EARLY EMBRYOGENESIS AND MATERNAL RECOGNITION OF PREGNANCY

Chapter 13; Pathway to Pregnancy and Parturition

AVS 222 (Instructor: Dr. Amin Ahmadzadeh)

I. THERMINOLOGY AND EMBRYO ATTACHMENT

A. Four steps must be achieved before embryo can attach to the uterus

- Development of embryo within confinement of the zona pellucida
- Hatching of the embryonic cells (blastocyst) from the ZP
- Formation of extra embryonic membranes (e.g placenta)
- Maternal recognition of the pregnancy

B. Embryo

- Refers to the early period of development in which no distinct anatomical structure has formed.

C. Fetus

- Defined as potential offspring that is still in the uterus (before birth) and generally recognizable as a member of given species.
- More advanced from an embryo
- In cattle, Usually is referred to an advanced embryo after approximately 30 days post-fertilization in

D. Conceptus

- Product of conception including early embryo, the embryo and extra-embryonic membranes during the implantation, and fetus and placenta

II. EMBRYO DEVELOPMENT (CLEAVAGE DIVISIONS)

(Figure 13-1)

Mitotic divisions transform a one-celled embryo (**zygote**) into a multicellular embryo

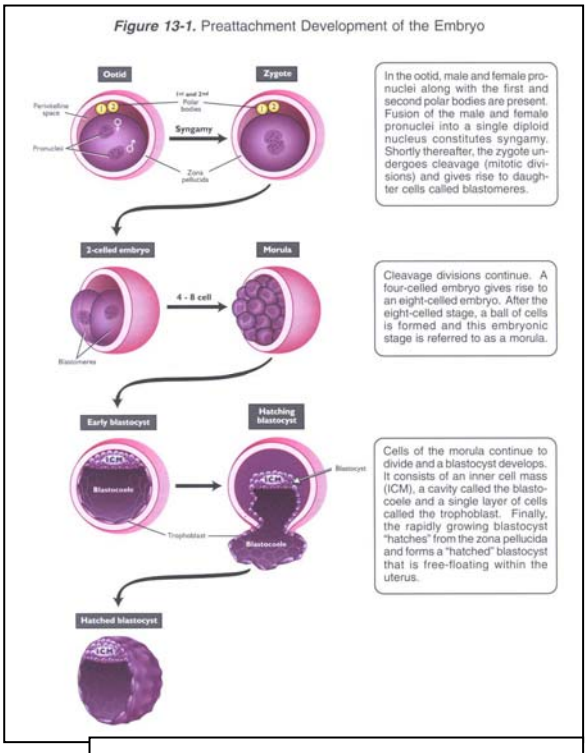
A. Zygote to 2-cell

- Each cell of embryo is called a **blastomere**
- There is no cell growth only division of the cytoplasm
  - a) Blastomere size decreases with cell divisions

B. 2-cell to 4- and 8- cell

- Each blastomere undergoes subsequent division yielding 4 and then 8 daughter cells

Figure 13-1. Preattachment Development of the Embryo



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- No cell growth

    a) Blastomeres are 1/4 and 1/8 original size

C. Divisions continue with embryos named for the number of cells present

- Eventually too many cells to count

D. **Morula** (Mulberry like!)

- Solid ball of cells (too many blastomeres to count)

    a) 16-32 cells

- Individual blastomeres become progressively smaller but the size of the embryo remains the same (still no embryo growth)
- In cattle that occurs around day six after fertilization and when embryo is non-surgically recovered (**flushing embryo**) for embryo transfer

II. CLEVAGE DIVISIONS (MORULA STAGE TO EMBRYO HATCHING)

(Figures 13-1 & 13-2 & Figure 13-3)

A. During late morula stage, blastomere cells begin to differentiation into two distinct populations, the inner and outer cells

B. Inner cells develop gap junctions

- Important for intercellular communication

C. Outer cells develop tight junctions

- Alter permeability of the outer cells allowing for fluid accumulation inside of the embryo

D. Development from morula to blastocyst

- Intracellular fluid creates a distinct cavity (hollow) inside of the embryo
- Hollow center of blastocyst called the **blastocoele**

E. Two cell types present (Figure 13-2 & 4-1)

-**Trophectoderm** (Outer single layer of cells)

    a) Develop into chorion and contributes to the placenta

- **Inner cell mass (ICM)**

    a) Develop into fetus

F. Blastocyst is the first stage where embryo grows in size

G. Passage through these stages in regard to time varies among species **(Table 13-1)**

III. DIFFERENTIATION

A. Involves formation of 3 germ layers

- Embryonic tissue which form all adult tissues & organs

B. The 3 germ layers are:

1. **Ectoderm**

    - In general forms exterior tissues including:

        Nervous system, and **mammary glands**

2. **Mesoderm**

- In general forms structural tissue including:

Muscle, Circulatory system, and **reproductive system**

3. **Endoderm**

- In general forms internal organs including:

Digestive system, liver, and **endocrine glands**

IV. FORMATION OF THE ORGANS

A. Differentiation starts at blastocysts stage

B. Completed early in gestation

- Day 35 in pigs; Day 45 in cattle & sheep

C. After differentiation fetus has all the necessary parts & mostly have an increase in size

V. FORMATION OF THE PLACENTA

(Figure 13-4)

Occurs after embryo hatching and involves massive growth of the conceptus

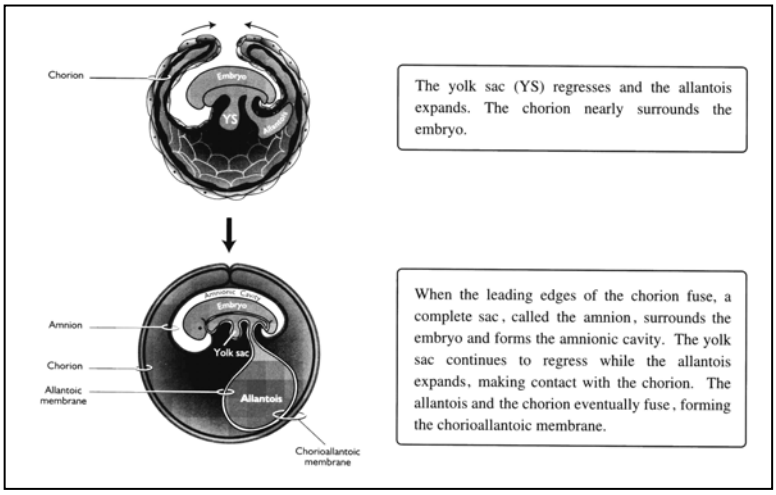
A. Development of **extra-embryonic membranes**

- Filamentous/threadlike structures in the pig. Sheep, and cow, but spherical in the horse

B. Used by fetus to attach to the uterus

C. Discarded after birth

D. Consists of 4 membranes



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1. **Amnion**

- Develops from trophoblast and endoderm
- Filled with fluid and serves to protect the embryo from mechanical perturbations

2. **Chorion**

- Like amnion, develops from trophoblast and endoderm
- Gives rise to fetus portion of the Placenta and becomes outermost layer of the placenta
- Does not contain blood vessels

3. **Allantois**

- Originates from splanchnic mesoderm and rises forms from the hindgut
- If fuses with the chorion forms the allantochorion and becomes fetus portion of

the palcenta

- Contains blood vessels

4. **Yolk sac**

- From splanchnic mesoderm and rises from midgut of embryo
- Site of primordial germ cells
- It regresses as the allantois develops
- Contains blood vessels

VI. VASCULARIZATION OF PLACENTA

A. Necessary for nutrient exchange

B. Only yolk sac and allantois can form blood vessels

1. Carnivores
2. Horses

C. If allantois fuses to chorion get allantochorial placenta

1. All other farm animals

VIII. MATERNAL RECOGNITION OF PREGNANCY

(Figures 13-5 to 13-7)

A. The developing embryo enters the uterus between d 2 and 5 after ovulation depending on the species

B. For the early embryo to become an established pregnancy, luteolysis must be prevented (the corpus luteum must be maintained)

- Two major events have to take place:

1) PGF2α synthesis and secretion must be stopped

2) Progesterone must be maintained

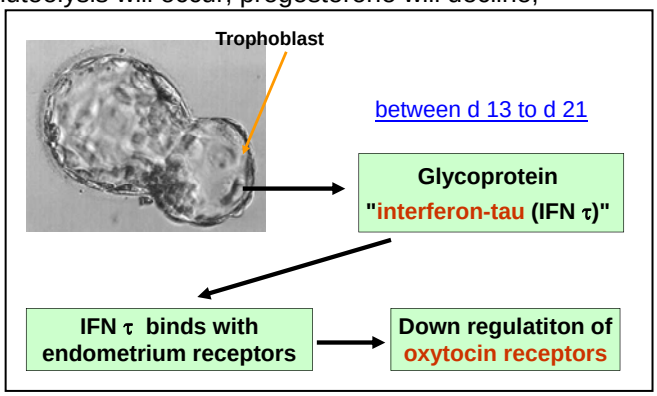
C. The conceptus must provide a timely (before luteolysis) biochemical signal

- Conceptus signals its presence to the dam
- Signals enable pregnancy to continue
- If a signal is not delivered quick enough, luteolysis will occur, progesterone will decline, and the early embryo will die

D. In the ewe and the cow: **(Figures 13-5)**

- The blastocyst begins to secrete **trophoblastic protein**
- Both ovine and bovine trophoblastic protein belong to a class of glycoprotein known as **interferons**

1) Ovine interferon-tau (oIFN τ) and Bovine interferon-tau (bIFN τ)



2) Interferons: glycoproteins that may possess antiviral action and alter the function of target cells

- The trophoblast produces oIFN-τ and bIFN-τ between d 13 to d 21 as the conceptus elongates (spherical to tubular to filamentous)

E. oIFN-τ and bIFN-τ do not enhance progesterone production directly, (NOT luteotropic)

- **Mechanism of action:**

oIFN-τ and bIFN-τ bind to the endometrium → inhibit endometrial oxytocin receptor synthesis (Fig. 13-5) → pulsatility of PGF2α does not change and therefore luteolysis does not occur

(remember, oxytocin, oxytocin receptors, progesterone, estradiol, and PGF2α all play a role in luteolysis; **Chapter 9 , Figures 9-12 & 9-12**)

- oIFN-τ and bIFN-τ also promotes protein synthesis thought to be critical to preattachment embryonic survival

F. In the sow: **(Figure 13-6)**

- Mechanism of action:

The conceptus of the pig produces estradiol between d 11 and 12 after ovulation (coincides with the elongation of the conceptus→ **Estradiol serves as the signal for maternal recognition of pregnancy**

What happens to PGF2α:

- **PGF2α** is produced by the endometrium re-routed into the uterine lumen and metabolized, rather than being drained by the uterine veins → luminal PGF2α has little access to the circulation and can't cause luteolysis
- The sow must have at least two conceptuses in each uterine horn for pregnancy to be maintained
- If there no two conceptuses, PGF2α is secreted in an endocrine manner and luteolysis will occur, and pregnancy will be terminated.

G. In the mare: **(Figure 13-7)**

Mechansim of action:

- The presence of the conceptus helps to prevent Luteolysis
- The equine conceptus does produce proteins; their role in maternal recognition is unknown
- The conceptus must migrate within the uterus between 12 to 14 times per day during days 12, 13, and 14 of pregnancy in order to inhibit PGF2α production.
    1) This migration appears to be very important because the early embryo does not elongate
    2) Conceptus must "touch" enough receptors or secrete "proteins" and place near

(on) receptors to maintain pregnancy

IX. THE MAIN OUT COME

Regardless of species, the desired outcome of maternal recognition of pregnancy is the maintenance of high blood progesterone concentrations.

Extra note: In the human:

- The basis of early pregnancy tests is human chorionic gonadotropin (**hCG**),
- hCG is produced by trophoblastic cells of the early embryo and is secreted as early as d 12 to 13 after ovulation

Maternal Recognition of Pregnancy

Definition:

Chemical message (Usually hormonal) which results in maintenance of the CL.

Establishment of Pregnancy	Sow	Mare	Cow	Ewe
Days of Estrous Cycle	**12, 15-18**	**14-16**	**16-17**	**12-13**
Embryonic Signal	**Estrogen**	**Small unknown Peptide**	**Bovine Interferon-τ**	**Ovine Interferon-τ**