Course Name :An Overview on Maternal Health Antenatal, Intranatal and Postnatal Care

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Implantation

So, hello students, hope you are all doing good. Welcome you all to today's session for the NPTEL online certified courses on the topic and overview on maternal health, the antenatal, intranatal and postnatal care. Myself, Dr. Barnali Ghosh, an obstetrician and gynecologist working at B.C.roy Medical College and Medical Research Center, IIT Kharagpur. Today, our topic of discussion is implantation. Following fertilization, there is the formation of the diploid zygote and this zygote will undergo different developmental stages and ultimately get implanted into the uterine cavity which will ultimately form the fetus in utero.

So, the concepts covered in today's class are the events of implantation, the growth stages of embryo and the different fetal growth periods. Key words being implantation, embryo, blastocyst and fetal growth. So, coming to the events that occur after fertilization right. So, coming to implantation, what we have already seen this fertilization will occur in the ampulla of the fallopian tube right.

So, this is the interstitial part, then the isthmus, then the ampulla, the widest and the longest portion of the tube followed by the infundibulum and the fimbriae. Now here is the release of the secondary oocyte with the corona radiata complex from the ovary during ovulation which reaches the ampulla of the tube and here it is fertilized by the sperm and they will form the zygote right, they will form the diploid zygote. So, let us complete the picture, this is the cervix, the uterine cavity and so now the zygote is formed in the ampulla of the fallopian tube where the fertilization takes place. This zygote from one cell it will divide into two cell by binary fission, then gradually two cell will become four cell, four cell will become eight cell and ultimately it will form a 16 cell structure right by binary fission or mitosis. This 16 cell structure will now enter into the uterine cavity, this is a 16 cell structure compactly adhered with one another forming a globular structure and this is called as the morula or the 16 cell stage.

It enters into the uterine cavity on day 4, this is day 4 of fertilization for the first 3 days it will remain in the fallopian tubes. So, the fallopian tubes will you know help in nourishment of the gametes and as well as the zygote for the 3 first 3 days of fertilization. On day 4 the morula or

the 16 cell structure reaches the uterine cavity, what happens in day 5. Now the zona pellucida which was encircling the ovum it is still present in the zygote and it is also present in this morula this is the zona pellucida. On day 5 there is shedding of the zona pellucida and release of blastocyst.

So, the morula now gets converted to blastocyst right. So, this is day 5, day 5 there is zona pellucida shedding and release of blastocyst. Blastocyst is nothing, but a fluid filled cavity this here there is fluid, fluid is actually due to imbibition this fluid is actually due to imbibition of uterine fluid. Now the water present in the uterine cavity this uterine cavity fluid will you know intravacet within the morula and will lead to the formation of cavity called as the blastosol and this structure is called the blastocyst which you know has two parts the inner cell. This is the inner cell mass and this outer lining cells of the blastosol these are the outer cell mass.

So, this is the events occurring on day 5 after fertilization. What happens on day 6? On day 6 this blastocyst well so, this is the inner cell mass and these are the outer cell mass and in between is the blastocoel cavity. So, the blast this is occurring on day 6. What happens in day 6? What happens in day 6? There is just you know opposition or just you know loosely attachment of the blastocyst to the endometrial lining. So, there is no opposition of the blastocyst to the endometrial lining which you know depicts the start of implantation.

So, 6th day after fertilization is the start of implantation. From day 7, the outer cell mass will now form will now differentiate into two structures you know the cytotrophoblast and the syncytiotrophoblast right and this syncytiotrophoblast will give some pinopod like structures or extensions within the you know decidua or the endometrium of the uterine cavity and these will further bind you know more strongly or adhere more strongly to the endometrial lining and thereby you know helping the embryo developing embryo to firmly attach to the endometrium. So, this is the inner cell mass and the outer cell mass. So, this occurs in day 7 where there is differentiation of the outer cell mass into syncytiotrophoblast which will form the pinopod like extensions or villi like structures and the cytotrophoblast right. Syncytotrophoblast is actually has hormonal action and it causes release of beta HCG which is the hormone of pregnancy.

Now, on day 8 you know day 8 what happens? Yes, this is the inner cell mass and the outer cell mass having differentiated into syncytium and the cytotrophoblast. Now, what I want to know say that this implantation is also called as interstitial implantation why it is so, why it is so? This interstitium this is the decidua right, this is the decidua or the endometrial lining of the pregnant uterus. This decidua actually will start covering the developing embryo and it will further cover the developing embryo fully right. So, this decidua will cover the developing embryo fully these are the decidua lining in the other walls of the uterus. So, now depending upon the location depending upon the location these have different names.

This decidua is called as the decidua basalis which is to the basal side towards the myometrium of the uterine wall. So, this is called as the decidua basalis this part which covers the developing embryo as a capsule is called as the decidua capsularis and the decidua on the opposite wall of the uterine cavity this decidua is called as decidua parietalis. So, you can appreciate that the 3 decidua what happens these are the 3 decidua. So, these this is the decidua lining and the embryo developing embryo this is the developing embryo and this decidua will cover the developing embryo of fully on all sides right. It will cover the developing embryo on all sides right.

So, as the embryo goes bigger and bigger this portion will grow. So, this is the uterine cavity which is still persistent, but as it grows larger as the embryo goes larger the cavity gets obliterated and slowly and slowly the decidua capsularis will fuse with the decidua parietalis thereby obliterating the uterine cavity right. So, I hope it is clear firstly we need to understand the steps of fertilization and then after fertilization zygote is formed and this zygote gradually you know the steps of implantation of the zygote will be discussed now right. So, coming to implantation proper. So, this is the diagram which I was drawing.

So, here in the ampulla there is fertilization the fertilized zygote will remain in the fallopian tube for the first 3 days and it reaches the uterine cavity on day 4 as morula. From day 4 gradually day 5 day 6 it will gain its development and from day 6 there is no attachment to the uterine wall and this formation of pinopores or more adhesion form adhesion to the uterine wall occurs on day 7 right. So, day 4 and day 5 the morula and the blastocyst will be floating in the uterine cavity within the endometrial fluid and from day 6 it will first loosely oppose with the loosely oppose with the decidua and then gradually you know it will adhere firmly within the decidua. So, zygote this is the zygote and we have discussed that it remains for first 3 days that is precisely for 80 hours in the fallopian tube and this single zygote will be forming 2 cell, then 4 cell, then 8 cell, gradually 16 cell stage, 16 cell stage which is called as the morula. So, these are by mitosis or by binary fission and this morula will reach the uterine cavity on day 4 after fertilization.

Morula is nothing, but a globular structure containing compactly adhered cells forming a solid mass right. Now, day 5 what happens day 5 this morula will imbibe water, morula will imbibe water and it will lead to formation of blastocyst. Blastocyst is nothing, but there is a cavity inside cavity inside called as the blastocoel right. So, this cavity inside this cavity inside is called the blastocoel and the cell gets divided into this is the inner cell mass right, this is the inner cell mass and this part is the outer cell mass, this is the outer cell mass or the tropho ectoderm layer. Now, we need to know that the outer cell mass will ultimately form the placenta and the membranes whereas, the inner cell mass will form the embryo proper or the whole of the fetus right and hatching.

So, blastocyst formation number 1 and hatching. What is hatching? The zona pellucida which was covering the morula will now give way, it will rupture and there will be release of the blastocyst from the zona pellucida into the uterine cavity. So, this is coming to the structure of the blastocyst, this is the inner cell mass, this is the blastocoel, this is the outer cell mass and this is the endometrial lining of the uterus endometrial endometrial lining of the uterus. So, blastocyst beneath the endometrium these are the maternal spiral arteries containing the maternal blood right. So, this is the structure of blastocyst which occurs in day 5 of fertilization.

Coming to hatching what happens? Yes, the morula structure it was present inside the zona pellucida and gradually there is formation of blastocyst in a fluid filled cavity inside and it will you know give pressure and the zona pellucida will break open and there will be release of the blastocyst outside the zona pellucida into the endometrial cavity or the uterine cavity right. So, these two phenomenon are occurring on day 5. So, these are the stages of embryo development. Yes, this is the zygote the 1 cell stage it divides by binary fission 2 cell, 4 cell, 8 cell stage this is a compact cell mass and this is the 16 cell stage or the morula which will ultimately convert to blastocyst right. You can see the cavity inside and this is this is the zona pellucida ultimately the zona pellucida will be shed off and this is called as hatching right.

On day 6 what happens in day 6? Yes, the blastocyst gets implanted not implanted, but it just loosely attaches to the endome you know decidua endometrial lining of the endometrial lining of a pregnant uterus is called as the decidua. So, it gets now just lightly attached to the decidua. So, attachment to the endometrial uterine wall and this signifies the start of implantation migration towards the decidua and this type of implantation where the decidua the embryo gains entry inside the decidua and the decidua covers the embryo from all sides this type of implantation is called as interstitial implantation. What happens in day 7? Yes, in day 7 so, the blastocyst the blastocyst here the blastocyst here it has been differentiated into inner cell mass and outer cell mass and this outer cell mass will form the tropho ectoderm layer which will now differentiate into cytotrophoblast inside and outside is the syncytiotrophoblast. The syncytiotrophoblast is actually you know a syncytium it is a multi nucleate structure without any intervening cell membrane and this syncytiotrophoblast will form pinnopod like structure to gain entry into the decidua.

This is actually know mostly hormonal action and it releases beta HCG hormone. What happens to the cytotrophoblast? The cytotrophoblast will form the placenta and the membranes it first divides into two parts the villas trophoblast and the extra villas trophoblast right. The villas trophoblast so, firstly was the inner cell membrane which will form the embryo or the fetus and the outer cell membrane or the tropho ectoderm dividing into cytotrophoblast and syncytiotrophoblast. Syncytiotrophoblast mostly hormonal action cytotrophoblast divides into or differentiate into villous trophoblast and extra villas trophoblast. This villas trophoblast will help in formation of villi or the chorionic villi that is chorionic frondosome.

We will see the structures during you know discussion about placenta. Extra villas trophoblast will again differentiate into endovascular trophoblast and interstitial trophoblast right. This endovascular trophoblast are actually you know invade the maternal blood vessels, invade the maternal spiral arteries you know and thus it will render the maternal blood vessels from high resistance to low resistance and thereby help in you know exchange of nutrients from mother to the baby right. So, this is day 7. Now day 8 we have seen that from the day 7 the syncytiotrophoblast starts release of beta HCG and just immediately one day later beta HCG is detected in the serum from day 8 and this beta HCG has similar structure as per the LH hormone.

So, it will take over the action of LH and it will help in maintenance of the corpus luteum called as corpus luteal rescue. This will you know have a important effect because this corpus luteum will secrete progesterone which will help in maintenance of pregnancy in maintaining the uterine quiescence and thereby you know help in progression of the pregnancy. Day 8 the beta HCG is detected in serum. Now on day 13 the beta HCG is detectable in urine very important these are all from the days of fertilization. Day 13 of fertilization will correspond to we have already discussed that mostly on an average in a 28 day menstrual cycle ovulation takes place on 14th day and taking that day that day of ovulation to be the day of fertilization.

So, day 13 of fertilization comes out to be day 13 plus 14 that is day 27 of the cycle. So, just one day prior to the expected date of menses just one day prior to the next menstrual to the date of the next menstrual cycle the beta HCG will be detected in urine. So, when the patient comes with a history of missed period maybe you know he she tells that yes doctor my menses were about to happen on 28th day of every month and, but I have missed my cycle. Now the beta HCG will be detected in urine and it can be you know done by a simple pregnancy kit test in a OPD basis we can detect beta HCG and thereby confirm the pregnancy right. So, thus day 13 will be the day of detection of beta HCG in urine.

Now coming to day 11 what happens day 11 the growing conceptus is covered by the decidua on all sides and this marks the completion of interstitial implantation. So, I have already drawn this picture. So, this is the embryo with the syncytium and the cytotrophoblast with the inner cell mass and it gradually buries into the decidua. It gradually buries into the decidua and the decidua will cover the embryo on all sides, the decidua will cover the embryo on the all sides right. So, this decidua will be covering the embryo on all sides by day 11.

So, this is the you know completion of interstitial implantation. So, this what is the implantation window it starts from the start of implantation to the last day of completion of implantation that is from day 6 to day 11 of fertilization. Coming to the menstrual cycle yes so, this is day 14 the day of ovulation as well as the day of fertilization. So, day 6 you know day 6

will be actually day 20. So, day 6 to day 11 so, this period day 6 to day 11 of the cycle this is called as the implantation window right.

So, this is a pictorial diagram where now how the blastocyst this is the uterine cavity and this is the endometrial lining of the uterus or the decidua. How the blastocyst from day 5 there was hatching release of the blastocyst in the endometrial cavity it will gradually attach just oppose on day 6 on the endometrial lining then gradually it will go inside the decidua you know by for different protein metalloproteinase or hydrolytic proteins as well as you know attachment of different glycoproteins they will help in movement of this developing embryo inside the decidua. This is the outer cell mass the red color which will differentiate into cytotrophoblast and the syncytiotrophoblast right and this blue is the inner cell mass and this is the blastocyst cavity right. Now as the formation of the structures of the villi you know they develop from the trophoblast these villi structures they get developed the embryo the inner cell also simultaneously adapts into hypoblast epiblast and ultimately this will form the embryonic disc which will form the whole of the fetus right and this is outer this part outer this part this is the cytotrophoblast and the syncytotrophoblast forming the villi. So, this is a structure of villi and this is a primary villi there are different stages of development of villi primary secondary tertiary which will ultimately help in formation of the placenta and thereby you know restoring or help in you know establishing the maternal the fetomaternal you know exchange of nutrients from the from the mother to the fetus right.

So, this is the stages of implantation. Coming to the implantation time yes we have just read it is day 6 to day 11 of fertilization very important this terminology after fertilization day 6 to day 11 which comes out as day 20 to day 25 of the menstrual cycle and where it occurs it occurs mostly in the upper uterine segment it occurs in the upper uterine segment. So, upper uterine segment in the middle in the posterior wall. So, this is the usual site of implantation of the embryo on the uterine wall. What are the process of implantation? There are three stages, opposition, adhesion and invasion.

Opposition as occurs on day 5. Now, day 5 there is blastocyst formation day 6 just you know loosely binding to the uterine decidua and there thus molecules you know playing an important role are interleukin 1, then your colony stimulating factor 1. These are you know there are various molecule molecules leukemia inhibiting factor 1, these molecules will bring about this opposition. Adhesion actually due to now integrins, integrins present on the blastocyst they will you know combine or they will attach with the different extracellular matrix protein on the decidua. So, this is the uterine decidua, these are the uterine glands and these are the extracellular matrix and here within the extracellular matrix there are different extracellular matrix proteins called as fibronectin and laminin attachment of these proteins will bring about adhesion. And ultimately invasion where the blastocyst gains entry inside the decidua and important factor here is this is you know positively it gets positive impact from matrix

metalloproteins enzyme.

It will help in invasion of the blastocyst whereas, it is inhibited by plasminogen activator inhibitor enzyme right. So, all these enzymes they work together in synchrony bringing about the implantation of the growing blastocyst inside the decidua. So, these are the stages of implantation I will mark. So, number 1 this is the blastocoel, this is the blastocyst on day 5 after fertilization and this is showing the blastocoel cavity, this is the inner cell mass and forming the embryo proper and this is the outer cell mass tropho ectoderm layer. Now on day 6 you know it will adhere loosely adhere with the uterine wall this is the epithelium of the endometrium right and these are the spiral arteries containing the maternal blood.

This is the endometrium. So, compactum there are different layers of the endometrium. So, this is the compactum layer of the endometrium. So, now there will be differentiation of the outer cell mass into cytotrophoblast inner is the cytotrophoblast which are mononuclear cells, outer is the syncytiotrophoblast which is multinucleate without any proper intervening cell membrane. They will form projections right and they will gain entry into the endometrium. Now see within the projections they form lacunae, they will ultimately form the inter villa the space which will be filled with maternal blood right and these are the villi.

These are the villi here this is primary villi gradually they will form secondary and tertiary villi and in the inner cell mass this cavity is called as the amniotic cavity right. So, this is the ectodermal layer the yellow colored is the endodermal layer and this cavity formed within the endodermal layer is the yolk sac and this endoderm ectoderm this is called as the embryonic disc with the intervening mesoderm will lead to the formation of the fetus right. So, now coming to gestational age and fetal age what does that mean I have already discussed that this last day of sorry first day of last menstrual period first day of last menstrual period right and this is the day of ovulation which is actually the taken to be the day of fertilization day of ovulation or day of fertilization right. So, when we talk about you know gestational age we always calculate from this first day of last menstrual period. So, if it is day 6 day of ovulation is day 14 from the LMP.

So, this is day 14 which is the day of ovulation and that is actually the day of fertilization. So, day 6 after fertilization day 6 after fertilization will correspond to plus 14. So, day 20 right. So, this is the gestational age and this is the fetal age. Fetal age is more accurate and it corresponds with the day of fertilization, but we do not know actually we cannot always very precisely say the day of ovulation.

So, more practical is to talk about the gestational age where the female knows her first day of last menstrual period and this gestational age is nothing, but fetal age plus gestational age is nothing, but fetal age plus 2 weeks. The age calculation from USG is actually the shows the fetal age. So, the age you know gestational age which has been calculated from USG it is actually

accurate and it comes out approximately 2 weeks you know less than the calculated gestational age from her LMP right. So, we get a idea about gestational age and fetal age. Now, what are the stages of fetal growth? There are 3 stages pre embryonic period, embryonic period and the fetal period.

What are they? The pre embryonic period, pre embryonic means from the day of fertilization to 2 weeks. This I have already told that gestational age is plus 2 weeks. So, 2 weeks to 4 weeks right embryonic period, embryonic period is 3 weeks, 3 weeks after fertilization to 8 weeks and fetal period is 9 weeks after fertilization up to delivery. So, correspondingly the gestational age can be calculated. Another point to remember is this embryonic period, this embryonic period is you know most teratogenic period.

Teratogenic period and it is very susceptible any insult during this period can cause defect in the fetus. Coming to double decidual sac sign, it is a USG finding and this is a finding suggestive of intrauterine life, you know intrauterine pregnancy. What does it mean that this gestational sac, this is the gestational sac and this is surrounded by decidua right on all sides. I have already explained in the implantation is your interstitial implantation.

So, it is surrounded by decidua on all sides right. So, this is the decidua capsularis which covers the sac as a capsule and this is the decidua basalis, this part which is below the developing gestational sac and the decidua on the opposite side, decidua on the opposite wall of the uterus, this is the decidua parietalis right. So, in USG you will find that these two decidua will come as white lines or hyper echoic structures and this gestational sac will come as a hypo echoic structure. So, double white line covering the hypo echoic structure, this is the endometrial cavity which will also come as hypo echoic. So, this structure when we see in USG, it is called as double decidual sac sign and it is confirmatory of intrauterine pregnancy.

This is the you know USG finding. So, this inside is the gestational sac and outside you can see these two white areas sorry outside you can see these two white areas, this is the decidua capsularis and this is the decidua parietalis. So, these two white lines surrounding the gestational sac, this is actually the pictorial representation and here this is called as the double decidual sac sign right. And we can you know say that up till the uterine cavity, uterine cavity is I mean up till it is patent we can appreciate this double decidual sac sign. Once the uterine cavity gets obliterated, the double decidual sac sign cannot be further appreciated and it obliterates on 16th week of pregnancy. Slowly, slowly the embryo will grow and by 16 weeks the whole of the uterine cavity will get obliterated that is the decidua capsularis will now merge with decidua parietalis right.

So, this uterine cavity will get obliterated by 16 weeks of pregnancy. Coming to the MCQs, very quickly we will go through them fertilization usually occurs in yes we know in the tubes

and it is in the ampulla of the tubes. Then, in which day the fertilize implantation starts, we have already said it is 6th day of fertilization very important. So, the fertilization after 6th day of fertilization implantation starts and the implantation window is day 6 to day 11. Which of the following happens immediately after fertilization? Restore the diploid number of chromosomes, formation of blastocyst, become haploid beginning of second meiosis.

So, immediately after fertilization there is union of two haploid gametes thereby restoring the diploid number of chromosome forming the zygote which contains 46xx or 46xy chromosome depending it is a female or a male fetus. During implantation which one of the following structures will invade the myometrium right. So, what will invade the myometrium sorry endometrium? So, endometrium will be invaded by the outer cell, outer cell mass and this outer cell mass will now differentiate into inner cytotrophoblast and outer syncytiotrophoblast. So, it will be invaded by the outer syncytiotrophoblast. 24 years old woman presented to the clinic with late period, missed period right.

So, now, she was referred to a lab for blood investigations which one of the following enzymes will be found it will the enzyme of pregnancy which we test is HCG more precisely it is the beta HCG which is secreted from the syncytiotrophoblast. In urine it is present on day 13 after fertilization. What is the site of implantation? Site of implantation is on the posterior wall of the body of the uterus. So, this is the correct answer outer cell layer of blastocyst is called outer cell layer that is the trophoblast or tropho ectodermal cells which will form the cytotrophoblast inside and the syncytotrophoblast outside in which later utero placental circulation begins it is day 11 right. When the implantation has been completed then the utero placental circulation will begin.

Next what is the phenomenon shown here? This is actually the zona pellucida. So, zona pellucida is giving way and this is called as zona shedding or hatching which occurs on day 5 of fertilization. What are these structures? 2 this is the outer cell mass or the trophoblast. 3 this is the epiblast.

4 so, this is the amniotic cavity and the hypoblast. I am very sorry this will be this will now this is a blastocyst stage. So, this will be the blasto seal right this will be the blasto seal. Identify the phenomenon occurring on occurring. So, here you know this is the blastocyst has ruptured from the zona pellucida and it getting attached to the uterine endometrium. So, on which what is the phenomenon this is called as adhesion because the outer cell mass is the has developed into the cytotrophoblast inside and this is the syncytotrophoblast which is multinucleate within without any intervening cell membranes.

This is the syncytotrophoblast this adhesion of the blastocyst with the endometrium and this occurs on day 7. Day 6 is loose apposition, day 7 is adhesion and differentiation into cyto and

syncytotrophoblast. Now bleeding during pregnancy which mimics menstruation why it happens? We have already seen this right. So, this is the endometrium and here there will be the developing embryo right. The gestational sac with the embryo inside and the decidua will cover the embryo on all sides.

So, the decidua will cover the embryo on all sides forming the decidua basalis, then the decidua capsularis and the decidua parietalis right. So, these this is the decidua basalis, this is the decidua capsularis and this is the decidua parietalis. So, as the embryo grows embryo will grow and this decidua this embryo will slowly grow and the decidua capsularis will slowly merge with the decidua parietalis. So, this endometrial space this endometrial space this was the endometrial cavity which will gradually get obliterated right with the growing embryo. Now till know if still it is not obliterated there is a chance of bleeding from the endometrium, there is a still a chance of bleeding from the endometrium from this endometrial lining and it happens during pregnancy there is some shedding of the endometrium.

This is called as the placental sign or the heart man sign. But to note that this phenomenon can occur till the cavity of the uterus is patent after obliteration of the uterine cavity there will be no shedding of the endometrium and thus it occurs up till 16 weeks of pregnancy. Actually it is it can happen, but it is very rare in occurrence right. So, this is the summary slowly the zygote is formed there is fertilization, there is cleavage forming the morula that is the 16 cell stage with the blastomeres, then there is compaction and differentiation leading to formation of the blastocyst with cavitation and formation of inner cell mass and the outer cell mass or the trophoblast. Then there will be zona hatching and will release of blastocyst which will get implanted into the uterine endometrium right or the decidua. And this you know whole of the embryo or whole of the blastocyst will get inside the decidua and ultimately slowly there will be formation of villi and placenta and also simultaneously there will be inner cell mass differentiation which will lead to formation of bilaminar disc ultimately forming the embryonic disc from which the fetus will grow right.

So, this is all for regarding implantation references taken are from D.C Dutta book of obstetrics, Speroff's clinical gynecologic endocrinology and infertility and Williams obstetrics. Thank you all for your patient hearing.