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
- Hepatic injury dose not differ clinically or morphologically from drug induced damage
- Occupational liver disease may be of secondary importance to damage
- Occupational history and result of personal or workroom air sampling

- Lack of sufficiently sensitive and specific tests
- Effects of multiple hepatotoxic exposure
- Remove the patient from exposure to the suspected workplace toxin

Routes of Exposure

- Inhalation
- Ingestion
- Percutaneous absorption

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

- 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

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

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
- Granoluma:
  - Beryllium, Copper
- Neoplastic changes:
  - VCM, Arsenic

Infectious Agents

HAV	Nursery & kindergarten staff 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 icterohaemorrhagiae	Sewer workers, farm workers

Hepatitis A

- **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**

- 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 HAY infection.**
- **Orthotopic liver transplantation**

Prevention

- Hand washing
- Avoiding tap water and raw foods in areas with poor sanitation.
- Heating foods appropriately >85°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**

- 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

- 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.

- 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.

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

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

- 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

- 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.

- 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.5

- 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.

- 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

Hepatitis B

- Prevalence rate of HBS-Ag in hospital staff : 1-2%
- Prevalence rate of Anti-HBS: 15-30%
- Prior to hepatitis B vaccine:
  - Most frequent occupational infection among health care, laboratory, and public safety workers following human blood or body fluid exposure
  - 10 times higher than general population
- **By Standard Precautions and preexposure vaccination: sharp decline**

Hepatitis B

- Blood contains the highest titers of virus in infected individual
- Low levels in other body fluids:
  - Cerebrospinal, Synovial, Pleural, Peritoneal, Pericardial, Amniotic
  - Semen and Vaginal secretions
- Viral titers in urine, feces, tears, and saliva are low enough not be routes of transmission
  - except in cases of human bites that usually involve some blood transmission

- HBsAg found in breast milk is also unlikely to lead to transmission,
- Hence HBV infection is not a contraindication to breastfeeding.

- The risk of infection with HBV depends on:

  the titer of virions in the infectious fluid

  And

  correlates with the presence or absence of

  hepatitis e antigen in the source patient.

- The risk of infection following percutaneous injury with both HBsAg- and hepatitis B e antigen (HBeAg)-positive blood is 22-31%;
- The risk of developing serologic evidence of HBV infection is 37-62%.

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

- 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 suggestive occupational liver disease**
  - **Little Prognostic valve**
  - **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 2-4 weeks**
  - **Repeat**
  - **A persistently elevated serum transaminase concentration suggests a non-occupational cause of liver disease or, rarely, chronic occupational liver disease.**