Section 1 Vaccination

Chapter 1

Vaccination in Pregnancy

Akanksha Sood

Introduction

Vaccination is one of the most cost-effective successful public health interventions. Maternal vaccination protects both mother and baby from the morbidity of certain preventable diseases.

Basics of Immunology

Immune response is the ability of the body to identify, recognise and defend against harmful toxins, infections or disease by making specific antibodies or sensitised white blood cells.[1,2]

The different antibodies produced by plasma cells as classified by isotype are five major isotypes (IgA, IgD, IgE, IgG and IgM).[3]

Immunity is produced by one of two body reactions:

1. **Active immunity** is the ability to produce immunity either by exposure to the disease, infection, organism or by vaccination (killed or weakened form of organism).[4] The protection is provided by a person's own immune system, is natural and often lasts for life.
2. **Passive immunity** involves administration of immunoglobulins which provides a quick but short-term immunity that wanes with time. These include varicella zoster hepatitis
   B immunoglobulin or transplacental transfer of antibodies from the mother.

Vaccination

Vaccination stimulates immune response against a specific antigen and provides protection from contracting the disease by forming antibodies.[5]

Types of Vaccines

1 Live Attenuated Vaccines

These vaccines contain pathogens, which have been weakened to diminish their infectivity and pathogenicity by repeated culturing. They do not cause illness, but retain their ability to replicate and stimulate production of antibodies. The immune response is virtually identical to the naturally produced long-term immunity with one dose, except oral vaccines which need repeating.[6]

Side effects of live vaccines are:

- The organisms might revert to a virulent form resulting in infection although of milder form
- Contraindicated in pregnancy as they have the potential to infect the fetus
- In immunocompromised individuals they cause uncontrolled replication of organisms, which may cause fatal reaction
- Vaccine can become ineffective by heat, light, presence of antibodies from other sources (transplacental or blood transfusion)[6]

Examples of a live attenuated vaccine are measles–mumps–rubella vaccine (MMR combined vaccine), varicella, measles, rotavirus, smallpox, chickenpox, yellow fever or the antibacterial vaccines, Bacillus Calmette-Guérin (BCG) vaccine and oral polio vaccine.

2 Live Inactivated Vaccines

These vaccines are produced by growing bacteria or the virus in culture media and then inactivating it with heat or chemicals. They are not alive and cannot replicate, and are therefore unable to cause disease even in an immune-deficient person.

Unlike live vaccines, these are not affected by circulating antibodies and hence can be given when antibodies are present in the blood, e.g. in infancy or following receipt of antibody-containing blood products. They require multiple doses. The first dose only primes the immune system. A protective immune response develops after the second or third dose.

Antibody titres diminish with time and, as a result, may require to be boosted with periodic supplemental doses.

Examples of inactivated vaccines: hepatitis A, flu, polio, rabies.

3 Recombinant Vaccines

Recombinant vaccines are produced by genetic engineering technology. Currently eight such vaccines are available:

1. Hepatitis B vaccine
2. HPV (human papillomavirus) vaccine
3. Live typhoid vaccine
4. Live attenuated influenza vaccine (LAIV)
5. Whooping cough (part of the diphtheria, tetanus and pertussis (DTaP) combined vaccine)
6. Pneumococcal vaccine
7. Meningococcal vaccine
8. Shingles vaccine

4 Toxoid Vaccines

Toxoid vaccines implies administration of the toxin produced by certain bacteria (tetanus or diphtheria) after making them harmless.

Vaccination in Pregnancy

Vaccination during pregnancy is not a routine event, and attenuated live virus vaccinations are generally contraindicated. A woman should be up to date with her routine immunisation before pregnancy against preventable diseases.

Vaccination during pregnancy is warranted when:

1. The risk of exposure is high
2. Infection poses risk to mother/fetus
3. Vaccine is unlikely to be harmful

The benefits to mother and fetus should outweigh the risk of vaccination. It is preferable to delay immunisation until the second trimester to avoid the period of organogenesis unless medically indicated; however, no evidence exists of risk to fetus from inactivated vaccines or toxoids.[7,8] [evidence levels EL 2 & 3]

In the clinical context, vaccines can be broadly divided into three groups.

1. Vaccines contraindicated during pregnancy: live attenuated vaccines could cross the placenta and result in viral infection of the fetus, e.g. MMR and the varicella vaccines.
2. Vaccinations specially recommended during pregnancy, e.g. the trivalent inactivated influenza vaccine during the influenza season.
3. Vaccinations recommended for women at risk of exposure (hepatitis B).[8]

Rubella

Vaccine against rubella is routinely given to all as part of childhood immunisation, and 97 per cent of women in the UK are immune.

Rubella vaccine is contraindicated during pregnancy as it is presumed to cause fetal anomalies; however, if the vaccine is inadvertently administered to a pregnant woman, or pregnancy occurs within 28 days of vaccination, it should not be the reason for termination of pregnancy. She should be counselled about the theoretical risks to the fetus and the need for close follow-up.[9]

At the preconception counselling, a non-immune woman (immunoglobin (IgG) levels <10 IU/mL) should be offered MMR vaccine as a single dose and counselled to avoid pregnancy for 28 days after vaccination.

A pregnant non-immune woman should be offered vaccination during the postpartum period even if she is breastfeeding. Rubella virus is secreted in breastmilk; seroconversion without serious infection is reported in breastfed infants.

Varicella Zoster (VZV)

Approximately 90 per cent of women are immune because of childhood vaccination or exposure.

Universal screening to check immune status is not recommended; however, in certain situations the immune status should be checked.[10]

1. Women with an uncertain or no previous chickenpox infection
2. Those who come from tropical or subtropical countries
3. Those who had an exposure to the infection

Varicella vaccine contains live attenuated virus derived from the Oka strain of VZV and is contraindicated in pregnancy due to theoretical risks of fetal infection.

If a woman is sero-negative, she should be offered postpartum immunisation of two separate doses four to eight weeks apart and advised to avoid pregnancy for four weeks after the second dose. She should be reassured about its safety during breastfeeding.

Women are advised to avoid contact with chickenpox or shingles and to inform a health care worker in case of significant contact. Contact with pregnant women should be avoided if a post-vaccination rash occurs. [EL 2]

If the pregnant woman is not immune to VZV and she has had a significant exposure, she should be offered varicella zoster immunoglobulin (VZIG) as soon as possible.[10]

Inadvertent exposure to vaccine in pregnancy is not an indication for termination as there has been no increase in the risk of fetal abnormality above the background risk.

A review of the Pregnancy Registry for VARIVAX following 362 pregnancies inadvertently exposed to varicella vaccine showed there was no case of congenital varicella syndrome and no abnormal features or birth defects in the infants. [EL 2]

Whooping Cough (Pertussis)

This is an acute bacterial infection. It is highly contagious, caused by *Bordetella pertussis* spreading through droplets (coughing and sneezing).

Vaccinating pregnant women against whooping cough has been highly effective in protecting newborn babies. It offers immediate protection to cover the newborn until they can have their first vaccination at two months of age.

Babies born to women vaccinated at least a week before birth had a 91 per cent reduced risk of becoming ill with whooping cough in their first weeks of life, compared with babies whose mothers were not vaccinated.[11]

In 2012, the UK experienced a nationwide epidemic of pertussis, resulting in serious complications (pneumonia, encephalitis, seizures, brain damage) including death, especially in young babies. A programme for the vaccination of pregnant women between 28 and 32 weeks against pertussis was introduced in October 2012.[11]

However, it can be given at any time until the start of labour, although after 38 weeks the fetus is less likely to be protected by maternal immunity.

The Joint Committee on Vaccination and Immunisation (JCVI) of the Royal College of Obstetricians and Gynaecologists (RCOG) recommended that from April 2016 the vaccination should be offered from 20 weeks (after the anomaly scan).[12]

Many countries including the United States, Spain, Australia, New Zealand, Belgium and Argentina currently recommend vaccination against whooping cough in pregnancy.

Pregnant women need to be vaccinated even if they have been vaccinated in childhood or in a previous pregnancy. Both randomised clinical trials and cohort studies support its safety (no increase in pregnancy complications, preterm birth, low birthweight, congenital anomalies, spontaneous abortion, or stillbirth).[13] [EL 1]

Vaccination of the close contacts of the neonate (mother's partner) is recommended as a strategy for newborn prevention, when the mother has not been timely vaccinated.[13]

Tetanus

Worldwide, each year, tetanus kills an estimated 180 000 neonates (about 5 per cent of all neonatal deaths, 2002 data) and up to 30 000 women (about 5 per cent of all maternal deaths).

Tetanus vaccine is a toxoid vaccine and protects against both maternal and neonatal tetanus.

All pregnant women should receive a tetanus toxoid vaccine during each pregnancy, irrespective of any previous history of immunisation.

The optimum time for passive antibody transfer is from the 27th until the 36th week. A booster dose is indicated if a pregnant woman is exposed to the risk of tetanus infection during or immediately after delivery.

Diphtheria

Diphtheria can lead to breathing problems, heart failure, paralysis and death. The Tdap vaccine has a dose of tetanus toxoid, reduced diphtheria toxoid and acellular pertussis.

All pregnant women should get a Tdap vaccination in each pregnancy.

Influenza

'The flu', as is it commonly known, is a highly contagious disease caused by an influenza virus which occurs in all parts of the world. It spreads by coughing and sneezing of an infected person.

There are three types of Influenza virus, type A (H1N1), type B (H3N2) and type C.

Type C generally causes mild respiratory illness and does not usually cause epidemics.[14]

Influenza A and B viruses cause outbreaks or epidemics and therefore should be included in seasonal influenza vaccine.

Pregnant women are particularly vulnerable to influenza. Strong evidence shows that pregnant and postpartum women are at higher risk of severe illness and complications than women who are not pregnant.

Due to reduced immunity during pregnancy, influenza increases the risk for both mother and fetus with resulting preterm and low birthweight babies.

Influenza vaccine is an integral element of preconception, prenatal and postpartum care.

Studies have shown that vaccination reduces the risk of serious maternal medical complications and provides passive protection to the neonate from influenza in the first six months before the baby is eligible for vaccination.

Recent systematic review has confirmed that decreased risk of laboratory-confirmed influenza infection in infants is associated with uptake of influenza vaccine during pregnancy.[15] [EL 1]

There are two types of vaccine: the inactivated (injection) and the live attenuated (intra-nasal spray).

The live attenuated nasal spray is not recommended for pregnant women.

Pregnant women should be counselled about the benefits of the single influenza vaccine for themselves and their unborn child. According to the Mothers and Babies Reducing Risk through Audits and Confidential Enquiries, UK (MBRRACE-UK) report 2010–12, 1 in 11 pregnant women died from flu, and more than half of these deaths could have been prevented by a flu vaccination.[16] Increasing immunisation rates in pregnancy therefore remain important.

Increasing immunisation rates in pregnancy against seasonal influenza must remain a public health priority.

It is recommended that all pregnant women have influenza vaccine at whatever stage of pregnancy when the pandemic starts. The vaccine protects against three of the most likely strains. It is important to have the vaccine every year as flu virus is very variable and strains change over time.

It is strongly recommended by RCOG that flu vaccine be offered[17]

- To all pregnant women
- In each pregnancy
- At any stage of pregnancy (first, second or third trimester)
- To have the vaccine in autumn before the outbreak of flu starts

The vaccine offered is given as intramuscular injection; it takes up to two weeks after vaccination to give protection and is 50 per cent effective.

Human Papillomavirus (HPV)

Human papillomavirus (HPV) infection during pregnancy is not well studied. There has not been any association with an increased risk of birth defects. A link between HPV infection and preterm birth was shown in a case control study.[18]

Currently there are two inactive recombinant HPV vaccines, the quadrivalent vaccine, which protects against HPV types 6, 11, 16 and 18, and a bivalent vaccine, which provides protection against HPV types 16 and 18.

The Centers for Disease Control and Prevention (CDC) do not recommend HPV vaccination during pregnancy, nor do they recommend testing for pregnancy before the routine HPV vaccination.[19,20]

If the vaccine has been inadvertently given to a pregnant woman, there is no need for termination of pregnancy, but the second dose should be postponed until after the pregnancy. If a woman has received an HPV vaccine and then plans to become pregnant, there is no need to delay pregnancy, as the HPV vaccines are inactive.

In a recent retrospective observational cohort study, quadrivalent HPV vaccine inadvertently administered in pregnancy or during the periconceptional period was not associated with adverse pregnancy or birth outcomes [EL 1].

Hepatitis A

This is a formalin inactivated vaccine. The theoretical risk to the developing fetus is expected to be low.

The safety during pregnancy has not been determined. The risk associated with vaccination should be weighed against the risk of hepatitis A in pregnant women. It is recommended for pregnant women who are at high risk due to travel or pre-existing high-risk condition, e.g.

- Long-term liver disease
- Haemophilia
- Intravenous drug users
- Occupational risk – working with or near sewage, working in institutions where levels of personal hygiene may be poor
- Working with primates (monkeys, apes, gorillas etc.)[20]

Hepatitis B (HBV)

Hepatitis B is spread by blood-to-blood contact and may also be present in other body fluids, e.g. semen, vaginal fluid and saliva. Hepatitis B infection in pregnancy may result in severe hepatic disease for the mother and chronic infection for the baby. If the mother is hepatitis B 'e antigen' positive, vertical transmission occurs in 90 per cent of pregnancies, and if she is hepatitis B 'e antigen' negative it occurs in only 10 per cent.

Most infected infants (90 per cent) become chronic carriers, with possible long-term effects (liver cirrhosis and hepatocellular carcinoma). Vaccination will not cure chronic hepatitis but it is 95 per cent effective in preventing chronic infections from developing.

Pregnancy is not a contraindication to vaccination, it is an inactivated hepatitis B surface antigen (HBsAg) subunit vaccine.

The risk to the fetus is negligible. Hence, pregnant women who are identified as being high risk for HBV infection during pregnancy should be vaccinated, e.g.

- Women with multiple sexual partners during the previous six months
- Women who have been treated for a sexually transmitted infection
- Recent or current injection drug use
- HBsAg-positive sexual partner
- Received regular blood or blood product transfusion
- Travelling to high-risk countries
- Female sex workers
- Working in settings that place women at high risk of contact with body fluids, such as doctors, nurses, dentists and laboratory staff
- Women who started immunisation series before becoming pregnant[20]

Infants born to infectious mothers are vaccinated both by HBsAg vaccine and hepatitis B immunoglobulin (HBIG) (200 IU i.m.) preferably within 12 hours. This reduces the vertical transmission by 90 per cent.[21]

Meningococcal

The CDC advice is that this vaccination should be deferred in pregnancy and lactating women unless the mother is at high risk of disease:

- Women with sickle cell disease or thalassemia
- Immunosuppressed
- Travel to high-risk endemic areas
- Contact with infected individuals

The two available vaccines are meningococcal group C conjugated vaccine (Men C) and meningococcal quadrivalent polysaccharide vaccine (Men ACWY).

The UK Department of Health recommends that the conjugated vaccine be used in preference to polysaccharide vaccine because it provides better and long-lasting protection.[20]

Pneumococcal

Ideally the vaccine should be given prior to conception, but indications for administration (patients with asplenia, sickle cell disease, HIV or splenectomy) are not altered by pregnancy. The pneumococcal conjugated vaccine is preferred over polysaccharide vaccine.

The use of this vaccine is limited among women of childbearing age, although no adverse consequences have been reported among newborns whose mothers were inadvertently vaccinated during pregnancy.[20]

Polio

Polio is caused by a virus that can lead to permanent paralysis. It has been eradicated from most countries.

There are two types of polio vaccines, the inactivated poliovirus vaccine (IPV) and oral poliovirus vaccine (OPV). A pregnant woman should avoid travel to polio-endemic areas, but if travel is unavoidable and she requires immediate protection against polio, IPV can be administered.

In a cohort study in Finland, it was concluded that oral polio vaccination is safe for pregnant women.

Inclusion of pregnant women in programmes of mass vaccination with OPV appears to be safe.[21] [EL 2]

Typhoid

No data have been reported on the use of typhoid vaccine in pregnant women. Live vaccines like Ty21a are contraindicated in pregnancy. Vi polysaccharide vaccine should be given to pregnant women only if required.

Pregnant women are advised to avoid travel to typhoid-endemic areas but if such exposure is unavoidable, inactivated typhoid vaccine can be given if clearly needed.[20]

Rabies

Because of the potentially fatal consequences of inadequately managed rabies exposure, pregnancy is not considered a contraindication to post-exposure prophylaxis.

Pre-exposure prophylaxes may be indicated in pregnancy. Rabies exposure or diagnosis should not be regarded as reasons to terminate the pregnancy. It is an inactivated viral vaccine, and studies have indicated no increased incidence of abortion, premature births or fetal abnormalities.[20]

Yellow Fever

Yellow fever is a mosquito-borne viral infection endemic to rural areas of sub-Saharan Africa and tropical regions of South America. The infection varies in severity, but can be associated with significant morbidity and mortality. It is prudent to advise pregnant women not to travel to yellow fever-endemic areas.

Yellow fever vaccines are contraindicated as they are attenuated live vaccines. If travel is unavoidable and the risk of yellow fever exposure is high, vaccination may be justified (due to high mortality associated) after discussion with an infectious disease specialist.

Although no specific data are available, a woman should wait four weeks after receiving yellow fever vaccine before conceiving.[20]

Anti-Tuberculosis Bacilli Calmette-Guérin (BCG) Vaccination

This is a live vaccine, and falls into FDA category C (potential benefits may warrant use of the drug in pregnant women despite potential risks).

It is usually not given during pregnancy even though no harmful effects of vaccination on the fetus have been observed. Further studies are needed to prove its safety.[20]

BCG immunisation causes some pain and keloid scarring at the site of injection. The injection is either given in the deltoid or the buttocks, because it provides better cosmetic outcomes.

Vaccinia (Smallpox)

Smallpox is a viral infection and has been eradicated from most countries. Pregnant women who have had a definite exposure to smallpox virus should be vaccinated, as the risks to the mother and fetus from clinical smallpox infection substantially outweigh any potential risks.

The vaccine has not been documented to be teratogenic; the incidence of fetal vaccinia is low.

If a woman is inadvertently vaccinated or if she becomes pregnant within four weeks after vaccination, it should not be a reason to terminate pregnancy. [20,21]

Anthrax

The vaccine is a cell-free vaccine (developed from mammalian cell lines rather than embryonic chicken eggs).[21,22]

In a pre-event setting in which the risk for exposure is low, vaccination of pregnant women is not recommended and should be deferred until after pregnancy. During pregnancy in a post-event setting, pregnancy is not a precaution nor a contraindication to post-exposure prophylaxis.

Antenatal and Prenatal Screening for Infectious Diseases

In the United Kingdom, all pregnant women should be evaluated for immunity to rubella and varicella, hepatitis B, HIV and syphilis.

Women susceptible to rubella and varicella should be vaccinated immediately after delivery.

A woman found to be HBsAg-positive should be monitored carefully to ensure that the infant receives HBIG and begins the hepatitis B vaccine series no later than 12 hours after birth and the infant completes the recommended hepatitis B vaccine series on schedule.[22]

Breastfeeding and Vaccination

Neither inactivated nor live vaccines administered to the lactating woman affect the safety of breastfeeding women or their infants. Live viruses in vaccines can replicate in the mother, but most live viruses in vaccines have not been demonstrated in breastmilk.

Rubella vaccine virus might be excreted in breast milk, but the virus usually does not infect the infant. Even if infection does occur, it is well tolerated as the virus is attenuated.

Inactivated, recombinant, subunit, conjugated polysaccharide vaccines, as well as toxoids, pose no risk for mothers who are breastfeeding their infants.

Yellow fever vaccine should be avoided in breastfeeding women. However, when nursing mothers cannot avoid or postpone travel to areas endemic for yellow fever in which the risk for acquisition is high, these women should be vaccinated.

Postpartum Vaccination

The two vaccines that should be specifically administered before discharge of postpartum women to protect both mother and neonate are MMR vaccine and varicella vaccine. The woman should be counselled to avoid pregnancy for four weeks after vaccination.

Yellow fever and smallpox are the only vaccines contraindicated postpartum or when breastfeeding.

Conclusion

Maternal vaccination should be carried out with clear understanding, and mothers should be made aware of the implications (benefits vs risks). It can prevent/reduce maternal, fetal and neonatal infection and reduce disease burden.

- Most of the vaccines during pregnancy should be given according to risk/benefit ratios.
- Clearly indicated vaccine recommendations include inactivated influenza vaccine, the Tdap pertussis, diphtheria and tetanus vaccine, and smallpox for post-exposure prophylaxis if there is a definite history of exposure.
- The clearly contraindicated vaccines include the live attenuated influenza vaccine (LAIV), the BCG, the MMR (measles, mumps, rubella), the varicella and the zoster vaccines.

References

1. Dubé E, Laberge C, Guay M, Bramadat P, Roy R, Bettinger J. Vaccine hesitancy: an overview. *Hum Vaccin Immunother*. 2013; **9**(8): 1763–73.
2. Oxford Living Dictionary. https://en.oxforddictionaries.com/definition/immunity.
3. Thermo Fisher Scientific. Introduction to Immunoglobulins. thermofisher.com/antibodies/antibodies-learning-center/antibodies-resource-library/.
4. Centers for Disease Control and Prevention. Immunity types. www.cdc.gov/vaccines/vac-gen/immunity-types.htm.
5. Biology Online. www.biology-online.org/dictionary/Vaccination.
6. World Health Organization. Module 2: Types of vaccine and adverse reactions. www.who.int/vaccine_safety/initiative/tech_support/Part-2.pdf.
7. ACOG Committee on Obstetric Practice. Influenza vaccination and treatment during pregnancy. ACOG Committee Opinion No. 305. *Obstet Gynecol*. 2004; **104** (5 Pt 1): 1125–6.
8. Centers for Disease Control and Prevention. Vaccination in pregnancy. www.cdc.gov/vaccines/pregnancy/hcp/guidelines.html.
9. Sukumaran L, McNeil MM, Moro PL, Lewis PW, Winiecki SK, Shimabukuro TT. Adverse events following measles, mumps, and rubella vaccine in adults reported to the Vaccine Adverse Event Reporting System (VAERS), 2003–2013. *Clin Infect Dis*. 2015; **60**(10): e58–65.
10. Royal College of Obstetricians and Gynaecologists. Chickenpox in Pregnancy. Green-top Guideline No. 13. www.rcog.orguk/en/guidelines-research-services/guidelines/gtg13/. January 2015.
11. NHS Choices. Whooping cough vaccination in pregnancy. nhs.uk/conditions/pregnancy-and-baby/pages/whooping-cough-vaccination-pregnant.aspx.
12. Public Health England. Vaccination against pertussis (Whooping cough) for pregnant women. 2016.
13. Amirthalingam G, Campbell H, Ribeiro S, Fry NK, Ramsay M, Miller E, Andrews, N. Sustained effectiveness of the maternal pertussis immunization program in England 3 years following introduction. *Clin Infect Dis*. 2016; **63** (suppl 4): S236–43.
14. Centers for Disease Control and Prevention. Types of Influenza Viruses. www.cdc.gov/flu/about/viruses/types.htm.
15. American College of Obstetricians and Gynecologists. Influenza Vaccination during Pregnancy, 2014.
16. MBBRACE-UK. Saving Lives, Improving Mothers' Care: surveillance of maternal deaths in the UK 2012–14 and lessons learned to inform maternity care from the UK and Ireland. Confidential Enquiries into Maternal Deaths and Morbidity. 2009–14. www.npeu.ox.ac.uk/mbbrace-uk/.
17. Royal College of Obstetricians and Gynaecologists. Flu vaccination in pregnancy protects both mothers and babies say doctors and midwives. www.rcog.org.uk/.
18. Gomez LM, Ma Y, Ho C, McGrath CM, Nelson DB, Parry S. Placental infection with human papillomavirus is associated with spontaneous preterm delivery. *Hum Reprod*. 2008; **23**(3): 709–15.
19. Narducci A, Einarson A, Bozzo P. Human papillomavirus vaccine and pregnancy. *Can Fam Physician*. 2012; **58**(3): 268–9.
20. Centers for Disease Control and Prevention. Guidelines for Vaccinating Pregnant Women. www.cdc.gov/vaccines/pregnancy/hcp/guidelines.html. 2016.
21. World Health Organization. WHO/UNICEF immunization summary: the 2007 edition. Geneva: World Health Organization. //whqlibdoc.who.int/hq/2007/who_ivb_2007_eng.pdf. 2007.
22. Audsley JM, Tannock GA. Cell-based influenza vaccines: progress to date. *Drugs*. 2008; **68**(11): 1483–91.

Section 2 Infections in Pregnancy

Chapter 2

Viral Hepatitis

Rashda Imran

Virology[1]

Viruses are small, non-living parasites, which cannot replicate outside a host cell.

Viruses are grouped according to their genetic material: DNA or RNA.

DNA viruses are mostly double-stranded while RNA viruses are single-stranded.

A virus injects its genetic information into a host cell and then takes control of the cell's machinery. This process enables the virus to make copies of its DNA or RNA and make the viral proteins inside the host cell. A virus can quickly make multiple copies of itself in one cell, release these copies to infect new host cells and make even more copies. In this way, a virus can replicate very quickly inside a host.

DNA Viruses (Deoxyribonucleic Acid)

DNA is a molecule that contains the instructions it needs to develop, live and reproduce. DNA viruses use DNA as their genetic material. Some common examples of DNA viruses are parvovirus, papillomavirus and herpes virus. DNA viruses can affect both humans and animals and can range from causing benign symptoms to posing a very serious health risk.

DNA looks like a double helix and a twisted ladder.

RNA (Ribonucleic Acid)

Unlike DNA, RNA comes in a variety of shapes and types.

Common examples of RNA viruses: hepatitis C virus (HCV), Ebola, SARS, influenza, polio, measles and retrovirus human immunodeficiency virus (HIV).

Introduction

Viral hepatitis in pregnancy is the commonest cause of hepatic dysfunction and jaundice. The viruses resulting in hepatitis are hepatotoxic and include hepatitis A virus (HAV), hepatitis B virus (HBV), hepatitis C virus (HCV), hepatitis D virus (HDV) and hepatitis E virus (HEV).

Epstein–Barr virus and cytomegalovirus could also be the causative agents for hepatitis in rare cases.

Viral hepatitis caused 1.34 million deaths in 2015, a number comparable to deaths caused by tuberculosis and higher than those caused by HIV.[2]

In May 2016, the World Health Assembly endorsed Global Health Sector Strategy (GHSS) on viral hepatitis 2016–21. The GHSS calls for elimination of viral hepatitis as a public health threat by 2030 (reducing new infections by 90 per cent and mortality by 65 per cent).[2]

The hepatoviruses are quite divergent in their structures, epidemiology and routes of transmission, incubation period, clinical presentation, natural history and diagnosis. Prevention and treatment options are also different.

Hepatitis A (HAV)

Hepatitis A is an acute self-limiting illness and does not cause chronic infection. Hepatitis A virus can cause mild to severe disease. A very small proportion of people infected with hepatitis A could die from fulminant hepatitis.[3] It is the second most common form of viral hepatitis in the United States.[4] It is rarely life-threatening, with an estimated mortality of 0.3–0.6 per cent.[5] Approximately 1.5 million new cases are reported annually. The true incidence might be higher as mild cases are not reported.[5]

Virology and Epidemiology

Hepatitis A virus is a non-enveloped RNA virus. The lack of lipid envelope makes it relatively hard and acid-resistant. It can remain infectious for weeks. Human beings are the important reservoir. Hepatitis A virus is highly prevalent in areas with poor sanitary

conditions. High endemic areas include Africa, central Asian countries and South America, and low endemic areas include Europe, Canada and the USA.

Pathogenesis and Transmission

The oral route is the primary mode of transmission, usually through ingestion of contaminated foods, especially raw and undercooked shellfish and person-to-person contact. Hepatitis A virus replicates in the small bowel and liver after ingestion, and is excreted via bile through feces. It has a short viraemia period, with peak infectivity during the two weeks before onset of symptoms.

Fetal Implications of Hepatitis A

The incidence of acute hepatitis A infection in pregnancy was quoted as less than 1:1000 prior to the introduction of HAV vaccine.[6]

Mother-to-child transmission (MTCT) of hepatitis A is very rare.

Only few cases of intrauterine transmission following maternal infection in the first trimester have been reported. The transmission resulted in fetal peritonitis and was confirmed by the presence of hepatitis A immunoglobulin M in fetal blood obtained by trans-abdominal blood sampling of the fetal umbilical cord, performed under ultrasound guidance (cordocentesis).[7]

There is increased risk of miscarriage and preterm labour.

Neonatal Implications

- Maternal infection in the third trimester of pregnancy may result in self-limiting neonatal cholestasis or asymptomatic neonatal infection.[8]
- Most viral infections are not affected by pregnancy.
- There have not been any reported maternal or fetal mortalities due to hepatitis A.
- Breastfeeding should not be discouraged, and the child should be protected through administration of immunoglobulin or the inactivated vaccine.[9]

Prevention

Safe water supply, food safety, improved sanitation and hand washing, especially before handling food, are important for its prevention.

Vaccination and Passive Immunisation

- The hepatitis A vaccine (HAVRIX, VAQTA) is the most effective way to combat the disease and should be considered for pregnant women and women of reproductive age before visiting HAV-endemic areas.
- Hepatitis A vaccination (an inactivated (killed) vaccine). **Two doses** are needed for long-lasting protection. It is prepared from inactive virus and is considered safe during pregnancy.[10]
- If a pregnant woman is exposed to hepatitis infection, passive immunisation with immunoglobulins within two weeks of exposure is safe in pregnancy.
- 0.02 mg/mL of immunoglobulin by single intramuscular injection provides protection for three months in 80–90 per cent of people.[7]

Clinical Presentation

The presentation in pregnant and non-pregnant women is the same:

1. Fever and chills
2. Anorexia, nausea and vomiting
3. Dark urine and pale stool
4. Jaundice and hepatomegaly

Most signs and symptoms resolve in three weeks.

Complications

- About 7 per cent of patients can have complications like cholestasis, prolonged jaundice, pruritus and fever.
- Fulminating hepatitis occurs in less than 1 per cent of cases.

Diagnosis

The specific diagnosis of acute hepatitis A is made by serology testing of the patient's blood; anti-HAV immunoglobulin M (IgM) is diagnostic. Detection of IgG anti-HAV alone indicates past infection.

The liver enzymes like transaminases are classically elevated by 10–100 times the normal range.[11]

Treatment

- The treatment of hepatitis A is supportive to maintain comfort and adequate nutrition.