Embryology
the anatomic basis of fetal medicine

Molecular mechanisms

Classic anatomic embryology

Correlation with prenatal and postnatal findings

Jan 30, 2013
Overview of Developmental Periods

• Week 1 - ovulation to implantation
• Week 2 – bi-laminar germ disk
• Week 3 – tri-laminar germ disk
• Week 4 to 8 - embryonic period

• 3rd month to birth – fetal period
  – Subsequent lectures will discuss specific tissue /organ development
Consequences of

- Mis-programming – errors in genetic code
  - i.e. consequences of trisomy 13,18,21
- Early developmental errors-
  - different than late? Does mal-development of one system predispose another to same?
  - i.e. VACTERL association
Terminology

• Week 1 - ovulation to implantation
  – Blastomeres / morula/ blastocyst
  – Trophoblast / embryoblast

• Week 2 - bilaminar germ disk
  – Endometrial embedding- development of placenta
  – Establishment of uteroplacental circulation by day 13
  – Embryoblast – forms bilaminar germ disk and amniotic cavity lining develops

• Week 3 - trilaminar germ disk
  – Gastrulation – formation 3 germ cell layers
  – Establishment of body axes
**Week one:** ovulation to implantation

Initial cleavage/mitosis-------forms Blastomere ------- Morula
This is only 27 units/cells!!!
Aberrancies in cleavage process

Monozygotic Twins

Completely separated after 2-cell stage – two chorions, two amnions
Aberrancies in cleavage process

Monozygotic Twins

Separation of inner cell mass at later stages of development, resulting in a common placenta - common chorionic cavity - mono-chorionic

Separate amnion (di-amnion) – common amnion (mono-amnion)
Which twins are at risk for Twin-twin Transfusion syndrome?

- Dichorionic, diamniotic membranes
- Monochorionic diamniotic membranes
- Monochorionic Monoamniotic membranes
Di-chorionic, Di-amniotic membranes

Mono-chorionic di-amniotic membranes

Mono-chorionic Mono-amniotic membranes
the Morula enters uterine cavity- and forms the blastocyst by day 9
Day 12 – further embedding into endometrium
Day 13: Established uteroplacental circulation
Bilaminar disk stage

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- Future umbilical cord
**Gastrulation:**
Development of tri-laminar disk
Derivation of the three germ cell layers

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Epiblast cells invaginate to form mesoderm
Gastrulation:
Development of tri-laminar disk
Derivation of the three germ cell layers

Establishment of body axes
Looking onto ectoderm from above

Fate map for epiblast cells
pm: paraxial mesoderm= somites
lm: intermed mesoderm= urogenital system,
Lpm: lateral plate mesoderm= lateral body wall,
eem: extraembryonic meso= chorion
Teratogenesis
Examples of failures at gastrulation

- **Holoprosencephaly**: injury to anterior midline of germ disk -
  alcohol exposure / via SHH gene?
- **Caudal dysgenesis** - Injury to caudal end of disk —
- **Situs inversus** – error in right/left patterning - ? Role of cilia
- **Sacroccocygeal tumors** – arise from remnants of primitive streak.
- **Conjoined twins** – partial splitting of primitive node

Holoprosencephaly with fusion of the eyes. Single nasal chamber
Teratogenesis

• Examples of failures at gastrulation
  – **Holoprosencephaly**: alcohol exposure – injury to anterior midline of germ disk
  – **Caudal dysgenesis** –
    • Injury to caudal end of disk

Example: 22-week fetus. The lower portion of the body is small compared with the midbody and chest. The lower extremities (arrows) appear abnormally extended and atrophied. Structures above the level of L3 and intracranial anatomy appear normal.

Source: radiology.rsna.org/cgi/content/full/230/1/229
Teratogenesis

- Examples of failures at gastrulation
  - *Situs inversus* – error in right/left patterning - ? Role of cilia-
  - *Sacroccocygeal tumors* – arise from remnants of primitive streak.
  - *Conjoined twins* – partial splitting of primitive node
Teratogenesis

- Examples of failures at gastrulation
  - Sacrococcygeal tumors – arise from remnants of primitive streak.
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Teratogenesis

• Examples of failures at gastrulation
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**The embryonic period**

- Ectoderm, mesoderm and endoderm give rise to specific tissues and organs

![Diagram showing embryonic development](image)
Germ Cell Derivatives

- **Ectoderm** –
  - neural system, skin and appendages that relate to external environment (eyes, ears...)

- **Mesoderm** –
  - musculoskeletal tissues, genitourinary system, body wall and membranes lining the cavities

- **Endoderm** –
  - foregut, midgut and hindgut – GI tract and appendages (liver, pancreas) respiratory tract, bladder
The embryonic period

- Complex set of folding patterns, cell migrations give rise to embryo structure/form
View along longitudinal axis (head – tail)
Specific embryology

• Development of
  – 1) the body cavities- thoracic/abdominal
  – 2) the respiratory system
  – 3) the GI tract
  – 4) the urogenital system
Ventral Body Wall Defects

- Failure of in-folding or incomplete development of component tissues

Consequences of failure:......
Gastroschisis

Herniation of bowel through defect in abdominal wall – always to the right of umbilicus - Exposed intestine

Question: Is it ever normal to see intestine outside the confines of the abdominal wall?

Omphalocele

Herniation through umbilical ring intestine covered by membrane
What we take for granted – separation of chest from abdomen
Pleuro-peritoneal separation and development of the diaphragm
Congenital diaphragmatic hernia
aka Posterolateral / Bochdalek hernia
Prenatal counseling prepares parents for this possible scenario
But not every baby with a diaphragm defect requires this.....
Morgagni Hernia – anterior defect in diaphragm
We expect swallowing and breathing to be achieved through two parallel conduits.
Development of Respiratory System

25 days

5 week embryo
Tracheo-esophageal separation

A. Tracheoesophageal ridge
B. Foregut
C. Esophagus

Respiratory diverticulum
Lung buds
Trachea
Failure of tracheo-esophageal separation

Which one(s) might you be able to dx prenatally?
Broncho-alveolar development
Pulmonary agenesis-
If bronchioles don’t grow-
Lung parenchyma doesn’t grow
Pulmonary agenesis-
If bronchioles don’t grow-
Lung parenchyma doesn’t grow

Cystic adenomatoid malformation
Proliferation of bronchioles, not alveoli- abnormal sac of lung tissue
Pulmonary agenesis-
If bronchioles don’t grow-
Lung parenchyma doesn’t grow

Cystic adenomatoid malformation
Proliferation of bronchioles, not alveoli

Pulmonary sequestration
Separate piece of lung – not connected to Tracheobronchial tree
Aortic blood supply
Pulmonary agenesis -
If bronchioles don’t grow-
Lung parenchyma doesn’t grow

Cystic adenomatoid malformation
Proliferation of bronchioles, not alveoli

Congenital lobar emphysema
Absent musculature on bronchus
Results in hyperinflation

Pulmonary sequestration
Separate piece of lung – not connected to tracheobronchial tree
Aortic blood supply
Other lesions

Bronchogenic Cyst
Diverticulum of tracheobronchial tree
w/o associated pulmonary parenchyma
Other lesions

Bronchogenic Cyst
Diverticulum of tracheobronchial tree w/o associated pulmonary parenchyma
Gastrointestinal tract

1. Defects in the continuity of the intestine

Some are consequences of failures of normal developmental processes

Some are accidents of nature when development has been fine
Gastrointestinal tract

1. Defects in the continuity of the intestine

Some are consequences of failures of normal developmental processes

Some are accidents of nature when development has been fine

Does this make a difference in what you expect the incidence of associated anomalies to be????
Gastrointestinal tract

Duodenal atresia/ stenosis: trisomy 21. cardiac defects, multiple atresias

Jejunoileal atresia: No association with Genetic disorders or Other organ involvement
Gastrointestinal tract

2. Defects in the rotation of the intestine
Gastrointestinal tract

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Gastrointestinal tract

2. Defects in the rotation of the intestine
Gastrointestinal tract

- Defects in innervation

Hirschsprung’s disease
Impact for fetal medicine

• Embryology:
  – Provides understanding of a given anomaly
  – Prompts us to consider organ defects in organs forming at same time
  – Allows us to search for genetic basis of disorders
  – Allows us to prepare parents for what the may need to expect postnatally even if not evident prenatally
References

- **Human Embryology**
  - Author: William J. Larsen
  - Edition: Third Edition

- **Langman’s Medical Embryology**
  - Author: T. W. Sadler
  - Edition: Ninth Edition