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Matric number: 18/mhs07/020

Department: Pharmacology

Course code: PHS 212

Question: write a short note on implantation

Implantation is a process in which a developing embryo, moving as a blastocyst through a uterus, makes contact with the uterine wall and remains attached to it until birth. The lining of the uterus (endometrium) prepares for the developing blastocyst to attach to it via many internal changes. Without these changes implantation will not occur, and the embryo sloughs off during menstruation. Such implantation is unique to mammals, but not all mammals exhibit it. Implantation consists of three stages:

- (a) The blastocyst contacts the implantation site of the endometrium (apposition);
- (b) Trophoblast cells of the blastocyst attach to the receptive endometrial epithelium (adhesion);
- (c) Invasive trophoblast cells cross the endometrial epithelial basement membrane and invade.

Furthermore, of those mammals that exhibit implantation, the process differs in many respects between those mammals in which the females have estrous cycles, and those mammals in which the females have menstrual cycles. Females in the different species of primates, including humans, have menstrual cycles, and thus similar processes of implantation. Before embryogenesis begins, the ovary releases an unfertilized egg cell, called an oocyte, which then travels down the fallopian tube. The egg is enveloped in an extracellular matrix called the zona pellucida. Sperm can fertilize the egg in the zona pellucida (ZP), which prevents the fertilized egg, called a zygote, from adhering to the wall of the fallopian tube. If the zygote implants in any area besides the uterus, the result is an ectopic pregnancy. This condition prevents the complete development of the embryo, and it can cause fatal hemorrhaging in the pregnant female. As the zygote moves through the fallopian tube it undergoes several rounds of cell division, a process

called cleavage. These cell divisions produce the inner cell mass (ICM), which will become the embryo, and the trophoblast, which surrounds the ICM and interacts with maternal tissues. Together, the ICM and the trophoblast are called the blastocyst. A blastocyst successfully implants in the uterus when, as the ZP exits the fallopian tube, the blastocyst leaves the ZP and binds to the endometrium. The endometrium is one of the few uterine surfaces to which a blastocyst cannot always implant. The properties of the endometrium change, and only in a brief window can the blastocyst implant on the tissue. In humans, that window includes days six through ten after ovulation. Just prior to ovulation, the endometrium begins to thicken and to expand in response to the release of estrogen from the ovaries. As the embryo moves through the fallopian tubes, the endometrium proliferates, changes in shape, becomes receptive to implantation, and produces a hospitable environment for the embryo. Signaled by the release of progesterone from the ovaries, a series of changes called decidualization occurs. Decidualization includes the gathering of white blood cells around endometrial arterioles, or blood vessels leading from arteries to capillary beds. As that vasculature forms, a molecule that stores energy, called glycogen, accumulates in the expanding connective tissues of the uterus. Furthermore, the endometrium swells as interstitial fluid accumulates in it. The endometrium, swollen with interstitial fluid, vasculature, and nutrients, provides a hospitable environment for embryogenesis. As the blastocyst moves through the uterus it realigns itself so that the inner cell mass is adjacent to the uterine wall, and the trophoblast contacts the endometrium. The position of the ICM in relation to the endometrium establishes the head to tail, or dorsal-ventral, axis of the embryo, with the dorsal side of the embryo facing the uterine wall. This is the first embryonic event that dictates the organization of the future body. Successful implantation depends on the blastocyst binding to the endometrium. There are many molecules that are thought to dictate this interaction, but integrins, a type of cell-adhesion molecule, have been identified as a primary component. Integrins extend from the lining of the uterus and from the surface of the blastula. Integrins have many functions in nearly all tissue types, and they have a role in cell adhesion, conveying information about the extracellular environment to the nucleus, and modulating the local immune response. Immediately following implantation, integrins help regulate

gene expression in the embryo. Doctors also look for high concentrations of integrin's when they look for areas of uterus receptive to implantation in assisted reproductive therapy (ART), and they use the lack of such concentrations to identify women who may be infertile.

Despite the contact between the blastocyst and the endometrium, implantation can fail. There are many potential causes of errors. If implantation does not occur, the endometrium breaks down and sheds, along with the blastocyst, as part of the menstrual cycle. However, if a blastocyst does implant, then the endometrium remains in the uterus, and together with uterine tissue, becomes the maternal portion of the placenta, called the decidua. Once the blastocyst adheres to the uterine wall, the trophoblast secretes enzymes that digest the extracellular matrix of endometrial tissue. The trophoblast cells then begin to intrude between the endometrial cells, attaching the blastocyst to the uterine surface. Further secretions of enzymes allow the blastocyst to bury itself deeply among the uterine stromal cells that form the structural components of the uterus. Subsequently, trophoblast cells continue to divide and form two extraembryonic membranes. These membranes form the fetal portion of the placenta called the chorion. Additional enzymes and signaling factors secreted by these membranes remodel the uterine vasculature to bathe the fetal or embryonic blood vessels in maternal blood. Chorionic villi are the folds of tissue and blood vessels that connect maternal and fetal blood pools. Maternal blood diffuses into the villi, and it travels through them into the fetus's vasculature. Similarly, fetal blood diffuses from the villi and into the maternal vasculature. Normally fetal and maternal blood do not mix, but the relationship between the two circulatory systems enables the transfer of nutrients and oxygen to the fetus or embryo, and carbon dioxide and urea from the fetus to the mother.

While unique to mammals as a reproductive process, implantation is not unique to the uterus and the trophoblast. The same trophoblast enzymes that digest the endometrium are also used by tumor cells to burrow into tissues throughout body. Tumor cells use the same growth factors as the trophoblast to attract maternal blood vessels, which then interact with the chorion, and to provide nutrients to the expanding

mass. In addition, the changes in the endometrium during decidualization such as swelling, the accumulation of white blood cells, and the general activation of the maternal immune system, are consistent with a response to the presence of pathogens or tumors.