REVIEW OF LITERATURE
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TORCH : Consist of -
Toxoplasma gondii.
Rubella virus.
Cytomegalo virus.
Herpes simplex virus.

TOXOPLASMA GONDII

Toxoplasma gondii is an obligate intracellular parasite with worldwide distribution found both in man & animals. Approximately 3300 infants born every year in the United States are congenitally infected with toxoplosmosis. Most infants are asymptomatic during neonatal period but subsequently develop adverse sequelae. Early treatment reduces the severity of the disease.

Historical Aspect of Toxoplasma gondii:

Toxoplasma was discovered by Nicole and Monceaux in 1908 in a small rodent gondii (Clenodactylus gondii) of Africa. Human importance of organism was realized 30 years after i.e. from the year 1939. Although 2 cases were reported in the interval, one in 1914. Castellavi from Srilanka and other in 1923 by Jonku. Toxoplasma gondii was first recognized as a cause of congenital infection and disease by Janku in Czechoslovakia in 1923.
We now realize that it is cosmopolitan in the human population and can cause disease. The importance of the organism as a human pathogen has stimulated a huge amount of research in recent years.

**Epidemiology:**

Toxoplasma gondii has a worldwide distribution found both in man & animal caused by a small protozoan. Approximately 3300 infants born every year in the United States are congenitally infected with Toxoplasmosis, most infants are asymptomatic during neonatal period. But subsequently develop adverse sequela. Early treatment reduces the severity of the disease.

Development forms include the oocyst, trophozoites, tissues cyst. Organism reproduce sexually in the intestinal mucosa of cats, the only definitive host to form oocysts, which are excreted in the stool. Oocysts becomes infectious when they undergo sporogony outside the body. Humans are infected following ingestion of oocysts from dried out faeces on tissue cyst from contaminated food especially undercooked meat. High rates are associated with tropical climates, poor sanitary condition, and prevalence of cats.

**Pathogenesis:**

Following the ingestion of T. gondii trophozoites disseminates throughout the body via the lymphatics & blood stream, organisms invade cells and multiply resulting in tissue destructions cyst containing several thousand slowly growing organisms may develop in any tissue but are common in CVS, Myocardium & skeletal
muscles HIV induced immuno-suppression permits reactivation-dissemination of latent infection.

**Clinical Features:**

Most human infections are asymptomatic. Clinically it is either acquired or congenital.

(I) **Acquired:**

A. **Cerebrospinal:** Common in children, presents as acute meningo-encephalitis.

B. **Lymphatic:** Present as lymphadinitis of one or more group, fever lasting for several weeks with constitutional symptoms.

C. **Exanthematous:** Mostly present in adults characterized by acute febrile illness with wide spread maculo popular rashes, diffuse interstitial pneumonia, myocarditis and occasionally meningo-encephalitis.

D. **Latent:** Does not produce any sign or symptoms and infection is detected by laboratory tests, it is found only in adults.

(2) **Congenital Toxoplasmosis:**

It results when infection is transmitted trans-placentally from mother to foetus. This occurs only when the mother gets primary toxoplasma infection whether clinical or asymptomatic during the pregnancy. Mother with chronic or latent toxoplasma infection
acquired earlier do not infect their babies. Most infected newborns are asymptomatic at birth & may remain so throughout. Some develop clinical manifestations of toxoplasmosis weeks, months or even years after birth. The manifestation may be chorioretinitis, strabismus, blindness, deafness, epilepsy or mental retardation. A few are born with manifestation of acute toxoplasmosis which may include fever, jaundice, diarrhoea, petechial rashes. Hydrocephalous, microcephaly cerebral calcifications microphthalmia, cataract, glaucoma, chorioretinitis, optic atrophy, lymphadenitis pneumonitis, myocarditis & hepatosplenomegaly.

If mother gets infected during pregnancy it often leads to abortion. If pregnancy continues foetus is so deformed that there may be a still birth.

**Diagnosis:**

Laboratory diagnosis may be made by **microscopic demonstration** of the parasite by its isolation or by serological tests.

**Giemsa stained** impression smears of lymph nodes, bone marrow, spleen or brain may occasionally show the trophozoites, which can be readily identified by their morphology. Tissue sections may show the cyst forms.

The commonest method of laboratory diagnosis is by **serology**. Several serological tests are available. These include the Sabin-Feldman dye test, indirect immunofluorescence, indirect Haemagglutination & complement fixation.
The Sabin-Feldman dye test is based on the specific inhibition by antibody of the staining of the trophozoite by alkaline methylene blue.

In direct fluorescent antibody would be the test of choice in the clinical laboratory provided that the equipment for fluorescent microscopy is available. If the laboratory is not so equipped the alternative serological method would be indirect haemagglutination test (Peter G Beach et al 1978).

The complement fixation test can contribute in making a serodiagnostic interpretation from a single serum sample but itself is not a good diagnostic method because of long delay, upto two months in becoming positive after exposure (Alexander Macdonal 1950).

All these tests detect IgG antibodies. Demonstration of specific antibody using an enzyme linked immunosorbent assay is easy and accurate method (Van Loon, A.M., et al 1980).

IgM antibody which indicates current infection can be detected by IgM fluorescent antibody assay or a double sandwich IgM ELISA. However 10-20% of adults which acute toxoplasmosis are IgM negative. Similarly, IgM antibody an be detected only in about 25% of infants with congenital toxoplasmosis.
Treatment:

A combination by pyrimethamine 25-50 mg, three to four times a day and sulphadiazine initially 2 gm and then 1 gm every 6 hourly for 14 days is given in all cases.

In primary, Azithromycin 500 gm 1 BD for 15 days.
Spiramycin 6-9 MIU per day in divided doses for 15 days.

Toxoplasmosis in Pregnancy:

Congenital toxoplasmosis was first reported by Jocoby and Sagenin (1948) in Britain. Complement fixing and neutralizing antibodies were present in some apparently healthy women (Macdonald 1949).

Sabin and Feldman (1949) investigated the dye test and complement fixing toxoplasma antibodies in 3 mothers who had given birth to a child with toxoplasmosis and then a normal child. They found that both types of antibodies were transmitted to the normal infant and almost disappeared after 4 or 5 months, they suggested when a mother has one child with congenital toxoplasmosis her subsequent children are likely to be normal.

Jirovec et al (1959) and Langer and Geissler (1960) believed that toxoplasmosis is on of the main infectious cause of repeated abortion in women, other workers believe that women who have congenitally infected child do not have another infected child in subsequent pregnancies, repeated abortion occurs if women developed only an incomplete immunity.
Eckerling, Neri and Eylan (1968) studied 40 women with positive serology who previously in 116 pregnancies had produced only 32 surviving infants and after treatment with pyrimethamine and sulphonamide before pregnancy and with tetracycline and sulphonamide during pregnancy and these 40 women had 42 pregnancies with 41 healthy children and one abortion. In the light of more recent knowledge that tetracycline is potentially tetragenic it should not be used.

Desmonts Georges et al (1974) studied 378 pregnant women with high initial toxoplasma antibody titres or sero conversion during pregnancy, 183 acquired the infection during pregnancy, a rate of 6.3 per 100 pregnancies. There were 11 abortion, 7 infants were still born toxoplasmosis occurred in 59 of the non aborted offspring. Severe disease was noted only when maternal infection were acquired during the first two trimesters, later resulted in subclinical or no fetal infection. Treatment with spiramycin during pregnancy reduced overall frequency of fetal infection but not the overt disease. Mothers with antibodies before they became pregnant had no infected infants.

Wilson et al (1980) found that infection late in pregnancy is usually subclinical at birth but of these children most develop convulsion and other neurological sequelae later in life so all pregnant women should be screened for toxoplasmosis and treatment should be given to positive cases.

Beattie et al (1984) suggested that in Britain, where meat is usually well or over cooked prevalence rate of toxoplasmosis are
lower and routine serology would not be cost effective, e.g. in the west of Scotland only 25% of population have antibodies and the seroconversion rate in pregnancy in only 0.2% (Williams et al 1981) compared with 0.4% and 0.6% respectively in French and Belgium studies and the incidence of congenital toxoplasmosis is usually 0.06 per 1000 birth.

Faulen et al (1984) suggested that antenatal drug treatment has some value in preventing transplacental infection when it is known that primary maternal infection has occurred especially in most dangerous early months of pregnancy, he used spiramycin cyclically as a 3 week course one week interval.

Francois Foresties et al (1988) reported a prospective study of 749 documented cases of maternal toxoplasma infection. Infection was diagnosed antenatally in 39 of 42 foetuses, 24 were terminated. 15 mothers were treated with spiramycin. If foetal infection was demonstrated pyremethamine and either sulfadoxine or sulfadiazine were added to the regimen, only 2 foetuses developed chorioretinitis, remaining were clinically well, so it was concluded that prenatal therapy in women who wish to continue their pregnancies reduces the severity of the manifestation of the disease.

Tomba Singh. et al (1992) he took 120 patients of high risk pregnancies and 100 normal pregnancies were studied incidence of maternal toxoplasmosis was 13.3% in high risk pregnancy while it was 4% in normal control group.
Kusuma Saxena et al (1993) studied 150 cases 50 control and 100 test group of bad obstetric history was 27%. Maximum positive cases were found in age group of 21-30 years, almost equal incidence of positive cases in rural & urban population. Positive cases were more non vegetarian and in patients who had history of contact with cats. The positivity was 26.2% in abortion cases 30.7% in cases with history of premature labour, 25% cases with history of still birth and 33.3% in cases with history of congenital malformation.

Berrebi A. et al (1993) has done prospective study of 176 cases to determine the value of antenatal diagnosis of congenital toxoplasmosis by ultrasound guided aspiration of cord blood for testing. As well as obtaining fetal blood and amniotic fluid and searched for specific IgM and culturing for the parasites on human fibroblasts and inoculation of mice, as well as researching them for non-specific signs of fetal infection. 149 children were able to be followed up one year after birth. 15% of the children (22/149) were infected with toxoplasmosis. 11 out of these were diagnosed positive antenatally. For the 11 others the diagnosis of fetal infection could only be made after birth, but the non-specific signs made it possible to expect early that they had been contaminated. 59% (13/22) had latent toxoplasmosis which only showed up after a mean interval of 34 months after birth. 41% (9/22) had clinical and/or paraclinical signs of toxoplasmosis (mainly unilateral non-macular chorioratinitis and intracranial calcifications) but they are well after a follow-up period averaging 30 months. Ultrasound alone, when it shows up fatal abnormalities, can make the diagnosis of the severity of the condition. The role of taking fetal specimens
is to make clear those infants that are infected because of specific signs, and to find those features which are at high risk because of non-specific signs in order to improve the management of the cases. This development has made it possible to avoid carrying out a large number of unnecessary terminations of pregnancy and has resulted in the birth of affected infants that had no functional sequelae from the infection.

**Portlong, F. et al (1994)** estimated high incidence of 0.5 to 1.5% and 30 to 50% of V in pregnancy. Among the studied 190 women, two third by seroconversion of toxoplasmosis antibody status and one third by rising IgG titre plus the presence of IgM, risk of infection was 4%, 17% and 53% respectively in first, second and third trimester, so antenatal screening is cost effective.

**F. Pratiary et al (1995)** studied a cohort of 286 antenatal patients for toxoplasma antibodies, 40 were positive he concluded importance of making diagnosis of toxoplasmosis antenatally in order to limit the number of medical abortion.
RUBELLA

Historical aspect of Rubella:

Clinical Rubella (three day measles or German measles) was first discovered in Germany about 200 years ago and was called Rothelin. In the late 1930's the viral agent was transmitted to man and monkeys, but was considered an inconsequential disease until 1941 when Gregg, an Australian ophthalmologist discovered the teratogenic property of rubella. He observed a sudden increase in congenital contract in infants and related it to maternal rubella.

Rubella virus was isolated in tissue culture in 1962 independently by two group of workers (Weller and Neva Parkman, Bueschan and Arkenstien). In 1969, the first rubella vaccine was licenced in United States.

Thus in a relatively short time cause of neonatal rubella was identified, pathogenesis explained and a preventive measure created and then public health measures reduced the incidence of disease.

Structure and properties of Rubella

Rubella is a RNA virus of Togavirus group, contains hemagglutinins. There are several stain of the virus, the virus is readily inactivated by heat and chemical agents. The viral particle is roughly spherical 50-70 nm in diameter surrounded by envelope. It is inactivated by ether, chloroform and formaldehyde. It is destroyed by heating at 56°C but survives for several years at 60°C.
Clinical Infection by Rubella virus during pregnancy:

Infection takes place though the nasopharynx, after that virus incubates in the lymphnodes for 15-21 days (20 days incubation pd), which is followed by prodromal viraemia marked by coryza, malaise and low grade fever.

This is followed by discrete maculopapular rash appearing first on face than spreading to neck trunk and disappears by 3rd day.

However about half to two third of cases of Maternal rubella are clinically inapparent.

Immune phenomenon in the body:

Anti-Rubella IgG antibody of maternal origin are transferred transplaceltally to the developing foetus. In event of in-utero infection immune response in the form of rubella specific IgG antibodies is seen for duration of two months in the foetus. It may last upto a year this is followed by IgG antibodies response which can last for around 10 years. Maternal IgG transfer across the placenta generally last for 6 months. In general it can be said that cases negative for antibodies are always at risk and cases positive for antibodies remains protected for a minimum of 10 year (Khare et al 1987, Bhaskanan et al 1991).

Diagnosis of Rubella:

The other store for the diagnosis of maternal rubella infection is serologic using. Most widely used test being.
Haemagglutination inhibition Test. It is time consuming and complex and being replaced by newer methods namely:

- Solid phase enzyme linked immnosorbent assay (ELISA).
- Passive Haemagglutination (PHA)
- Immunofluorescent assay (IFA)
- Radial immunodifussion test (RID).

**Contribution of rubella to bad obstetrics:**

Maternal rubella in the first trimester of pregnancy is likely to result in birth of a malformed baby or induction of spontaneous abortion. Such sequelae of congenital rubella as gross cardiac lesions, hepatitis, Meningoencephalitis and interstitial pneumonia are often fatal to infants. Other such as pancytopenia, retinopathy, hepatosplenomegaly, Lymphadenopathy and bone lesions are usually self limited and seems to pose no long term risks. In adult who have survived congenital rubella major handicap with psychomotor, perceptual and cardiac abnormalities as less common complication.

The original concept of congenital rubella syndrome consisting of the triad of contract, congenital heart disease and deafness in the new born is no longer accepted as the only evidence of rubella infection (Marshal 1973).

**Criteria for diagnosis of Congenital Rubella Syndrome:**

Have been laid down by centre of disease control, Atlanta Georgia in two categories. These are –
1. A confirmed case which shows a congenital defect typical of congenital rubella syndrome. This can be followed by either isolation of rubella virus or rubella specific IgM antibodies and a persistently high HIA.

2. A comparable case which has sufficient laboratory data associated with two of the congenital malformations, cataract, glaucoma, patent ductus arteriosus, deafness or lymphadenopathy.

**Rubella vaccination:**

In 1969, two vaccines were licenced in United States, the HPV 77- DES and cenderhill strain. HPV 77 was most commonly used vaccine until it is replaced by RA 27/3 in 1979. RA 27/3 mimics natural rubella better and more consistently than other vaccines. It is a live attenuated vaccine and is contraindicated in pregnancy however; the risk of foetal infection after vaccination is between 3% to 5%. Vaccine produces seroconversion in 95 to 98% of susceptible individuals and causes symptoms resembling mild rubella in 10% to 15% of recipient.
CYTOMEGALOVIRUS INFECTION

Cytomegalovirus is a ubiquitous D.N.A. virus belonging to the family of human herpes virus, that includes herpes simplex virus, Ebstein barr virus, varicellazoster virus. The virus ranges in size form 180 to 250 nm in diameter and has a genome in the range of 150 million daltons.

Epidemiology:
Most people are infected with CMV some time during their life. Antibodies to CMV have been detected in over 90% of homosexual men and 60% of women attending sexually transmitted disease clinics in the United States. Cytomegalovirus can be cultured from saliva, semen, vaginal secretions, blood or infected tissues.

CMV infection can be acquired at the time of vaginal delivery. Another common route of infection is breast feeding. Virus is transmitted in the breast milk of 25.7% of women with serologic evidence of CMV infection.

Other potential route but rare source of infection is introduction of virus into foetal blood stream or amniotic fluid during intrauterine transfusion or amniocentesis.

Severe congenital infection:
Infants born with severe congenital infection exhibits hepatosplenomegaly, thrombocytopenia with petechiae & purpura,
hepatitis associated with icterus, pneumonitis and chorioretinitis, abnormality that results from faulty neurologic development includes microcephaly, optic atrophy, Aplasia of various parts of brain and microphthalmia. Incidence of foetal growth retardation is 30-40%. The presence of intracranial calcification is an indication that the infant will have at least moderate to severe retardation. Mental retardation affects 95% of newborns with severe infection, auditory deficiency is the most common handicap affecting 25% of congenitally infected newborns.

Diagnosis:

1. **Culture**: the gold standard for the diagnosis of CMV infection is the viral culture. Virus can be cultured by conventional technique or by the shell viral methods. Culture for CMV is expensive and virus may require up to three weeks to grow.

2. **Histology**: Histologic examination of biopsy specimens may demonstrate typical CMV inclusions, tissue necrosis or both. Definitive histologic diagnosis of CMV infection requires the presence of characteristic 'OWL's eye cells' with cytomegaly and large intranuclear or intracytoplasmic inclusions surrounded by a halo. Immunofluorescent staining of frozen section using an anti CMV monoclonal antibody may facilitate diagnosis and increase the sensitivity of cytologic examination.

3. **Serology**: serologic tests are useful in the diagnosis of acute infection characterized by IgM antibodies. Recurrent
infection is characterized by at least four fold increase in IgM titres. Antibodies may be absent in AIDS patients with severe CMV infection and a negative titre does not excludes the possibility of active disease, therefore serologic testing for CMV is of little diagnostic utility in HIV infected patients.

4. **Treatment**: Cytomegaloviral infection is neither preventable nor curable. Efforts are being made to produce a vaccine. Antiviral agent gancyclovir is a potent inhibitor of CMV replication. The medication is available only for intravenous administration and has significant toxicity.

**Reynolds et al (1974)** suggested that some of the estimated 1 in 1000 cases of unexplained profound deafness in American children may be caused by congenital CMV infection.

**Lawrence Hatherley (1985)** said 12 neonates in 47,320 consecutive births cytomegalic inclusion disease confirmed by viral studies, an incidence of approximately 1 in 4000 deliveries, further 4 cases were diagnosed in 738 (1 in 185) neonates for intensive care. Congenital CID was diagnosed in 12 to 16 neonates and post natal infection in remaining 4 infant, the sexes were equally represented which included 1 set of twin. Five deaths occurred in hospital between 6 hours and 135 days of delivery. 112 infants were discharged for follow up and 7 showed CMV infection.
Griffith and Babrobin (1992) pointed that foetal loss occurred in 4/25 (5%) of early CMV infection. The transmission of CMV from mother to foetus in early pregnancy is very high.

Transmission of CMV = Transmission of HIV – 1 in 8 weeks foetus.

They are suggested that potential CMV carrier may transmit CMV to their foetus in early pregnancy. The rate of CMV IgM is 5.6% but the incidence of congenital CMV infection of chronic villi in early pregnancy was 23.5%.

Chiba (1992) said congenital CMV infection after secondary maternal infection, common in Japan. Did not describe the route of infections whether hematogenous or ascending or in the birth canal (Chibe, et al 1992, Ahlfors et al 1993).

In patients, post transfusion infection could be excluded since the infant was positive for anti CMV IgM before receiving transfusion, the breast milk was doubtful source of infection since the period of incubation is too short for seroconversion. Transmission through birth canal is unlikely by caesarean delivery, CMV had ascended from vagina via ruptured membrane to reach the decidua or amniotic fluid. The foetus then aspirated the virus to develop a congenital pneumonia.
HERPES SIMPLEX VIRUS

Herpes simplex virus is of major obstetric interest because it is one of the most common sexually transmitted diseases and because of its potential to cause severe foetal and neonatal infection.

Epidemiology:

HSV belongs to the herpes virus family who have the ability to persist throughout the life of their host to produce recurrent infection. Primary infection occurs 2-12 days after the introduction of the infectious secretions into the oral cavity (HSV-1) genital area (HSV-2) skin or eyes. 50% of adults have antibodies to HSV with a higher prevalence in certain populations including male homosexual and those from developing countries.

Clinical Features:

In Infants:

1. Acute gingivostomatitis: Common age of occurrence is of 10 months to 3 years, onset is abrupt with fever, generalized malaise, irritability and soreness of the mouth lesions are seen just inside the lips. After healing mucosal lesions do not reoccur but skin lesions may reappear over a period of many years, these vesicles are called cold sores. common precipitating cause of recurrence is febrile illness, trauma, and exposure to sunlight.
2. **Genital Herpes**:

**Vulvovaginitis**: In female infants HSV may be the cause of vulvovaginitis typically there are herpetic eruption around the vulva area becomes inflamed and painful. In males there may be herpes of glans penis.

3. **Infection of the eye**: The most common herpetic infection of the eye in infants is acute oedematous conjunctivitis with chemosis and stickyness of the lids. The preauricular lymphnodes are enlarged and tender. Corneal involvement leads to formation of dendritic ulcer and loss of vision.

4. **Skin Infection**: Eruption involves any area of the skin, common are napkin area of the skin.

5. **Meningitis**: It may be the rare cause of meningitis.

6. **Acute generalized infection**: Neonatal infection with HSV is often life threatening and causes severe morbidity amongst some infants.

Genital herpes simplex in pregnancy poses a risk for transmission of infection to the foetus at birth during prolonged rupture of membrane as well as possibly a risk for congenital malformation of the unborn. In late 1960 it was discovered that there are types of herpes simplex virus infecting humans. Type-1 causes a majority of oral infection and type-II causes genital infection, with either type is often asymptomatic but often gives a long lasting IgG response. Neonatal infection with HSV is often life
threatening and causes severe morbidity among some infants (Whitley et al 1980 Stone et al 1988). Genital herpes in pregnancy are associated with increasing foetal and maternal morbidity and mortality (Nahmians et al 1971). HSV has been reported to increase spontaneous abortion and neonatal death in this study comparing the pregnancy outcome of 15 patients with primary genital herpes and 14 with non primary 1st episode disease complicating pregnancy. 6 of the 15 (40%) patients with primary infection developed a serious obstetrical and perinatal complication.

Adverse outcome increased with advancing gestation with 1 of the 5 cases in 1st trimester, 1 of the 5 cases in second trimester and 4 of the 5 cases in third trimester demonstrating 1 or more of these complications.
The human immuno deficiency virus is the cause of acquired immuno deficiency syndrome (AIDS), a condition that affects hundreds of thousands of individuals in the United States and many more throughout the world. The demographics of this disease are changing, and HIV is infecting a growing number of women of reproductive age. As a consequence, the number of infants born to HIV-infected mothers is also rapidly increasing.

Virology:

There are five known human retroviruses (HIV-1, HIV-2, HIV-I, HIV-II, and HIV-IV), and three of them are associated with human disease. HIV-1 and HIV-2 cause AIDS, and HIV-I most probably is the causal agent of T-cell leukemia/lymphoma. HIV-I, the most common cause of AIDS in the United States, has an envelope formed by three glycoproteins (gp160, gp120, and gp41) surrounding a core that contains other proteins (p55, p40, p24, p17), reverse transcriptase, and endonucleases.

Attachment of the virus to the host cell is a critically important step in the mechanism of infection. The virus only infects susceptible cells that express in their surface a glycoprotein called CD4. CD4 is recognized by the glycoprotein gp120 that is present in the viral envelope. The best-known susceptible cells in humans is the CD4 or T4 helper-inducer T lymphocyte. Invasion and eventual destruction of these cells by the HIV-I virus will cause the profound alteration in the immune system that is characteristic of AIDS.
Once inside the cell, retroviruses follow a unique reproductive cycle that involves reverse transcription of their ribonucleic acid (RNA) into deoxyribonucleic acid (DNA), incorporation of the newly synthesized DNA into a host cell DNA, transcription of the viral components. The viral DNA may remain incorporated into the host cell DNA for prolonged latent periods until viral synthesis is activated. What conditions until viral synthesis is activated is unclear.

**Maternal infection:**

Women account for approximately 10% of AIDS cases. The large majority of them are black or Hispanic and between 15 and 35 years of age. Most of them are intravenous drug abusers, have multiple sexual partners, and have intercourse with partners at high risk.

Maternal HIV is acquired primarily by sexual contact or by parental exposure to blood or blood products. Most sexual transmission is the result of receptive vaginal or anal intercourse with infected partners. Transmission by exposure to blood or blood products is usually the result of needles or syringes being shared between intravenous drug abusers. Rarely, maternal infection results from the administration of blood or blood products, especially if they were received before April 1985 when individuals from high risk groups were not excluded as donors.

The initial infection with HIV is asymptomatic. Serologic evidence that infection has occurred may be obtained 2 to 8 weeks after the initial infection, but in some cases it takes up to 6 months
before an antibody response. Then infected individuals undergo a prolonged period without symptoms, during which they are shedding virus into most body fluids and are infective. Most pregnant women with HIV infection are in this phase of asymptomatic carriers. At some point in the evolution of the disease, infected individuals develop symptoms and signs called AIDS-related complex, or ARC. ARC is characterized by generalized lymph node enlargement, fever, night sweats, weight loss, and unusual recurrent infections such as herpes or candidiasis. ARC is followed by the final stage of the disease, or AIDS, that is a condition characterized by the consequences of a severe dysfunction of the immune system. Patients with AIDS develop a series of systemic or local infections by opportunistic organisms such as candidiasis, cytomegalovirus, herpes, histoplasma, Cryptococcus and Pneumocystic carinii or develop Kaposi’s sarcoma. Lymphoma of the brain, or multiple recurrent bacterial infections.

Prospective studies have demonstrated that maternal HIV infection does not affect the outcome of pregnancy. However, since a significant number of infected mothers are IV drug abusers, they are at increased risk for preterm delivery and low birth weight infants. Also, there is no evidence that pregnancy accelerates the progression of HIV infection.

**Diagnosis:**

The diagnosis of HIV infection is serologic, by virus culture or by detection of viral DNA or RNA using polymerase chain reaction (PCR). The screening procedure is an ELISA test may produce false-positive results, and all positive tests should be
followed by Western blot analysis. Western blot detects antibodies against glycoproteins p24, p31, gp41, and gp160. The presence of antibodies against these structural and envelope proteins is a reliable indication of infection. Results of the Western blot are given as positive, negative or undetermined. The probability of a false-positive diagnosis is almost nil if two ELISAs and one Western blot are positive. Once the presence of infection has been demonstrated, it is possible to use determination of CD4 cells to assess the severity of the immunologic dysfunction.

Viral cultures and PCR may be used for diagnosis of HIV under special circumstances. Cultures are labor intensive, expensive, and less sensitive than serologic testing. PCR is a very sensitive technique that has the potential to become the test of choice for the diagnosis of HIV infection.

**Fetal transmission:**

Approximately 24% of infants born to HIV-infected mothers will demonstrate the presence of the disease by 1 year of age. It is not clear if the infection is transmitted during pregnancy, during delivery, or shortly after birth, although there is evidence that fetal infection may occur by transplacental transmission, by contact with infected secretions, and through breastfeeding.

Significant effort has been directed to the identification of factors predictive of fetal infection. Once of these factors is the previous birth of an infected child. Another is severely depressed immune function as shown by low CD4 counts. The presence of maternal antibodies against certain epitopes or against the principal
neutralizing domain of the envelope protein gp120 is also predictive of the absence of new born infection.

The majority of babies born to HIV-positive mothers have no physical signs of infection. A few of them may exhibit the so-called HIV embryopathy characterized by growth retardation, microcephaly, and craniofacial abnormalities. All infants of HIV-infected mothers have positive HIV serology as a consequence of passive transfer of maternal antibodies. Levels of these antibodies decline gradually, and by 6 months of age, most noninfected newborns will be seronegative. The presence of positive serology resulting from passive transmission of antibodies makes difficult the diagnosis of HIV infection in the newborn. In this situation viral cultures and PCR testing should be done to confirm or rule out infection.

**EPIDEMIOLOGICAL ASPECTS**

**Global distribution of HIV:**

The epidemiology of AIDS in developed countries in Western Europe, North America has recently been received by Alder 1988.

WHO estimates that by 1993 more than 2.5 million adult full blown cases may have occurred world wide, although AIDS was first recognized in USA in 1981, earlier case were found by retrospective analysis to have occurred in 1978 in the USA and in the late 1970’s in equatorial Africa (WHO 1986).

The number of AIDS cases gives a forecast rather than a true reflection with a virus that takes many years to causes illness.
An explosion of HIV has recently occurred in South East Asia, particularly in Thailand, Burma and India where with in only a few years over two million people may have already been infected, during the next decade HIV is likely to reach most of the communities around the world and geographic boundaries cannot protect against HIV.

**HIV infection in India**

The first group of seropositive individual in India detected in April 1986 were ten prostitutes, with in short span of 18 months it became obvious that the seropositivity rate was low 4/1000 and heterosexual promiscuity was the major mode of transmission in India (ICMR).

As the contraceptive use is quite low and birth rate continues to be high in India, it is therefore not surprising that pregnancies among seropositive women were reported in 1986 itself, first seropositive pregnant mother was detected in Sept. 1986 (ICMR). First seropositive infant was detected in 1987.

Till Nov-Dec. 1990 out of 44 Indian AIDS patients reported to ICMR, 8 were women.

No patients of paediatric AIDS was reported till Dec. 1990.

1st Dec. is being observed as world AIDS day since 1988. 1990-91 being observed as *women and AIDS* with following aims.

To continue to increase awareness about HIV/AIDS.
To strengthen the world wide efforts to stop AIDS by highlighting the impact of HIV/AIDS in women the world.

AIDS Surveillance:

Govt. Of India has established a network of surveillance centres in the country to screen high risk group (Govt. of India 1991). This includes establishment of nine referral centres (e.g. National institute of virology Pune, Christian Medical College Vellore, All India Institute of Medical Sciences, New Delhi and National institute of Communicable Diseases, Delhi) where higher level diagnostic facilities are available. By the end of 1992, Govt. of India has established 62 surveillance centres for screening persons practicing high risk behavior. Realizing the gravity of epidemiological study of HIV in the country a separate wing “National AIDS control organization” has been set up under the Ministry of Health and Family Welfare.

Jovaicas et al (1985) gave termination of pregnancy in an antibody positive women at wks gestation and foetal sample were found to contain HIV. So HIV seropositive among pregnant women is therefore a great risk to unborn child.

Gloeb et al (1988) report of 50 HIV seropositive pregnant women found that 35 seropositive women have complicated perinatal courses and most commonly premature labour or infections complication. Premature labour complicated 35% of pregnancies among HIV infected women.
Glaeb and colleagues (1988) followed the clinical course of 50 HIV infected women ante partum and or post partum. Three patients died of complications related to AIDS. Two of these were asymptomatic when first seen in the course of their pregnancy and two developed pneumocystis carinii pneumonia and died during pregnancy and third developed toxoplasma gondii encephalitis at 18 weeks gestation and died four months after delivery. Another two patients developed AIDS related symptoms in the third trimester.

Jean Pape (1988) obtained information about sexual activity on 151 HIV seropositive and 131 seronegative spouses of male AIDS followed from 1983 to 1986. As a result 14% (22/151) of the seropositive sex partner have become pregnant during a mean period of follow up of 15 months (range 2-36 months) and 18 months (range 2-38 months) respectively. 27% of the seropositive pregnant women (6/22) had a miscarriage compared to 13% of the seronegative pregnant women.

Embers (1989) studied HIV infection on foetus growth failure may be seen in 75% or more of infected infants it has been suggested that deformities including microcephaly, ocular hypertension, prominent forehead, flat nasal bridge long palpebral fissures, and blue sclera and patulous lips may be associated with congenital infection, however, the relationship of these features to HIV infection has been challenged.

Lakshmi & Gururaj kumar (1989) studied 2 pregnant women, one of 400 were found to be seropositive for HIV antibody
by ELISA, the positive rate being 0.5% both of them were primigravida in mid term pregnancy came from urban area and belonged to low socioeconomic status. There was also history of multiple sexual partners, drug abuse, and blood transfusion in the past and their husbands had history of STDs.

Kell et al (1991) reported a 26 year old Ugandan woman presented 10 weeks gestation in her second pregnancy to a direct general hospital causality department complaining of shortness of breath or excretion, fever and productive cough for 1 week, six year back she had an uneventful pregnancy, as she had arrived in British as a political refuge. Only two weeks before initial physical examination revealed tachypnoea (70/min) and pyrexia. Her chest x-ray was suggested of an interstitial pneumonia. Arterial blood goes on air showed a po2 of 10.0 kpa. She was treated with intravenous ampicilline and erythromycin for 3 days, she continued to deteriorate. A blood sample was taken to test for HIV antibody after the patients was conselled the result was found to be positive. This case represents to be reported in Britain, diagnosis of HIV seropositivity affect the outcome.

Johnstone et al (1992) believes that the pregnancy is associated with mild impairment of cell mediated immunity and increased virulence of some infections.

European collaboration study group (1992) demonstrated in 30 Nov. 1992. 1200 mother child pairs were enrolled (19 European centres). Children with known HIV infection (born to women with HIV positive antibody at or before the delivery) status were
available for present analysis. All multiple pregnancies and children whose HIV infection status was still indeterminate were excluded. 3 months were known to receive Zidovudine during pregnancy and all 3 infants were uninfected.

Caroline et al (1994) said that at least two hypothesis can be suggested for the effect of pregnancy on HIV diseases progression, first the short term risk of developing AIDS or HIV related disease may be much higher during pregnancy, with no residual excess risk once the pregnancy is over. The immediate risk of developing AIDS returns to what it would have been if the pregnancy has not occurred, alternately pregnancy might accelerate HIV disease progression irreversibly leaving women who have been some time if the pregnancy have never occurred multiple pregnancies would produce a cumulative detrimental effect on risk.

**Corelation between TORCH and HIV infection**

**Corelation between HIV and Toxoplasma:**

Women infected with HIV are at risk for transmission of Toxoplasma Gondii infection to the foetus both of they are seronegative for T. gondii antibodies and acquire T gondii infection during pregnancy and if they are seropositive for T gondii antibodies and suffer reactivation of their latent T gondii infection because of immune deficiency from HIV infection.

Mitchell et al (1990) revealed a congenital transmission rate for women who are dually infected with HIV and T gondii that was remarkably higher when compared to non HIV infected, Toxoplasma seropositive pregnant women.
All infants with congenital Toxoplasma born to mother who were HIV infected also were infected with HIV.

The initial clinical presentation of congenital Toxoplasma in HIV infected infants is similar to that and non HIV infected infants but appear to run a more rapid and progressive course. The infants often appear normal at birth. In the ensuing month, they fail to gain weight or develop opportunity. The majority develop, multisystem organ involvement including CNS, Heart, Lungs.

Corelation between Toxoplasma and Rubella:

Chitra Raghunandan (1993) said the present study was conducted in 25 cases of missed abortion between 6-20 weeks of gestation and 25 cases of unexplained intrauterine death between 21-40 weeks of gestation, 25 cases of MTP and 25 cases of normal pregnancy were taken as control. Their sera were tested by ELISA for IgM specific antibodies to Toxoplasma gondii and rubella.

The 50 cases of study group, 16 cases (32%) showed antibodies to Toxoplasma, (6 cases) Rubella, (1 case) and Syphilis (9 cases) as compared to all the control cases with more than one etiological agent. All 6 cases seropositive for Toxoplasma as well as 1 case of Rubella were associated with missed abortion were 8 cases out of 9 cases of Syphilis associated with late foetal death.
Correlation between Toxoplasma gondii, Rubella, Cytomegalovirus and Herpes simplex virus:

P. Prabhaker (1990) seroprevalence of Toxoplasma gondii, Rubella virus, Cytomegalovirus and Herpes simplex virus infection and Syphilis were determined in order to assess and the immunosusceptibility foetus in American pregnant women in 1986 the positive rate were 57% (T. gondii), 69% (Rubella), 97% (CMV), 91% (HIV) and 4.9% (Syphilis) respectively. The rate of reactivity for syphilis ranged from 2.1% in the Kingston and St Andrew at 7.3% in rural parishes. The seropositivity for syphilis ranged from 21% and the seropositive rate for Rubella was over 50% in parishes, the highest being 85% in St Thomas.

The seroprevalence of T. gondii was lowest in Trelawny (37.5%). There were no significant differences in seropositivity of CMV and HSV infected women in various parishes.