens

- HCV

- risk of transmission

- needlestick: 1.8%
 - mucous membranes: rare
 - non-intact skin: very rare



Bloodborne Pathogen Standard

- Exposure Control Plan
- Exposure Determination
- Engineering and Work Practice Controls
- Personal Protective Equipment
- Housekeeping



Bloodborne Pathogen Standard (cont.)

- Regulated Waste
- Training
- Hepatitis B Vaccination and Post-Exposure Evaluation and Follow-up
- Communication of Hazards to Employees (signs and labels)
- Record Keeping



Bloodborne Pathogens of Most Concern in the Workplace

- Human Immunodeficiency Virus (HIV)
- Hepatitis B Virus (HBV)
- Hepatitis C Virus (HCV)



Hepatitis B Virus

- Virus affects the liver
- Symptoms include:
nausea, vomiting, fever, abdominal
pain, jaundice
- 100 times more infectious than HIV



Hepatitis B Virus (cont.)

- 6-30% chance of infection from a puncture wound (contaminated needle)
- Up to 30% of infected individuals can become carriers without having symptoms
- Vaccine preventable



Hepatitis C Virus

- Virus affects the liver.
- Symptoms include:
nausea, abdominal pain, jaundice,
fatigue, dark urine.
- No vaccine to prevent HCV.



Preventing Needlesticks



ENGINEERING CONTROL EXAMPLES

- Sharps disposal containers must be provided and used.
- Sharps disposal containers must be leakproof, puncture resistant, able to be closed, and labeled or color-coded.



LABELS

The standard requires that warning labels be attached to:

- Containers of regulated waste;
- Refrigerators and freezers containing blood or OPIM;
- Other containers used to store, transport, or ship blood or OPIM;
- Contaminated equipment prior to shipping.

Red bags or containers may be substituted for labels.



BIOHAZARD

Engineering/Work Practices

Controls (cont.)



Sharps must be contained in puncture resistant container!

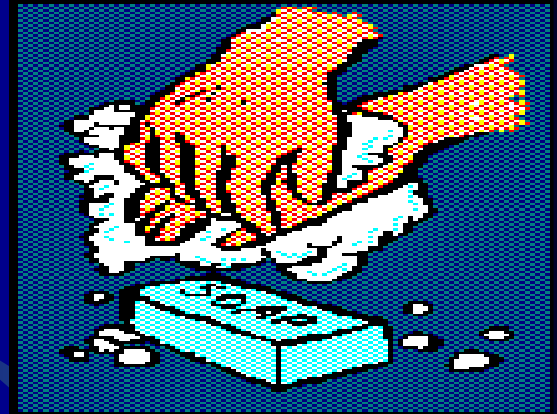


Use Safe Clean-up Practices:

- Wear appropriate gloves and other required PPE
- Never pick up broken glass or similar items with hands
- Put glass, etc. in “puncture resistant”



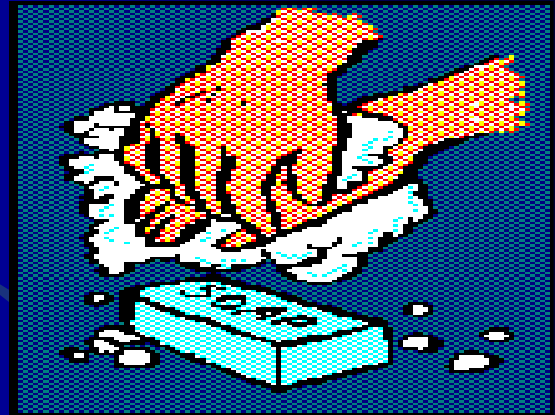
Handwashing



- One of the most important work practice controls!
- Handwashing facilities should be readily accessible and adequately stocked or utilize a waterless hand disinfection system



Handwashing (cont.)



- Always wash hands after taking off gloves
- If you are using an antiseptic hand cleaner or wipes, you must wash your hands with soap and water as soon as possible after contact with blood or other body fluids



Personal Protective Equipment (PPE)

Personal protective equipment is specialized clothing or equipment worn or used by you for protection against a hazard. Provides a barrier between you and the hazard.



PPE (cont.)

Examples of PPE:

Latex gloves

Non-Latex gloves

Lab coats

CPR masks

Face shields

N-95 Respirators

Surgical Mask

Isolation Masks

REMOVE ALL PPE IN AREA OF USE !!!



PPE (cont.)

Latex, Synthetic Latex or nitrile gloves are probably the most important protective apparel that can be worn to protect yourself from bloodborne pathogens



PPE (cont.)

Anytime there is a risk of splashing of contaminated fluids, and/or other eye protection should be used to protect your eyes



PPE (cont.)

Waterproof clothing such as lab coats or aprons may be worn to protect your clothing and to keep blood or other contaminated fluids from soaking through to your skin.



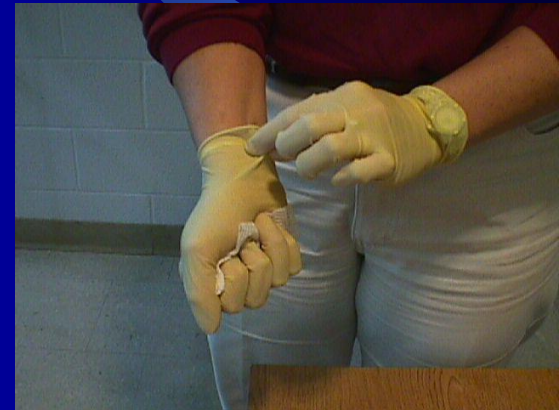
PPE (cont.)

Face shields may be worn in addition to goggles to provide additional face protection. A face shield will protect against splashes to the nose and mouth



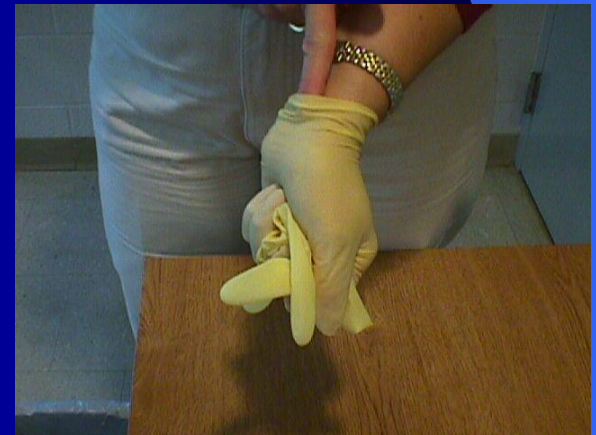
Proper Glove Removal

1. Before removing disposable gloves, gather any contaminated materials and dispose of in red biohazard bag.
2. Strip off one glove from the wrist, turning it inside out so the “clean” side is on the outside.



Proper Glove Removal

3. Place the glove in the other hand and strip off the glove on that hand, turning it inside out.



Proper Glove Removal

4. Dispose of the gloves/material in a regulated waste container.

Make sure bag is intact and that there is no danger of leaking. If the bag is torn or punctured or is contaminated on the outside, place the bag inside a second biohazard bag.

DO NOT throw the biohazard bag into the regular trash.



Limitations

- Engineering controls, work practices and personal protective equipment all have limitations.
- Exposure incidents are reduced but still may occur.



Hazard Communication LABELS!!!



Recordkeeping

Medical Records – including dates of Hepatitis B vaccinations and related information as well as medical evaluations and reports. These records must be maintained for the duration of employment plus 30 years and must be kept confidential.

Training Records – including the dates of training and the name(s)/title(s) of the individual(s) who provided the training. These records must be maintained for three years. A copy of these records must also be maintained by Safety and Health.



Exposure Control: Protect Yourself

- Read the Exposure Control Plan
- Use engineering and work practice controls
- Use personal protective equipment
- Know what to do in case of an exposure



Thank You for Attention

