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BIO380F—HUMAN DEVELOPMENT

Professor Danton H. O'Day

Lecture Test 2—March 10, 2008

2 Hours; 100 Marks Total

Answer all questions giving the best or most appropriate answer in each case. No aids allowed.

1. Based upon the primary diagnoses for ART procedures, list the three major causes of infertility (3 marks):

a. Problems with fallopian tubes

b. Male infertility (low sperm count, sperm motility problems…)

c. Endometriosis

Note: "Unexplained" can be substituted for any of above

2. List two methods that are being used to select sperm that will give rise to either a male or female child in IVF (2 marks):

a. Selection based on swimming rates (male sperm faster)

b. Selection based on DNA content (X chromosome smaller, less DNA, than X)--FACS

3. Using short sentences or clearly stated point form, compare the mitotic cycle of cleavage cells to normal cells and explain what the implications of this difference are to early human development (5 marks).

-Normal cells: G1, S, G2, M (1 Mark)
-Cleavage cells: S,M no G1 or G2 (1 Mark)
-Cleavage is faster than normal cell division--important to get embryo multicellular rapidly, (prepares cells for implantation by time embryo reaches the uterus) (1 Mark)
-Key point: no intervening growth: Zygote is divided up into smaller and smaller cells that can be moved around during gastrulation and neurulation (2 Marks)

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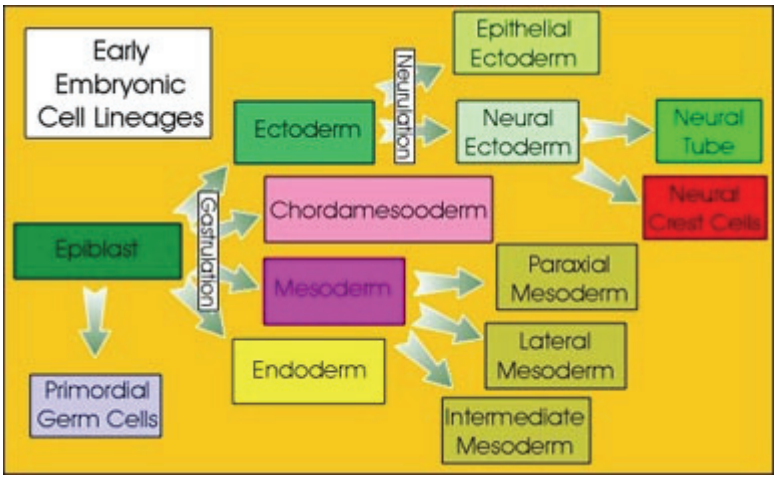
4. In concise point form and short phrases with or without diagrams answer the following questions. What are bottle cells, where do you find them, what is their function, what allows them to separate from the other cells, describe their behaviour and what drives their change in shape? Provide some experimental evidence for the last point. (10 marks)

-a special elongated, independently motile cell seen in embryonic development (1 Mark)
-occur during gastrulation and neurulation (1 Mark)
-driving force behind ingression of cells during both gastrulation and neurulation. (1 Mark)
-loss of E-cadherin allows cells to dissociate and move internally (1 Mark)
-Change in shape is driven by microtubules (elongation of cells; 1 Mark) and microfilaments (actin filaments cause constriction of apical region; 1 Mark)
-Colchicine (inhibits microtubules) stops elongation of cells and neurulation/gastrulation (2 Marks)
-Cytochalasin (inhibits actin filaments) stops constriction of apex of cells and neurulation/gastrulation (2 Marks)

5. Draw a simple chart of the embryonic cell lineages that have been established once neurulation is complete (15 marks).



1 Mark each; 3 marks if completed fully and correctly

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6. Using short sentences and point form define the term "Pattern and Polarity" and provide some indication on how they are established (14 marks).

Gastrulation lecture, See sections "Mammalian Pattern & Polarity", "Hox and the AP Axis"

Mammalian Pattern & Polarity
-Embryo establishes 3 axes early in development: (anterior-posterior axis); (dorsal-ventral axis); (right-left Axis). (3 marks)
- anterior-posterior axis is likely established at implantation (1 mark)
-the A-P Axis defines the orientation of the primitive streak. (1 mark)
- The A-P axis of all animals appears to be specified by the expression of Hox genes (1 mark)
-Retinoic acid is a natural morphogenetic agent that affects A-P axis formation and HOX gene expression. (1 mark)
-the node (Hensen's node) that appears at gastrulation at the anterior end of the primitive streak oversees the construction of the whole body form. (1 mark)
-After the endoderm has migrated internally, the "anterior visceral endoderm" instructs the formation of head components. (1 mark)
-Together the two signaling centres regulate gene expression in specific regions (1 mark)
- The node expresses genes called Noggin and Chordin that are not expressed by the anterior visceral endoderm. (2 marks)
-The anterior visceral endoderm expresses genes called Lim-1, Hesx-1 and Otx-2 which are essential for head development. (2 marks)

7. Using your knowledge from all of the lectures so far, starting at the zygote draw and label a timeline of the major events that occur during the first 3 weeks of human development. Without defining them be sure to include all of the major events that have been covered (16 Marks).

0 Days	1-3 Days	3-4 Days	4 Days	5 Days	6 Days
Zygote	Cleavage to Morula	Compaction, Cavitation	Blastocyst	Hatching	Implantation Starts

7-15 Days	15 Days	18 Days	20-21 Days	
Implantation Continues	Gastrulation Starts	Neurulation Starts	Gastrulation done	Heart Development starts

Notes:
-Above timeline is worth 12 marks (1/event; Compaction, Cavitation, 1 each); dates can be approximate but must be close
-Clarification of the separation of cell lineages within the first 7-15 days or so (1 mark); comments on specific cell layers that form (e.g., of blastocyst, gastrula and/or neurula), 2 marks.

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8. Describe the process of capacitation explaining how the sperm prepares for egg penetration? Make sure any terms or components that are mentioned are clearly explained. (15 marks)

Material from Lecture 7:
"Capacitation" through "Effects of Capacitation on Sperm" plus "Some Major Acrosomal Enzymes" through "Human Acrosin"

-define capacitation; Essential changes in spermatozoa that enables them to fertilize the egg (1 mark); occurs in mammals not lower animals (1 mark)
-Then clarify this definition: role of female genital tract in causing capacitation (1 mark); calcium ions and cAMP via kinases (e.g., PKA, others?) important to phosphorylate proteins for increased motility (3 marks); cholesterol reduced to increase membrane fluidity for fusion (1 mark); Galactosyltransferase (GalTase) modified for zona binding (2 marks) to ZP3 ; Acrosomal enzymes are activated to digest proteins (e.g., human Acrosin—acrosomal serine protease, 1 mark) and carbohydrates (1 example at least; 1 mark) which is important for penetration of extracellular matrix of cumulus oophorus and corona radiata cellular layers (2 marks) and then for zona pellucida binding (ZP2, ZP3) and penetration (protein digestion) (2 marks).

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9. Define ART and in order of current usage list the types of ART procedures that are carried out with a clear definition of each of those procedures. Then list the full sequence of events for a successful ART procedure with an indication of what the typical success rate is for such procedures. (20 marks)

ART = Assisted Reproductive Technologies (2 marks)—must be exact

Types of ART procedures (3 marks each = 9 total)
IVF (In Vitro Fertilization) involves extracting a woman's eggs, fertilizing the eggs in the laboratory, and then transferring the resulting embryo(s) into the woman's uterus through the cervix.
GIFT (Gamete IntraFallopian Transfer) involves using a fiber-optic instrument called a laparoscope to guide the transfer of unfertilized eggs and sperm (gametes) into the woman's fallopian tubes through small incisions in her abdomen.
ZIFT (Zygote IntraFallopian Transfer) involves fertilizing a woman's eggs in the laboratory and then using a laparoscope to guide the transfer of the fertilized eggs (zygotes) into her fallopian tubes.
Most IVF, GIFT, and ZIFT cycles used fresh, nondonor eggs or embryos.

Successful ART—Sequence of Events (1.5 marks each = 7.5 total)
1. Assessment of Egg Production. An ART cycle is started when a woman begins taking medication to stimulate the ovaries to develop eggs or, if no drugs are given, when the woman begins having her ovaries monitored (using ultrasound or blood tests) for natural egg production.
2. Egg Retrieval. If eggs are produced, the cycle then progresses to egg retrieval, a surgical procedure in which eggs are collected from a woman's ovaries. Once retrieved, eggs are combined with sperm in the laboratory.
3. Egg Transfer. If fertilization is successful, one or more of the resulting embryos are selected for transfer, most often into a woman's uterus through the cervix (IVF).
4. Implantation Signals Clinical Pregnancy. If one or more of the transferred embryos implants within the woman's uterus, the cycle then progresses to clinical pregnancy.
5. Live Birth. Finally, the pregnancy may progress to a live birth, the delivery of one or more live-born infants. (The birth of twins, triplets, or more is counted as one live birth.)

Success rate: ~30% (number within 28-35% range is okay) (1.5 marks)

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