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AKANSHA
COURSE - BSC
ZOOLOGY (H)
SEMESTER - VIth
SUBJECT - DEVELOPME
NTAL BIOLOGY
TOPIC - IMPLICATIO
NS IN DEVELOPMENTAL
Biology.

*Seen
Anulaja
16.4.2024*

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I would like to express my special thanks of gratitude to my teacher Dr. Anita Duda ma'am as well as our principal who gave me the golden opportunity to do this wonderful project on the topic "Implication in developmental Biology". which also helped me in doing a lot of Research and I come to know about so many new things.

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TERATOGENESIS

Teratogenesis is a process that causes birth defects or malformations in an embryo or fetus (due to environmental factors) or teratogens are exogenous agents that cause birth defects. OR Teratology is the study of the causes and underlying mechanisms leading to birth defects or malformations.

Most teratogens produce their effects during certain critical periods of development. Human development is usually divided into two periods.

1. Embryonic period (to the end of week 8) when most of the organ systems form.
2. Fetal period (the remaining time in the uterus) when growth and modeling occur.

The period of maximum susceptibility to teratogens is between weeks 3 and 8 since that is when most organs are forming. The nervous system however is constantly forming and remains susceptible throughout development. Before week 3 exposure to teratogens does not usually produce congenital (by birth) abnormalities because a teratogen encountered at this time either damages most or all of the cells of an embryo, resulting in its death or kills only a few cells, allowing the embryo to fully recover.

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* TERATOGENICITY

The ability of the teratogens to induce the teratogenic effects or developmental malformations. chemicals and drugs can not cross the placental barrier but some of them are able to do so and cause the developmental defects.

The ability of the teratogenicity depends on their ability to cross the placenta.

The Embryo is more susceptible to teratogens during the period of rapid differentiation.

Different organs are more susceptible during a particular period of gestational development as heart first 3 to 6 week of development central nervous system first 3 to 7 week of embryonic period.

TERATOGENIC AGENTS

1. CHEMICALS :-

Alcohol, cocaine, cigarette, smoking (Nicotine), medicinal drugs (as Thalidomide, valproic acid), heavy metals as cadmium, pollutants, pesticides, antibiotics (Tetracycline, streptomycin) etc.

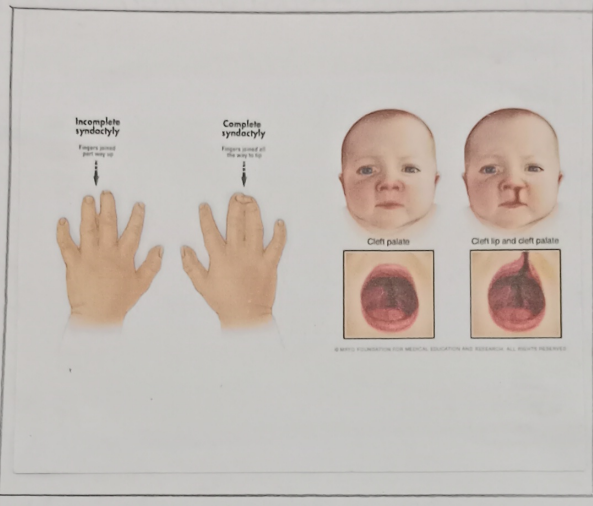
2. INFECTIOUS AGENTS (PATHOGENS)

Zika virus, Rubella virus, Herpes simplex virus.

3. PHYSICAL AGENTS AND IONIZING RADIATION

X-rays.

TERATOGENIC EFFECTS



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4. MATERNAL FACTORS :
Gestational diabetes, malnutrition

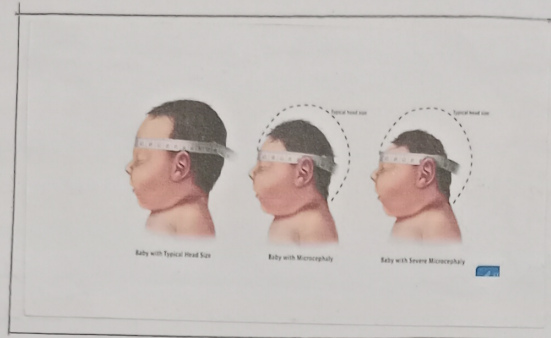
TERATOGENIC AGENTS AND THEIR EFFECT ON EMBRYON - IN DEVELOPMENT

I Ethanol, Smoking and Various drugs

4. Fetal Alcohol Syndrome (FAS) :- Patients with FAS must have three characteristic prenatal and post-natal growth retardation ($< 2SD$ for length and weight), facial abnormalities and CNS dysfunction. The full picture of FAS usually occurs in babies born to alcoholic mothers or those who drink regularly or binge drink. However, no amount of alcohol is safe. Even light or moderate drinking can ~~not~~ affect the developing fetus. Acetaldehyde is implicated as the cause of FAS through its inhibiting effects on DNA synthesis, placental amino acid transport and development of the fetal brain (96-98). The biologic basis of FAS is related to genetic polymorphisms identified for alcohol dehydrogenase (ADH) which converts alcohol to acetaldehyde and acetaldehyde dehydrogenase (ALDH2) which converts acetaldehyde to acetate.

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MICROCEPHALY



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2. Thalidomide :-

Thalidomide was used clinically in the 1960s. It caused limb reduction defects, facial hemangiomas, esophageal and duodenal atresia, cardiac defects, renal agenesis, urinary tract anomalies.

3. Chloroquine :-

Malformation in three half siblings included up slanting palpebral fissures, flat philtrum, thin upper lip and brachy-dactyly of the fifth finger. Maternal chloroquine use during pregnancy may be associated with auditory, vestibular, mental and other neurologic dysfunction in children.

4. Tobacco Smoking - Nicotine is a vasoconstrictor that results in uterine vascular constriction and intrauterine growth retardation. The increased mortality is attributed to abruptio placentae, placental previa, spontaneous abortion, prematurity and IUGR. Carbon monoxide from cigarette smoke also crosses the placenta and produces an increase in blood carboxyhemoglobin (HbCO) levels.

5. Marijuana :-

The active ingredient of marijuana is δ ,9-tetrahydrocannabinol which is fat soluble, crosses the placenta easily and may persist in the fetus for as long as 30 days. Intrauterine retardation and malformations are reported after marijuana use during pregnancy, especially in the first trimester. Increased risk of non-lymphoblastic leukemia has been reported.

SS TIME

6. Lysergic acid diethylamide (LSD)

defects of the limbs, eyes CNS and ophthalmology-
ptosis may be present.

7. Sedatives -

Increased frequency of cleft lip, cleft palate and congenital heart disease have been reported after maternal phenobarbital exposure. Ben-zodiazepine containing drugs, taken in large amounts may produce IUGR, cleft lip and facial features that resemble the findings of FAS although studies have shown little or no increase in congenital anomalies.

8. Isotretinoin -

The risk of fetal abnormality when isotretinoin is taken by a pregnant woman is 25%. The critical period of exposure is 4 to 10 weeks of gestation. The defects include microcephaly, microphthalmia, cerebellar dysgenesis, depressed nasal bridge, microtia or absent external ears, cleft palate anomalies of the aortic arch, cardiac defects and hypoplastic adrenal cortex.

II. Radiation -

Ionizing radiation can injure the developing embryo due to cell death or chromosome injury. The most critical exposure period is 8-15 week after fertilization. Because of its extended periods of organogenesis and histogenesis the central nervous system retains the greatest sensitivity of all organ systems to the detrimental effects of radiation through the latter fetal stages. In utero radiation produces

INFECTIOUS AGENTS

Teratogen	Fertilization Age	Malformation
Rubella virus	0-60	Cataract or heart diseases more likely.
Thalidomide	21-40	Reduction defects
Hyperthermia	18-30	Anencephaly
Male hormones		
(androgens)	<90	Clitoral hypertrophy and labial fusion
	>90	Clitoral hypertrophy
Warfarin		
(Coumadin)	<100	Hypoplasia of nose and stippling of epiphyses
Diethylstilbestrol	>100	Possible mental retardation
	>14	50% vaginal adenosis
	>98	30% vaginal adenosis
	>126	10% vaginal adenosis

Microcephaly and mental retardation

III. Infectious agents -

The lethal or developmental effects of infectious agents are the result of mitotic inhibition direct cytotoxic effects or a vascular disruptive event on the embryo or fetus.

1. Influenza virus - There is no compelling evidence to incriminate Influenza virus infection during pregnancy as a cause of malformations.
2. Varicella - When a woman has a varicella infection during the first 20 weeks of pregnancy there is a 2% chance that the baby will have a group of defects called the congenital varicella syndrome. Which includes scars, defects of muscle and bone malformation and paralyzed limbs, small head like blindness, seizures and mental retardation.
3. Mumps virus - Mumps virus during pregnancy does not cause malformation but encephalitis has been noted in infants with positive mumps antigen skin test.
4. Parvovirus - Human parvovirus B-19 is able to cross the placenta and result in foetal infection which may occur whether the mother is symptomatic or asymptomatic. It is associated with a higher than average foetal loss and may lead to spontaneous abortion in the first trimester, hydrops fetalis in the second trimester and stillborn at term. Generalized myocarditis, myositis of skeletal muscles and abnormalities of the eyes are reported.

IV. Toxic Metals :-

1. Lead - Lead crosses the placenta as early as the 12th to 14th weeks of gestation and accumulates in fetal tissue. The adverse effects of lead include spontaneous abortion and stillbirth. A small but significant increase in minor malformations, including haemangiomas, lymphangiomas, hydroceles, skin tags, skin papillae and undescended testes were seen in infants with high level in the umbilical blood.
2. Methylmercury - Methylmercury poisoning produces atrophy of the granular layer of the cerebellum and spongy softening in the visual cortex and other cortical areas of the brain, polymyositis can also occur.
3. Lithium - The ratio of lithium concentration in umbilical cord blood to maternal blood is uniform. Infants with high lithium concentration at delivery have significantly lower Apgar scores.

(V) Chemical Exposures -

1. Polychlorinated and polybrominated biphenyls. Poisoning have. Infants with percutaneous like skin with desquamation and brown discoloration, dark coloured nails, conjunctivitis, low birthweight, exophthalmos and natal teeth.
2. Toluene - Toluene embryopathy includes prenatal and postnatal growth deficiency, microcephaly, anencephaly, development delay, cardiac and limb defects and craniofacial anomalies similar

to fetal alcohol syndrome.

VI. Maternal Conditions -

1. Obesity - During pregnancy, obesity is associated with adverse outcomes that include macrosomia, hypertension, pre-eclampsia, gestational diabetes mellitus and fetal death.
2. Diabetes mellitus - Hyperglycaemia leads to inhibition of the myoinositol uptake that is essential for embryonic development during gastrulation and neurulation stages of embryogenesis. Deficiency of myoinositol appears to cause perturbations in the phosphoinositide system that lead to abnormalities in the arachidonic acid-prostaglandin pathway.
3. Cretinism and Iodine deficiency - There is a role of maternal T4 in neurologic embryogenesis before the onset of fetal thyroid function and therefore, it's protective role in fetal thyroid failure. In early pregnancy, iodine deficiency induces a critical decrease of T4 levels with consequent TSH increase responsible for hypothyroidism in about 50% of iodine-deficient pregnant women. Congenital hypothyroidism associated with deafness and mental retardation is found in the offspring of hypothyroid mothers. Deafness persists in spite of thyroid replacement therapy. Developmental changes in the brain and cerebellum have been described.
4. Phenylketonuria - Maternal phenylketonuria leads to defects that include intrauterine and postnatal growth retardation.

And to prevent her baby from haemolytic anaemia.

RISKS

Amniocentesis is performed between the 15th and 20th week of pregnancy. Performing this test earlier may result in fetal injury. The term early amniocentesis is sometimes used to describe use of the procedure between weeks 11 and 13.

Complications of amniocentesis include premature labour and delivery, respiratory distress, postnatal deformities, chorioamnionitis or intra-amniotic infection, fetal trauma and alloimmunisation or Rh disease of the mother. Amniotic fluid embolism or AFE has also been described as a possible outcome. Additional risks include amniotic fluid leakage and bleeding. These two are of particular importance because they can lead to spontaneous abortion in pregnant patient.

→ /split by alpha - fetoprotein level.
Rare metabolic disorders.

2. Infection — This process can detect infections via decreased glucose level a gram stain showing bacteria or abnormal differential count of WBCs.

3. Lung maturity —

This can predict fetal lung maturity, which is inversely connected to the risk of infant respiratory distress syndrome. Several tests are available including the —

→ Lecithin — sphingomyelin ratio: if the result is less than 2:1 the fetal lungs may be surfactant deficient.

→ The presence of phosphatidylglycerol (PG) indicates fetal lung maturity.

→ The surfactant / albumin ratio the result is given as mg of surfactant per gram of protein. An S/A ratio < 35 indicates immature lungs 35-55 is intermediate and > 55 is mature surfactant production.

4. Decompression of polyhydramnios :-

Polyhydramnios can be relieved via decompression. amniocentesis can also be used to diagnose potential causes of polyhydramnios.

5. Rh Incompatibility —

This process can be used to diagnose Rh incompatibility a condition when the mother has Rh-negative blood and the fetus has Rh+ve blood. Early detection is imp to treat the mother with Rh immunoglobulin and to treat the mother with Rh immunoglobulin

amniotic fluid. This procedure can be performed with a single needle and double needle technique. These techniques have their own variations in how they are performed including guidance of needle insertion location and angle of needle insertion.

- From the pool of amniotic fluid the first 2ml is typically discarded due to mixture with maternal blood cells to ensure high quality fluid sampling.
- Fetal cells are separated from the amniotic fluid and placed in a culture medium that stimulates them to grow and divide, then fixed and stained under a microscope. the chromosomes are examined for abnormalities.
- After the procedure the puncture seals and the amniotic sac replenishes the liquid over the next 24-48 hours.

MEDICAL USES

1. Genetic diagnosis -

Early in pregnancy, amniocentesis is used for diagnosis of chromosomal and other fetal problem sources.

- Down Syndrome (Trisomy 21)
- Patau Syndrome (Trisomy 13)
- Edwards Syndrome (Trisomy 18)
- Sex chromosome aneuploidies.
- Neural tube defects (diseases where the brain and an incomplete skull) and spina bifida

Amniocentesis does not detect all birth defects, but it can be used to detect the following conditions if the parents have a significant genetic risk of

- Down Syndrome.
- Sickle cell disease
- Cystic fibrosis.
- Muscular dystrophy.
- Tay - Sachs disease.

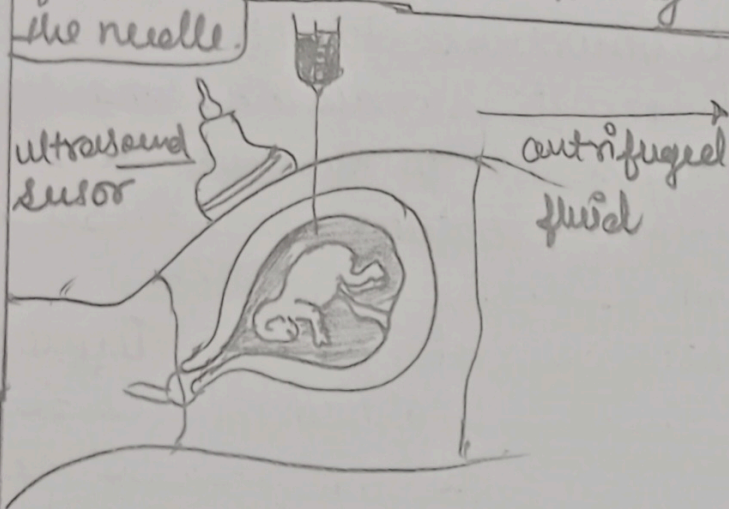
* Procedure :-

Amniocentesis is routinely performed as an outpatient procedure either with or without the use of a local anaesthetic.

- Ultrasonography is used to locate the position and movements of the fetus, location of placenta, and characteristics of the amniotic fluid in the uterus.
- With the aid of ultrasound guidance a long sterile needle is inserted through the abdominal wall of the uterus at an angle through the muscle then through the wall of uterus and finally into the amniotic sac.
- The physician then punctures the sac in an area away from the fetus and extracts approximately 20ml of amniotic fluid. This procedure can be performed with a single needle and double needle technique. These techniques have their own double needle technique. These techniques have their own variants in how they are performed including guidance of needle insertion, location and angle of needle insertion from the 20ml of amniotic fluid the first and

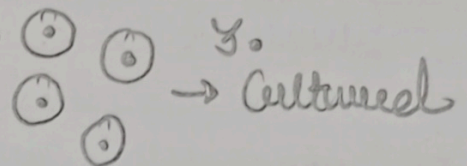
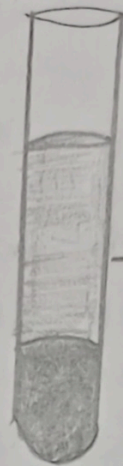
AMNIOCENTESIS PROCEDURE

1. Under the guidance of ultrasound a sterile needle is inserted through the abdominal wall into the amniotic sac. A small amount of amniotic fluid is withdrawn through the needle.



2.

The amniotic fluid contains fetal cells, which are separated from the amniotic fluid.



4. Tests are then performed on the cultured cells.

Chemical Analysis

And DNA Analysis

↓
Chromosomal Analysis

AMNIONCENTESIS

Medical procedure used for prenatal genetic testing for chromosomal abnormalities (presence or absence of certain chromosomes, genes or enzymes) fetal infection as well as for sex determination to obtain a sample of amniotic fluid a pregnant woman. A long sterile needle is inserted through the abdominal wall as for sex determination to obtain a sample of amniotic sac to obtain the fluid.

Amniotic fluid - the substance that fills the amniotic sac and surrounds the developing fetus - contains fetal cells that can be used for genetic testing.

• Why is an Amniocentesis performed?

This process is performed to look for certain types of birth defects because amniocentesis presents a small risk for both mother and her baby the prenatal test is generally offered to women to women who have a significant risk for genetic diseases including those who:

• Have an abnormal ultrasound or abnormal lab screens.

Have a family history of certain birth defects.

Have previously had a child or pregnancy with a birth defect.

Had an abnormal genetic test result in the current pregnancy.

genetic and chromosomal disorders a month and a half earlier than standard amniocentesis. The techniques are now used by many pregnant women and prospective parents especially couples who have a history of genetic abnormalities or where the woman is over the age of 35.

*. Repair of DNA damage -

Differentiated somatic cells and ES cells use different strategies for dealing with DNA damage. For instance, human foreskin fibroblasts are a type of somatic cell use non-homologous end joining as the primary pathway for repairing double-strand breaks during all cell cycle stages. Because of its error prone nature, NHEJ tends to produce mutations in a cell, clonal descendants. ES cells use a different strategy to deal with DSBs. Because ES cells give rise to all of the cell types of an organism including the cells of the germ line mutations arising in ES cells due to faulty DNA repairs are a more serious problem than in differentiated somatic cells. Thus mouse ES cells predominantly use high fidelity homologous recombination repair (HRR) to repair DSBs. This type of repair depends on the interaction of the two sister chromosomes formed during S phase and present together during the G2 phase of the cell cycle. HRR can accurately repair DSBs in one sister chromosome by using intact information from the other sister chromosome.

Cardiac progenitors are to be used in clinical trials of patients with severe heart failure.

* Drug discovery :-

Besides becoming an important alternative to organ transplants, ESCs are also being used in field of toxicology and as culture screens to uncover new chemical entities that can be developed as small molecule drugs.

Studies have shown that cardiomyocytes derived from ESCs are validated in vitro models to test drug responses and predict toxicity profiles. ES derived cardiomyocytes have been shown to respond to pharmacological stimuli and hence can be used to assess cardiotoxicity. ESC-derived hepatocytes are also useful models that could be used in the preclinical stages of drug discovery -

* Models of genetic disorders -

Several new studies have started to address the concept of modelling genetic disorders with ESCs. Either by genetically manipulating the cells, or more recently by deriving diseased cell lines identified by prenatal genetic diagnosis, modelling genetic disorders is something that has been accomplished with stem cells. This approach may very well prove valuable at studying disorders such as fragile X syndrome, cystic fibrosis and other genetic malades. Researchers, developed prenatal diagnosis testing methods to determine

Therapies have been proposed for regenerative medicine and tissue replacement after injury or disease. Pluripotent stem cells have shown promise in treating a number of varying conditions, including but not limited to spinal cord injuries, age related macular degeneration, diabetes, neurodegenerative disorders, AIDS etc. In addition to their potential in regenerative medicine ESCs provide a possible alternative source of tissue. Indeed ESCs can also be used for research on early human development, certain genetic disease and in vitro toxicology testing.

Human embryonic stem cells have the potential to differentiate from ESC have or are currently being developed include cardiomyocytes, neurons, hepatocytes, bone marrow cells, islet cells and endothelial cells. These are in current research.

* Clinical potential -

- ESCs have been differentiated to neural cells and bone tissue.
- Researchers have differentiated ESCs into dopamine producing cells with the hope that these neurons could be used in treatment of Parkinson's disease.
- Studies involving ESCs are underway to provide an alternative treatment for diabetes. For example, researchers were able to differentiate ESCs into insulin producing cells to produce large quantities of pancreatic beta cells from ES.
- An article describes a translational process of generating human embryonic stem cell-derived.

Leukemia inhibitory factor or serum-free media supplements with two inhibitory drugs the MEK inhibitor PD03259010 and GSK-3 inhibitor CHIR99021.

Known -

ESCs divide very frequently due to a shortened G1 phase in their cell cycle. Rapid cell division allows the cells to quickly grow in no. but not size which is important for early embryo development. In ESC cyclin A and E proteins involved in G1/S transition are always expressed at high levels, CDK2 that promote in the G1/S transition are always expressed at high levels. CDK2 that promote cell cycle progression are overactive in part due to downregulation of their inhibitors. Retinoblastoma (Rb) protein that inhibit that transcription factor E2F until the cell is ready to enter S phase are hyperphosphorylated and inactivated in ESCs leading to continued expression of proliferation genes.

These changes result in accelerated cycles of cell division. Although the shortened G1 phase has been linked to maintenance of pluripotency ESCs grown in serum free 2i condition do express hypo-phosphorylated active Rb protein and have an elongated G1 phase. Pluripotency factors Oct4 and Nanog play a role in transcriptionally regulating the ESC cell cycle.

* Uses :-

Due to their plasticity and potentially unlimited capacity for self-renewal embryonic stem

these traits that makes them valuable in the scientific and medical fields. ESCs have a normal karyotype, maintain high telomerase activity to differentiate into any embryonic cell type and by their ability to self-renew it is these traits that makes them valuable in the scientific and medical fields. ESCs have a normal karyotype maintain high telomerase activity and exhibit remarkable long term proliferative potential.

1. Pluripotent :-

Embryonic stem cells of the inner cell mass are pluripotent, meaning they are able to differentiate to generate primitive ectoderm, which ultimately differentiates during gastrulation into all derivatives of the three primary germ layers, ectoderm, endoderm and mesoderm. These germ layers generate cells of the more than 220 cell types in the adult human body when provided with the appropriate signals. ESCs initially from precursor cells that is subsequently differentiated into the desired cell types. Pluripotency distinguished embryonic stem cells from adult stem cells, which are multipotent and can only produce a limited number of cell types.

2. Self-renewal and repair of structure -

Under defined conditions, embryonic stem cells are capable of self-renewing indefinitely in an undifferentiated state. Self-renewal condition must prevent the cell from clumping and maintain an environment that supports an unspecialized state. Typically this is done in the lab with media containing serum and

Reprogramming. Through altering the genes in the adult cells, researchers can reprogramme the cells to act similarly to that of embryonic stem cells.

* Perinatal stem cells — Researchers have discovered stem cells in amniotic fluid as well as within umbilical cord blood. These cells have the ability to change into specialized cells when required.

EMBRYONIC STEM CELLS

ESCs are pluripotent stem cells derived from the inner cell mass of a blastocyst or early-stage pre-implantation embryos. Human embryos reach the blastocyst stage 4-5 days post fertilization at which time they consist of 50-150 cells, isolating the embryoblast or inner cell mass results in destruction of the blastocyst, a process which raises ethical issues, including whether or not blastocyst a process which raises ethical issue, including whether or not embryos at the pre-implantation stage should have the same moral considerations as embryos in the post-implantation stage of development.

* Properties :-

Embryonic stem cells (ESCs), derived from the blastocyst stage of early mammalian embryos are distinguished by their ability to differentiate by their ability to differentiate into any embryonic cell type and by their ability to self-renew. It is

ESCs



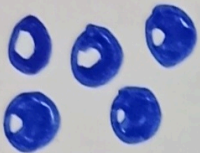
Fertilised egg



Totipotent stem cell



Blastocyst containing pluripotent stem cells

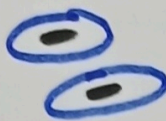


Isolated pluripotent stem cells from inner cell mass



HSCs

Blood cells



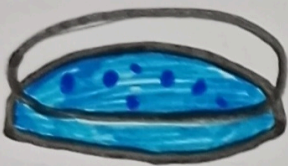
Neural stem cells

Neurons



MSC

Bone, Cartilage



-ally into the female genital tract to achieve fertilization.

- F. Tubal Embryo Stage Transfer (TEST) - In this technique, a multi cell embryo of 2-cell, 4-cell & 8 cell stage is transferred to fallopian tubes after in-vitro fertilization. Thus TEST is an extension of ZIFT.

STEM CELLS

Stem cells are new cells found within the Human body from which all other cells with specialized functions are generated. In proper experimental conditions these stem cells can be divided to create daughter cells. These daughter cells can either be new stem cells themselves by the way of self-renewal or end up being functional cells.

- *. Embryonic Stem cells :- These stem cells come from embryos that are 3-5 days old. They are by far the most versatile and can thus be used for both regenerative and cell replacement purpose.
- ∴ Adult Stem cells :- These stem cells are found in most adult tissues (such as bone marrow or fat). Compared with embryonic stem cells, these have a more limited ability to produce various cells found in the body. These can be versatile, but not to the extent found in embryonic cells.
- ∴ Adult cells altered to have properties of embryonic stem cells :- Scientists have successfully transformed regular adult cells into stem cells using genetic

- *. Different combinations or variants of IVF with other technique can also be applied to achieve better results. The other techniques are
- Intracytoplasmic sperm Injection (ICSI) - In this method the sperm are directly introduced into mature oocytes which are retrieved by IVF method. It helps to increase the probability of fertilization. ICSI is used when there is abnormal sperm motility or failure of sperm cells to develop into spermatozoa.
 - Gamete Intra Fallopian Transfer (GIFT) - In this technique the gametes (both the egg and sperm) are placed in a fallopian tube so that they will mate naturally. In case the female has immunological problem of sperm rejection or blocked fallopian tubes, the gametes can be placed directly into the female genital tract.
 - Zygote Intra Fallopian Transfer (ZIFT) - It is a combination of IVF and GIFT where the oocyte are collected by IVF and fertilized *in-vitro*. The zygote is then laposcopically transferred to the fallopian tube. This technique is also known as Tubal Embryo Transfer (TET). This is done for the women who have severe infertility problems.
 - Peritoneal (Pronuclear Stage) Tubal Transfer (PROST) - In this technique the *in-vitro* fertilized oocyte (zygote) at pronuclear stage is transferred into fallopian tubes of the female. This is a relatively newer method of ART.
 - Artificial Insemination (IA) - Spermatozoa from fresh or frozen semen is transferred intravagin-

To 1ml mature oocyte culture. After insemination the oocytes are examined microscopically to find the presence of two pronuclei and two polar bodies is evidence of successful fertilization. Fertilized eggs are cultured for a day or two.

4. Embryo Culture - The fertilized oocytes are cultured in vitro in sterile medium for 1-2 days to obtain pre-embryos with normal early development upto 32-cell stage. These pre-embryos are placed back into the uterus of recipient for implantation and subsequent growth by the technique called embryo culture Transfer (ET).

5. Embryo Transfer - After embryo culture the embryos are introduced into the uterine cavity for implantation using a Catheter called Embryo Transfer (ET). The transfer of morula or blastocyte into the fallopian tube is called intra fallopian Transfer (IFT) and into the uterus is called Intra uterine Transfer (IUT). The embryos when transferred in the cleavage stage has better chance of implantation. In case implantation fails, assisted hatching of embryo from its Zona pellucida layer is done and inserted in the uterus. The remaining embryos are cryo-preserved to be used again for ET if abortion occurs. The embryos can be transferred after IVF in the uterus of another woman who acts as surrogate mother.

Thus treatment of infertility through In-vitro fertilization and embryo transfer (IVF-ET) has gained much popularity although it is used as last resort for carefully selected patients.

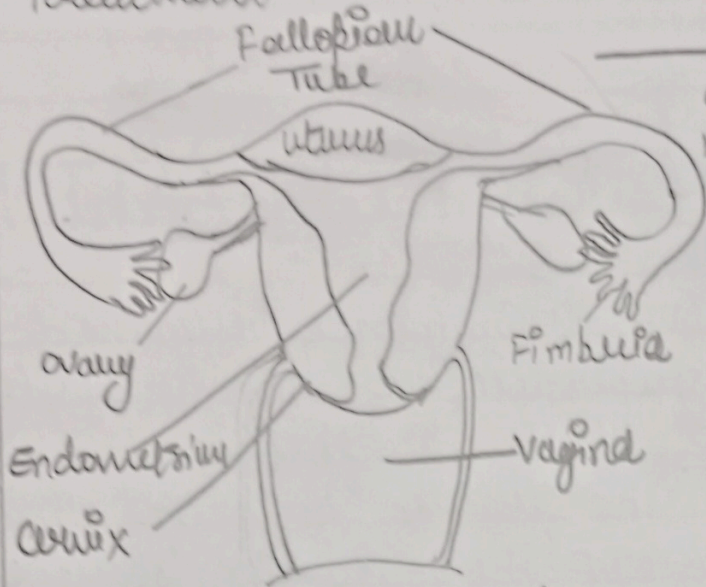
Nonfunctional ovaries and uterine endometriosis and immunological problems etc.

2. IVF is also beneficial for the couples who have family history of genetic abnormalities. Presence of deleterious genes can be tested during preimplantation diagnosis of the in-vitro fertilized embryo.
3. IVF is also done to obtain zygotes with desired genetic characteristic for experimental purpose and also to study early embryonic development.

IVF PROCEDURE

1. Stimulation and monitoring of ovary:- The ovaries are stimulated to produce a large number of mature follicle. This is achieved by administering gonadotropin or clomiphene treatment. Superovulation is done to obtain large number of oocyte for fertilization in vitro which has limited success rate. Development of follicles and time of ovulation is monitored by clinical tests.
2. Oocyte aspiration:- The oocytes at metaphase II stage are retrieved from antral follicles by using ultrasound guided laparoscopy which needle aspiration (trans vaginal oocyte retrieval).
3. Insemination and fertilization in-vitro:- The semen is collected from the male partner or frozen semen is also used. Healthy sperm are selected and processed for in-vitro capacitation. a total of 10,000 to 50,000 motile sperm are

Re-stimulation Treatment



Monitoring follicle development and hormone measurements → and help time of injections and Egg Retrieval

Oocyte Retrieval

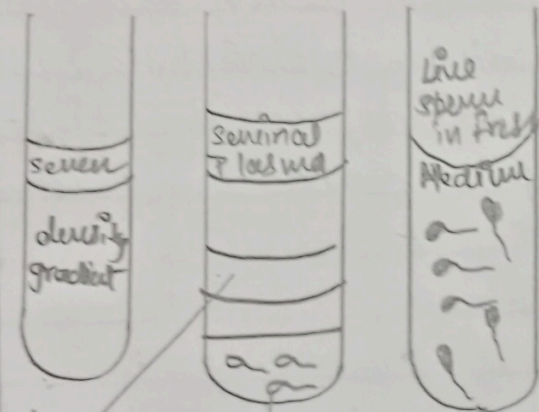
Follicles are observed

Intravenous sedation

Injury and infection are rare

Evaluation of uterus and Ovarian stimulation

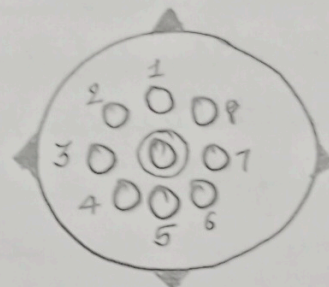
Semen



debris and dead sperm

live sperm

Embryology Lab procedures



Eggs and sperm in culture medium or the ICSI technique

Embryo Transfer

→ using the micro injection into the female reproductive tract.

Semen collection protocols is used diff for IUI and IVF cases.

IN VITRO FERTILIZATION

In vitro fertilization (IVF) is commonly performed procedure of Assisted reproductive Technology (ART) to treat infertility in which the fertilization of oocytes is done outside the female body in the laboratory dish. For IVF the eggs and sperm of the parents are retrieved and made to fertilize in vitro in the culture dish to obtain embryos which undergo cleavage and then they are transferred in the uterine cavity for implantation and complete gestation. The babies born using this technology are commonly called Test-tube babies. The basic steps of IVF are Super-ovulation, oocyte aspiration, insemination, fertilization, embryo culture and embryo transfer.

* HISTORY :-

The first successful attempt of IVF was done by Charles Tibbault and Louis Dauxelle using rabbit sperm for humans the technique was developed by RB Edwards and PC Steptoe. RB Edwards was awarded with Nobel prize in 2010 for the same. The first test tube baby Louise Brown was born on 25 July 1978 in England.

* NEED OF IVF :-

It is usually needed for a couple who may have infertility problems due to variety of reasons. Some causes of female infertility are tubal

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