Embryology
the anatomic basis of fetal medicine
Prenatal consult

- You meet with expectant parents and tell them that a congenital malformation has been identified.
- You proceed to explain the birth defect.
Predictable questions

- Why did that happen?
- Is it something we passed on to the baby?
- Did we expose the baby to something that caused this?
- What else can be wrong?
- What does it take to fix everything?
- Can we do something to prevent problems before the baby is born?
Embryology

- Fundamental understanding of key events in development of the fetus
- Basis for rational prenatal evaluation
- Basis for postnatal evaluation and Treatment
“Early Cellular” events

- Fertilization, cleavage….Blastomere to morula

- “Physical events”
  - Twin gestations, incomplete separation,

- “Information events” – heritable/sporadic
  - Genetic disorders
Monozygotic Twins

Aberrancies in cleavage process

Completely separated after 2-cell stage – two chorionic cavities, two amniotic cavities.

Separate uterine implantations
Aberrancies in cleavage process

Monozygotic Twins

Separation of inner cell mass at later stages of development - resulting in common placenta –

One chorionic cavity mono-chorionic
A) separate amniotic cavities
B) Single amniotic cavity
Which twins are at risk for Twin-twin Transfusion syndrome?

- Dichorionic, diamniotic membranes
- Monochorionic diamniotic membranes
- Monochorionic Monoamniotic membranes
Wolf Hirschhorn Syndrome

- Transmission of faulty genetic “directions”
- Example: microdeletion on short arm of chromosome 4
- Aneuploidy disorders – some fatal
- Mitochondrial disorders -

<table>
<thead>
<tr>
<th>Table 1. Characteristic features in Wolf-Hirschhorn Syndrome</th>
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<tbody>
<tr>
<td><strong>Branch of medicine</strong></td>
</tr>
<tr>
<td>Otolaryngology</td>
</tr>
<tr>
<td>Ophthalmology</td>
</tr>
<tr>
<td>Gastroenterology</td>
</tr>
<tr>
<td>Cardiology</td>
</tr>
<tr>
<td>Orofacial Surgery &amp; Dentistry</td>
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<tr>
<td>Dermatology</td>
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<td>Neurology</td>
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<td>Others</td>
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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 of 3 germ cell layers
  - Establishment of body axes

- **Week 4-8 embryonic period**

- **3rd month to birth = fetal period**
Events have to occur in correct spatial and correct time sequence.

This is only 27 units/cells!!!
the **Morula** enters uterine cavity- and forms the **blastocyst** by day 9

1) Trophoblast (green)
2) Embryoblast (blue/yellow)
Day 12 – further embedding into endometrium
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<thead>
<tr>
<th>Trimester 1</th>
<th>Trimester 2</th>
<th>Trimester 3</th>
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</table>

**Week 2**

Day 13: Established uteroplacental circulation
Bilaminar disk stage
Gastrulation:
Development of tri-laminar disk
Derivation of the three germ cell layers

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
Im: intermed mesoderm= urogenital system,
Lpm: lateral plate mesoderm= lateral body wall,
eem: extraembryonic meso= chorion

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<tr>
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<th>Trimester 2</th>
<th>Trimester 3</th>
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<td>Week 3</td>
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Teratogenesis

Examples of failures at gastrulation

- **Holoprosencephaly:**
  - Injury to anterior midline of germ disk
  - Alcohol exposure / via SHH gene
  - Fusion of the eyes.
  - Single nasal chamber
Teratogenesis

- Examples of failures at gastrulation
  - **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.rsajnl.org/cgi/content/full/230/1/229

Day 28 of gestation
Affects mesodermal derivatives
?lack of vascular supply?
May be related to mat’l diabetes
Teratogenesis

- Examples of failures at gastrulation
  - **Situs inversus** –
  - Generally autosomal recessive disorder
  - 5-10% have CHD most often transposition of the great vessels
  - If situs with levocardia (1in 2Mill) then 95% risk CHD
  - 25% will have primary ciliary dyskinesia (PCD)
  - 50% of PCD have Situs inversus = Kartagener syndrome
  - siuts, sinusitis, bronchiectasis male infertility
Teratogenesis

- Examples of failures at gastrulation
  - Sacrococcygeal tumors – arise from remnants of primitive streak.
Midline cervical mass

Dermoid cyst or thyroglossal duct cyst?
Principle of “cyst” excision is complete excision

- Dermoid cyst – simple excision of the mass
- Thyroglossal duct cyst –
- Must understand embryology of thyroid descent
- Requires excision of mid-portion of hyoid bone to avoid recurrence
The embryonic period

- Ectoderm, mesoderm and endoderm give rise to specific tissues and organs
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
Pleuro-peritoneal separation and development of the diaphragm
Congenital diaphragmatic hernia
aka Posterolateral / Bochdalek hernia
Morgagni Hernia – anterior defect in diaphragm
Development of Respiratory System

25 days 5 week embryo
Tracheo-esophageal separation
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
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 they may need to expect postnatally even if not evident prenatally
References

[Image of Human Embryology by William J. Larsen]

[Image of Langman’s Medical Embryology by T. W. Sadler]
Di-chorionic, Di-amniotic membranes

Mono-chorionic di-amniotic membranes

Mono-chorionic Mono-amniotic membranes
Dizygotic twins

2 oocytes
Simultaneously fertilized – usually separate membranes, although they can fuse
Teratogenesis

- Examples of failures at gastrulation
  - **Conjoined twins** – partial splitting of primitive node

http://library.med.utah.edu/WebPath/PEDHTML/PED022.html
Urogenital System

- Renal
  - parenchymal development, retroperitoneal vs pelvic location, midline fusion
- Ureteral
  - Duplication anomalies, Insertion in bladder
- Bladder
  - Size/innervation/musculature
  - Development of bladder neck, continence