


# Occupational Liver Disease



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# Introduction

- The liver is the target organ of many occupational and environmental chemicals and plays a central role in their detoxification and elimination
- Occupational hepatic injury does not differ clinically or morphologically from drug induced damage
- Occupational liver disease may be of secondary importance to damage
- Effects of multiple hepatotoxic exposure
- Lack of sufficiently sensitive and specific tests





# Introduction

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- Occupational history
  - result of personal or workroom air sampling
  - Remove the patient from exposure to suspected toxin



# *Routes of Exposure*

- Inhalation
  - Ingestion
  - Percutaneous absorption
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- Inhalation the most important route particularly for volatile solvent
  - Percutaneous absorption is the most important for lipophilic agent

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- Oral intake of hepatotoxic agents is usually of importance only in the rare case of accidental ingestion
  - Mouth breathing and gum and tobacco chewing can increase the amount of gaseous substances absorbed during the workday.

# *Physical agent induced liver disorders*

- **Hyperthermia ( Heat Stroke)**
  - **Acute hepatic injury**
    - **Centrilobular necrosis**
    - **Cholestasis**
- **Ionizing radiation**
  - **A cumulative dose in excess of 3000 to 6000 Rad**
  - **Accidental intense exposure**
  - **Hepatitis 2-6 Week later**

# *Chemical agents associated with occupational liver disease*

|                            |  |                                  |
|----------------------------|--|----------------------------------|
| <b>Arsenic</b>             | <b>Cirrhosis, Hepatocellular carcinoma, Angiosarcoma</b> | <b>Pestiside</b>                 |
| <b>Beryllium</b>           | <b>Granulomatosis diasease</b>                           | <b>Ceramics workers</b>          |
| <b>Ccl4</b>                | <b>Acute hepatocellular injury, cirrhosis</b>            | <b>Dry cleaning</b>              |
| <b>Dimethylnitrosamine</b> | <b>Hepatocellular carcinoma</b>                          | <b>Rocket mfg</b>                |
| <b>Dioxin</b>              | <b>Porphyria cutanea tarda</b>                           | <b>Pestiside</b>                 |
| <b>Halothane</b>           | <b>Acute hepatocellular injury</b>                       | <b>Anesthesiology</b>            |
| <b>Hydrazine</b>           | <b>Steatosis</b>   | <b>Rocket mfg</b>                |
| <b>Nitropropane</b>        | <b>Acute hepatocellular injury</b>                       | <b>painter</b>                   |
| <b>PCB</b>                 | <b>Subacute injury</b>                                   | <b>Electrical utility</b>        |
| <b>TNT</b>                 | <b>Acute or Subacute hepatocellular injury</b>           | <b>Munitions workers</b>         |
| <b>Trichloroethylene</b>   | <b>Acute hepatocellular injury</b>                       | <b>Cleaning solvent sniffing</b> |
| <b>Vinylchloride</b>       | <b>Angiosarcoma</b>                                      | <b>Rubber workers</b>            |

# *Acute hepatic injury*

- Cytotoxic injury or cholestatic injury
- Latent period 24 - 48 hours
- Clinical symptoms are often extra hepatic origin
- Anorexia, nausea, vomiting, jaundice, hepatomegaly
- In massive necrosis coffee-ground emesis, abdominal pain, reduction of liver size, ascites, edema, hemorrhagic diathesis
- During 24-48 hours somnolence and coma



# *Carbon Tetrachloride*

- Use as a liquid solvent, dry cleaning agent, fire extinguisher
- Dizziness, Headache, Visual disturbance, Confusion
- Hepatic disease occurs after 2-4 days
- Hepatomegaly, Splenomegaly, Jaundice
- Elevated serum transaminase, prolonged PT
- Hemorrhage, Hypoglycemia, Encephalopathy
- Renal failure may ensue a few days after the hepatic damage becomes manifest
- N- acetylcysteine



# Sub acute injury

- **Rare**
- **Most common: necrosis**
  - **TNT, Tetrachloroethane, PCB**
- **Symptoms:**
  - **Anorexia, Nausea, vomiting, Hepatomegaly & Jaundice**

# Chronic injuries

- **Asymptomatic until advanced stages**
- **Cirrhosis:**
  - Arsenicals, dimethylnitrosamine, CCL4, TNT, PCB
- **Steatosis:**
  - DMF, CCl4
- **Hepatoportal Sclerosis:**
  - VCM & Arsenic
- **Hepatic porphyria:**
  - Dioxin
- **Granuloma:**
  - Beryllium, Copper
- **Neoplastic changes:**
  - VCM, Arsenic

# Infectious Agents

|                                   |   |
|-----------------------------------|---|
| HAV                               | Nursery & kindergarten staff<br>Sewer workers             |
| HBV & HCV                         | HCWs with blood and body fluid contact                    |
| Cytomegalovirus                   | Pediatric health care workers                             |
| Coxiella burnetti                 | Animal care workers, farm workers, slaughterhouse workers |
| Leptospira<br>icterohaemorrhagiae | Sewer workers, farm workers                               |

# Hepatitis A



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- **High Risk Occupations:**
  - **HCWs**
    - Emergency rooms, surgery, laundry, children's psychiatry, dentists, neonatal intensive care units
  - **Waste water treatment plant workers**
  - **Waste pickers,**
  - **home health workers**
  - **food handlers**
- **Incubation period:** 15-50 days (28-30 days)
- **Symptoms:** Abrupt onset, with fever, malaise, anorexia, nausea, abdominal discomfort, and jaundice
- **Transmission:** fecal-oral, Blood (rare)



# Hepatitis A

- **Highest concentration of virus excretion in Fecal:**
  - During the incubation period
  - Early in the prodromal phase
  - It diminishes rapidly once jaundice appears
- **Greatest infectivity:**
  - 2-week period immediately before the onset of jaundice or elevation of liver enzymes
- **Not chronic carrier**

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- Fulminant hepatitis occurs rarely (<1% overall), but rates are higher with **increasing age** and in those with **underlying chronic liver disease**, including those with chronic hepatitis B or C infection.
  - Hepatitis A does not appear to be worse in HIV-infected patients when compared to HIV-negative persons

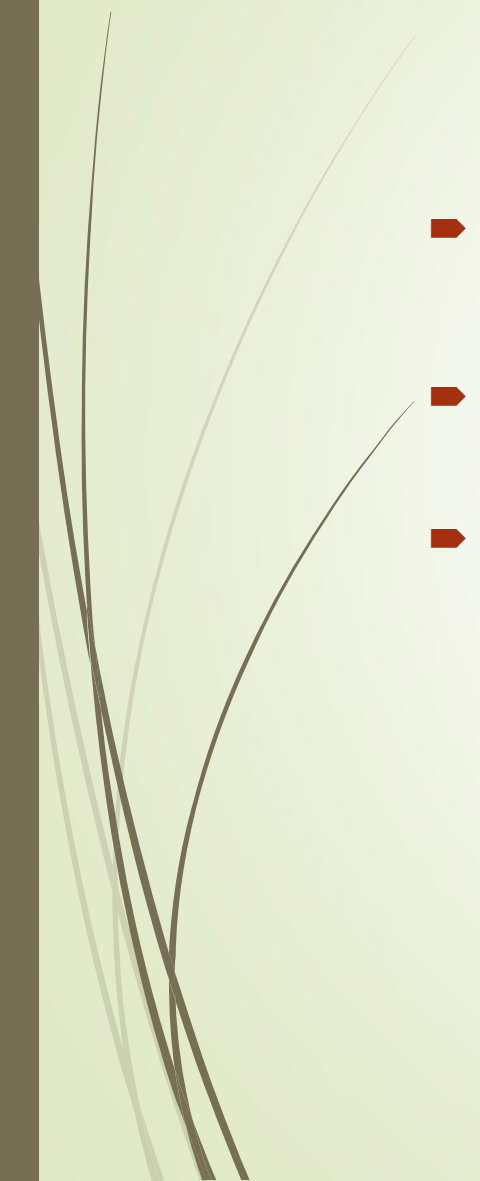
The diagnosis of acute hepatitis A is confirmed by:

- Presence of immunoglobulin IgM class anti-HAV in serum collected during the acute or early convalescent phase of the disease.
- IgG antibodies appear in the convalescent phase and remain positive for life
- The presence of IgG anti- hepatitis A antibody indicates either previous exposure or immunization





# Treatment

- symptomatic, with rest, analgesics, and fluid replacement
  - Fulminant hepatic failure occasionally follows acute HAV infection.
  - Orthotopic liver transplantation
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# Prevention

- Hand washing
- Avoiding tap water and raw foods in areas with poor sanitation.
- Heating foods appropriately  $>85^{\circ}\text{C}$  for 1 minute
- Chlorine, iodine, and disinfecting solutions (household bleach 1:100 dilution)



# Prevention

- A single intramuscular dose of 0.02 mL/kg of immune globulin (immune serum globulin, gamma globulin) given before exposure or during the incubation period

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- **Pre exposure prophylaxis in persons who plan to travel in areas with high or intermediate hepatitis A endemicity depends on the duration of the travel:**
    - up to 1 month: 0.1 mL/kg**
    - up to 2 months: 0.2 mL/kg**
    - 2 months or longer: repeat dose of 0.2 mL/kg every 2 months**
  - **Post exposure prophylaxis, it is 0.1 mL/kg.**


# Prevention

- Once the diagnosis of acute infection is made, **close contacts** should be given HAV vaccine and/ or immune globulin promptly within **2 weeks** of exposure to prevent development of secondary cases.
- close contacts include:
  - staff of day-care facilities
  - food handlers (in establishments with a food handler diagnosed with hepatitis A)
  - institutions for custodial care
  - hospital staff if an unsuspected patient has been fecally incontinent

- Immune globulin can be used in cases where hepatitis A vaccination is contraindicated
- where travel is imminent
- It is less protective and only for short periods of time

## **Routine immune globulin administration is not recommended**

- **The usual office or factory conditions for persons exposed to a fellow worker with hepatitis A**
  - **Teachers with schoolroom contact**
- BUT**
- **Restaurant employees(food handlers) ,patrons**

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- Food handlers should receive immune globulin when a common-source exposure is recognized
  - Restaurant patrons when the infected person is involved directly in handling uncooked foods without gloves.



This is especially the case when the patrons can be identified **within 2 weeks of exposure** and the food handler's hygienic practices are known to be deficient



- **Pregnancy or lactation is not a contraindication to immune globulin administration.**

# hepatitis A vaccine

- Persons traveling to or working in countries with intermediate or high HAV endemicity
- laboratory workers with exposure to live virus
- Animal handlers with exposure to HAV-infected primates
- Men who have sex with men (MSM),
- Illicit drug users (injections and non injection)
- Individuals with chronic liver disease,
- Individuals with clotting factor disorders
- Individuals with direct contact to others who have hepatitis A and homeless individuals.


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- **Protective antibodies remain for as long as 4 years after two-dose vaccine series**
  - **There is no need for HAV booster vaccination after completion of the primary two-dose vaccination series**


## **Routine hepatitis A vaccination is not recommended for :**


- **Child-care workers**
- **Hospital workers**
- **Teachers**
- **Correctional workers**
- **Restaurant employees**
- **sewage treatment employees,**
- **Staff in institutions for the developmentally disabled.**

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- **When outbreaks are recognized in these settings:**


**use of HAV vaccine and/ or immune globulin promptly within 2 weeks of exposure for persons in close contact with infected patients or students is recommended**


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- If a food handler has been in contact with an individual who is acutely infected with hepatitis A. If he has been immunized against hepatitis A with documented evidence of a completed course of hepatitis A vaccine in the past 10 years, or one dose of monovalent vaccine within the past 12 months, they can be considered immune.
  - Those who have had laboratory- confirmed hepatitis A (previous anti- HAV IgG positive, or HAV RNA positive) can also be considered immune and then no further action is required

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- If the contact with the source case of hepatitis A is within 14 days, provided they are **healthy and aged under 60**
  - the food handler should be given a first dose of monovalent hepatitis A vaccine and a second dose 6– 12 months after the initial dose.

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- Food handlers **aged 60 years and over** should be offered hepatitis A immunoglobulin in addition to monovalent hepatitis A vaccine.
  - A second dose of vaccine is recommended 6– 12 months after the first dose to ensure long- term protection.<sup>5</sup>



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- If the food handler has not been immunized within 14 days of exposure
  - they are at high risk of acquiring infection and should be **removed from activities** which involve preparing and handling ready- to- eat foods until 30 days post exposure.

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- If a worker is suspected of being infected with hepatitis A, should be excluded from work **until 7 days** after the onset of jaundice or
  - If there is no history of jaundice, 7 days after the onset of symptoms



# Cytomegalovirus Infection

- Pediatric and immunosuppressed adult units
- kindergarten teachers
- Child-care workers
- Hepatitis
- Neonate with a congenital malformation



# *Coxiella burnetii*

- **Animal-care technicians**
- **Laboratory research personnel**
- **Abattoir workers**
- **Farmers**
- **Acute hepatitis occurs in up to 50% of cases and usually is self-limited.**



# *Malignant Liver Disease*

## ➤ **Hepatic Angiosarcoma**

- Vinyl chloride monomer
- Arsenic ( vineyard workers )
- Copper ( pesticide )
- Anabolic steroids
- Thorium dioxide( Thorotrast)



# Hepatocellular carcinoma



- ☐ vinyl chloride
- ☐ Arsenic
- ☐ Dimethylnitrosamine



# Adjustments at work

- In patients with oesophageal varices, there is no restriction on occupation once the varices have been treated.
- Patients with ascites may experience difficulty with lifting, bending, or stooping.
- Patients with chronic or intermittent encephalopathy should not be employed in intellectually demanding work or jobs requiring a high degree of vigilance, including :

**Safety critical work or operating machinery**

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- **Individuals suffering from hepatic cirrhosis with chronic encephalopathy or those who are cognitively impaired must not drive and must notify the Driver and Vehicle Licensing Agency (DVLA)**
  - **Group 1 and 2 licenses will be revoked or refused until recovery is satisfactory and other medical standards for fitness to drive (e.g. for psychiatric conditions) are satisfied.**





# Implications for employment

- **patients with chronic liver disease with ongoing inflammation or liver damage should not work with hepatotoxins.**
- **All patients working with hepatotoxins should avoid alcohol misuse and enzyme- inducing agents such as anticonvulsants, in particular phenobarbitate and phenytoin.**

# Medical Surveillance

- **Biochemical tests**
  - AST, ALT
  - ALP
  - LDH
  - Bilirubin
  - Urine bilirubin
- **Tests of synthetic liver function**
  - Alb
  - PT
  - Alpha fetoprotein
  - Ferritin
- **Clearance tests**
  - Sulfobromophthalein
  - Indocyanine green
  - Antipyrine test
  - Aminopyrine breath test
  - Serum bile acid
  - Urinary D-glucaric acid



# Transaminase

## ➤ **AST & ALT:**

- Most useful indicators of hepatocellular damage
- Sensitive not specific
- >8-10 folds: acute injury
- 2-3 folds chronic or mild acute
- In alcoholics ALT>300 is uncommon

➤ **Positive result:** Strongly suggest liver injury

➤ **Negative data:** Cannot rule out it

# Transaminase

## ➤ *High levels:*

- Viral
- alcoholic
- ischemic
- extrahepatic obstruction
- obese individuals

## ■ A serum AST:ALT ratio $> 1$ may suggest occupational liver disease

- Little Prognostic value
- Not correlate with extent of liver necrosis on biopsy



# Clinical Management of OCCUPATIONAL Liver Disease

- **Occupational & medical Hx**
  - Exposure to hepatotoxins
  - PMH of liver dis, medication
  - Review of symptoms(CNS Toxicity due to solvent exposure)
  - Travel to areas with endemic parasitic or viral disease
  - Steroid use, glue sniffing, recreational solvent use
  - Previous blood transfusion, tattoos, needle sticks, IV drug ...
  - Use of protective work practices
  - MSDS
  - Ask about other employees



# Clinical Management of OCCUPATIONAL Liver Disease

## ➤ Physical Examination

### ■ Acute liver disease

RUQ tenderness

Hepatosplenomegaly

Jaundice

### ■ **Chronic liver disease**

Spider angioma

Palmar erythema

Testicular atrophy

Ascites

Gynecomastia



# Clinical Management of OCCUPATIONAL Liver Disease

- **Elevated serum transaminase level**
  - **R/O non-occupational causes**
  - **Remove for 3-4 weeks**
  - **Repeat**
  - **A persistently elevated serum transaminase concentration suggests a non-occupational cause of liver disease or, rarely, chronic occupational liver disease.**



