PREVENTION & CONTROL

HEPATITIS A VACCINES

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As countries prosper, anti-HAV seroprevalance decreases; that is why infection is more commonly encountered in advanced age cases in developed countries. The presence of the risk of developing fulminant hepatitis and the increase in touristic travels to endemic areas, emphasizes the importance of active immunization. Studies for preparing a vaccine started in the late 70's and the first vaccine was introduced in 1992.

INACTIVATED VACCINES

Today, many firms introduced several vaccines obtained from different cell cultures.

HAVRIX®, (SmithKline Beecham Biologicals): The strain used in this vaccine is HM-175. It is purified by ultrafiltration and colon chromatography, and inactivated in 37°C in 250 µg/ml formaldehyde for 15 days. Inactivated virions are absorbed to aluminum hydroxide which is an adjuvant. The vaccine is available in two formulations: pediatric form provides a 0.5 ml dose containing 720 ELISA units; and the adult form provides 1 ml containing 1440 ELISA units. It is recommended to be stored at 2-8°C and its shelf life is 2 years. The vaccine is safe and immunogenic. Within one month from vaccination a seroconversion rate of 100% is reported. Recommended adult dosage is 1440 or 2x720 ELISA units and the pediatric dosage is 2x360 ELISA units. The vaccine should be administered using a 3-dose schedule; initially at month 0, then month 1 and a booster at month 6 to 12. The vaccine, which is available in our country, is claimed to be protective for as long as 20 years.

VAQTA®, (Merck & Co., Inc.): The strain that is used is CR326F. The vaccine has two formulations; 50 U/ml for adults and 25 U in 0,5 ml for children. This vaccine should also be stored in 2-8°C and has a shelf life of 2 years. The vaccine is safe and efficient for both children and adults. Again, this vaccine is well tolerated.

AVAXIM®, (Pasteur – Merieux Serums & Vaccines): In this vaccine GBM strain of HAV is used. After purification by ultrafiltration and chromatography it is inactivated by using formaldehyde. A 2-dose schedule is recommended for administration. Two doses of 160 ELISA units should be given at month 0 and 1. After immunization a seroconversion rate of at least 90% is reported.

EPAXAL BERNA®, (Swiss Serum and Vaccines Institute): It is produced by using the RG-SB strain of HAV. Influenza virosomes are used as adjuvant. The seroconversion rate of this vaccine is reported to be 100% after the second dose. Recommended schedule of administration is 500 ELISA Units given with 1 year's interval. The side effect rate of this vaccine is said to be very mild, just like the others.

AIMMUGEN®, (Japanese Chemo Sero Therapeutic Research Institute): Clinical studies about this vaccine are still in progress.

All vaccines of this type are stable and may be stored for 2 years at 2-8°C. They should be kept away from direct sunlight, should not be diluted or mixed with any other vaccines in the same syringe. They should be administered intramuscularly to deltoid muscle. Gluteal region should be avoided since the effectiveness diminishes. Subcutaneous administration is not recommended other than for hemophiliac patients. Vaccine should not be given to patients with febrile disease or pregnant patients if not clearly indicated. Side effects of the vaccines are usually mild and negligible. Moderate fever, malaise, headache, bone ache, myalgia has been reported. Pain, sensitivity, erythema and bulging on injection site are the local side effects. These vaccines are summarized below on Table I.

Table I: Commercially available, inactivated HAV vaccines.

	Havrix	Vaqta	Epaxal Berna	Avaxim
Manufacturer	SmithKline Beecham	Merck	Swiss Serum	Pasteur Merieux
Formaldehyde Inactivation	Yes	Yes	Yes	Yes
Strain	HM-175	CR326F	RG-SB	GBM
Cell line	MRC-5	MRC-5	MRC-5	MRC-5
Virosomal	No	No	Yes	No
Dose schedule	0, 1 – 12 months	0, 6 months	0, 12 months	0, 1 months

LIVE, ATTENUATED VACCINES

Many vaccines using several HAV strains, which are inactivated in different levels, are developed and tested on marmosets, chimpanzees and humans. Attenuation is done in cell cultures at temperatures of 32-35°C, in consecutive passages. Such vaccines, which are tested only in China, are cheaper and said to have a longer immunity period than inactivated vaccines. No increase in side effect profile is reported. Administration of live, attenuated vaccines simultaneously with immunoglobulins can prevent immune reactions. Thus an interval of at least 3 months is necessary between administration of live vaccines and immunoglobulins. Differences between live-attenuated and inactivated vaccines are summarized on Table II.

Table II: Characteristics of inactivated and live attenuated HAV vaccines.

	Inactivated (killed)	Attenuated (live)
Main source	HAV cultured in vitro	HAV cultured in vitro
Attained by	Formalin inactivation	Multiple passages in cell culture
Immunogenicity	Contains alum as adjuvant Evokes anti-HAV	Adjuvant is not needed Evokes anti-HAV
Advantage	Unlikely to cause infection (killed virus)	In theory, a single dose would be sufficient
Disadvantage	Multiple doses needed	Theoretical possibility of reversal to virulence and ability to cause infection
Availability	Commercially available	Still at research level

COMBINED VACCINES

Recently a new combined vaccine, called Twinrix®, containing both hepatitis A and B vaccines has been produced by SmithKline Beecham Biologicals. This vaccine contains 720 ELISA Units of hepatitis A antigens and 20μg of hepatitis B surface antigens. The vaccine is safe and possesses adequate immunogenicity. Several studies carried out in different countries to compare combined vaccination with separate hepatitis A and B vaccinations showed that combined vaccination is tolerated much better and stimulates a stronger immune reply with higher antibody titers. In these studies no increase in side-effect profile of combined vaccines has been reported.

WHO SHOULD BE VACCINATED?

- International travellers to developing countries
- Persons with chronic liver disease
- Military personnel
- Persons who are hemophiliac and frequently administered factor VIII
- Illegal drug users
- Health care workers
- Mentally handicapped persons (during epidemics)
- Day care personnel
- Homosexuals
- Food handlers

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