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

<table>
<thead>
<tr>
<th>Category of Agent</th>
<th>Incidence</th>
<th>Experimental Reproducibility</th>
<th>Dose Dependent</th>
<th>Example</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Intrinsic toxin</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Direct</td>
<td>High</td>
<td>Yes</td>
<td>Yes</td>
<td>Carbon tetrachloride</td>
</tr>
<tr>
<td>Indirect</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cytotoxic</td>
<td>High</td>
<td>Yes</td>
<td>Yes</td>
<td>Dimethylnitrosamine</td>
</tr>
<tr>
<td>Cholestatic</td>
<td>High</td>
<td>Yes</td>
<td>Yes</td>
<td>Methyleneedianiline</td>
</tr>
<tr>
<td><strong>Host idiosyncrasy</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypersensitivity</td>
<td>Low</td>
<td>No</td>
<td>No</td>
<td>Phenytoin</td>
</tr>
<tr>
<td>Metabolic abnormality</td>
<td>Low</td>
<td>No</td>
<td>No</td>
<td>Isoniazid</td>
</tr>
</tbody>
</table>
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
  - biochemical tests of liver function
    - test of hepatic metabolism
    - test of hepatic synthetic function

- **Anatomic Tests**

- **Liver Biopsy**
# Inflammatory Liver Disorders

<table>
<thead>
<tr>
<th>Agent</th>
<th>Occupation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hepatitis A virus</td>
<td>Nursery and kindergarten staff</td>
</tr>
<tr>
<td></td>
<td>Sewer workers</td>
</tr>
<tr>
<td>Hepatitis B and C viruses</td>
<td>Health care workers with blood and body fluid contact</td>
</tr>
<tr>
<td>Cytomegalovirus</td>
<td>Pediatric health care workers</td>
</tr>
<tr>
<td>Coxiella burnetii</td>
<td>Animal care workers</td>
</tr>
<tr>
<td></td>
<td>Farm workers</td>
</tr>
<tr>
<td></td>
<td>Slaughterhouse workers</td>
</tr>
<tr>
<td>Leptospira icterohaemorrhagiae</td>
<td>Sewer worker</td>
</tr>
<tr>
<td></td>
<td>Farm workers</td>
</tr>
</tbody>
</table>
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**

<table>
<thead>
<tr>
<th>Target organs</th>
<th>Agents</th>
<th>Industry</th>
<th>Tumour type</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung</td>
<td>Asbestos, Arsenic, Mustard gas, nickel, PAH (poly aromatic hydrocarbons), Tobacco smoke</td>
<td>Shipyard &amp; 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</td>
<td>Squamous, large cell and small cc, adenocarcinoma</td>
</tr>
<tr>
<td>Pleura</td>
<td>Asbestos</td>
<td></td>
<td>Mesothelioma</td>
</tr>
<tr>
<td>Oral cavity</td>
<td>Tobacco smoke, alcohol beverage, Nickel</td>
<td>Boot &amp; shoe productions. Furniture manufacture, Alcohol productions</td>
<td>Squamous cell carcinoma</td>
</tr>
<tr>
<td>GI</td>
<td>Smoked, salted, pickled food, Tobacco, alcohol</td>
<td>Rubber Industry</td>
<td>adenocarcinoma</td>
</tr>
<tr>
<td>Liver</td>
<td>Aflatoxin, vinyl chloride, tobacco, alcohol, thorium dioxide</td>
<td></td>
<td>Hepatocellular C, Hemangiosarcoma</td>
</tr>
</tbody>
</table>
## Chemical Carcinogenesis in humans

<p>| Tissue     | Carcinogenic Agents                                      | Carcinoma Type                                      | \n|------------|----------------------------------------------------------|-----------------------------------------------------|
| Kidney     | Tobacco Smoke, phenacetin                                | Renal cell Carcinoma                                |
| Bladder    | Tobacco, phenacetin, benzidine                           | Magneta manufacture, auramine manufacture           |
|            |                                                          | Transitional cell carcinoma                         |
| Prostate   | Cadmium                                                  |                                                     |
| 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                                  |</p>
<table>
<thead>
<tr>
<th>Type of Cancer</th>
<th>Related to Occupational Exposure Estimated % (USA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung</td>
<td>6.3-13%</td>
</tr>
<tr>
<td>Bladder</td>
<td>3-19%</td>
</tr>
<tr>
<td>Mesothelioma</td>
<td>?</td>
</tr>
<tr>
<td>Leukemia</td>
<td>0.8-2.8%</td>
</tr>
<tr>
<td>Laryngeal</td>
<td>1-20% (men)</td>
</tr>
<tr>
<td>Skin Cancer (non-melanoma)</td>
<td>1.5-6% (men)</td>
</tr>
<tr>
<td>Sinonasal and nasopharyngeal</td>
<td>31-43% (men)</td>
</tr>
<tr>
<td>Kidney</td>
<td>0-2.3%</td>
</tr>
<tr>
<td>Liver</td>
<td>0.4-1.1 (vinyl chloride only; men)</td>
</tr>
</tbody>
</table>
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” 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

<table>
<thead>
<tr>
<th>Hepatitis B</th>
<th>Hepatitis C</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Virus</strong></td>
<td>DNA</td>
</tr>
<tr>
<td><strong>Spread</strong></td>
<td>Blood, sexual</td>
</tr>
<tr>
<td><strong>Presentation</strong></td>
<td>Fever, malaise, anorexia, nausea, arthralgia, jaundice, RUQ pain</td>
</tr>
<tr>
<td><strong>Investigation</strong></td>
<td>See below. Biopsy</td>
</tr>
<tr>
<td><strong>% Chronic</strong></td>
<td>5-10%</td>
</tr>
<tr>
<td><strong>Treatment</strong></td>
<td>Supportive. Chronic: antivirals (nucleoside analogues). Transplant</td>
</tr>
</tbody>
</table>

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 world.


HBsAg prevalence
- ≥8% High
- 2%-7% Intermediate
- <2% Low

HBV = hepatitis B virus.
Virology of HBV Infection

- HBV is a partially double-stranded DNA virus which primarily infects liver cells\(^1\)

- Liver inflammation and fibrosis/cirrhosis are consequences of host’s immune response\(^1\)

- The virus can evade the immune system during early phases of infection
  - Therefore, acute infections are primarily asymptomatic\(^1\)

\[\text{cccDNA=covalently closed circular DNA.}\]

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

Routes of HBV Transmission

HBV Carrier

Horizontal transmission

- Prolonged close contact (eg, household)
- Injection drug use
- Sexual contact
- Exposure to blood or body fluid
- Organ, blood, and semen donors
- Hemodialysis

Vertical transmission via mother

Child

HBcAg: hepatitis B core 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


Chronic Infection is defined as the persistence of positive test results for hepatitis B surface antigen or HBV DNA for at least 6 months. Percentages are 5-year cumulative incidence rates.

HCC = hepatocellular carcinoma.

Serologic Markers of HBV Infection

HBsAg
- Hallmark of infection
- Major tool for screening and diagnosis of CHB (if present ≥6 months)

Anti-HBs
- Antibody to HBsAg
- Marker of immunity to HBV
- Only detectable marker of successful immunization

Anti-HBc
- Antibody to HBV core antigen
- Marker of prior exposure
- HBC is a marker of recent infection

HBeAg
- Marker of risk of transmission of infection

HBV DNA
- Measure of viral load; indicates ongoing viral replication
- Correlates with infectivity and risk of major liver disease

HBV Infection Can Be Prevented

Screen for HBV Infection

Involves simple blood tests for serologic markers of infection

Identify CHB-infected patients

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

Identify unprotected patients for HBV vaccination

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

HBV Screening Tests

Screening tests for virologic markers of HBV infection include HBsAg, anti-HBs, and anti-HBc₁,²

<table>
<thead>
<tr>
<th>HBsAg</th>
<th>Anti-HBs</th>
<th>Anti-HBc</th>
<th>Interpretation</th>
<th>Recommended Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>+</td>
<td>−</td>
<td>+</td>
<td>Acute or chronic infectionᵇ</td>
<td>Contact patient for evaluation and further testing</td>
</tr>
<tr>
<td>−</td>
<td>+</td>
<td>+</td>
<td>Patient has immunity from previous infection</td>
<td>Follow up as appropriateᶜ,d</td>
</tr>
<tr>
<td>−</td>
<td>+</td>
<td>−</td>
<td>Patient has immunity from vaccination</td>
<td>No further action required</td>
</tr>
<tr>
<td>−</td>
<td>−</td>
<td>−</td>
<td>Patient is at-risk for HBV infection</td>
<td>Vaccinate</td>
</tr>
</tbody>
</table>

¹Anti-HBc refers to total anti-HBc.²
²Patient is chronically infected if HBsAg+ for ≥6 months.³
³Patients who are anti-HBc positive should be monitored closely during and after the administration of cytotoxic chemotherapy for signs of HBV reactivation.⁴
⁴Patients with cirrhosis may need to be monitored for hepatocellular carcinoma per the AASLD guidelines.⁴

HBV Vaccination

Populations recommended for HBV vaccination by the CDC

- All newborns
- 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 months

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

First dose (0 month) 30%-55% with protective immunity
Second dose (1 month) 75% with protective immunity
Third dose (6 months) >90% with protective immunity

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

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.
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.
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.
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