Genetics

Biology Dept.3rd stage

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Lec-14- 2- infections (biological pollution) :

a-Viral :

-German measles (Rubella) : deafness, blindness, cataract, retinopathy, glaucoma, microcephaly, mental retardation . Attenuated virus causes damage to the fetus, so give vaccine before pregnancy by three months

-Hepatitis, small pox, chicken pox : may cause abortion, stillbirth, skin diseases, hepatitis … etc .

b-bacterial :

Syphilis: hydrocephalus & mental retardation, deafness, tooth malformation, meningitis & CNS disturbances .

Tuberculosis : Wt. loss, refusal to suckle, hepato-splenomegaly

c-protozoal :

toxoplasmosis : it is transmitted to pregnant women by feces of domestic cats & birds causing hydrocephalus, CNS disturbance, microcephaly, hepatosplenomegaly & blindness .

3- maternal diseases :

- uncontrolled diabetes mellitus, hyperthermia &thyrotoxicosis(hyperthyroidism) teratogenicity & toxemia of pregnancy

4-Alcohol :

Fetal Alcohol syndrome (FAS) : growth failure & delayed development, microcephaly & mental retardation , defects in the eye, face (cleft palate) , congental abnormalities in heart, skin & kidneys .

5-Drugs :

-Highly teratogenic drugs as" thalidomide,warfarin ,corticosteroids , anticancer drugs .

-The following drugs are hazardous if given during the 2nd or 3rd trimester, some of them are hazardous also if given during the 1st trimester :

6- malnutrition :

Vit. A anophthalmia .

Vit. D bone and teeth malformation .

Folic acid malformations .

A wide range of different chemicals and environmental factors are suspected or are known to be teratogenic in humans and in animals. A selected few include

•Nicotine (Tobacco(

It is estimated that about 30% of all women of childbearing years smoke, and 25% of all women will continue on smoking during pregnancy. Many studies have been conducted in the past few decades which link maternal cigarette smoking during

pregnancy with adverse pregnancy outcomes, including intrauterine growth retardation, preterm delivery, perinatal mortality, and spontaneous abortions.

•Caffeine

High doses of caffeine have been reported to cause adverse developmental effects of the central nervous system. Although caffeine is not classified as a human teratogen, it is likely that excess consumption during gestation can result in embryotoxic effects.

•Ethanol (Alcohol) fetal alcohol spectrum disorder(

Binge drinking during pregnancy is associated with birth defects such as intrauterine growth retardation, microcephaly, cardiac abnormalities and maxillary hypoplasia. Studies show that approximately one third of the children born to alcoholic mothers suffer from fetal alcohol syndrome and all affected children exhibit developmental delay. High risk of exposure constitutes chronic consumption of 6oz of alcohol per day. If the mother drinks less than 2 oz of alcohol per day, fetal alcohol syndrome is unlikely to develop. Acetate, an ethanol metabolite, is 10 000 more embryotoxic. It is likely that the mechanism of action of these two agents differs substantially. The primary effect of alcohol on the fetus is the inhibition of cell growth and altered placental transport of amino acids to the fetus, as demonstrated in the mice and rat animal models.

•Coumarin (Warfarin)

Coumarin in-utero exposure is known to cause risk of nasal hypoplasia, calcific stiffing of secondary epiphysis, and central nervous system abnormalities in 10 to

25% of exposed infants. Coumarin inhibits the formation of carboxyglutamyl residues, decreasing the ability of proteins to bind calcium. A useful animal model has not yet been reported

Cyclophosphamide

Defects caused by this agent include growth retardation, ectrodactyly, cardiovascular defects and other smaller anomalies. Experimental evidence gathered in rat, mice, rabbit and monkey models has shown a high susceptibility of the nervous system and mesenchymal tissues. These reaction products are though to produce teratogenic effects associated with exposures to cyclophosphamide by interacting with cellular DNA which results in cell death.

•Tetracyclines

Antimicrobial tetracyclines prevent bacterial protein synthesis by inhibiting access of aminoacyl tRNA to the mRNA-ribosome complex. Tetracyclines can readily cross the placenta and they have been shown to cause teeth discolouration, depression of skeletal bone growth and extremely high doses may result in hypoplasia of tooth enamel. Tetracyclines can complex with calcium and organic matrix of newly forming bone.

•Thalidomide

Thalidomine was first synthesized in 1954 and marketed in 1956 in Germany. It was studied in rodents for a variety of toxicities, and even when administered at

very high doses, no side effects were observed. With increasing sales in 46 counties, it was marketed for treatment of influenza and promoted as a remedy for sleeplessness. It was never approved in the United States for commercial sale; however thousands of samples were distributed to physicians. It was often prescribed to pregnant women to treat morning sickness. In 1961, a significant increase in congenital limb defects in exposed newborns became apparent. Today, there are 5000 thalidomide survivors worldwide and they are in their late forties. The stress placed on their body structures is causing further physical deterioration, resulting in new disabilities.

•Aspirin

Chronic high exposure of pregnant women to aspirin has been associated with low birth weight and a variety of maternal and placental complications.

•Retinol (Vitamin A(

Vitamin A in the form of retinoic acid, is a potent teratogen. Its two primary modes of action have been established: direct cytotoxicity and interactions with DNA, which collectively cause a delay in differentiation and/or inhibition of protein synthesis. [It is now appreciated that retinoids play a widespread critical role in developmental control. Some phenotypic abnormalities followed by excess Vitamin A included abnormal brachial arch development, ear malformations or cleft palate. Vitamin A deficiency in pigs resulted in offspring being born with no eyeballs.

•Vitamin D

Excess of Vitamin D during pregnancy has increased the incidence of a syndrome consisting of supravalvular aortic stenosis, elfin facies, and mental retardation in humans.

Environmental chemicals

•Polychlorinated biphenyls (PCBs(

First teratogenic potential of PCBs was identified in Japan in 1968 when consumption of contaminated cooking oil by pregnant women resulted in pigmented children with low birth weights, pigmentation of gums, nails and groin, calcification of the skull, rocker bottom heal and conjunctivitis

•Methylmercury

Mercury is known to interfere with metabolism and function by combining with phosphoryl, carboxyl, amide and amine groups resulting in enzyme inhibition and protein precipitation. The most documented case of human exposure took place in Japan in 1953 where the local population ingested fish caught in a bay heavily polluted by methylmercury. Resulting congenital abnormalities in infants born to exposed mothers included cerebral palsy and associated microcephaly.

•Other: ethidium bromide, polycyclic aromatic hydrocarbons (polynuclear aromatic hydrocarbons(

Ionizing radiation

•Iodine-131

Exposure to radioactive iodine creates a potential risk to the developing fetal thyroid, especially once it begins to concentrate iodine at 10 to 12 weeks of gestation.

•Radiation therapy

Damage to cell chromatin is the direct result of radiation. Most common malformations associated with therapeutic radiation in pregnant mothers include intrauterine growth retardation, gross malformations and embryonic cell death..

•Other: uranium, background radiation, diagnostic x-rays, Iodine-131

Infections

Viral

•Cytomegalovirus • Herpes virus • Parvovirus B19 • Rubella virus (German measles) • Venezuelan equine encephalitis virus

Metabolic imbalance

• Diabetes • Folic acid deficiency • Iodine deficiency • Maternal Starvation • Obesity • Other: Hyperthermia, phenylketonuria, rheumatic disease, congenital heart block, virilizing tumors, Endemic cretinism.