

hello students Welcome to our preclinical pharmacology Channel today we are going to discuss some introductory part about the reproductive toxicology this is very important topic as pharmacology and toxicological screening methods are concerned and that is there with the syllabus of mform pharmacology so let's start with the introduction part what is reproductive toxicity so reproductive toxicity is a study of occurrence means appearance then causes manifestations and sequential adverse effect of exogeneous Agents on reproduction this is very important that the effect of exogeneous Agents on reproduction which which always occur and you observed are nothing but the study of all these things are nothing but the reproductive toxicity now what is developmental toxicity it is actually related to the abnormal structure or functional development following exposure of pregnant or lactating females so again it is the same but when the exposure to exogeneous agents will causes the abnormal structure or functional development in the fetus during the pregnancy and lactation female the study of all these things are under the developmental toxicity now this reproductive toxicity is the subject which dealing with the causes mechanism effects and prevention of disturbances throughout the reproductive cycle including fertility induced by the chemical so this is another way by which you can Define the reproductive toxicity then the reproductive toxicity is mainly occurs because of the exposure of human reproduction to xenobiotics such as drugs various drugs will affect on the reproductive system then substances of abuse like morphine Codine all these things then industrial chemicals various industry they releases the chemicals which are really toxic to the human body then pesticides like DDT and all these things Airborne contaminants then Trace Metals these metals like cadmium lead and uh arsenic which are there in the nature in very tress uh level and food additives and lifestyle so apart from all this thing lifestyle plays a very important role in reproductive toxicity then the causes of this infertility uh as we have seen here that these are the different causes which leads to the human uh reproduction problem in human reproduction but still there are oneir male and oneir female and oneir between the couple the causes are unknown and they are remain unknown and that's why many a time it happens that everything is manage but still the uh pregnancy is not occurs so this reproductive hazards means the what problem arises once the reproductive toxicity occurs this are produced in the mothers and father as well as The Unborn and the newborn child so this includes loss of libido then sterility mutag Genesis teratogenesis abortion fatal death perinal death and delayed toxicity so these are the mainly major effect which occurs on reproduction by the exposure to various this Hazard materials now if you see uh what are the components of male reproductive system so this figure indicate that these are the various components of of male reproductive system like testes epid diis then was difference prostate glandular vesiculosa then glandular bulbo urees then urinary bladder urethra so all these near about 15 components are there which plays a major role in male reproductive system and this allows the male to produce sperm sperm cells which gets the female pregnant so here this system is involved in the spermatogenesis and these sperm cells are responsible for uh producing the pregnancy in the female likewise female reproductive cell they having the various components similar to the male if you observed here the main components are the ovary then OV duck uterus survice vagina urethra then uh different parts are there that is laia minora labia majora and then colog then rectum and anus so 20 different components or parts are involved in the female reproduction and it has been observed that the female

reproductive cycle is quite complicated as compared to the male and this system involves that the female to make the eggs and to get pregnant to produce babies with the male so by in that way the male reproductive organs and female reproductive organs both are equally important and involved in the development of the newborn babies now what are the neuroendocrine system which are involved in the reproductive toxicology so neuroendocrine Target so whenever this genetics are affected on the reproductive system so what are the mechanism by which it produces the reproductive problems and that includes like environmental toxicants and these environmental toxicant can disturb the reproductive function mainly by the three different mechanism first is the endocrine system that is they alter the endocrine system they are called as endocrine disruptors and they mainly disturb the hormonal system another is the altering gene expression and that is pertaining to spermatogenesis as well as the steroidogenesis and third is the exerting epigenetic effects and which can be result in abnormality in the reproductive system of male offspring up to the four generation following in utero exposure next is the generation of oxidative stress nowadays oxidative stress plays a very important role and change in the lifestyles are the one of the factor for this oxidative stress and many metal ions and environmental toxicant they produces the oxidative stress so it has been observed that this oxidative stress can be seen in up to 80% of clinically proven infertility man and exposure to environmental toxic is a major factor contributing to such increase so this is nowadays many research is going on related to the role of oxidative stress in various disorders and diseases now endocrine disruptors which is related to hormonal irregularity their course of action by acting on either as Agonist or antagonist at the receptor side thereby minimizing or blocking the cellular response in such endocrine gland as the adrenal thyroid and ovary so this endocrine disruptors they affect act on The receptors which are present at different sites and they blocks the cellular responses and next is the altering any of all these system can lead to impaired neurological development depending on the timing and duration of exposure of The Offspring in the pregnant woman so this is very important line that though these alter the neurological development but still it is depending on the time of exposure and duration of exposure of The Offspring in the pregnant woman then immune toxicant so some environmental toxicants are there which affect the immune system so immune toxicant they disturb the cytokine secretion by macrophages and activated T cells thereby preventing normal activation of other T and B cells so thus these chemicals may disturb cytokine mediated communication between immune cell impairing normal immune responses that may be fundamental to reproduction so these are the neuroendocrine targets of the reproductive toxicity now here this hypothalamic pituitary gonadal axis plays a very important role or we can say that it plays a central role in reproductive toxicology so in your previous classes you have studied on this endocrine system so just for understanding if you can observe here that this hypothalamus it increases the production of the gonadotropin releasing hormone that is GnRH and this gonadotropin releasing hormone they triggers they shows the effect on the pituitary anterior pituitary thereby releases the luteinizing hormone and follicle stimulating hormone so this luteinizing and follicle stimulating hormone they have the various effects on testes as well as the ovaries and thereby they produces testosterone and estrogen from the ovaries and they have the different effect on the reproductive organs like estrogen if estrogen is released from the ovary it causes follicular Genesis

then it will also responsible for female secondary sex characters like breast development and maturation hips broaden and for pubic hair growth likewise if testosterone are releases they are responsible for spermatogenesis and apart from that the male secondary sex characters are developed because of this testosterone including the penis and scrotum growth then facial hair grows then larynx elongates lowering voice shouters broaden then body armpit and public hair growth pic hair growth and musculature increases and body weight so these are the uh hormones in male as well as the female which are responsible for secondary characters and the main process of reproduction like follicular genesis and spermatogenesis they also having the some feedback mechanism now uh what are the endocrine disturbers and female reproduction means when endocrine disturbers affect on the female reproduction what uh what are the outcomes here we have discussed with some species like Marine molus there is a morphological changes in reproductive organs if it occurs in the fish it reduce fertility and hormone autism if it occurs in the birds then abnormal clut size female female pairing embryonic deformities in reptiles it produces abnormal sexual development and in woman it increases risk of breast cancer early puberty altered Menses decrease fertility increase miscarriage rate and early menopause similarly if this endocrine distur effect on the male reproduction it also produces several different types of the alteration suppose the male reproductions are exposed to the Organo chemicals and pesticides like dbcp DDT and dextrin these are given or heavy metals like lead Mercury cadmium it produces decrease fertility decrease liido embryo fetal loss birth defect cancer estrogen effect poor cement quality so uh these are the different effects on the male reproductive system after exposure to this environmental then biological and pharmacological agents so here the details are given then what is the mamal uh reproductive cycle this is the general picture of the memal reproductive cycle so it start with the sexual maturation then come to the release of GTs then fertilization transport of zygote implantation embryogen isogenesis birth then fetal development development and growth and again it so this embryogenesis can also involved in the maturation and production of the gamuts which leads to release of the gamuts so this reproductive toxicology this covers a wide spectrum of Toxic effect at all the stages of reproductive cycle starting with the female and male fertility from here it will start and prenatal and postnatal development and culminating in late manifestation that can only be detected in the Next Generation so it is a complex phenomena and in this uh toxicant will affect on any of the stage of this reproductive cycle

So based on this in 1966 the usfda was the first regulatory Authority which issues a uh series of guidelines for evaluating the novel Pharmaceuticals for their effects on reproduction function and develop this guideline describe three studies and these three studies including the segment one study which is the fertility segment two that is embryotoxicity or teratogenicity and segment three that is prenatal and postnatal toxicity so in the same reproductive cycle if you observed what is the segment one fertility so here fertility is it is given in the figure that segment one it involves production and release of gamuts fertilization transport of zygote implantation that is actually the meeting process then segment two it is also called as the teratogenicity and it involves actually the gestation period like embryogenesis and fatal development so this is segment two of this study and segment three that is prenatal and postnatal toxicity here you can observe prenatal and postnatal toxicity it involves the curation lactation post Nal development development and growth so this part involves the segment three and this part

involves segment two and this involves segment one so as per the syllabus how to detect uh how to study the segment one segment two and segment 3 for that we will going to post a separate video for all the three uh different segment study these are again uh another picture which gives you the idea about the segment one segment two and segment three study what are the different uh steps are there and where this will affects then uh for carried out the reproductive toxicity there are certain essential features which one has to understand that is adverse effect may only occurs in the Next Generation or offspring so many of time it's happen that if the toxicity is occurs but the adverse effect you can notice in Next Generation or The Offspring then adverse effect on the vital function of all organs may also indirectly induce adverse effect on reproduction itself means if the vital organ is affected then you can observe the uh if effect indirectly on the reproduction itself then if you want to assess the potential of chemicals to interfere with reproduction so test method in experimental animal must cover the following essential steps first step is that growth and maturation of the sperm and US sites are important then fertilizations is important like Fusion of O sites and sperms then normal cleavage division implantation intrauterine development birth and postnatal development throughout the period of lactation is also equally important then normal development of The Offspring to fertile adult animals which are able to produce a second generation so these are the some essential criteria essential steps which are required if you want to check the potential of chemicals on the reproductive toxicity then next is the there are certain guidelines for study the reproductive toxicity these are the guidelines I guidelines are there which are used for the uh segmental study like segment one segment two and segment 3 apart from that oecd Glide guideline is there that is for industrial and Organo chemicals this is for the drugs industrial and Organo chemicals you have various guideline like teratology study TG 414 one gener study TG 415 two generation study TG 416 reproduction and developmental screening then combined repeated dose and developmental screening developmental neurotoxicity study uterotrophic assay osteogenic properties so all these oecd guidelines are also available on the website then what are the spaces required for evaluating the reproductive end point so if you are doing the study in case of the male and his well in different spaces like mouse rat rabbit pig and monkey so if you are using the mouse and it is male then you have to evaluate this much parameter like spermatogenesis testicular pathogenesis epd dial sperm fertility invitro fertilization if the mouse is there but it is a female then you go with the embryogenesis over and pathogenesis EST cycle endometrium in case of the Rat you can go with this much of the parameter in case of male in case of female in rabbit these are the parameter in case of female rabbit you can evaluate this parameter in case of pig and monkey uh in if male is there there is no specific parameter is reported but in case of the female you can go with the following parameter so this is all about the general basic introduction of reproductive toxicology the details about the male and female reproductive toxicology and the different segments we will going to post as soon as possible so if you like this video then circulate in your friends and also like you give the comments what you are expected from this uh Channel I am always wel welcome to solve the problem thank you once again for your patience listening

thank you