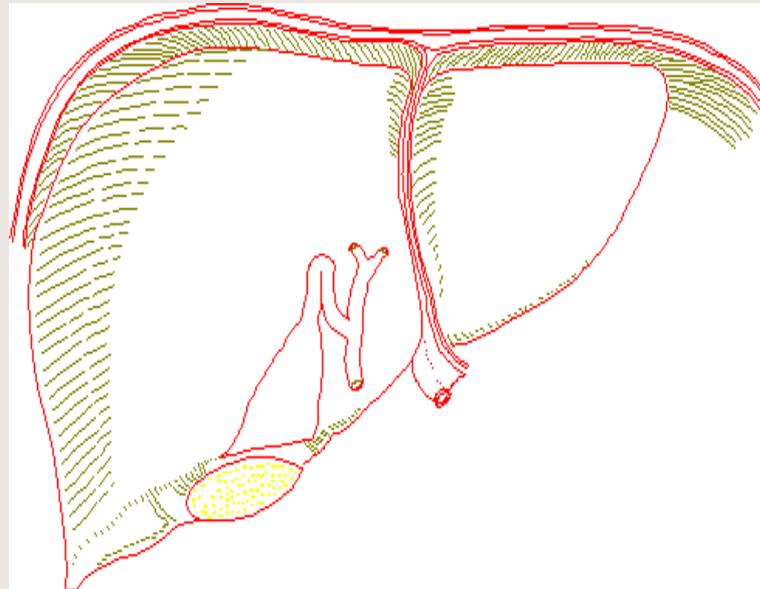


# HEPATITIS



VACCINATE DON'T PROCRASTINATE – LIVE HEALTHY  
NYS OASAS

# NEW YORK STATE OFFICE OF ALCOHOLISM AND SUBSTANCE ABUSE SERVICES

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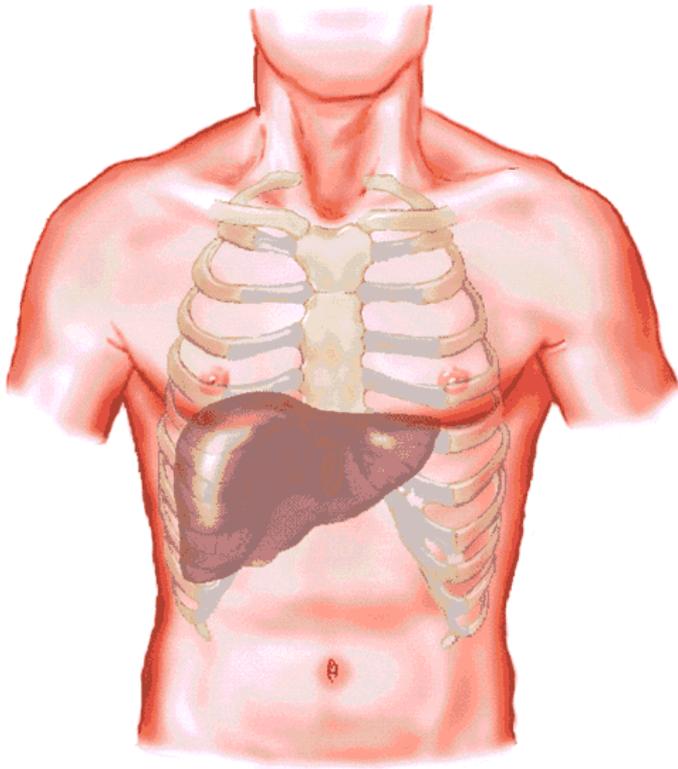
Workbook prepared by the  
Office of the Medical Director and  
the Bureau of Treatment:

Steven Kipnis MD, FACP, FASAM

Robert Killar, CASAC

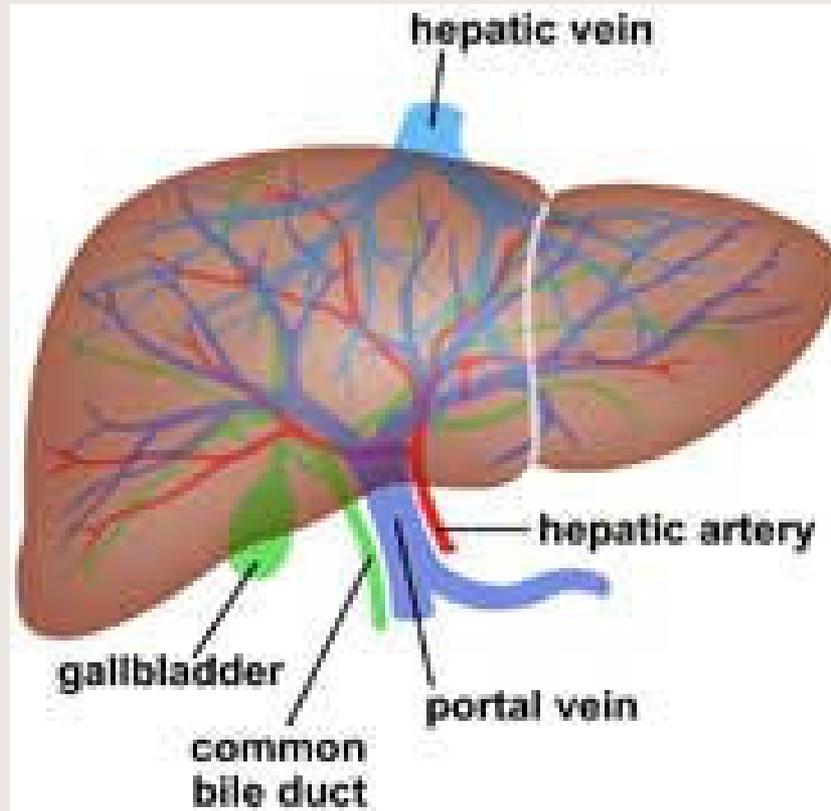
Patricia Lincourt, LCSW

# THE LIVER



- WEDGE SHAPED ORGAN
- LOCATED UNDER RIGHT RIB CAGE
- WEIGHS ABOUT 3 LBS.

# ANATOMY





## LIVER IN ABDOMINAL CAVITY

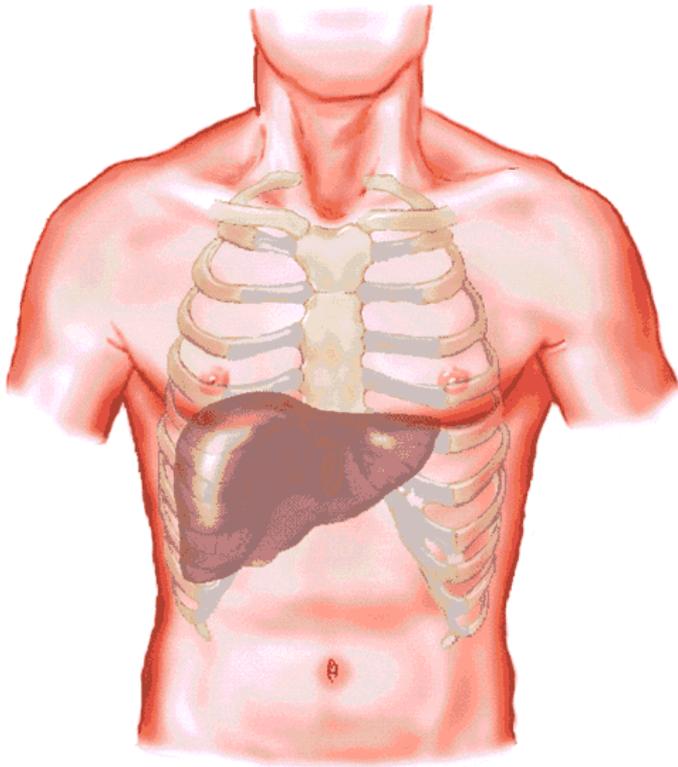
VACCINATE DON'T PROCRASTINATE – LIVE HEALTHY  
NYS OASAS



## LIVER REMOVED FROM ABDOMINAL CAVITY

VACCINATE DON'T PROCRASTINATE – LIVE HEALTHY  
NYS OASAS

# THE LIVER



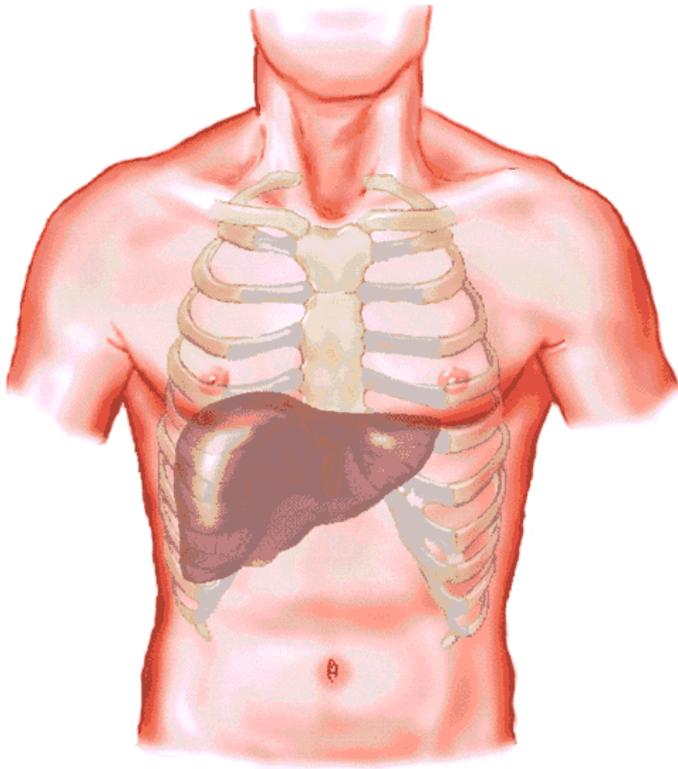
- FUNCTIONS OF THE LIVER:
  - MAKES PROTEIN NEEDED FOR BLOOD CLOTTING
  - STORES VITAMINS, IRON AND GLYCOGEN
  - METABOLIZES SUGAR, PROTEIN AND FAT TO PRODUCE ENERGY
  - REMOVES WASTE PRODUCTS AND FILTERS TOXIC SUBSTANCES FROM BLOOD

# EVALUATING THE LIVER

- Liver disease may be detected during a physical examination. During part of the exam, the doctor will lightly tap your abdomen above the liver (percussion). The resulting sound may indicate a change in the size or position of the liver.
- Liver health can also be determined by gently pressing over the right upper part of the abdomen.
- Further evaluation can involve blood tests looking for elevations of liver enzymes (see next page).

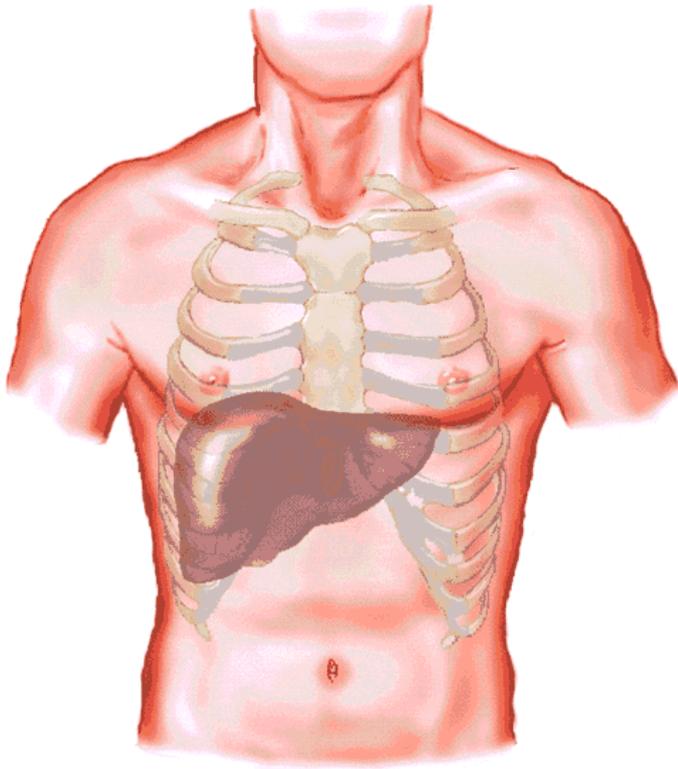


# THE LIVER



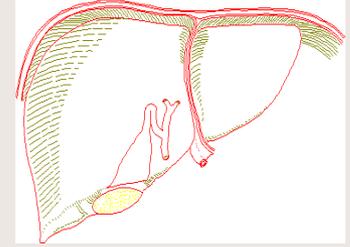
- Enzymes (proteins) from the liver are normally found in the blood as a result of normal aging and degeneration of liver cells (called LFT'S – liver function tests)
  - ALT
    - Almandine aminotransferase
  - AST
    - Aspartate aminotransferase
  - GGTP
    - Gamma -glutamyltransferase

# THE LIVER



- Liver enzymes (LFT's)
  - 6% of all patients have elevated enzymes. The most common causes are:
    - Alcohol use
    - Obesity
    - Hepatitis C

# HEPATITIS

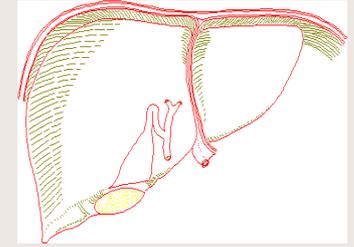


“INFLAMMATION OF THE LIVER”

CAUSED BY:

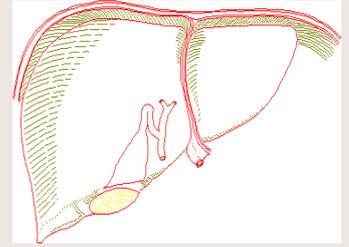
- VIRUSES - HEPATITIS A, B, C, D, E, G
- OTHER INFECTIONS (MONONUCLEOSIS)
- CHEMICALS
  - ALCOHOL
  - ACETAMINOPHEN

# HEPATITIS



A virus is much smaller than a human cell and much simpler. It is a string of genes (DNA or RNA) covered by a coat of protein. The virus cannot accomplish all the complex functions that normal cells can and in fact can really only reproduce using the human cell as a host. (When a virus invades a cell, it can use the cell's own mechanisms to reproduce) The hepatitis virus invades the liver cell and ultimately, using it to reproduce, causes damage (release of liver enzymes) and death of the liver cell.

# HEPATITIS

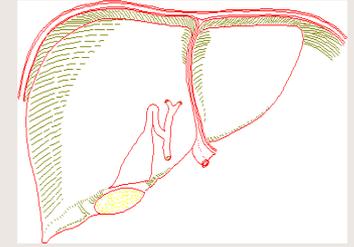


## Symptoms of acute hepatitis:

Mild hepatitis - malaise, jaundice,  
abdominal pain

Severe hepatitis - all of the above plus  
bleeding, fluid retention, altered mental  
status

# HEPATITIS



- Acute hepatitis is where the disease develops quickly, has symptoms and lasts less than 6 months.
- Chronic hepatitis is where the symptoms and disease last longer than 6 months.
- ACUTE HEPATITIS CAN RESOLVE TOTALLY OR GO ON TO A CHRONIC STAGE

# VIRAL HEPATITIS

---

- VIRAL HEPATITIS TYPES

- A

- CALLED “INFECTIOUS HEPATITIS” (HAV)

- B

- CALLED “SERUM HEPATITIS” (HBV)

- C

- PREVIOUSLY CALLED NON - A NON - B, NOW HCV

- D

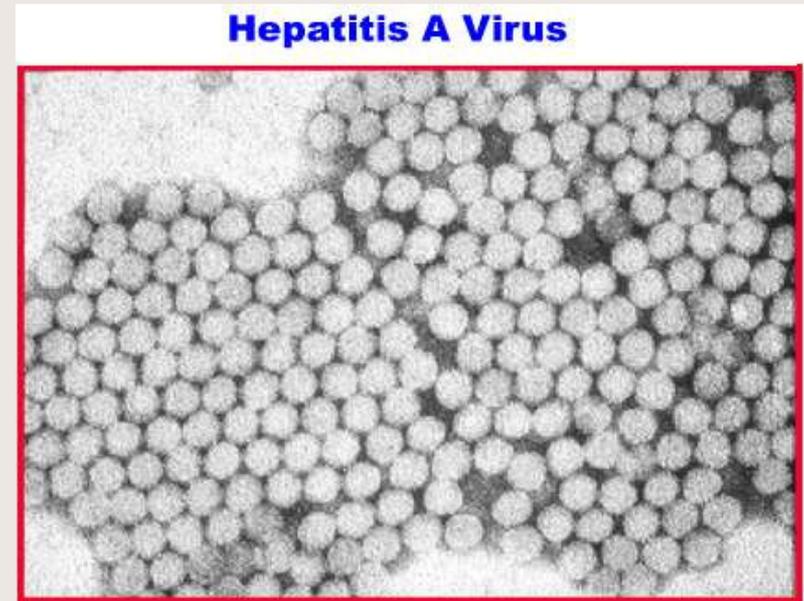
- DEFECTIVE RNA VIRUS
    - NEEDS B TO INFECT

- E

- LIKE A, ORAL/FECAL TRANSMITTED

# HEPATITIS A (HAV)

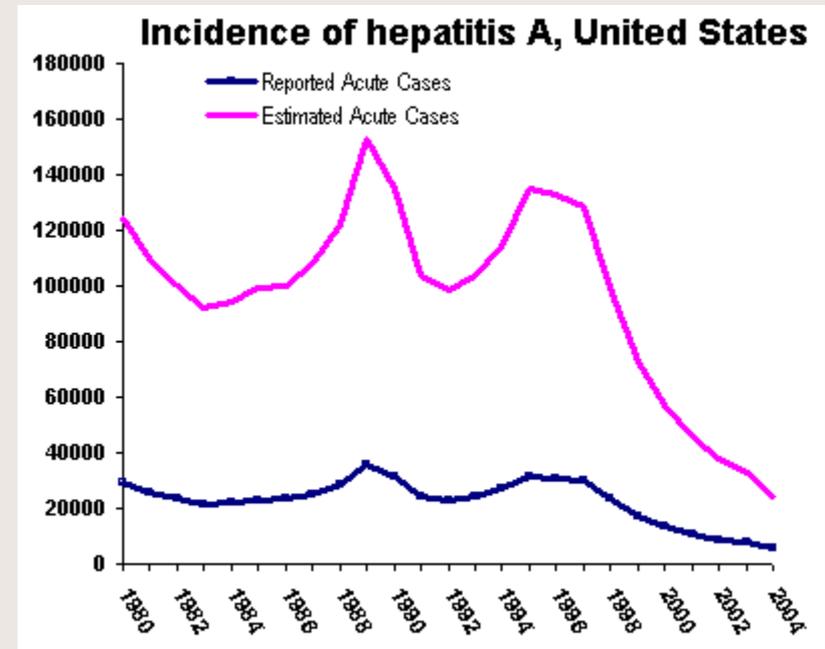
- Hepatitis A is caused by infection with the hepatitis A virus, which is an RNA virus in the picornavirus family.
- Only one virus has been discovered, unlike some other viruses that have subtypes.
- This type of hepatitis is vaccine preventable



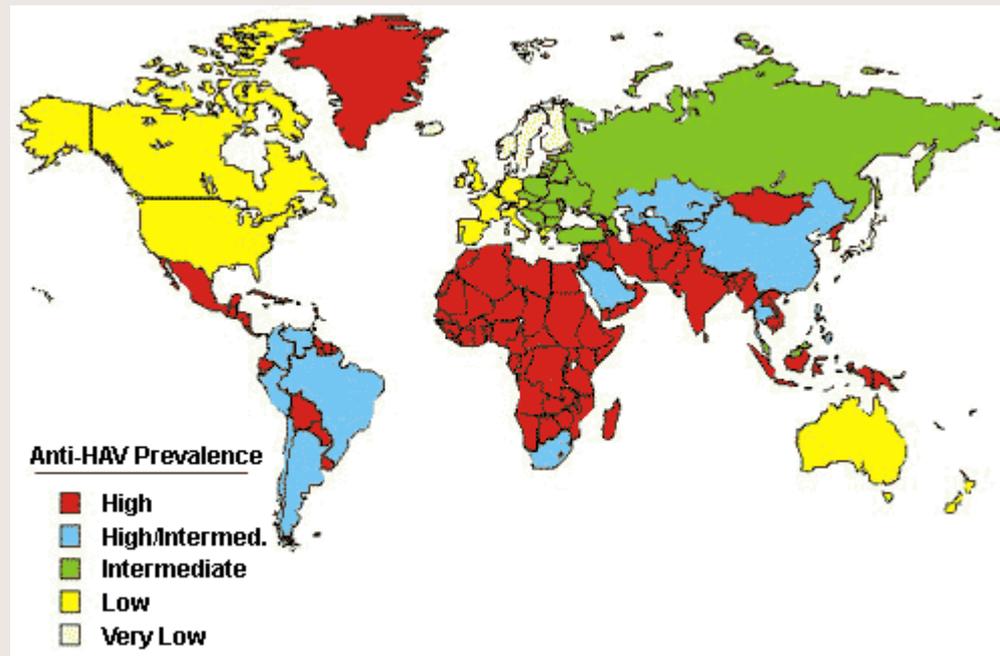
Source: Center for Disease Control

# HEPATITIS A (HAV)

- Hepatitis A is responsible for about 20,000 to 40,000 infections a year in the United States. While most are associated with symptoms, death is rarely associated with this type of hepatitis (due to fulminant hepatitis – liver failure)

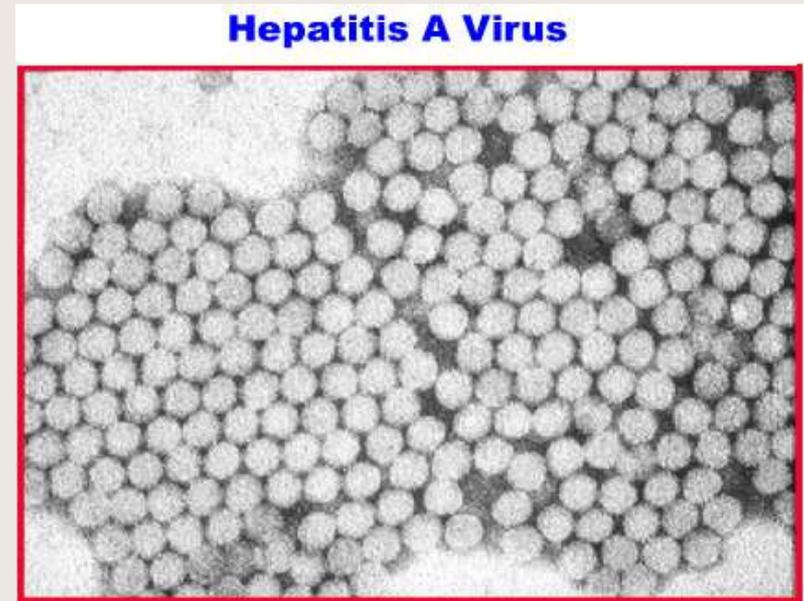


# WORLDWIDE HEPATITIS A PREVALENCE (CDC)



# HEPATITIS A (HAV)

- Clinical Features
  - Incubation period is usually about 30 days after exposure, the range is 15 – 50 days
  - Jaundice (turning yellow) is most commonly seen in the older patients
    - Under 6 years old (10%)
    - 6 to 14 years old (40 – 50%)
    - Greater than 14 years old (70 – 80%)
  - Fatigue
  - Dark urine
  - Fever
  - Nausea and vomiting
  - Abdominal pain
    - Complications of this type of viral infection include rare liver failure and relapsing hepatitis
    - Chronic sequelae are not seen
  - 33% of the US population has evidence of past infection and thus immunity

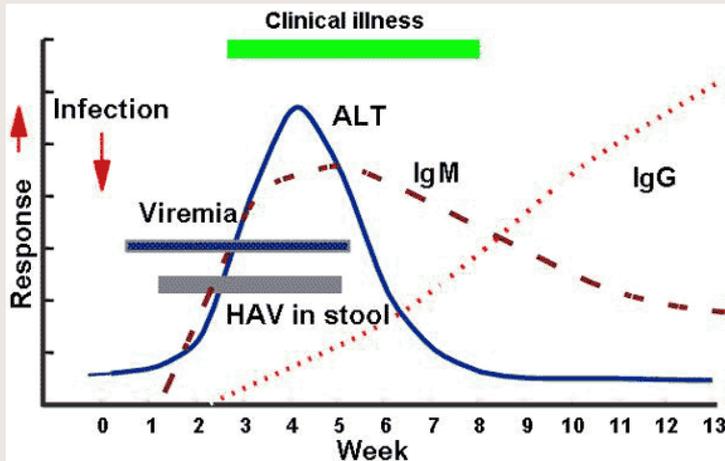


# HEPATITIS A (HAV)

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- Diagnosis - Hepatitis Panel
  - For diagnosis of Hepatitis A -IgM anti-HAV
  - Liver Enzymes

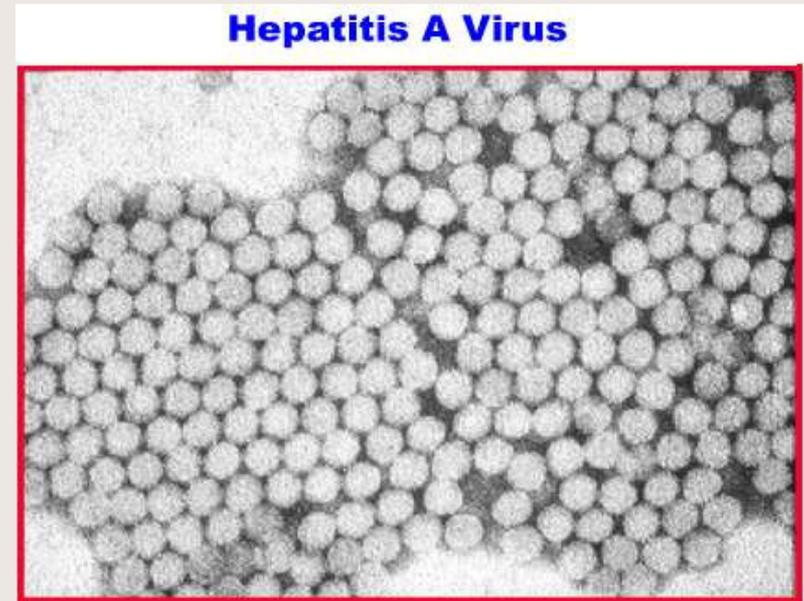
# EVENTS IN HEPATITIS A INFECTION (CDC)



- As the immune system responds to the infection, the amount of virus in the blood (viremia) and in the stool (HAV in stool) disappears. The liver enzyme, ALT goes up at the beginning of the infection, but decreases to normal at about 8 weeks. IgM shows acute infection and IgG is positive long – term.

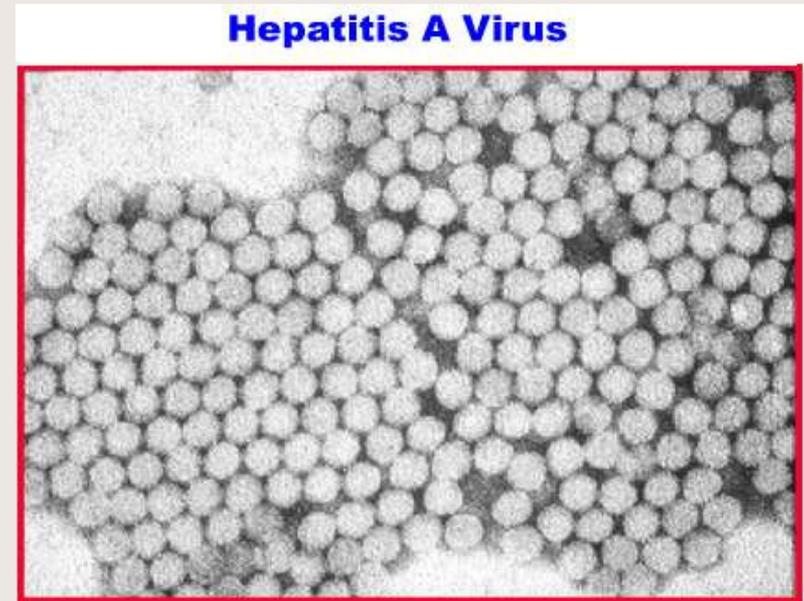
# HEPATITIS A (HAV)

- HAV Transmission
  - Close personal contact
    - Household member
    - Sex contact
    - Childcare centers
  - Contaminated food or water
    - Fecal – oral contact
    - Contaminated shellfish
    - Infected food handlers
  - Blood exposure
    - rare



# HEPATITIS A (HAV)

- HAV Treatment
  - No specific medical treatment
  - Avoid alcohol and all medications that are metabolized in the liver
  - Manage symptoms
  - If the spleen is enlarged avoid activities that could lead to abdominal pressure or injury



# HEPATITIS A (HAV)



- HAV Prevention
  - Wash hands
  - Use gloves when appropriate
  - Risk reduction if involved in oral/anal sexual practices
  - Risk reduction if involved in intravenous drug use
  - Vaccination

# HEPATITIS A (HAV)

- HAV Prevention (continued)

- Vaccination

- Pre-exposure Vaccination

- Persons at increased risk for infection:

- » Travelers to intermediate and high HAV-endemic countries
        - » Homosexual and bisexual men (men who have sex with men)
        - » Persons with HIV/AIDS
        - » Drug users
        - » Persons with chronic liver disease including Hepatitis C
        - » Persons with a diagnosis of clotting factor disorder
        - » Persons with occupational risks

- Communities with high rates of hepatitis A [e.g., Alaska Natives, American Indians]

- Routine childhood vaccination



# HEPATITIS A (HAV)

- HAV Prevention (continued)

- Immune Globulin (IG)



- Sterile preparation of concentrated antibodies (immunoglobulins) made from pooled human plasma
      - Only plasma tested negative for hepatitis B, HIV, and antibodies to hepatitis C are used
    - Provides protection against hepatitis A through passive transfer of antibody
    - When administered within 2 weeks after an exposure to hepatitis A virus, IG is 80 – 90% effective in preventing hepatitis A

# HEPATITIS A (HAV)

- HAV Vaccines – first licensed in 1995
  - Vaccines are virus vaccines where the virus has been inactivated
  - Both vaccines are highly immunogenic where 100% of those vaccinated with 2 doses will seroconvert to a protected level
  - New recommendations in 2005 are for routine vaccination of all children in the US beginning at 1 year of age



- HAVRIX

- The standard primary course of vaccination with **HAVRIX** consists of two doses, the first administered at the elected date and the second one month later. If necessary, the second dose may be administered a minimum of two weeks following the first dose. A booster is recommended at any time between 6 and 12 months after the initiation of the primary course in order to ensure long term antibody titers. In the event a subject is expected to be exposed to a high risk of contracting hepatitis A before the completion of the primary immunization scheme, concomitant administration of **HAVRIX ISG** might be considered.
  - **HAVRIX** is indicated for active immunization of persons  $\geq 2$  years of age against disease caused by hepatitis A virus (HAV). HAVRIX will not prevent hepatitis caused by other agents such as hepatitis B virus, hepatitis C virus, hepatitis E virus, or other pathogens known to infect the liver.
  - There is also a combined HAV and HBV vaccine available – **TWINRIX** – which offers the added advantage of providing protection against two viral hepatitis infections.
- *Source: GlaxoSmithKline Pharmaceuticals.*

# HEPATITIS A (HAV)

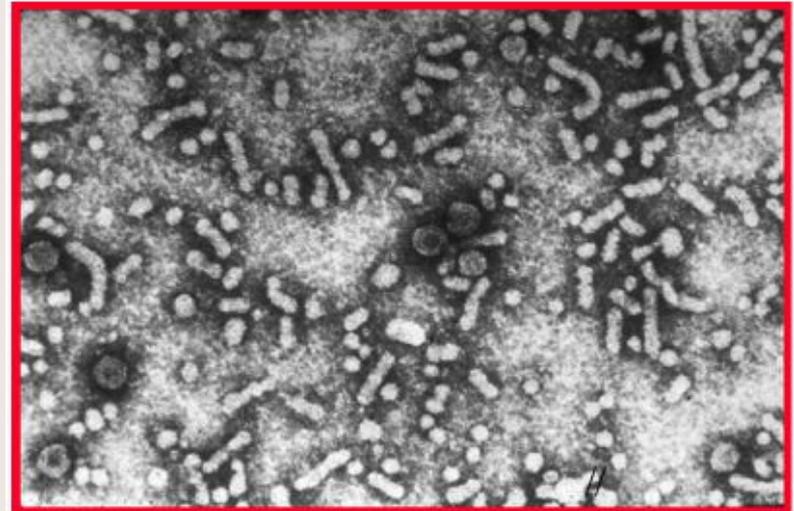


- HAV Vaccines
  - VAQTA is indicated for active pre-exposure prophylaxis against disease caused by hepatitis A virus in persons 2 years of age and older.
  - VAQTA is for intramuscular injection. A booster dose of VAQTA may be given at 6 to 12 months following the initial dose of other inactivated hepatitis A vaccines (e.g., HAVRIX).
  - Primary immunization should be given at least 2 weeks prior to expected exposure to HAV.
  - Source: Merck & Co., Inc

# HEPATITIS B (HBV)

- Hepatitis B is a DNA virus of the class of viruses known as hepadnaviridae.
- The Hepatitis B virus is 100 times more infectious than the HIV virus.
- Hepatitis B is vaccine preventable.
  
- Source: Center for Disease Control

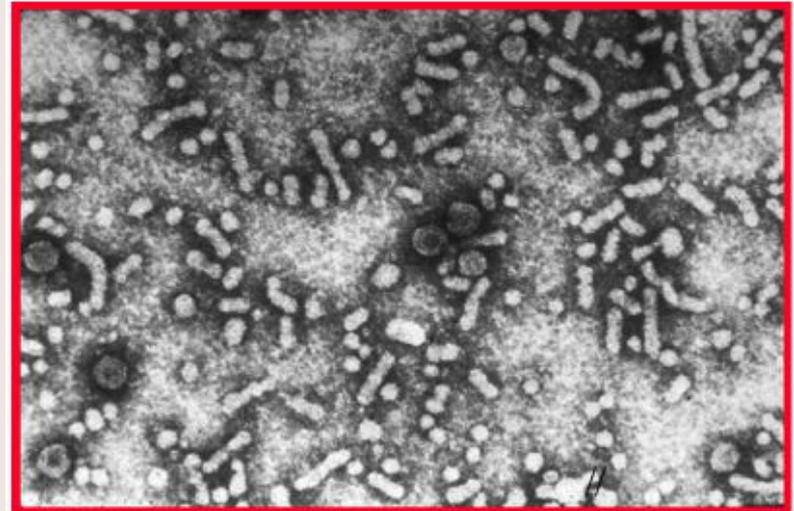
**Hepatitis B Virus**



# HEPATITIS B (HBV)

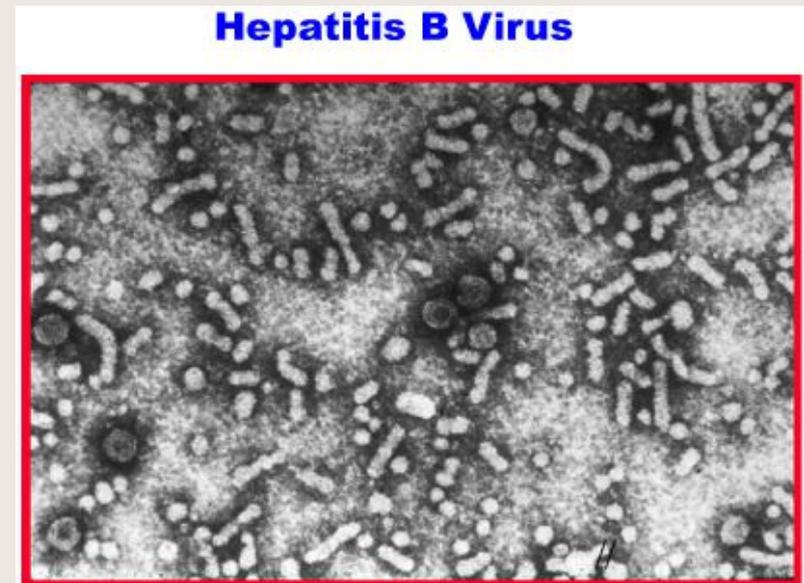
- Hepatitis B virus is composed of several different parts
  - Hepatitis B Surface Antigen
    - Outer surface membrane
    - Primary component of Hepatitis B vaccines
    - This structure causes the production of a protective, neutralizing antibody that provides long - term protection from the Hepatitis B virus

**Hepatitis B Virus**



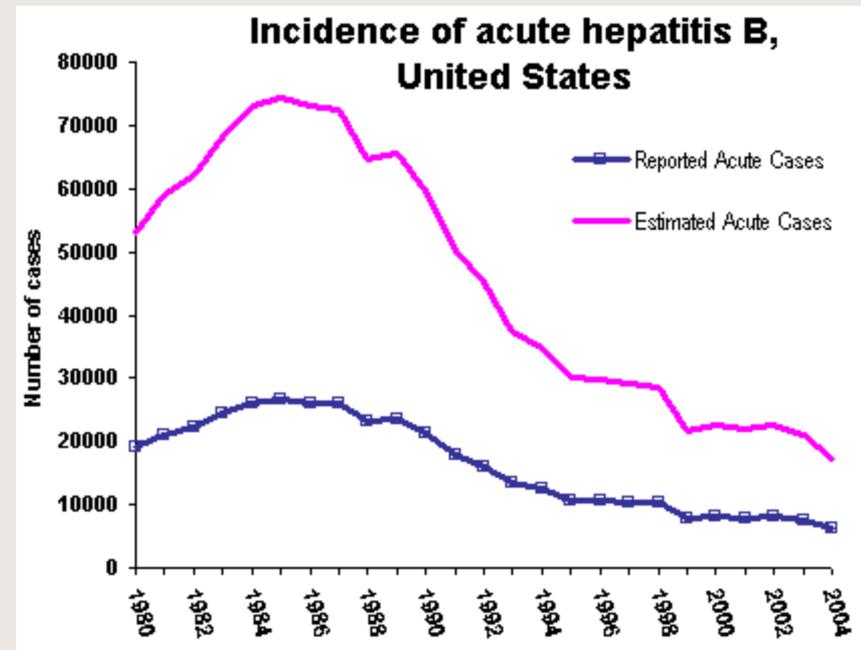
# HEPATITIS B (HBV)

- Hepatitis B virus is composed of several different parts
  - The inner core contains
    - Hepatitis B core antigen (HBcAg)
    - Hepatitis B e antigen (HBeAg)



# HEPATITIS B (HBV)

- Hepatitis B virus infection is seen in Americans each year



# HEPATITIS B (HBV)

- Hepatitis B virus infection
  - Of the total number of those infected, a small percentage die from cirrhosis (top picture) and primary liver cancer (bottom picture)



# HEPATITIS B (HBV)

---

- Clinical course – symptoms
  - Jaundice
  - fatigue/abdominal pain
  - appetite loss
  - nausea/vomiting
  - mild fever
  - dark urine
    - One third of adults & 90% of children have no symptoms
    - Symptoms last 1-4 weeks up to 6 months
    - 90-95% recover within 6 months with lifelong immunity
    - 50% develop acute liver disease

# HEPATITIS B (HBV)

- Clinical course – 10% of adults who are infected do not clear the virus\* and develop what is called Chronic HBV infection.
  - These patients develop chronic liver disease which can be either persistently mild or aggressive. 20 – 25% of these patients die prematurely due to cirrhosis or liver failure.

\* 30 – 50% of all infected 1 to 5 year olds and 80 – 90% of all infants develop chronic infection

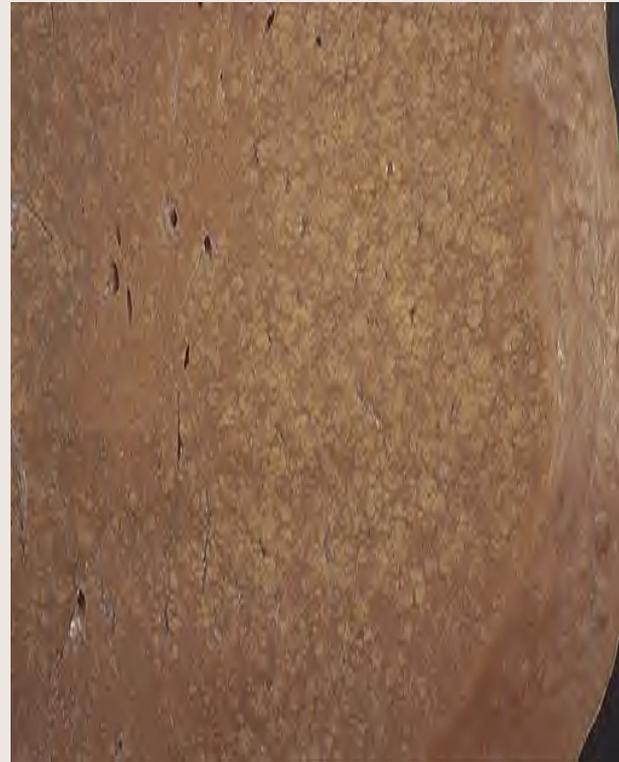
# WHAT IS CIRRHOSIS ?

- Scarring of the liver with loss of function
- Liver function tests may be normal due to a decrease in the number of normal liver cells





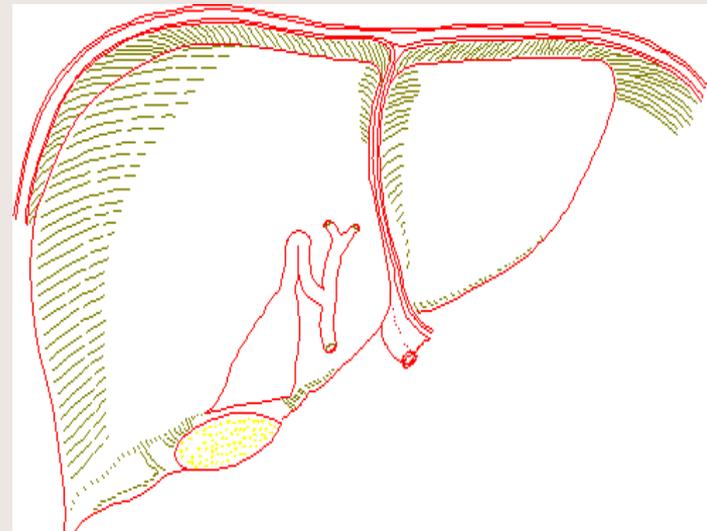
**NORMAL BIOPSY**



**BIOPSY OF CIRRHOSIS**

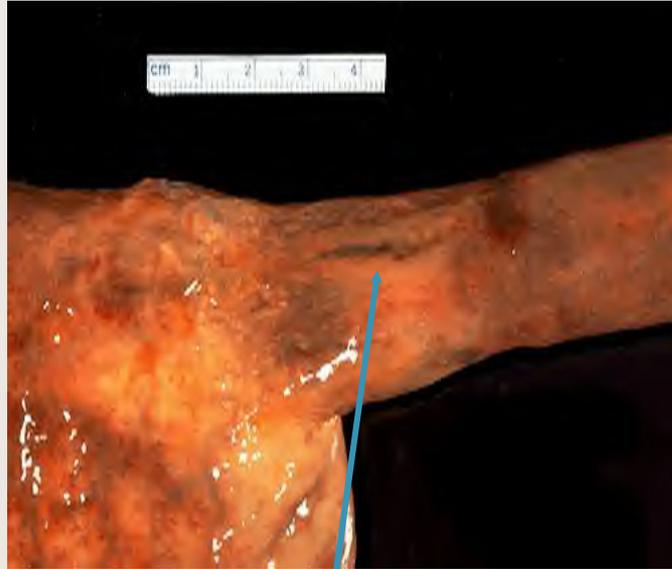
# WHAT IS CIRRHOSIS ?

- Complications:
  - Encephalopathy (altered mental status)
  - Ascites (fluid in abdomen)
  - Edema (fluid in lower extremities)
  - Spontaneous bacterial peritonitis (spontaneous infection in the abdomen)
  - Coagulopathy (impaired blood clotting mechanism)





**CIRRHOSIS COMPLICATION  
CAPUT MEDUSA  
(DILATED ABDOMINAL VEINS)**



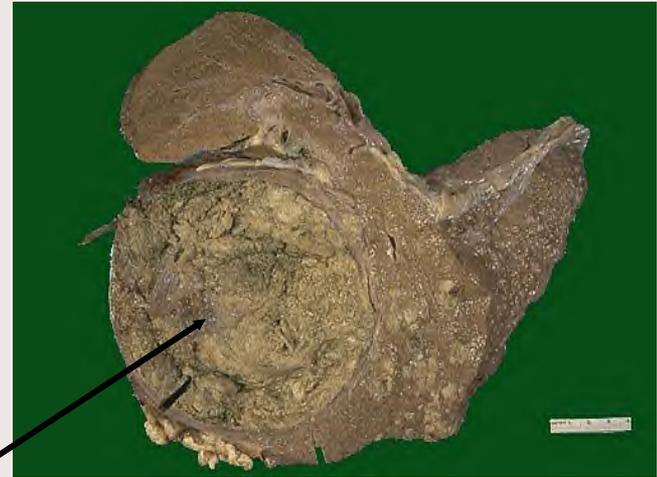
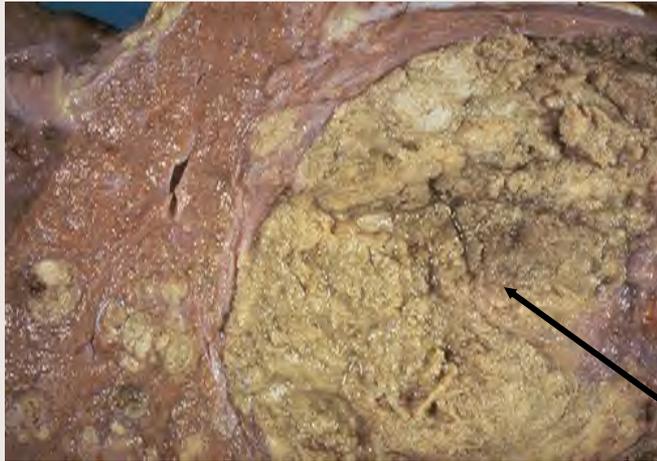
**CIRRHOSIS COMPLICATION  
ESOPHAGEAL VARICES  
(DILATED ESOPHAGEAL VEINS)**



PATIENT WITH END-STAGE LIVER FAILURE DUE TO CIRRHOSIS

VACCINATE DON'T PROCRASTINATE – LIVE HEALTHY  
NYS OASAS

# CIRRHOSIS COMPLICATIONS



HEPATOCELLULAR CARCINOMA  
(HCC)

# HEPATITIS B (HBV)

- Transmission
  - Percutaneous = virus enters through the skin
    - Contaminated needle stick [injection drug use/occupational exposure]
    - Hemodialysis
    - Human bite
    - Transplantation/transfusion
    - Acupuncture, tattooing, body piercing
  - Mucosal = through the mucous membranes (mouth, vagina, etc)
    - Sex – oral, anal, vaginal
    - Perinatal – mother to child
    - Infected household items, [i.e., toothbrush w/blood, razors]
    - Intranasal drug use, sharing straws for snorting

# HEPATITIS B (HBV)

- Transmission
  - There is high concentration of the Hepatitis B virus in blood, serum and wound secretions (exudates)
  - There is a moderate concentration of Hepatitis B virus in semen, vaginal fluid and saliva
  - There is a low or absent concentration of Hepatitis B virus in urine, feces, sweat, tears and breast milk

\*the higher the concentration = the easier to get infected

# HEPATITIS B LABORATORY NOMENCLATURE

([WWW.IMMUNIZE.ORG](http://WWW.IMMUNIZE.ORG))

HBsAg:	<i>Hepatitis B surface antigen</i> is a marker of infectivity. Its presence indicates either acute or chronic HBV infection.
anti-HBs:	<i>Antibody to hepatitis B surface antigen</i> is a marker of immunity. Its presence indicates an immune response to HBV infection, an immune response to vaccination, or the presence of passively acquired antibody. (It is also known as <i>HBsAb</i> , but this abbreviation is best avoided since it is often confused with abbreviations such as <i>HBsAg</i> .)
anti-HBc (total):	<i>Antibody to hepatitis B core antigen</i> is a nonspecific marker of acute, chronic, or resolved HBV infection. It is not a marker of vaccine-induced immunity. It may be used in prevaccination testing to determine previous exposure to HBV infection. (It is also known as <i>HBcAb</i> , but this abbreviation is best avoided since it is often confused with other abbreviations.)
IgM anti-HBc:	<i>IgM antibody subclass of anti-HBc</i> . Positivity indicates recent infection with HBV ( $\leq 6$ mos). Its presence indicates acute infection.
HBeAg:	<i>Hepatitis B "e" antigen</i> is a marker of a high degree of HBV infectivity, and it correlates with a high level of HBV replication. It is primarily used to help determine the clinical management of patients with chronic HBV infection.
Anti-HBe:	<i>Antibody to hepatitis B "e" antigen</i> may be present in an infected or immune person. In persons with chronic HBV infection, its presence suggests a low viral titer and a low degree of infectivity.
HBV-DNA:	<i>HBV Deoxyribonucleic acid</i> is a marker of viral replication. It correlates well with infectivity. It is used to assess and monitor the treatment of patients with chronic HBV infection.

# HOW TO INTERPRET COMMON HEPATITIS B LAB TESTS (UPDATED 11/05 [WWW.IMMUNIZE.ORG](http://WWW.IMMUNIZE.ORG) )

Tests	Results	Interpretation	Vaccinate?
HBsAg anti-HBc anti-HBs	negative negative negative	susceptible	vaccinate if indicated
HBsAg anti-HBc anti-HBs	negative negative positive with ≥10mIU/mL*	immune due to vaccination	no vaccination necessary
HBsAg anti-HBc anti-HBs	negative positive positive	immune due to natural infection	no vaccination necessary
HBsAg anti-HBc IgM anti-HBc anti-HBs	positive positive positive negative	acutely infected	no vaccination necessary
HBsAg anti-HBc IgM anti-HBc anti-HBs	positive positive negative negative	chronically infected	no vaccination necessary (may need treatment)
HBsAg anti-HBc anti-HBs	negative positive negative	four interpretations possible†	use clinical judgment

\* Postvaccination testing, when it is recommended, should be performed 1–2 months after the last dose of vaccine. Infants born to HBsAg-positive mothers should be tested 3–9 months after the last dose.

†1. May be recovering from acute HBV infection

2. May be distantly immune, but the test may not be sensitive enough to detect a very low level of anti-HBs in serum

3. May be susceptible with a false positive anti-HBc

4. May be chronically infected and have an undetectable level of HBsAg present in the serum

# HEPATITIS B (HBV)

- Prevention
  - Avoid sharing injection drug equipment
  - Avoid unprotected sex [oral, vaginal or anal]
  - Screen pregnant women and vaccinate all exposed infants
  - Routine early childhood vaccination – 1991
  - Vaccinate active IDU's, non-monogamous adults, healthcare workers, & household contacts
  - Standard precautions used to prevent exposure to blood – healthcare workers, tattoo artists, body piercing. Wear protective gear such as gloves, goggles, etc
  - Don't use an infected person's toothbrush, razor, or anything else that could have blood on it

# HEPATITIS B (HBV)

- Prevention
  - Vaccination should be offered to
    - Persons with more than one sex partner in 6 months
    - Men who have sex with men (MSM)
    - Persons diagnosed with a sexually transmitted disease (STD)
    - Commercial sex workers
    - Illegal injectable drug users
    - Persons with HIV/AIDS
    - Persons with chronic liver disease including Hepatitis C
    - Inmates
    - Healthcare workers
    - Staff and clients (developmentally disabled)
    - Persons receiving hemodialysis
    - Alaskan Natives and Pacific Islanders
    - Adopted persons from HBV endemic countries
    - Recipients of certain blood products

# HEPATITIS B (HBV)

- Prevention
  - Vaccine first licensed in 1981
  - Two inactivated virus vaccines available in the US
    - Engerix – B made by GlaxoSmithKline
    - Recombivax HB made by Merck
  - Both vaccines are highly immunogenic where after 3 doses, 90% of young adults and 95% of infants, children and adolescents develop an antibody response
  - Immune memory lasts 15 years
    - Hepatitis B vaccine produces antibody response – series of three injections
    - Give initial dose, then next one at 1 month and last one 6 months later for adults and older children, though dosing can be at 2 and 4 months after initial shot, or 1 and 4 months after initial shot (all schedules are approved)
    - All high risk babies should get vaccinated. Infants get their first shot within 12 hours after birth, the second shot at age 1 to 2 months and the third shot between the ages of 6 to 18 months.
    - Peak level achieved 7-10 months after initial dose

# HEPATITIS B (HBV)

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- Prevention
  - Twinrix is a combination hepatitis A and B vaccine made by GlaxoSmithKline and approved for persons aged 18 years and older. It is indicated for persons at risk for both hepatitis A and B
    - It is administered in a 3 dose series at 0, 1, and 6 months

# HEPATITIS B (HBV)

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- Prevention Note
  - If a patient does not complete the series of vaccines indicated, they should just restart where they left off. There is not need to restart from the first dose.

# HEPATITIS B (HBV)

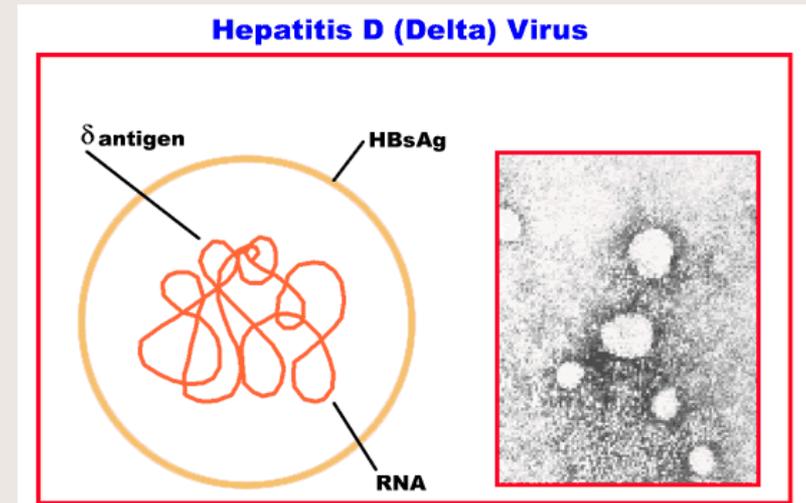
- Treatment for Hepatitis B
  - Alpha-interferons were the first drugs approved in the United States for the treatment of chronic hepatitis B.
    - Interferon treatment is recommended for individuals who have "replicative disease" (HBeAg positive).
    - About 40% of such individuals will lose serum HBeAg after 16 weeks of treatment with interferon-alpha.
    - Loss of HBeAg is correlated with an improved prognosis.
    - Patients with severe, decompensated liver disease (eg. encephalopathy, ascites, very high serum bilirubin, prolonged prothrombin time, etc.) should not generally be treated with interferon alfa except in the setting of an approved clinical study.
    - The recommended dose of interferon alfa-2b for the treatment of chronic hepatitis B is 5,000,000 units daily, administered by subcutaneous or intramuscular injection, for a total of 16 weeks. The patient must be monitored carefully during the treatment period for side effects including flu-like symptoms, depression, rashes, other reactions and abnormal blood counts.

# HEPATITIS B (HBV)

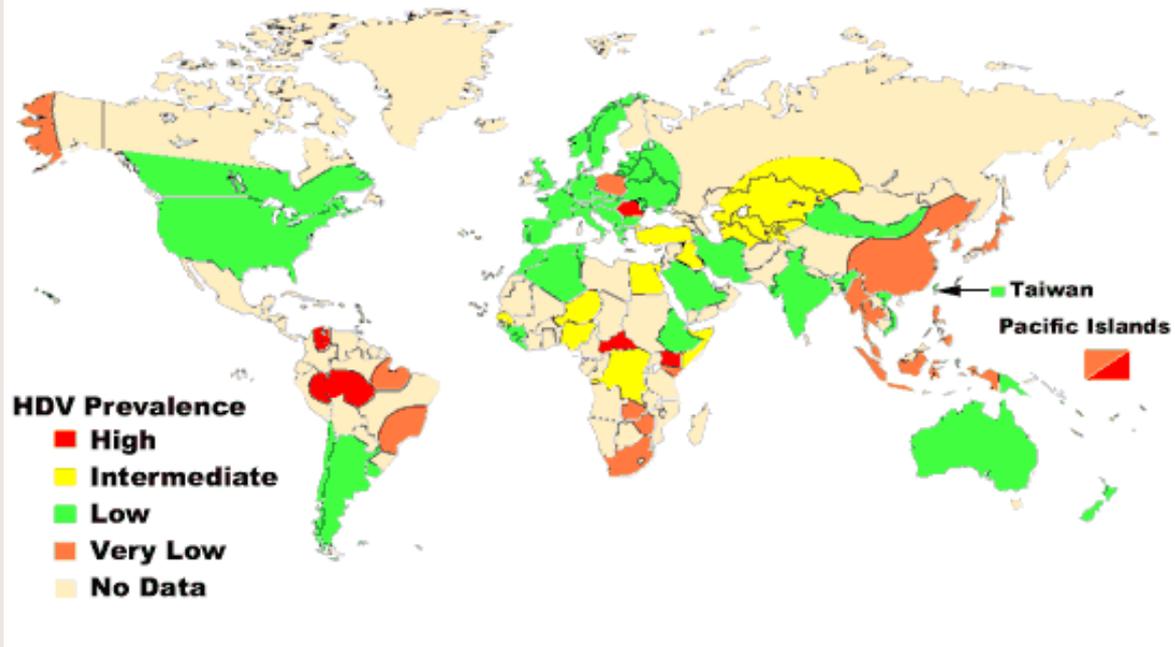
- Treatment for Hepatitis B (continued)
  - Other treatment options for chronic hepatitis B include nucleoside analogues
    - Lamivudine , also known as 3TC and is also effective against HIV.
      - Lamivudine is taken orally at 100 mg/day for chronic hepatitis B.
    - In studies where they were compared, lamivudine was equally effective to interferon-alpha in inducing a loss of serum HBeAg. It also has been shown to improve liver biopsy results.
    - Adefovir dipivoxil
    - The dose is 10 mg/day for chronic hepatitis B.
- At the present time, other nucleoside analogues are being studied in clinical trials. The combination of interferon-alpha and a nucleoside analogue, two nucleoside analogues together (such as lamivudine and adefovir) are also under investigation.

# HEPATITIS D (HDV)

- HDV is a defective single-stranded RNA virus that requires the helper function of HBV to replicate. HDV requires HBV for synthesis of envelope protein composed of HBsAg, which is used to encapsulate the HDV viral nucleic acid.
- Source: Center for Disease Control

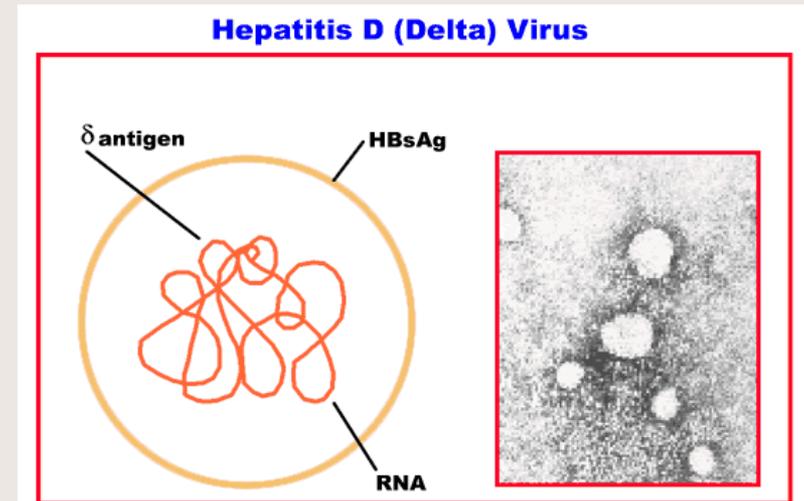


## Geographic Distribution of HDV Infection



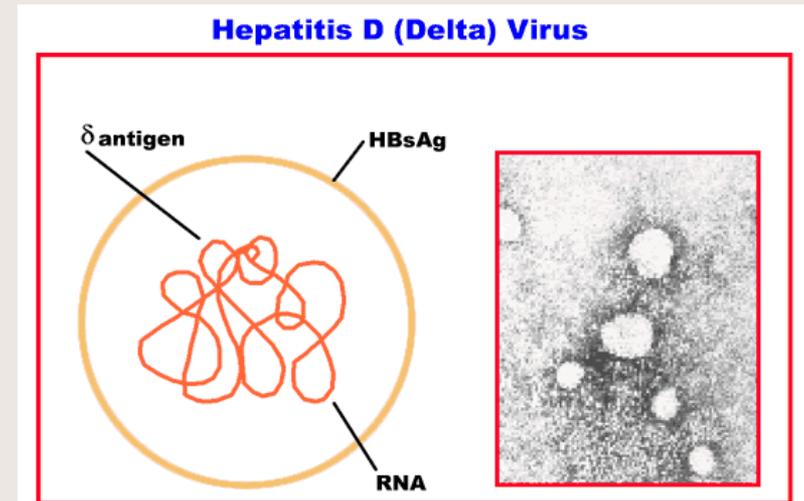
# HEPATITIS D (HDV)

- Clinical
  - HDV infection can be acquired either as a co-infection with HBV or as a superinfection of persons with chronic HBV infection.
  - Persons with HBV-HDV co-infection may have more severe acute disease and a higher risk of fulminant hepatitis (2%-20%) compared with those infected with HBV alone
  - Chronic HBV infection appears to occur less frequently in persons with HBV-HDV co-infection.

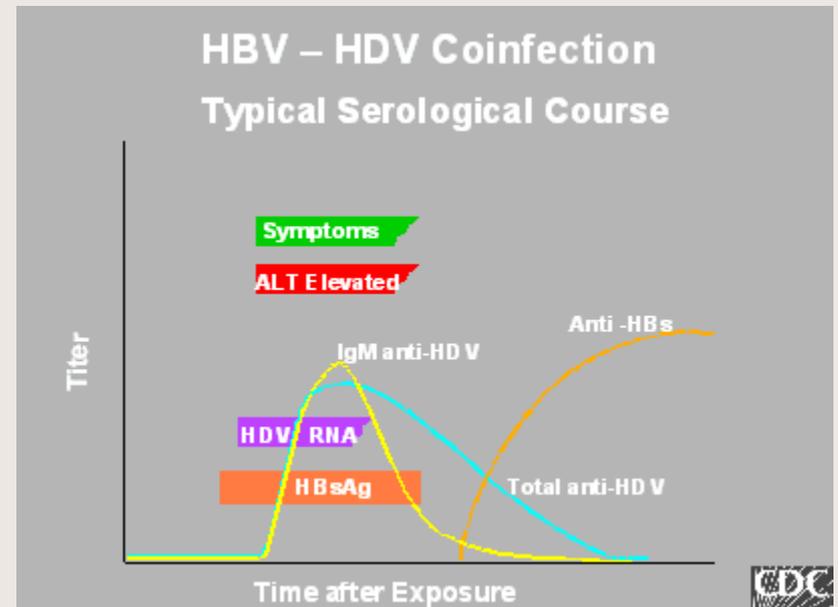


# HEPATITIS D (HDV)

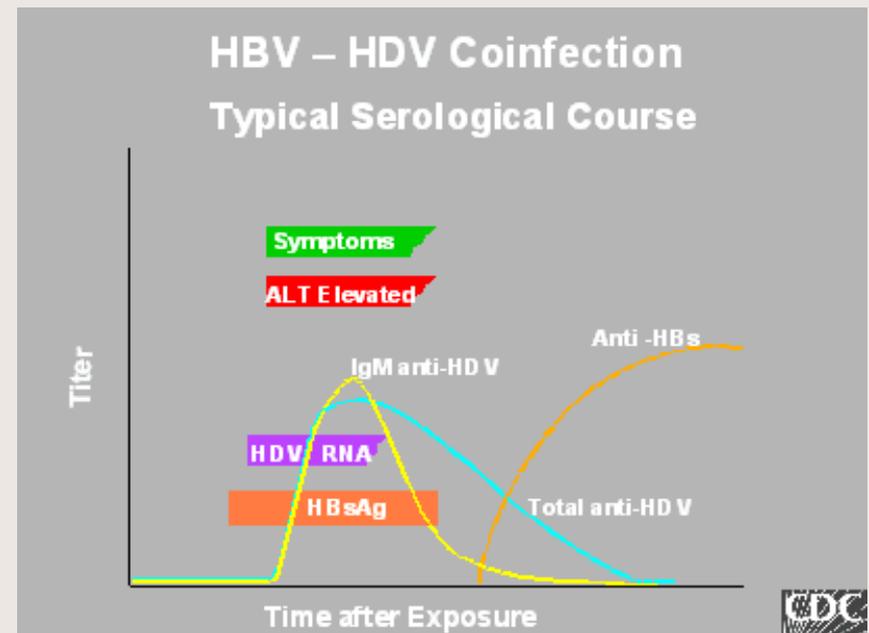
- Clinical (continued)
  - Chronic HBV carriers who acquire HDV superinfection usually develop chronic HDV infection.
  - In long-term studies of chronic HBV carriers with HDV superinfection, 70%-80% have developed evidence of chronic liver diseases with cirrhosis compared with 15%-30% of patients with chronic HBV infection alone



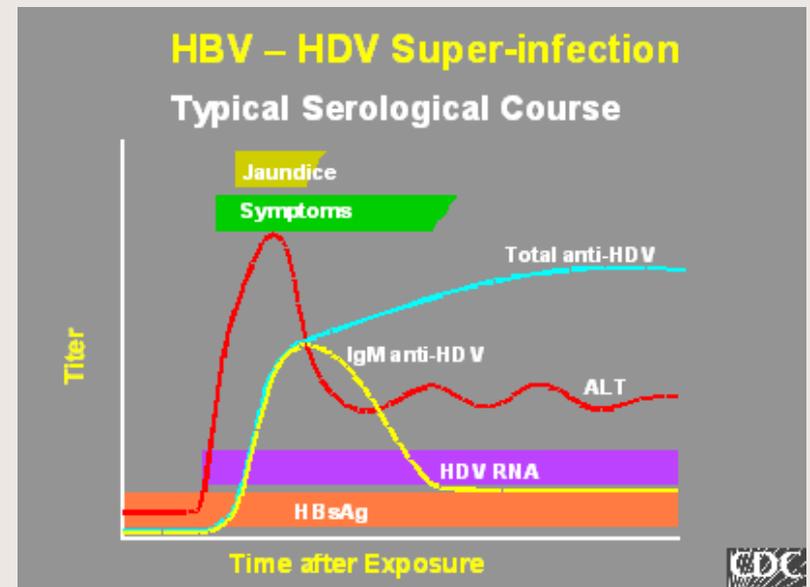
- In most persons with HBV-HDV co-infection, both IgM antibody to HDV (anti-HDV) and IgG anti-HDV are detectable during the course of infection.
- However, in about 15% of patients the only evidence of HDV infection may be the detection of either IgM anti-HDV alone during the early acute period of illness or IgG anti-HDV alone during convalescence.
- Anti-HDV generally declines to sub-detectable levels after the infection resolves and there is no serologic marker that persists to indicate that the patient was ever infected with HDV.



- Hepatitis Delta Antigen (HDAg) can be detected in serum in only about 25% of patients with HBV-HDV coinfection. When HDAg is detectable it generally disappears as HBsAg disappears and most patients do not develop chronic infection.
- Tests for IgG anti-HDV are commercially available in the United States.



- In patients with chronic HBV infection who are super-infected with HDV several characteristic serologic features generally occur, including:
  - the titer of HBsAg declines at the time HDsAg appears in the serum
  - HDsAg and HDV RNA remain detectable in the serum because chronic HDV infection generally occurs in most patients with HDV superinfection, unlike the case with co-infection
  - high titers of both IgM and IgG anti-HDV are detectable, which persist indefinitely.



# HEPATITIS D (HDV)

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- Transmission
  - The modes of HDV transmission are similar to those for HBV, with percutaneous exposures the most efficient (blood from an infected person enters the body of a person who is not immune). Sexual transmission of HDV is less efficient than for HBV. Perinatal HDV transmission is rare.

# HEPATITIS D (HDV)

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- Transmission
  - Risk groups include
    - Injection drug users
    - Men who have sex with men
    - Hemodialysis patients
    - Sex contacts of infected persons
    - Healthcare and public safety officers
    - Infants born to infected mothers (very rare)

# HEPATITIS D (HDV)

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- Prevention
  - Because HDV is dependent on HBV for replication, HBV-HDV co-infection can be prevented with either pre- or postexposure prophylaxis for HBV.
  - However, no products exist to prevent HDV superinfection of persons with chronic HBV infection. Thus, prevention of HDV superinfection depends primarily on education to reduce risk behaviors.

# HEPATITIS D (HDV)

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- Treatment
  - Acute HDV
    - Supportive care
  - Chronic HDV
    - Interferon – alfa
    - Liver transplant

# HEPATITIS E (HEV)

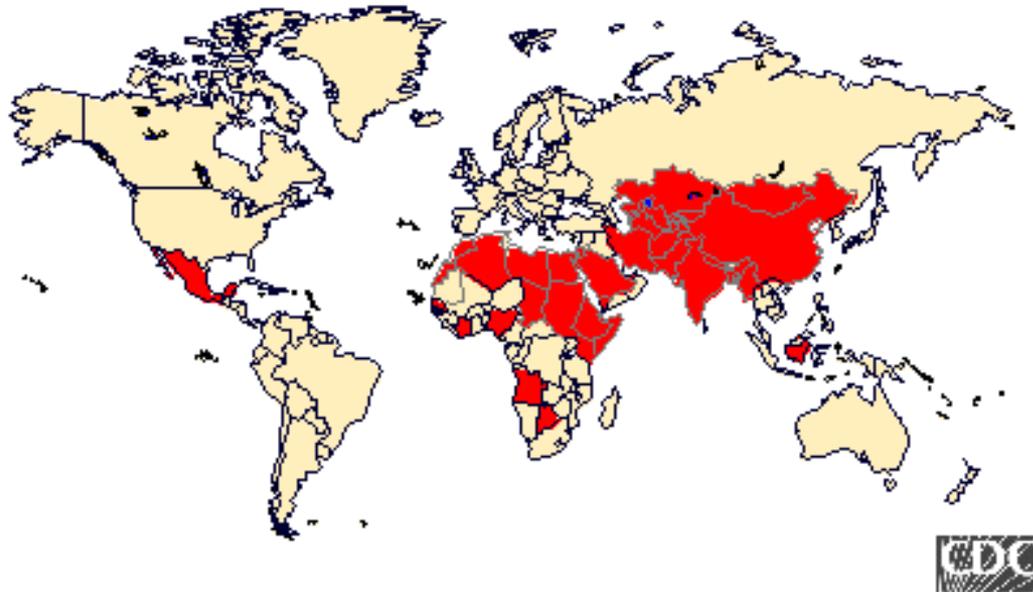
- Hepatitis E virus (HEV), the major etiologic agent of enterically transmitted non-A, non-B hepatitis worldwide, is a spherical, non-enveloped, single stranded RNA virus. HEV belongs to a genus of HEV-like viruses (unassigned genus).
- Source : Center for Disease Control

**Hepatitis E Virus**



## Geographic Distribution of Hepatitis E

Outbreaks or Confirmed Infection in > 25% of Sporadic Non-ABC Hepatitis



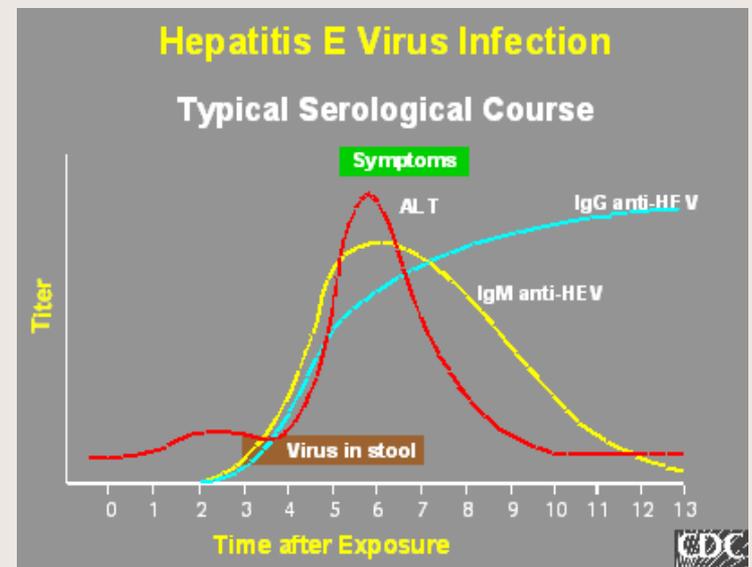
# HEPATITIS E (HEV)

- **Clinical Features**
- The incubation period following exposure to HEV ranges from 15 to 60 days (mean, 40 days).
- Typical clinical signs and symptoms of acute hepatitis E are similar to those of other types of viral hepatitis and include
  - Abdominal pain
  - Anorexia
  - dark urine
  - Fever
  - Hepatomegaly
  - Jaundice
  - Malaise
  - Nausea, and vomiting
  - Other less common symptoms include arthralgia, diarrhea, pruritus, and urticarial rash.

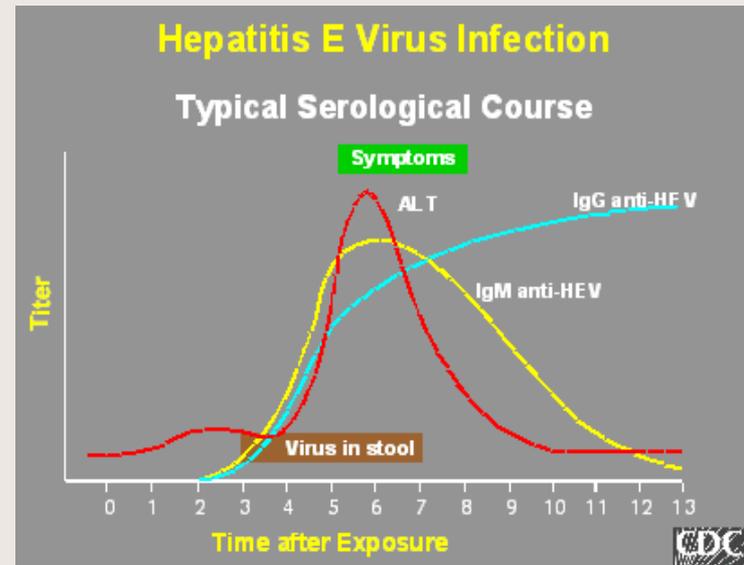
**Hepatitis E Virus**



- The typical serologic course following HEV infection has been characterized using experimental models of infection in nonhuman primates and human volunteer studies.
  - In two human volunteer studies, liver enzyme elevations occurred 4-5 weeks after oral ingestion and persisted for 20-90 days.
  - Virus excretion in stools occurred approximately 4 weeks after oral ingestion and persisted for about 2 weeks.
  - Both IgM and IgG antibody to HEV (anti-HEV) are elicited following HEV infection.
  - The titer of IgM anti-HEV declines rapidly during early convalescence.
  - IgG anti-HEV persists and appears to provide at least short-term protection against disease.



- No serologic tests to diagnose HEV infection are commercially available in the United States.



# HEPATITIS E (HEV)

- **Clinical Features**

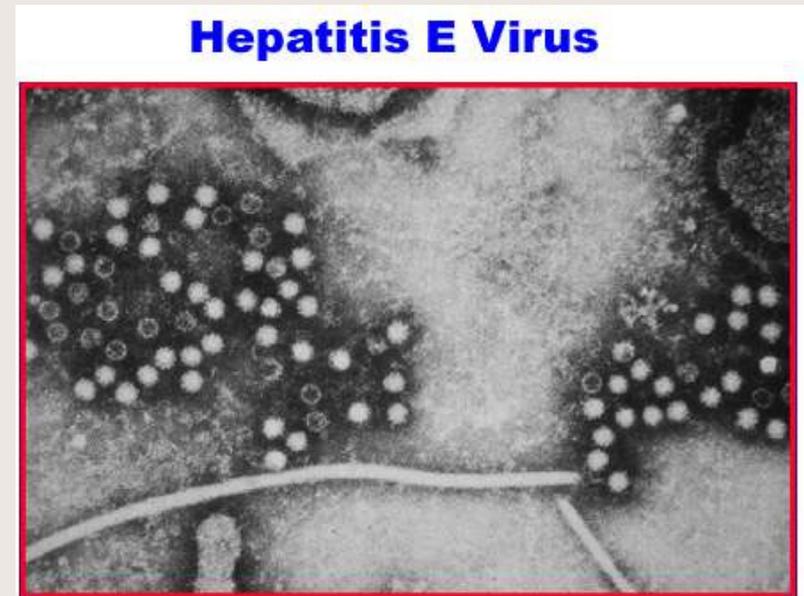
- The period of infectivity following acute infection has not been determined but virus excretion in stools has been demonstrated up to 14 days after illness onset.
- In most hepatitis E outbreaks, the highest rates of clinically evident disease have been in young to middle-age adults
- No evidence of chronic infection has been detected in long-term follow-up of patients with hepatitis E.

**Hepatitis E Virus**



# HEPATITIS E (HEV)

- **Clinical Features**
  - Case-fatality rate:  
Overall, 1%-3%  
Pregnant women,  
15%-25%
  - Illness severity is  
increased with age
  - Chronic sequelae:  
None identified



# HEPATITIS E (HEV)

- Transmission
  - HEV is transmitted primarily by the fecal-oral route and fecally contaminated drinking water is the most commonly documented vehicle of transmission.
  - Although hepatitis E is most commonly recognized to occur in large outbreaks, HEV infection accounts for >50% of acute sporadic hepatitis in both children and adults in some high endemic areas.
  - Risk factors for infection among persons with sporadic cases of hepatitis E have not been defined.
  - **Unlike hepatitis A virus, which is also transmitted by the fecal-oral route, person-to-person transmission of HEV appears to be uncommon.** However, nosocomial transmission, presumably by person-to-person contact, has been reported to occur. Virtually all cases of acute hepatitis E in the United States have been reported among travelers returning from high HEV-endemic areas.

# HEPATITIS E (HEV)

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- Diagnosis
  - No serologic tests to diagnose HEV infection are commercially available in the United States.

# HEPATITIS E (HEV)

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- Prevention
  - Prevention of hepatitis E relies primarily on the provision of clean water supplies.
  - Prudent hygienic practices that may prevent hepatitis E and other enterically transmitted diseases among travelers to developing countries include avoiding:
    - drinking water (and beverages with ice) of unknown purity
    - uncooked shellfish
    - uncooked fruits or vegetables that are not peeled or prepared by the traveler
  - No products are available to prevent hepatitis E.

# HEPATITIS E (HEV)

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- Treatment
  - Supportive
    - No medications are available
    - Treat symptoms with PRN (as needed) medications

# HEPATITIS G (HGV)

- Hepatitis G is a newly discovered form of liver inflammation caused by hepatitis G virus (HGV), a distant relative of the **hepatitis C** virus.
  - HGV, also called hepatitis GB virus, was first described early in 1996.
  - HGV is a positive-strand RNA virus belonging to the family Flaviviridae.
  - Little is known about the frequency of HGV infection, the nature of the illness, or how to prevent it. What is known is that transfused blood containing HGV has caused some cases of hepatitis.

# HEPATITIS G (HGV)

- HGV has been identified in between 1-2% of blood donors in the United States.
- Often patients with hepatitis G are infected at the same time by the hepatitis B or C virus, or both.
- In about three of every thousand patients with acute viral hepatitis, HGV is the only virus present.
- The virus has been identified in as many as 20% of patients with long-lasting viral hepatitis, some of whom also have hepatitis C.

# HEPATITIS G (HGV)

- **Clinical**

- Some researchers believe that there may be a group of GB viruses, rather than just one. Others remain doubtful that HGV actually causes illness. If it does, the type of acute or chronic (long-lasting) illness that results is not clear.
- Diagnosis is made by confirming the presence of HGV in the blood by detecting HGV-RNA.
- When diagnosed, acute HGV infection has usually been mild and brief.
- There is no evidence of serious complications, but it is possible that, like other hepatitis viruses, HGV can cause severe liver damage resulting in liver failure.

# HEPATITIS G (HGV)

- **Transmission**

- Transfused blood containing HGV has caused some cases of hepatitis. For this reason, patients with **hemophilia** and other bleeding conditions who require large amounts of blood or blood products are at risk of hepatitis G.
  - HGV has been identified in between 1-2% of blood donors in the United States.
  - Also at risk are:
    - Patients with kidney disease who undergo hemodialysis
    - Injection drug users
    - It is possible that an infected mother can pass on the virus to her newborn infant
    - Sexual transmission also is a possibility

# HEPATITIS G (HGV)

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- **Treatment**

- There is no specific treatment for any form of acute hepatitis. Patients should rest in bed as needed, avoid alcohol, and be sure to eat a balanced diet.

- **Prognosis**

- What little is known about the course of hepatitis G suggests that illness is mild and does not last long.

- **Prevention**

- Since hepatitis G is a blood-borne infection, prevention relies on avoiding any possible contact with contaminated blood. Drug users should not share needles, syringes, or other equipment.

# SPECIAL CONSIDERATIONS

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- **Chemically Dependence Counselors**

- In the typical counseling setting, it is virtually impossible to contract hepatitis
- The chemical dependence patient may exhibit some symptoms early in the disease process that could mimic mild withdrawal (especially opiate withdrawal)
- Remember to reinforce the facts that Hepatitis A is a self – limited disease and that there are treatments available for Hepatitis B and C.
- Remember to reinforce the fact that use of alcohol and other drugs is detrimental to the course of hepatitis

# SPECIAL CONSIDERATIONS

- **Chemically Dependent Patients**
  - Alcohol will worsen all forms of hepatitis
  - Alcohol alone can cause a form of hepatitis (alcohol induced hepatitis)
    - More than 2 million Americans suffer from alcohol-related liver disease. Its symptoms include fever, jaundice (abnormal yellowing of the skin, eyeballs, and urine), and abdominal pain. Alcoholic hepatitis can cause death if drinking continues. If drinking stops, this condition often is reversible. About 10 to 20 percent of heavy drinkers develop alcoholic cirrhosis, or scarring of the liver.
  - Alcohol can also cause a condition know as fatty liver, which is sometimes misinterpreted as hepatitis. The liver enzymes are elevated and the liver is enlarged on examination. However, this is due to the body using alcohol as an energy source and the fat from the food intake being stored in the liver. The condition will resolve in several weeks once alcohol use is stopped.

# SPECIAL CONSIDERATIONS

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- **Chemically Dependent Patients**
  - Some medications can cause or worsen hepatitis
    - Naltrexone used as an opiate blocker or alcohol craving reducer
    - Statins used to treat hypercholesterolemia
  - Any drug that impacts negatively on the immune system can have a detrimental effect on the course of liver disease

# SPECIAL CONSIDERATIONS

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- **Chemically Dependent Patients**
  - **Drugs associated with hepatitis (non-viral)**
    - **Prescription pain medications that contain acetaminophen (over 4 grams a day can cause significant liver toxicity)**

# SPECIAL CONSIDERATIONS

- **Chemically Dependent Patients**
  - **Drugs associated with hepatitis (non-viral)**
    - **Cocaine**
      - Cocaine related fulminant liver failure Campos Franco J; Martínez Rey C; Pérez Becerra E; González Quintela A An Med Interna. 2002; 19(7):365-7
        - » A 23 year-old woman developed biochemical signs of acute severe hepatitis together with confusion and flapping tremor after snorting a large dose of cocaine. Blood levels of cocaine were very high and a liver biopsy was performed a few days later showing centrilobular necrosis. She recovered completely with conservative measures.
        - » Cocaine toxicity should be considered in similar cases of fulminant liver failure.

# SPECIAL CONSIDERATIONS

- **Chemically Dependent Patients**
  - **Drugs associated with hepatitis (non-viral)**
    - **Glue sniffing**
      - A case of toxic hepatitis induced by habitual glue sniffing Park CK; Kwon KT; Lee DS; Jo CM; Tak WY; Kweon YO; Kim SK; Choi YH Taehan Kan Hakhoe Chi. 2003; 9(4):332-6
        - » The link between toxic hepatitis and exposure to organic solvents is relatively well-documented, but there are no specific laboratory or histologic findings diagnostic of chemical-induced hepatitis. Clinical history, therefore, is very important in making a diagnosis. A history of glue sniffing is sometimes overlooked and glue sniffing has not received much attention as a cause of hepatitis. Toluene, a main organic solvent in glue, is known to cause disturbances in various organs such as the heart, nervous system, liver and kidneys. We present a case of hepatitis in an individual who has sniffed glue for euphoria for 3 years.
        - » There is an increasing tendency towards glue sniffing among young adolescents today, so toxicity caused by exposure to organic solvents should be considered as one possible cause of hepatitis in young adolescents.

# SPECIAL CONSIDERATIONS

- **Chemically Dependent Patients**

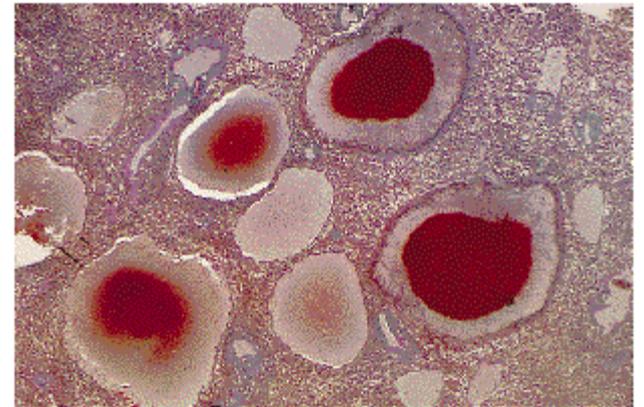
- **Drugs associated with hepatitis (non-viral)**

- **Buprenorphine**

- Hepatitis after intravenous buprenorphine misuse in heroin addicts. Berson A; Gervais A; Cazals D; Boyer N; Durand F; Bernuau J; Marcellin P; Degott C; Valla D; Pessayre D J Hepatol. 2001; 34(2):346-50
        - » **BACKGROUND:** Sublingual buprenorphine is used as a substitution drug in heroin addicts. Although buprenorphine inhibits mitochondrial function at high concentrations in experimental animals, these effects should not occur after therapeutic sublingual doses, which give very low plasma concentrations.
        - » **CASE REPORTS:** We report four cases of former heroin addicts infected with hepatitis C virus and placed on substitution therapy with buprenorphine. These patients exhibited a marked increase in serum alanine amino transferase (30-, 37-, 13- and 50-times the upper limit of normal, respectively) after injecting buprenorphine intravenously and three of them also became jaundiced. Interruption of buprenorphine injections was associated with prompt recovery, even though two of these patients continued buprenorphine by the sublingual route. A fifth patient carrying the hepatitis C and human immunodeficiency viruses, developed jaundice and asterixis with panlobular liver necrosis and microvesicular steatosis after using sublingual buprenorphine and small doses of paracetamol and aspirin.
        - » **CONCLUSIONS:** Although buprenorphine hepatitis is most uncommon even after intravenous misuse, addicts placed on buprenorphine substitution should be repeatedly warned not to use it intravenously. Higher drug concentrations could trigger hepatitis in a few intravenous users, possibly those whose mitochondrial function is already impaired by viral infections and other factors

# SPECIAL CONSIDERATIONS

- **Chemically Dependent Patients**
  - **Drugs associated with hepatitis (non-viral)**
    - **Anabolic Steroids**
      - **Peliosis Hepatitis (Blood filled cysts in the liver)**



# SPECIAL CONSIDERATIONS

- **Chemically Dependent Patients**
  - **Drugs associated with hepatitis (non-viral)**
    - **Ecstasy-induced toxic hepatitis** *Aknie X Presse Med. 2004; 33(18 Suppl):18-20*
      - **INTRODUCTION:** The use of ecstasy (MDMA) has developed in the young since the eighties. Among the severe adverse events induced by this synthetic drug, the hepatotoxicity related to MDMA and to its physiopathological mechanism warrant attention.
      - **OBSERVATION :** A 21 year-old man consulted for anaemia that had persisted over the past months with abnormality in hepatic profile. The imputability of ecstasy in perturbations in his hepatic profile was highly probable in view of the fact that his transaminase level returned to normal one month after he stopped taking the drug, all the viral markers of hepatitis became negative and in the absence of concomitant consumption of any psycho-active drugs other than cannabis.
      - **DISCUSSION:** A review of the literature showed the great variability in clinical pictures related to the hepato-toxicity of ecstasy, ranging from acute to lethal, fulminating hepatitis. The physiopathological mechanism of this phenomenon is little known. Various hypotheses are evoked with, among others, immuno-allergic-type hypersensitivity, phenomenon of apoptosis, vitamin E deficiency, and the role of occasionally concomitant malignant hyperthermia. The part played by the metabolites of the synthetic drug has also been suggested as well as individual variations in genetic origin with regards to the risk of developing acute hepatitis after ingestion of ecstasy.
      - The hepato-toxicity of this drug does not appear to be dose-dependant nor related to the cumulated duration of exposure

# SPECIAL CONSIDERATIONS

- **Chemically Dependent Patients**
  - **Drugs associated with hepatitis (non-viral)**
    - **Herbs used to treat Hepatitis**
      - Hepatitis associated with Chinese herbs. McRae CA; Agarwal K; Mutimer D; Bassendine MF *Eur J Gastroenterol Hepatol.* 2002; 14(5):559-62
        - » Traditional Chinese herbal medicines are widely available in Western society and are popular as a form of 'natural' alternative medicine. Their use is increasing, as they are perceived to be free of side effects, but they remain largely unregulated. We describe two patients who suffered severe hepatitis, one of whom died, after taking Chinese herbal remedies for minor complaints. We also review the English-language literature on hepatitis associated with Chinese herbs. Two products appear to be implicated frequently: Jin bu huan was taken by 11 patients, and *Dictamnus dasycarpus* was taken by six patients, including both fatal cases. It is difficult to provide conclusive evidence of what caused hepatitis, as these products are mixtures that may contain adulterants. These cases highlight not only the potential dangers of these products to consumers but also the need for greater control of their manufacture and use.

# SPECIAL CONSIDERATIONS

- **Chemically Dependent Patients**
  - **Drugs associated with hepatitis (non-viral)**
    - **Cannabis use and progression of fibrosis**
      - Daily cannabis smoking as a risk factor for progression of fibrosis in chronic hepatitis C. Hézode C; Roudot-Thoraval F; Nguyen S; Grenard P; Julien B; Zafrani ES; Pawlotsky JM; Pawlostky JM; Dhumeaux D; Lotersztajn S; Mallat AHepatology. 2005; 42(1):63-71
        - » Cannabinoids present in Cannabis sativa (marijuana) exert biological effects via cannabinoid receptors CB1 and CB2. We recently demonstrated that CB1 and CB2 receptors regulate progression of experimental liver fibrosis. We therefore investigated the impact of cannabis smoking on fibrosis progression rate in patients with chronic hepatitis C (CHC). Two hundred seventy consecutive untreated patients with CHC of known duration undergoing liver biopsy were studied. Patients were categorized as noncannabis users (52.2%), occasional users (14.8%), or daily users (33.0%), and the relationship between cannabis use and fibrosis progression rate (FPR) or fibrosis stage was assessed. In conclusion, daily cannabis smoking is significantly associated with fibrosis progression during CHC. Patients with ongoing CHC should be advised to refrain from regular cannabis use.

# SPECIAL CONSIDERATIONS

- **Chemically Dependent Patients**

- Hepatitis-associated knowledge is low and risks are high among HIV-aware injection drug users in three US cities. Heimer R; Clair S; Grau LE; Bluthenthal RN; Marshall PA; Singer M *Addiction*. 2002; 97(10):1277-87
  - AIMS: Injection drug use is a major risk factor for HIV and hepatitis infections. Whereas programs to prevent new infections have focused on HIV, they have generally neglected hepatitis B and C. This study was designed to examine the interrelationships among HIV and hepatitis knowledge, risky drug preparation and injection practices, and participation in syringe exchange programs (SEPs).
  - DESIGN : Surveys of injection drug users (IDUs) collected data on socio-demographics, medical history, drug use and injection practices, and HIV- and hepatitis-related knowledge.
  - SETTING : Inner-city US neighborhoods in Chicago, IL, Hartford, CT and Oakland, CA.
  - PARTICIPANTS : The study population was a convenience sample of 493 IDUs recruited using street outreach and snowball sampling strategies
  - FINDINGS : HIV knowledge was significantly higher than hepatitis knowledge among SEP customers and non-customers alike. Elevated hepatitis knowledge was associated with a history of substance abuse treatment, hepatitis infection, hepatitis B vaccination and injection practices that reduced contact with contaminated blood or water but not with SEP use. SEP customers were consistently less likely to engage in risk behaviors, with the notable exception of safely staunching blood postinjection.
  - CONCLUSION : Increased hepatitis awareness among IDUs is necessary for reducing hepatitis transmissions. Although SEPs continue to effectively disseminate HIV prevention messages-as evidenced by lowered risk behaviors among their customers-they must do more to prevent hepatitis transmissions.

# SPECIAL CONSIDERATIONS

- **Chemically Dependent Patients**

- Validity of injecting drug users' self report of hepatitis A, B, and C. Schlichting EG; Johnson ME; Brems C; Wells RS; Fisher DG; Reynolds G Clin Lab Sci. 2003; 16(2):99-106
  - **OBJECTIVE:** To test the validity of drug users self-reports of diseases associated with drug use, in this case hepatitis A, B, and C.
  - **DESIGN:** Injecting drug users (n = 653) were recruited and asked whether they had been diagnosed previously with hepatitis A, B, and/or C. These self-report data were compared to total hepatitis A antibody, hepatitis B core antibody, and hepatitis C antibody seromarkers as a means of determining the validity of the self-reported information.
  - **SETTING:** Anchorage, Alaska.
  - **PARTICIPANTS:** Criteria for inclusion included being at least 18-years old; testing positive on urinalysis for cocaine metabolites, amphetamine, or morphine; having visible signs of injection (track marks).
  - **RESULTS:** Subgroup analyses revealed significant differences in sensitivity associated with previous substance abuse treatment experience for hepatitis B self-report and with gender for hepatitis C self-report.
  - **CONCLUSION:** Given the low sensitivity, the validity of drug users, self-reported information on hepatitis should be considered with caution.

# SPECIAL CONSIDERATIONS

- **Chemically Dependent Patients**

- Hepatitis B virus infection and vaccination among young injection and non-injection drug users: missed opportunities to prevent infection. Kuo I; Sherman SG; Thomas DL; Strathdee SA  
Drug Alcohol Depend. 2004; 73(1):69-78
  - INTRODUCTION: We examined correlates of HBV infection and vaccination and the missed vaccination opportunities among young injection drug users (IDUs) and non-injection drug users (NIDUs).
  - METHODS: Two hundred IDUs and 124 NIDUs aged 15-30 years were studied.
  - RESULTS: More IDUs had been infected with HBV in the past than NIDUs (37% versus 19%,  $P = 0.001$ ). Among male and female IDUs, injection drug use behaviors were significantly associated with past infection. For female IDUs, being African-American and trading sex were also associated with previous infection. Among NIDUs, being female and longer time since sexual debut were associated with past infection. Overall, 11% were vaccinated (10% IDU versus 14% NIDU,  $P = 0.30$ ). Younger age and drug treatment history were associated with vaccination. Most susceptibles (84%) experienced at least one missed opportunity for vaccination.
  - CONCLUSION: Young drug users remain at high risk for HBV infection. Vaccination rates remain low despite multiple opportunities for vaccination. An integrated HBV immunization effort should be coordinated among venues frequented by young drug users.

# SPECIAL CONSIDERATIONS

- **Chemically Dependent Patients**

- An outbreak of hepatitis A amongst injecting drug users. O'Donovan D; Cooke RP; Joce R; Eastbury A; Waite J; Stene-Johansen K Epidemiol Infect. 2001; 127(3):469-73
  - This descriptive study investigated an outbreak of hepatitis A virus (HAV) infection among injecting drug users (IDUs) and their contacts. Twenty-seven cases of acute HAV infection were identified in a 5-month period. Connections with the local injecting drug using (IDU) population were established for 25 of the cases of whom 14 admitted to injecting drug use. HAV RNA genotyping revealed two HAV variants, closely related to variants found in Scandinavian IDUs and in South East Asia. The study demonstrates that once HAV enters the IDU population extensive outbreaks are possible.
  - We recommend that all IDUs should be tested for HAV and hepatitis B virus (HBV) infections and offered combined hepatitis A and B vaccines if non-immune.

# SPECIAL CONSIDERATIONS

- **Chemically Dependent Patients**

- What do intravenous drug users think about hepatitis? Grimnes G Tidsskr Nor Laegeforen. 2005; 125(16):2164-6
  - **BACKGROUND:** Intravenous drug users have a high frequency of infectious diseases related to their needle usage, and a higher risk of death. The purpose of this study was to illustrate how intravenous drug users see their health, diseases, and related risks. This article focuses on results related to hepatitis.
  - **MATERIAL AND METHODS:** Seven informants were recruited from a low-threshold civic health centre. The sole criterion for joining the study was previous or current intravenous drug use. Semi-structured interviews were recorded, and the data edited and analysed with a qualitative approach.
  - **RESULTS AND INTERPRETATION:** The informants had experience with and were generally well informed about hepatitis, though some of their perceptions were in disagreement with existing medical knowledge. Self-treatment with intravenous hydrogen peroxide was described as a cure for hepatitis. Despite their accurate knowledge about the risks of infection, the informants still described various methods of sharing their needles and syringes. Their reasons for sharing could be limited access to clean equipment, and an inability to cope.
  - Knowledge alone is inadequate in order to reduce risk behaviour, and a variety of methods, such as access to clean drug equipment, should remain the focus of preventive efforts.

# SPECIAL CONSIDERATIONS

- Risk of occupational exposure to HBV
  - Related to degree of contact with blood in the workplace
    - Most healthcare workers cannot remember a needle injury and exposure may have resulted from direct or indirect blood or body fluid exposures that inoculated HBV into cutaneous scratches, abrasions, burns and other lesions or mucosal surfaces.
  - Related to the hepatitis B e antigen (HBeAg) status of the source person
    - Risk of developing hepatitis after needle injury was 22 – 31% if the source person was hepatitis B surface antigen and Be positive
    - Risk of developing hepatitis after needle injury was 1 – 6% if the source person was HBsAg positive but HBeAg negative.

# SPECIAL POPULATIONS

## Post exposure procedures for healthcare workers

Vaccination and antibody response status of exposed worker	Treatment		
	Source: Hepatitis B surface antigen positive patient	Source: Hepatitis B surface antigen negative patient	Source: unknown or not available for testing
Unvaccinated	Hepatitis B immune globulin (HBIG) x's 1 Hepatitis B vaccine series	Hepatitis B vaccine series	Hepatitis B vaccine series
Previously vaccinated and known positive response to vaccine	No treatment	No treatment	No treatment
Previously vaccinated and known negative responder to vaccine	HBIG x's 1 and initiate revaccination or give HBIG x's 2	No treatment	If known high risk source, treat as if source were hepatitis B surface antigen positive
Previously vaccinated but unknown response to vaccine	Test exposed person for antibody to hepatitis b surface antigen (HBsAg): if adequate antibody – no treatment, if inadequate give HBIG x's 1 and vaccine booster	No treatment	Test exposed person for antibody to hepatitis B surface antigen: if adequate do not treat, if inadequate levels, administer hep B vaccine booster and recheck titer in 1 – 2 months

# ADDITIONAL INFORMATION

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- HEPATITIS FOUNDATION INTERNATIONAL
  - [www.hepfi.org](http://www.hepfi.org)
  - (800) 891 -0707
- CDC, HEPATITIS BRANCH
  - (800) 443 - 7232
- AMERICAN LIVER FOUNDATION
  - [www.liverfoundation.org](http://www.liverfoundation.org)
  - (800) 223 - 0179
- NATIONAL DIGESTIVE DISEASES CLEARING HOUSE
  - (301) 654 - 3810
- <http://www.cdc.gov/nicdod/diseases/hepatitis/c/fact.htm>