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GENETICS

Meaning

The term genetics was introduced by Bateson in 1906. It was derived from Greek word gene'- "to become" or to grow into'. Therefore, Genetics is the science of coming into being

Definition

Genetics is that branch of biological sciences which deals with the transmission of characteristics from parent to offspring"

Prenatal development begins at the cellular level through a process referred to as fusion when the male germ cell, the sperm, unites with the female germ cell, the ovum to create a new cell referred to as a zygote. The zygote contains the base genetic prototype from which all the remaining cells will develop.

The developing cellular process is divided into two processes :

1. Meiosis - cellular divisions occurring prior to fertilization. This process provides for random combinations of genetic materials from each parent through production of haploid germ cells. Haploid germ cells contain half the number of chromosomes found in other body cells.

2. Mitosis - cellular divisions occurring after fertilization that create the ongoing growth and development of the organism. This process creates the diploid cells containing a complete chromosome number. The diploid cells are the result of a combination of one maternal X chromosome with one paternal X or Y chromosome to create either an a) XX female or b) XY male.

TERATOGENESIS

Teratogenesis refers to the production of defects in the fetus. A Teratogenic agent is responsible for producing such a defect. The term teratogen usually is cited in the context of causing anatomical defects in an embryo that was previously differentiating normally. The time during embryogenesis when the fetus is exposed to a potential Teratogens is crucia. The capability of formation of congenital anomalies in fetus is known as teratogenicity

Teratogens include radiation, chemicals (drugs), Stressors, malnutrition and infectious agents. This chapter reviews principles of teratology and discusses drug use in pregnancy.

Harmful substances such as drugs or radiation that invade the womb and result in birth defects are called Teratogens. Teratogens are especially damaging in the embryonic stage because it is a critical period in prenatal development. Later, during the fetal stage, the environment provided by the mother affects the baby's size, behaviour, intelligence and health, rather than the formation of organs and limbs.

DRUGS AND BIRTH DEFECTS

The clinical consequences of drug teratogens must be placed in the overall context of developmental defects in humans. Defects may be from genetic, environmental, or unknown causes. Approximately 25% are known to be genetic in origin (e.g., Mendelian, chromosomal). Approximately 65% of defects are of ostensibly unknown etiology but probably reflect combinations of genetic and environmental factors.(polygenic/multifactorial).

The risk for malformation after exposure to a drug must be compared with the background rate, which for major malformations in the general population usually is cited as 2-3%. A major malformation is defined as one that is incompatible with survival, such as anencephaly; or one requiring major surgery for correction.

VARIABLES AFFECTING TERATOGENESIS

Specificity of Agent

Some agents are more teratogenic than others. Less obvious is the axiom that an agent may be teratogenic in only certain species. For example, thalidomide

produces phocomelia in primates but not in rodents. Within a given species, however, a given teratogen may affect many organ systems. Some organ systems are preferentially affected, but the pattern of anomalies also reflects the organ systems differentiating at the time the agent was administered. For example, administering thalidomide between days 35 and 37 causes ear malformations administering the agent between days 41 and 44 causes amelia or phocomelia

Dosage

Although high doses of a proven teratogen usually are more deleterious than low doses, this is not always true. At any given time, an embryo can respond to a teratogen in one of three ways: (1) at a low dose, there is no effect: 2) at an intermediate dose, a pattern of organ-specific malformations can result; and (3) at a high dose, the embryo may be killed, causing the organ-specific teratogenic action to go unrecognized.

Timing

The effect of a teratogen on the developing organism depends on what period in the pregnancy (in development) the child is exposed to the teratogen. some teratogens cause damage only during specific days of weeks in early pregnancy other teratogens are harmful at any time during the pregnancy--for example, for behavioral teratogens. there is no safe period---the brain and nervous system can be harmed throughout the pregnancy.

Genotype

The genotype of the mother and the fetus influences the efficacy of a teratogen. For example, genotype determines the prevalence of cleft palate in inbred strains of mice whose mothers are administered cortisol during pregnancy.

Drug Interactions

Simultaneous administration of two(Drugs) teratogens may produce a different effect from that existing when the two are administered separately

Other Factors

Variability in teratogenic response sometimes is associated with other environmental or morphologic factors: maternal or fetal weight, in utero position of the fetus, proximity to other affected litter mates, uterine vasculature, and diet.