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TERATOGENICITY: A BASICS REVIEW

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ABSTRACT:

Teratogens are environmental agents that can cause birth defects or abnormalities in a developing fetus when a pregnant mother is exposed to them. These agents can be physical substances or conditions affecting the mother, resulting in physical or functional defects in the embryo. Exposure to teratogens during pregnancy can significantly impact fetal development, with approximately 4-5% of birth defects attributed to teratogen exposure. The critical period of susceptibility is believed to be between 10-14 days after conception, when the blood supply connection forms between the fetus and the pregnant individual. Since the term *"Teratogens"* was first coined in Paris in 1932, research has highlighted the importance of identifying and mitigating teratogen exposure to ensure healthy fetal development. This knowledge is crucial for expectant mothers, healthcare providers, and policymakers seeking to prevent birth defects and promote optimal prenatal care.

KEYWORD: teratogen, FDA, term teratogen, Pregnant person, etc.

Definition

Teratogens are agents that, after coming into contact with a pregnant mother, cause an abnormality in the developing fetus. A teratogen can be a physical substance or a maternal condition. The resulting abnormality can be a physical abnormality or a functional defect during the embryo called teratogenicity.

A teratogen is an environmental factor to which a person is exposed during pregnancy, which can affect the development of the child, leading to birth defects. In fact, about 4-5% of birth defects are the result of exposure to teratogens. When the child has developed and a blood

connection is established between the child and the pregnant person, everything that the pregnant person is exposed to, including Teratogens, can be transmitted to the child and affect its development. For this reason, it is believed that teratogens can affect the child between 10 and 14 days after conception.

INTRODUCTION

The term teratogen was first written in Paris, France in early 1932. The term teratogen comes from the Greek word teras, which means monster or wonder. Teratogens are environmental agents such as drugs, viruses, lack of nutrients and physical or chemical elements, which in contact with the embryo / fetus Can cause congenital anomalies, generating permanent functional or morphological changes in the newborn. An agent is now considered teratogenic if its administration to the pregnant mother causes, directly or indirectly, structural or functional abnormalities in the fetus, or in the postnatal child, which may not be apparent until later in life. A human teratogen is an agent that alters the growth or structure of a developing embryo or fetus, thereby causing birth defects. The first human teratogen identified in 1941 by an ophthalmologist, Norman Gregg, was maternal rubella infection during pregnancy, which caused a triad of malformations (cataracts, heart defects, and deafness) in children. After the identification of thalidomide, an antinausea agent, as a major human teratogen causing severe birth defects in 1961, teratological research began to expand and awareness of the potential teratogenic impact of maternal exposure during pregnancy was noted. A teratogen can cause chromosomal abnormalities, prevent implantation of the conceptus, and cause early embryo abortion, late fetal death, congenital malformations, or intrauterine growth retardation. In the newborn, there can be a functional dysfunction, for example deafness. Behavioral abnormalities and mental retardation may also occur.

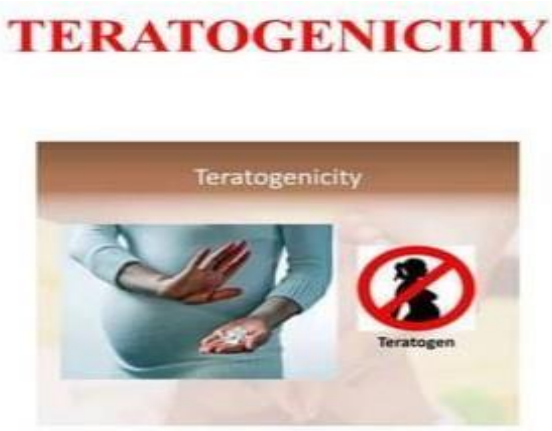


Fig. No. 01

Most pregnant women take at least one medication during pregnancy, although the safety of these medications during pregnancy is not always known. We examined the safety during pregnancy of 172 drugs approved by the US Food and Drug Administration (FDA) between 2000 and 2010 using the TERIS risk assessment system. We also examined safety information for 468 drugs approved by the FDA Between 1980 and 2000 to determine whether risk category revisions had been made in the past 10 years. The teratogenic risk during human pregnancy was "undetermined" for 168 (97.7%) of the drug treatments approved between 2000 and 2010. In addition, the amount of data available regarding safety during Pregnancy was described as "none "for 126 (73.3%) from these drugs. Among drugs approved between 1980 and 2000, only 23 (5%) changed their risk category completely or more in the last 10 years. The data sources that led to the revised risk emerged from exposure cohort studies conducted through data linkage studies, teratogen information services, case-control studies in large-scale population-based Registries, and registries of pregnancy The median time for a treatment initially classified as an "undetermined" risk to be assigned a more accurate risk was 27 years (95% confidence interval 26-28 years). The lack of information needed to assess the safety of drug treatments during human pregnancy remains a serious public health problem. A more active approach to post-marketing surveillance of teratogenic effects is needed.

Birth defects are the leading cause of infant mortality in high-income countries and the second most Common cause in many middle-income countries. Such conditions appear during fetal development and can be inherited or influenced by environmental factors, such as drug exposure. Teratogenesis refers to structural malformations during fetal development, as distinguished from other types of drug-induced fetal damage, such as growth retardation, dysplasia (e.g., iodine deficiency goiter), or asymmetric Reduction of l art. Exposure to teratogenic chemicals before conception, during prenatal development, or after birth results in manifestations of developmental toxicity, including death of the developing Organism, structural abnormalities, impaired growth, and functional dysfunction.[4] A recent review of the available data concluded that exposure to small amounts of nitrous oxide is not associated with impaired fertility or an increased risk of developing cancer;however, recent studies seem to suggest a correlation between nitric oxide anesthesia and hyperhomocysteinemia, an independent risk factor for heart disease. Long-term exposure to high concentrations of nitric oxide can cause megaloblastic Depression of the bone marrow and neurological symptoms. Teratogenic", meaning that a chemical agent or other agent may have some property of being

teratogenic or non-teratogenic. We use the term "teratogenic exposure" to include not only an agent, but also the level of exposure (dose) and Considerations related to the timing of exposure. We worry about classifying X-rays, for example, as teratogenic and about someone giving bad advice to a woman who had a chest X-ray in early Pregnancy.The development of malformations in an embryo. Growth, ontogenesis, ontogenesis, maturation, development (biology) the process of organic growth of an individual organism; a purely Biological flow of events involved in an organism gradually passing from a simple level to a more complex level; "He proposed an indicator of bone development in children "After an egg is fertilized by a sperm, the resulting zygote moves to the uterus and develops into an embryo. Cells begin to divide,increasing the size of the embryo and it migrates from the fallopian tubes to the uterus, where it eventually settles, being implanted in the uterine wall. This happens about a week after conception. After implantation, the growth of supporting structures such as common blood vessels begins. Finally, about 2 to 3 weeks after fertilization, the embryo shares a blood supply with the mother. It is during this period that the embryo Can be affected by teratogenic agents.

History of teratogenicity

A description of the events from year to year, including the scientific and social content of the annual meetings and changes in the activities of the Society, is given, in many cases, with the help of comments from past presidents. The valuable and unique diversity of the membership is discussed and illustrated, showcasing the Major disciplines and research areas of the chairs. The number of submissions and the different Categories are tabulated, calculating the average number and type in the four time periods. During 10 In recent years, a significant increase in the number of submissions dealing with epidemiology and Developmental biology is evident. The development of Society is compared to that of man and the question is asked: Have we reached the maturity stage of old age or old age, or is society still mature? This issue requires more discussion from all members.

The 49-year history of the Teratology Society is reviewed. A brief history is presented in tabular form, with a list of Warkany's conferences, continuing education courses and company officials. The original article has been updated to include the years 2000 to 2010. Over the past 50 years, we have developed the Scientific basis for preventing birth defects caused by rubella, alcoholism, and folate deficiency, and even other prenatal exposures. Now benefit of progress in many areas to begin forming the Teratology Society of the 21st century.

A story should record and honor the past, help plan for the future, and entertain the Reader. In 1998, Philip Mirkes, president of the Teratology Society, asked the authors to write a history of the Teratology Society to coincide with the year 2000. For the society's 50th annual meeting in 2010, the The original story article was updated by John Rogers. Teratology is the science that studies the causes, mechanisms and patterns of abnormal development. Teratology as a modern science began in the 1930s with the publication of a series of experiments in which pregnant sows were fed a diet low in vitamin A. All these pigs suffered from various malformations, mainly the absence of the eyes.

The first human teratogen Identified in 1941 by an ophthalmologist, Norman Gregg, was maternal rubella infection during pregnancy, which caused a triad of malformations (cataracts, heart defects, and Deafness) in children. Almost 60 years ago, thalidomide was prescribed to treat morning sickness in pregnant women. What followed was the largest medical disaster ever caused by man, with more than 10,000 children born with a variety of severe defects and disabilities. Despite this, the drug is now used Successfully to treat a variety of diseases in adults, including multiple myeloma and complications of leprosy.

Table no. 1 Historical events in modern teratology [9].

Year	Historical event
1905	The first experimentally induced developmental toxicity in mammals. Embryonic lethality induced by X-rays in cats (Tousey)
1921	The first experimentally induced teratogenicity in mammals. Disorders in limbs in pigs induced by lipid diet (Zilva et al.).
1929	The first description of malformations in humans caused by exogenous factors. Microcephalia caused by X-ray irradiation of the pelvis (Goldstein and Murphy).
1935	Recognition of food deficiency leading to malformations in animals. Eye disorders in pigs due to hypovitaminosis A (Hale).
1937	Hormones causing alterations in sexual differentiation in animals. Masculinisation of female foetuses in mice due to theaction of androgens (Raynaud)
1941	Report on virus-induced human malformations. Rose-rash induced eye disorders (Gregg).
1944	The first evidence of postnatal effect following prenatal administration of a chemical substance. Decreased learning ability inrats caused by the administration of sodium bromide (Hamiltonand Harned).
1948	General recognition of chemically induced teratogenicity. Experiments with alkylating agents (Haskin) and trypan blue(Gillman et al.).
1952	The first report on malformations caused by drugs in humans.Multiple malformations in foetuses caused by aminopterin(Thiersch).
1959	The first report on human malformations induced by environmental pollutants. Disorders of the central nervous system anddentition caused by methyl mercury (Kitamura et al.).
1961	Thalidomide-induced embryopathy

In the 1930s, a series of studies were published with pregnant sows fed a diet low in vitamin A, which marked the beginning of teratogenesis as a modern science. Most of the abnormalities encountered by these eyeless piglets were similar. Osef Warkany, doctor, is

recognized as the founder of experimental teratogenesis. He was the first to demonstrate, in the 1930s and 1940s of the last century, that external causes can also cause CDD in mammals. Various Important events in history related to teratogenesis.

Update on teratogens in children

Applying the principles of teratology can help assess the potential for exposure to teratogens. The Identification of the Zika virus as a teratogen, the most recently identified teratogen, has enabled public health measures to mitigate its spread. Risk management strategies for teratogenic drugs have resulted in a reduction, but often not elimination, of prenatal exposure. Failure to include pregnant women in clinical trials makes them less likely to receive the necessary medications and vaccines at the right time. Pediatricians play an important role in the prevention of teratogenic exposure. It is essential to provide optimal care for patients with chronic diseases that may increase the risk of congenital malformations during pregnancy due to the disease itself or its treatment. For patients who may become pregnant and Are taking teratogenic medications, it is also important to provide effective contraception. Involvement of pregnant women in clinical trials and research studies will be essential to advance our knowledge about the safety of medications and other exposures during pregnancy.

Teratogen Update: - Zika Virus and Pregnancy

The Zika virus was first identified in Uganda in 1947, but received little attention until 2015, when a large outbreak of Zika virus disease followed by a number of growth of children born with microcephaly occurred in Brazil. The Zika virus spread rapidly in the Americas and was identified in 2016 as a cause of microcephaly and other serious birth defects. Since then, much has been learned about the Zika virus. The virus spreads mainly From the bite of the Aedes mosquito; however, other forms of transmission (for example, sexual and intrauterine) are recognized. Although postnatal Zika virus infection usually causes mild or no symptoms, the effects on babies born to prenatally infected mothers can be severe and include structural birth defects and neurodevelopmental effects. The risk of structural birth defects in children born to mothers infected or suspected of having the Zika virus during pregnancy is between 5 and 10%. The timing of Zika virus infection during pregnancy affects the risk, with the highest risks when infected in the first trimester.

Neurodevelopmental effects are seen even in children who appear normal during the neonatal period. Although cases of Zika virus infection have decreased in the Americas, Zika virus remains an active threat in some parts of the world. Developing a vaccine for the Zika virus

will require continued attention and investment. Until a vaccine against the Zika virus is available, preventive measures for Pregnant women include avoiding travel to areas with active Zika virus transmission, avoiding mosquito bites for those living or traveling to areas with Zika virus transmission, and protecting themselves against sexual transmission.

Infections and viruses

Infections, viruses, parasites and other bacterial diseases can be a serious threat to the pregnant woman and the fetus. The acronym TORCH allows us to classify some of them:

- Toxoplasmosis (an infection spread through cat feces).
- Other infections such as group B streptococcus, listeria, candidiasis and sexually transmitted infections (STIs).
- Rubella.
- Cytomegalovirus (CMV).
- Herpes simplex virus.
- Syphilis.

Other infections and viruses that can cause pregnancy complications or problems in the fetus are

- Chicken pox and herpes.
- Hepatitis B, hepatitis C and other viral hepatitis.
- HIV.
- The fifth disease.

Identification of human teratogens: an update

A human teratogen is an agent that alters the growth or structure of a developing embryo or fetus, thereby causing birth defects. The first human teratogen identified in 1941 by an ophthalmologist, Norman Gregg, was maternal rubella infection during pregnancy, which caused a triad of malformations (cataracts, heart defects, and deafness) in children. After the identification of thalidomide, an antinausea agent, as a major human teratogen causing severe birth defects in 1961, research in 1961.

Teratology began to develop and awareness of the potential teratogenic impact of maternal exposure during pregnancy increased. Several factors that determine the teratogenicity of an exposure have been defined as Wilson's principles of teratology, which guide researchers in the study and understanding of teratogens. These include, but are not limited to, the

following: Abnormal development produced by teratogenic exposure manifests as death, malformation(s), growth retardation, or functional dysfunction. These include neurological disorders, such as mental retardation, and long-term effects on cognition and behavior that may appear later in childhood. A second principle of teratogenesis states that susceptibility to teratogenesis varies according to the stage of development at the time of exposure, and a third state that the manifestations of abnormal development depend on the dose and duration of exposure. These principles indicate that not all exposures considered teratogenic are actually teratogenic all the time; The timing and dose of a given exposure during pregnancy often determine the type and extent of its Teratogenic potential. The embryonic period, during which organogenesis takes place, is between implantation, about 14 days, and about 60 days after conception. This is generally the period most susceptible to teratogenesis, when exposure to a teratogenic agent is most likely to produce a malformation. For example, the administration of several known teratogenic drugs, such as isotretinoin, valproic acid, warfarin, or high-dose methotrexate, in specific periods of pregnancy during the first trimester is associated with a high risk of having a child with birth defects. But the risk decreases significantly during the second or third trimester of pregnancy. In some cases, several periods of Sensitivity can be for a single organ, as in the case of craniosynostosis, an abnormality that occurs as a result of the premature fusion of the sutures of the skull. In addition, for some teratogens there is a level of exposure below which no effects are demonstrated for the embryo, as in the case of methotrexate, an antagonist of folic acid.

FACTORS DETERMINING DRUG TERATOGENICITY

1. Type of drug (chemical and pharmacological properties)
2. Dose level and duration
3. Maternal dose modulation
4. Access to the concept
5. Stage of development at the time of drug administration
6. Regulation in the concept

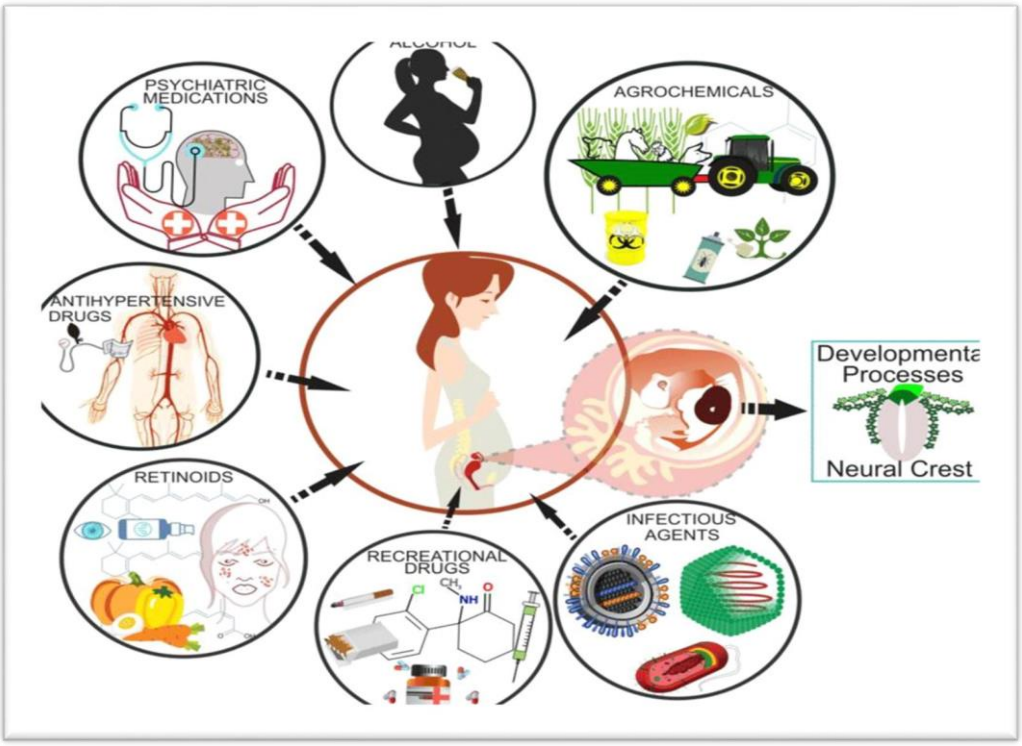


Fig. No: 02

Medications

Some over-the-counter and prescription medications are considered teratogenic. It is therefore important to tell your doctor about any medication you are taking. Read labels before taking over-the-counter medications or supplements. If you are unsure about the safety of a substance, call your healthcare professional. It is better to avoid the substance until you hear from her.

Some examples of teratogenic drugs include:

- Antiepileptic drugs (AED)
- Antimicrobial.
- Anticoagulants (anticoagulants)
- Antithyroid drugs
- Vitamin A (a common ingredient in skin care products)
- Hormonal drugs

Health care providers weigh the pros and cons of using prescription drugs to determine which pose the least risk to pregnancy. For example, phenytoin is a drug used for epilepsy. It has adverse effects on the fetus, but it may be medically necessary for the pregnant person.

Example of teratogenicity

1) Nitrous product

Beast

Teratogenicity was observed in studies of rats, rabbits, cats and hamsters exposed to nitrous oxide. A bioassay of the carcinogenicity of nitric oxide in rats exposed 4 hours per day, 5 days per week for 78 weeks, revealed no appreciable neoplastic or non-neoplastic lesions associated with nitric oxide.

HUMAN

Occupational exposure has been associated with impaired psychological functioning, but these effects are not found in trace concentrations. A recent review of the available data concluded that exposure to small amounts of nitrous oxide is not associated with impaired fertility or an increased risk of developing cancer; however, recent studies seem to suggest a correlation Between nitric oxide anesthesia and hyperhomocysteinemia, an independent risk factor for heart disease. Long-term exposure to high concentrations of nitric oxide can cause megaloblastic Depression of the bone marrow and neurological symptoms. Bone marrow depression has been observed in humans exposed for 4 days to high concentrations of nitrous oxide as part of treatment for tetanus. Nitric oxide is a common inhaled drug and severe myeloneuropathy has been observed as a complication. Nitrous oxide is classified as A4 (not classified as a human carcinogen) by the American Government Conference. Industrial Hygienists (ACGIH).

2) IMIDACLOPRID:- Developmental toxicity

The potential of imidacloprid to produce developmental toxicity, including teratogenicity, was examined in rats and rabbits. In rats, no fetal malformations were evident at any dose, the maternal no observed level (NOEL) was 10 mg kg-1 day-1 and the fetal no observed effect level (NOEL) was 30 mg kg-1 day – 1. In rabbits, embryotoxicity was evident only at a maternally toxic dose, and no fetal malformations were evident at any dose; the maternal no observed effect dose (NOEL) was 8 mg kg-1 day-1 and the fetal no observed effect dose (NOEL) was 24 mg kg-1 day-1.U the results obtained in these species indicate that imidacloprid is not a primary embryotoxicant and is not teratogenic.

3) Thalidomide

Between the 1950s and 1960s, thalidomide was widely used as a sedative and to treat morning sickness during pregnancy in Europe, Australia, Canada, Japan and Brazil. The use

of thalidomide during pregnancy caused limb malformations in thousands of newborns, leading to its ban in most countries since 1961 (Kim and Scialli, 2011). The thalidomide tragedy sparked a growing interest in drug exposure during pregnancy and the mechanism of action of teratogens in the development of embryo-fetal abnormalities.

MECHANISM OF TOXICITY

The mechanism of teratogenesis is divided into broad categories according to the etiology of congenital malformations: (a). Genetic programming errors based on deviations in embryonic Genotypes or low error probability of normal genotype; and (b). Environmental agents or factors that interact with an embryo during the development period (drugs, chemicals, radiation, Hyperthermia, infections, abnormal maternal metabolic states, or mechanical factors).

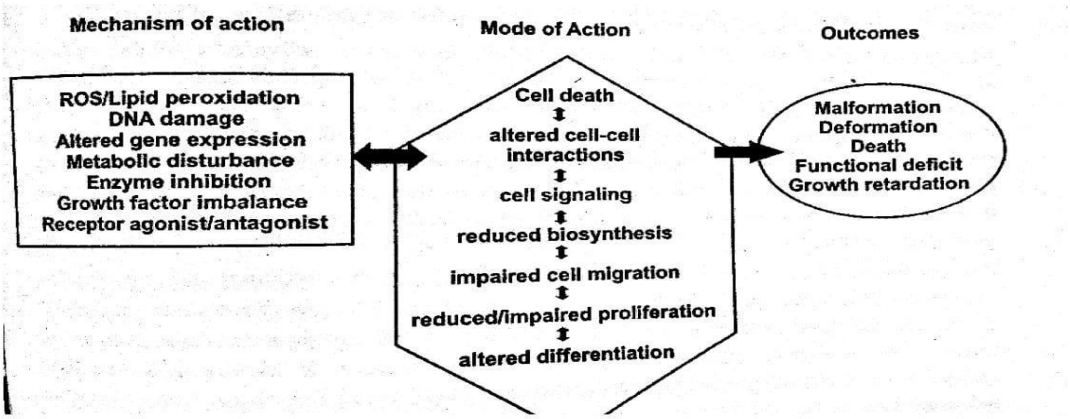
The etiology of human malformations involves genetic and environmental factors

Mammalian fetal development passes through three phases

(i) blastocyst formation

(ii) organogenesis

(iii) histogenesis and maturation of function.



- **Blastocyst formation**

The main process of cell division occurs during blastocyst formation. Medications can kill the embryo by preventing cell division. During this stage, the embryo survives, its further development is generally not affected. At this stage, ethanol is an exception, which affects development.

- **Organogenesis (17-60 days)**

During this stage, the medications administered can cause Significant malformations. During this period, the structural organization of the embryo occurs in a well- defined sequence: skeleton and limbs, eye and brain, heart, palate, major vessels and genitourinary system. Therefore, the type of malformation produced depends on the time of exposure to the teratogen.

- **Histogenesis and functional maturation**

Adequate nutrient intake plays an important role in fetal development in the final stage of histogenesis and functional maturation, which is regulated by various hormones. Significant structural malformations do not result from exposure to mutagens at this stage, but drugs can interfere with the distribution of nutrients or the hormonal environment and have deleterious effects on growth and development. Exposure of a female fetus to androgens at this stage can cause masculinization. For example, stilbestrol has been commonly administered to pregnant Women with a history of recurrent miscarriage.

- **Cholesterol imbalance**

A high amount of cholesterol is necessary for the development of the fetus. This biomolecule is provided by the mother at the beginning of pregnancy and is transported to the fetus through the placenta, while at the end of pregnancy, cholesterol biosynthesis depends on the Production of the fetus itself (Waterham, 2006). Drugs used to treat high cholesterol, such as statins, Work by blocking HMG-CoA reductase, the enzyme involved in the biosynthesis of cholesterol. HMG-CoA reductase is converted to mevalonate (Charlton-Menys and Durrington, 2008), disrupting cholesterol synthesis and therefore can cause adverse effects in the developing fetus (Edison and Muenke 2004).

Teratogenicity Causative factor

1) Obesity

The prevalence of obesity is increasing alarmingly throughout the world. Particular attention should be paid to the increase in obesity rates among women of reproductive age. According to the National Health and Nutrition Examination Survey (NHANES), the prevalence of obesity (body mass index ≥ 30 kg/m2) among women aged 20 to 39 reached 37% in 2013-2014 in the United States and it is estimated that half of the women who present for the first prenatal visit are overweight. In Europe, obesity prevalence Estimates range from 7.1% in

Poland to 25.2% in the United Kingdom. Several meta-studies have reported a global mean prevalence of obesity during pregnancy ranging from 1.8% to 70.3%.

The importance of these figures lies in the fact that pregestational obesity has been associated with an increased risk of negative outcomes at every stage of pregnancy, including periconceptional difficulties and health consequences for the newborn. During pregnancy, obese mothers have a higher risk of Spontaneous and recurrent miscarriages, preeclampsia and gestational diabetes mellitus. During labor, the chances of needing a caesarean section in obese mothers are twice as high as in thin mothers, and the frequency of anaesthetics complications or massive blood loss occurs in one in three births . For the Newborn, there is a higher risk of macrosomia and back dystocia, as well as obesity later in childhood. In addition, there is an increase in the rate of birth defects, mainly due to neural tube and heart defects. Congenital anomalies are the result of abnormal organogenesis in the uterus during the first trimester of pregnancy in humans. UT he mechanisms involved in obesity-induced teratogenesis have not been Elucidated.

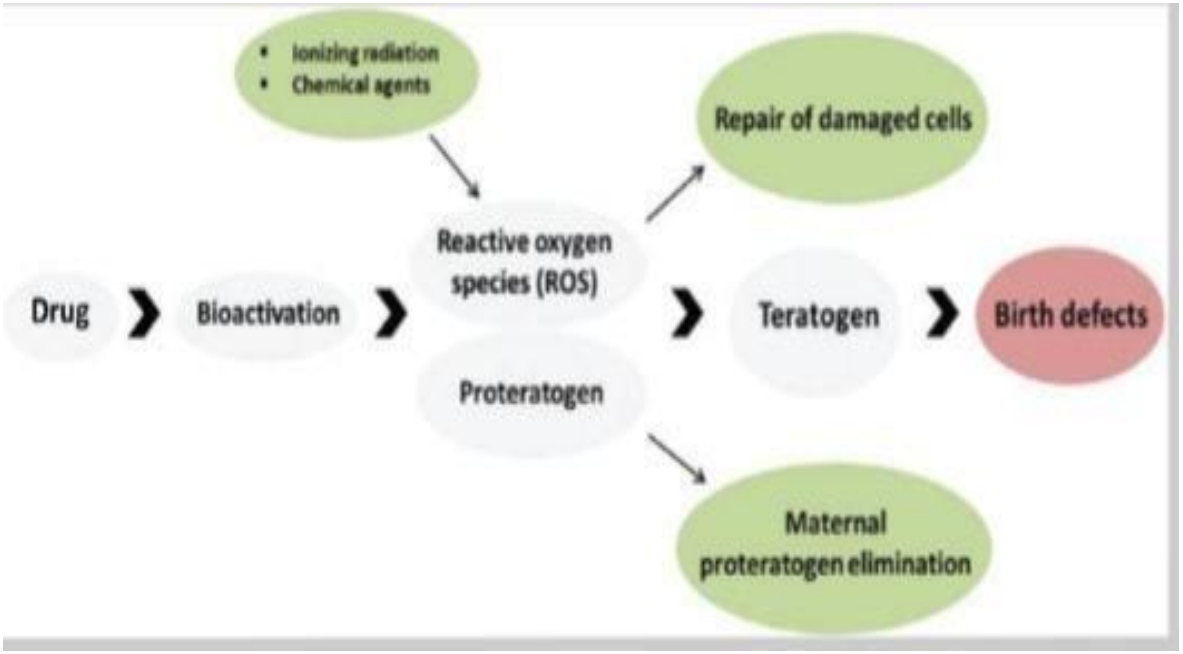


Fig no: 04

1) Oxidative stress

Oxidative stress (OS) has been proposed as a common underlying mechanism for malformations caused by maternal diabetes or obesity. Obesity and pregnancy are, in themselves, situations characterized by an imbalance between the production of reactive oxygen species and their elimination by antioxidant defenses. In fact, increased markers of

oxidative stress have been reported in pregnant women with pregestational obesity compared to lean pregnant women, which is positively Related to oxidative markers in newborns. SO has been suggested as a possible mechanism in Teratogenesis induced by ionizing radiation, cocaine and alcohol abuse, hypoxia, smoking or drugs such as valproate and thalidomide, as well as diabetes. In addition to a possible direct effect on DNA damage and repair, OS inhibits the expression of Pax3, a gene expressed in neuroepithelium and neural crest Cells and which is necessary for the closure of the neural tube and the separation of the cardiac outflow tract. Due to altered Pax3 expression, cardiac crest neuro-epithelial and neuronal cells undergo apoptosis through a p53 tumor suppressor protein-dependent process, resulting in neural tube and cardiac outflow defects. OS also inhibits Pax3 expression in a murine embryonic stem cell (ESC) neuro-epithelial Differentiation model and inhibition of Pax3 expression leads to activation.p53-dependent apoptotic pathways. Thus, OS can be teratogenic by altering the expression of genes necessary to prevent apoptosis during the development of embryonic structures.

2) Alcohol, cigarettes and recreational drugs

Alcohol, cigarettes and recreational drugs are known teratogens. Alcohol affects the central nervous system of the fetus. Alcohol during pregnancy increases the risk of fetal alcohol syndrome in the fetus. Fetal alcohol syndrome is a disorder that can Cause abnormal facial features, head and cerebellum, and other physical and behavioral disabilities. No amount of alcohol is considered safe during pregnancy. Smoking is associated with impaired fetal growth, premature birth and miscarriage. Smoking also affects sensitive lung tissue and the fetal brain. The use of substances such as cocaine, methamphetamine, heroin and marijuana during pregnancy can lead to low birth weight, heart problems and neonatal withdrawal syndrome. This is the detachment of the child after birth. Sharing needles can also cause infection. About 5% of people use these substances during Pregnancy.

3) Antibiotics

Many antibiotics are known to be teratogenic and should be avoided entirely during Pregnancy. These include streptomycin, kanamycin and tetracycline, which interrupt fetal development. These medications can cause hearing loss, hypoplasia and rusting of long bones and teeth, respectively. In addition, broad-spectrum antibiotics can extend the latency period. Narrow-spectrum antibiotics are considered safer than broad-spectrum antibiotics. For sure, every pregnant woman may consider the following measures. The use of antibiotics for the

time prescribed by a specific doctor or, if necessary, to take. Avoid antibiotics during the first trimester of pregnancy, because the major structural transformation of the fetus takes place during this period. Thus, avoiding the risk of iatrogenic exposure. Use a low dose of antibiotics. Limiting the use of over-the-counter medications will help avoid the interdependence of the chemical properties of prescribed drugs versus self-administered over-the-Counter medications.

Clindamycin	Major congenital malformations including musculoskeletal system anomalies and ventricular/atrial septal defect
Doxycycline	Increased risk for cardiac malformations and ventricular/atrial septal defect
Erythromycin	Nephrotic system malformations
Macrolides	Digestive system disorders
Moxifloxacin	Respiratory abnormalities
Ofloxacin	Major congenital malformations
Phenoxymethylpenicillin	Nervous system malformations
Quinoline	Urinary system abnormality
Tetracycline	Permanent discoloration of a child's teeth and bone disorders

Environmental toxins, chemicals or other physical agents

Certain chemicals and substances can cause birth defects. These congenital disorders include spinabifida, left palate or neurological problems. Some examples of toxins or chemicals include:

- Exposure to radiation (X-rays) or chemotherapy.
- Jacuzzi, sauna or other sources of heat that increase body temperature.
- Mercury (present in some types of fish).
- Lead (commonly found in paint and pipes in older homes).
- Toxic chemicals or heavy metals present in the workplace or production facilities.

What birth defects do teratogens cause?

Teratogens cause many known congenital disorders. Some of the more common abnormalities include:

- Problems with the brain or spine, such as anencephaly.
- Physical or structural malformations, such as small bones or missing body parts.

- Left lips and palates.
- Cognitive disorders or neurological problems.
- Cardiovascular problems or heart problems.

How are medications evaluated for safety during pregnancy?

The Food and Drug Administration (FDA) of the United States has created five categories to classify the risks of drugs during pregnancy. These are categories A, B, C, D and X. Although useful, the category system simplifies a very complex subject. A new system called the Pregnancy and Lactation Labeling Rule (PLLR) came into effect in 2015. Remove previous source categories above. PLLR provides health care providers with information about decision making when treating people pregnant or breastfeeding. It takes many other factors into account and puts the data in a better context for providers. It is better to let your pregnancy doctor decide the safety of the medication based on his expertise.

How to avoid teratogens during pregnancy?

The best way to avoid teratogens is to plan pregnancy, if possible. Planning your pregnancy allows you to control your chronic diseases and make lifestyle changes, such as quitting smoking. However, this is not always possible. When you are pregnant, there are steps you can take to reduce your risk of exposure to teratogens:

- Talk to your healthcare professional about the medications you are taking.
- Avoid cigarettes, alcohol and recreational drugs.
- Do not take supplements, medications, or prescription medications without consulting your healthcare professional.
- Avoid cleaning litter boxes.
- Avoid hot tubs, saunas, and anything that raises your body's internal temperature.
- Eliminate tuna, swordfish and other mercury-rich fish from your diet.
- Talk to your supervisor or human resources about harmful chemicals in your workplace.
- It is important to have an open and honest conversation with your obstetrician during pregnancy.
- This includes being honest about your alcohol or drug use. It is here to ensure that your pregnancy is safe and healthy. Don't be afraid to check with your doctor before taking any
- Medication or supplement. It is better to be very careful during pregnancy. Protecting the fetus from teratogens during pregnancy can help prevent birth defects. The first step is to

know that some harmful substances can reach the fetus in the womb and damage its development.

- Avoiding teratogens helps promote a healthy pregnancy and gives your baby a healthy start in life. Then, talk openly with your healthcare provider about the medications you are taking, as well as your alcohol consumption and work or living conditions. It can help answer questions about substances that can cause birth defects and to ensure the safety of you and the fetus.

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Part C: Seminars in Medical Genetics / volume 157, Issue 3 / p. 175-182 Article.

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