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L XIII

Viral Hepatitis

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Viral Hepatitis

- ❖ Define as infection of liver caused by dozen of viruses.
- More than 30 years ago only hepatitis A virus (HAV) and hepatitis virus B (HBV)were known.
- Hepatitis non-A, non-B (HNANB)
- Today's HAV. HBV, HCV. HDV HEV, and HGV have been identified and are recognised as aetiological agent of viral hepatitis.
- In addition many other viruses may be implicated in **hepatitis as**
  - **Cytomegalo-virus,**
  - **Epstein-Barr virus,**
  - **Yellow fever virus**
  - **Rubella virus .**
  - **Herpes simplex viruses,**
  - **Varicella viruses and**
  - **adenoviruses**

HEPATITIS A

Hepatitis A

is an acute infectious disease caused by hepatitis A virus (HAV). (formerly known as "infectious" hepatitis or epidemic jaundice)

- **The disease is having nonspecific symptoms such as**
- ***fever, chills, headache, fatigue, generalized weakness and aches and pains, followed by anorexia, nausea, vomiting, dark urine&jaundice.***

➢ Disease spectrum is **characterized by the occurrence of**

➢ **subclinical or asymptomatic cases.**

➢ **HAV disease** is **benign** with **complete recovery** in **several wks**

- **Case Fatality rate of icteric cases is <0.1%**, usually **from**

➢ **acute liver failure and mainly affects older adults.**

Hepatitis A

- HAV is endemic in most developing countries, with
  - frequent minor or major outbreak
- The exact incidence of the disease is difficult to estimate
  - because of the high proportion of asymptomatic cases.

However

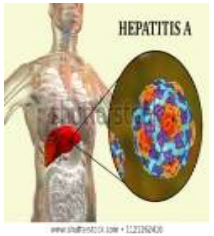
- WHO estimates the global burden that about
- 1.4 million cases /y or about
- 10-50 persons /100,000 annually affected WW
- Poor standard of hygiene and sanitation, facilitated the spread of infection

- For practical purposes the world divided into areas

Geographical areas having

I. *Areas with* high, levels of HAV infection
II. *Areas with* intermediate levels of HAV infection or
III. *Areas with* low levels of HAV infection

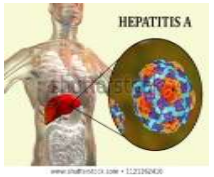
- ***Areas with High Levels of* HAV *infection*** (**High Endemicity**)
- **In developing countries with very poor, sanitation and hygienic practices**
- **Most infection occurs at Early childhood and are asymptomatic**
  - **Thus clinically apparent HAV is rarely seen in these areas**
- **Most children (90%) have been infected with the HAV before the age of 10 yrs.**
  - **Those infected in childhood do not experience any noticeable symptoms.**
- **Epidemics are uncommon because older children and adults are generally immune.**
  - **Symptomatic disease rates in these areas are low and**
    - **outbreaks are rare ??**



Areas with intermediate levels of HAV *infection*

(Intermediate Endemicity)

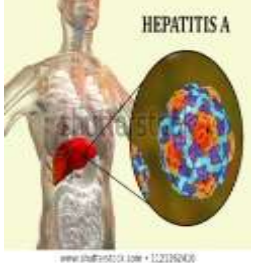
- Countries transit from developing to developed economies,
  - where sanitary conditions are variable gradually
  - will move from high endemicity to intermediate endemicity
  - HAV become more serious problems in these areas.
- children often escape infection in early childhood. and
  - reach adulthood without immunity
  - but are expose later in life.
- so in these areas most cases occurs during
  - late childhood & early adulthood..
- Ironically, these improved economic and sanitary conditions
  - may lead to a higher susceptibility in older age groups and
- Higher disease rates, occur in adolescents and adults, and
- large outbreaks can occur.
  - Thus, interestingly



- Thus, interestingly
  - **with the transition from high to intermediate endemicity,**
  - **the incidence of clinically significant hepatitis A increases.??**

- ***Areas with low levels of* HAV *infection* (Low Endemicity)**
  - **In developed countries with good sanitary and hygienic conditions**
  - **infection rates** are **low.**
    - ✓ **Disease may occur among adolescents and adults in high-risk groups**, such as,
    - ✓ **homosexual men, people travelling *to* areas of high endemicity**

Epidemiological determinants



AGENT FACTORS

The causative agent, the HAV,

It multiplies only in hepatocytes.

❖ **Faecal shedding of the HAV is at its highest during**

*** the later part of the incubation period and**

***early acute phase of illness.**

(b) Resistance

- ❑ **The virus is fairly resistant to**
  - **low pH, heat & chemicals.**
  - **It survive more than 10 wks**
  - **in well H2O**
  - **It withstands heating to 60 Cº**
  - **for one hour,**

- ✓ **The virus is inactivated by ultraviolet rays and**
- ✓ **by boiling for 5 minutes**
- ✓ **or autoclaving**
- ✓ **Formalin is an effective disinfectant**

- ❑ **not affected by chlorine doses usually employed for chlorination**

Reservoir of Infection :

- **The human cases are the only reservoir of infection.**
  - The **cases range from asymptomatic to severe infections**
    - **Asymptomatic (anicteric)** infections are especially **common in children**.
- These cases **play an important role in maintaining the chain of transmission in the community.**
  - **There is no evidence of a chronic carrier state**.

(d) Period of Infectivity :

- **Risk of HAV transition is greatest**
  - **from 2 weeks before to 1 week after** the **onset of jaundice.**
    - **infectivity falls rapidly with the onset of jaundice**

(e) Infective Material :

- **Mainly man's faeces.**
  - **Blood, serum and other fluids are infective** during the **brief stage of viremia**

(F) Virus Excretion :

- HAV is excreted in the faeces for about 2 weeks before the onset of jaundice and for up to 2 weeks thereafter.
- virus may also be excreted in the urine
- There is little evidence for HAV transmission by exposure to urine or nose-pharyngeal secretions of infected patients

HOST FACTORS

(a) AGE :People from all ages may be infected if susceptible.

- Infection with HAV is more frequent among children than in adults.
  - In young children, infections tend to be mild or subclinical
  - the clinical severity increases with age.
- The ratio of anicteric to icteric cases in adults is about 1 :3;
- in children, it may be as high as 12: 1.
  - However, faecal excretion of HAV antigen and RNA persists longer in the young than in adults

(b) SEX : Both sexes are equally susceptible

(c) Immunity:

- **Immunity after attack probably lasts for life;**
- **second attacks** have been reported in **about 5 %** of patients.
- **Most people in endemic areas acquire immunity through subclinical infection.**

Who is at risk?

- **Anyone who has not been vaccinated or previously infected can get HAV infection**
- In a **high endemicity** areas **most HAV infection occur during early child hood.**
- **Risk factors in intermediate and high endemicity areas include:**

***poor sanitation;**

**** lack of safe water;**

***travelling to areas of high endemicity without being immunized**

*****Living in a household with an infected person;**

****being a sexual partner of someone with acute HA infection**

Environmental Factors

Cases may occur throughout the year.

Poor sanitation and overcrowding favour the spread of infection

- ❖ giving rise to water-borne and food-borne epidemics.
- ❑ when standards of hygiene and sanitation are improved, morbidity may increase.?????

Incubation Period (IP)

- ❖ 10-50 days (usually 14-28 days}.
- ❖ Length of the IP is proportional to the dose of the virus ingested

❑ Clinical Spectrum

- ❖ The onset of jaundice is often preceded by as nausea, vomiting
- ❖ BUT anicteric hepatitis is more common.
- ❑ 98 % of HAV cases resolves completely

The outcome of infection with HAV is as shown

outcome of infection with HAV

outcome	Child	Adult
Unapparent (subclinical infection)	80-95%	10-25%
Icteric disease	5-20%	75-90%
Complete recovery	>98%	>98%
Chronic disease	None	None
Mortality rate	0.1%	0.3-2.1%

Modes Of Transmission

(a) Faecal-Oral Route :

This is the **major route** of transmission. **It may occur by**

- **DIRECT (person-to-person) contact** or
- **INDIRECTLY by contaminated water, food or milk**.

- **in developed** countries **Water-borne** transmission**, is not a major factor, where food-borne outbreaks are becoming more frequent**. *For example, consumption of salads and vegetables, and of raw or inadequately cooked shellfish* **and** *oysters cultivated in sewage* **polluted water is associated with epidemic outbreaks of hepatitis A. ?????**

- **Food handlers** are **critical role in common-source food-borne** HAV transmission.

- **Children play an important role in HAV transmission ???? as they generally have asymptomatic or unrecognized illness**

(b) *Parenteral Route*:

- HAV very **is rarely**, (i.e. by blood and blood products or by skin penetration through contaminated needles.
- **This may occur during the stage of viraemia**.
- **Health care personnel** do not have an increased prevalence of **HAV infection** and **nosocomial HAV transmission is rare**.

(c) *Sexual Transmission*:

- mainly may occur among homosexual men because of oral-anal contact.

Diagnosis

HA cases clinically are not distinguishable from other types of acute viral hepatitis.

abnormal liver function tests, such as serum alanine amino transferase (ALT) and bilirubin,

- **Anti-HAV appears in the IgM fraction during**
  - **the acute phase,**
  - **peaking about 2 weeks after elevation of liver enzymes.**

Anti-HAV **IgM**

- Anti-HAV **IgM** usually **declines to non-detectable levels**
- **within 3-6 months**.
- Anti-HAV **IgG** appears **soon after** the **onset** of disease and
- **persists for decades**.

- Thus, **detection of IgM-specific** anti-HAV in the **blood of an acutely infected patient confirms the diagnosis of HAV**
- **Demonstration of HAV particles or** HAV antigens **specific viral antigens in the faeces, bile and blood.**
  - **HAV is detected in the stool from about**

- **2 weeks prior** to the **onset of jaundice, up to 2 weeks after.**

- **Additional tests include reverse transcriptase polymerase chain reaction (RT-PCR) to detect the hepatitis A virus RNA, and may require specialised laboratory facilities**

The clinical, virologic and serological events following exposure to HAV are as shown in Fig. 1.

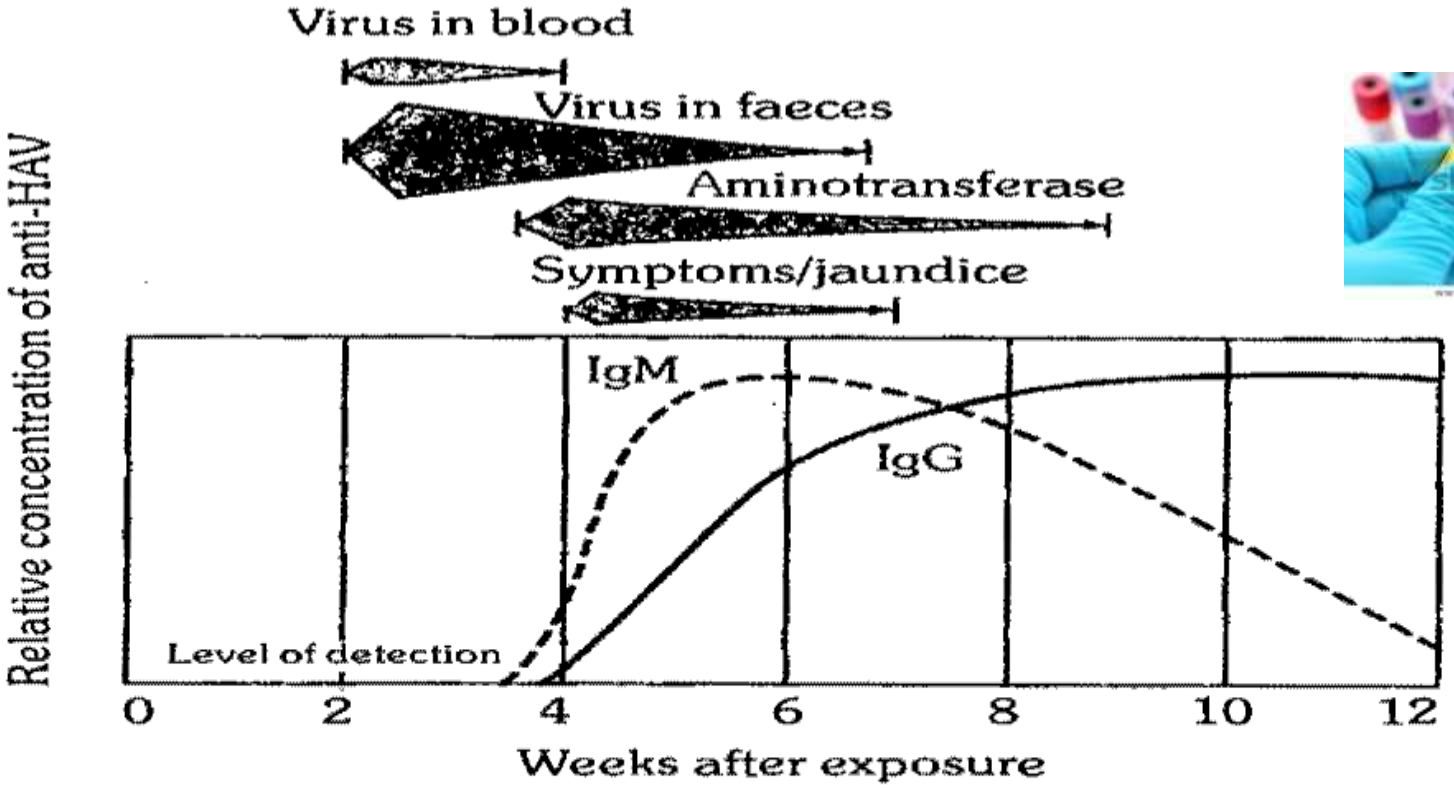


FIG. 1
Immunologic and biologic events associated with human infection with hepatitis A virus.

Source : *(6)*

PREVENTION AND CONTAINMENT

I. *Control of Reservoir*

Control of reservoir is DIFFICULT because of the following

(a) faecal shedding of the virus is at its height during the incubation period and early phase of illness

(b) the occurrence of large number of subclinical cases

(c) absence of specific treatment, and

(d) low socio-economic profile of the population usually involved.

- Strict isolation of cases is not a useful control measure because of (a)&{b)
  - However, attention should be paid to the usual control measures such as notification, complete bed rest and disinfection of faeces and fomites.

The use of 0.5 %sodium hypochlorite has been strongly recommended an effective disinfectant

II. *Control of* Transmission

The best means of reducing the spread of infection is by

- **promoting of personal and community hygiene,**
  e.g. ***hand washing before eating and after toilet***;
- **Sanitary disposal of excreta**
- **Prevent H2O, food & milk** contamination
- **purification of community water with**
  - **adequate chlorination 1mg/L of free** residual chlorine

can **cause distraction** of the **virus in 30 minutes** at Ph ≤ 8.5

- **boiling water** is recommended **during epidemic**
- . Proper **autoclaving of needles syringes other equipment**

III . *Control of susceptible population*

Targeted protection of high-risk groups should be considered **in low and very low endemicity, settings.**

Groups at increased risk of hepatitis A include

- **Travellers to areas of intermediate or high endemicity,**
- **Men having sex with men,**

❑ **In addition, pts with chronic liver disease are at increased risk**

- **for fulminant hepatitis A** and ***should be vaccinated*** .

1. Vaccines :

Two types of hepatitis A vaccines are currently used (WW)

(a) Formaldehyde inactivated vaccines –produced in **several countries** and which are most commonly used WW

{b) Live attenuated vaccines –which are manufacture **in China** and are available in several countries.

❑ Inactivated hepatitis A vaccine

- ❖ licensed for **use in persons ≥12 months** of age.
- ❖ **2 dose administration into the deltoid muscle**.
- ❖ **The interval between the first** (primary) dose **and second** (booster) dose is commonly **6-12 months**;
  however, the interval between the doses is flexible and can be **extended to 18-36 mths**
- ❖ **It can be administered simultaneously with other vaccines.**
- ❖ **Protective efficacy** is about **94 %.**.

❑ Live attenuated vaccine is

- ❑ administered as a **single subcutaneous dose**

Both inactivated and live attenuated hepatitis A vaccines are highly immunogenic and immunization will generate long-lasting possibly life-long, protection against the disease in **children** and **adults.**

Immunization

- **Vaccination** against HA **should be part of a comprehensive plan**
- for the **prevention and control** of viral hepatitis.

Generally speaking,

- **Countries with intermediate endemicity** will benefit **the most from universal immunization of children**.
- **Countries with low endemicity may consider vaccinating**
- **high-risk adults**.
- In **countries with high endemicity**, the **use of vaccine is limited as most adults are naturally immune**

Human Immunoglobulin to induce passive immunity

- **Recommended for**;

a-susceptible person traveling to endemic areas.

b- close personal contacts of Pt with HVA .

c- for the control of outbreaks in institutions

Gamma globulin given:

Gamma globulin given

❖ **Gamma globulin** given:

Before exposure to virus **or Early during IP** will **prevent or attenuate a clinical** illness **BUT NOT always prevent infection and excretion of the virus**

➢ **unapparent** or **subclinical illness may develop.** .

The efficacy of the passive immunization given in proper dosage

❖ **within 1-2 Ws of exposure it prevent 80-90%**

❖ **if given after onset of symptoms no benefit**

❖ **duration of protection is,, limited** to approximately

➢ **1-2 months and 3-5 months following administration of lgG at dose of 0.02 and 0.06 ml/kg body weight, respectively.**

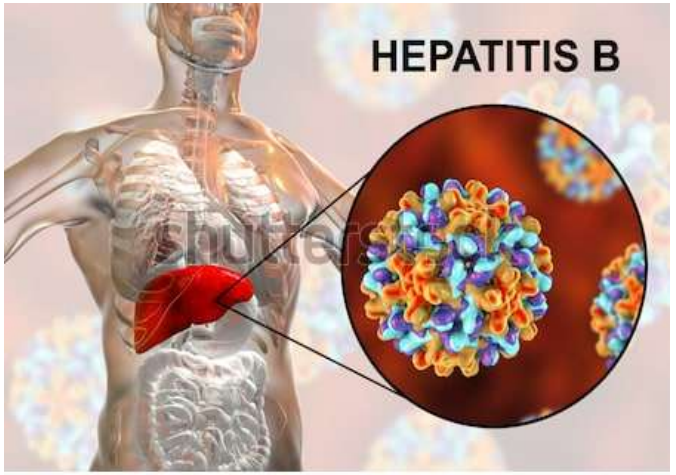
Hepatitis A vaccine in Jordan

The Hepatitis A vaccine is **part of the Jordan National Immunization Program**

The vaccine given to all children within the Kingdom, regardless of their nationality or citizenship status .
they focus on children younger than six years, as they are the most vulnerable to the disease.

The vaccine is given in two doses, six months apart, after the age of one, and is 94% effective in children.

-	2000	2001	2002	2003	2004	2005	2006	2007	2008	2010	2011	2012	2013	2014	2015	2016	2017
Capital Directorate	229	120	100	116	62	40	53	34	35	65	48	110	160	50	48	36	37
Madaba Directorate	15	6	5	4	3	6	10	6	7	3	14	7	28	5	0	2	0
Balqa Directorate	80	60	21	28	22	16	23	52	31	39	26	20	73	37	25	10	8
Ramtha Directorate	67	56	30	27	22	33	25	36	17	7	9	52	85	23	23	10	16
Ma'an Directorate	32	17	3	34	22	11	11	0	0	1	0	1	51	18	3	10	1
Deir Alla Directorate	26	4	5	3	13	5	10	10	34	4	12	11	18	25	1	3	11
Agwar Shamaliyah Directorate	14	22	150	116	26	26	102	38	15	65	73	73	10	11	3	1	2
Tafeileh Directorate	3	11	2	3	6	2	6	0	5	1	0	0	8	2	5	2	5
Bani Kenaneh Directorate	4	3	4	30	16	2	2	6	4	2	1	8	16	5	3	2	12
Badia Shamaliyah Directorate	27	47	6	18	7	2	0	2	5	4	1	6	160	18	0	7	35
Betra Directorate	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2
Irbid Directorate	96	71	35	20	11	5	104	16	19	17	50	67	68	24	36	13	15
Ajloun Directorate	62	32	7	13	27	13	9	5	0	7	23	26	16	13	1	0	5
Mafraq Directorate	71	92	20	13	35	8	56	28	74	38	33	22	143	128	34	14	25
Karak Directorate	45	25	4	9	3	4	3	18	17	7	13	6	2	21	34	25	8
East Amman Directorate	18	18	38	38	14	21	22	48	29	14	13	10	52	11	13	14	20
Shounah Janoobiyah Directorate	11	4	5	2	4	5	4	10	10	2	19	24	9	1	3	10	0
Koura Directorate	5	9	27	22	4	4	2	8	2	1	0	4	14	10	2	1	0
Zarqa Directorate	125	81	33	35	21	27	25	34	101	40	49	49	138	91	30	7	32
Aqaba Directorate	0	13	0	4	2	0	0	5	4	0	0	0	1	6	2	7	5
Jerash Directorate	17	63	11	17	22	36	14	30	47	60	34	8	24	45	25	77	26
Agwar Janoobiyah Directorate	-	-	-	-	-	-	1	1	8	0	0	5	6	0	0	0	1
Total	947	754	506	552	342	266	482	387	464	377	418	509	1082	544	291	251	266



HEPATITIS B

Brucellosis	467
Incidence Rate	4.645