Introduction

This lecture will introduce development of the special sensory structures associated with hearing, vision, smell and taste. Due to time limitations the lecture will focus on hearing development and if time is available vision and other senses will be introduced in general.

We use the sense of balance and hearing to position ourselves in space, sense our surrounding environment, and to communicate. Portions of the ear appear very early in development as specialized region (otic placode) on the embryo surface that sinks into the mesenchyme to form a vesicle (otic vesicle = otocyst) that form the inner ear.

This region connects centrally to the nervous system and peripherally through specialized bones to the external ear (auricle). This organisation develops different sources forming the 3 ear parts: inner ear (otic placode, otocyst), middle ear (1st pharyngeal pouch and 1st and 2nd arch mesenchyme), and outer ear (1st pharyngeal cleft and 6 surface hillocks).

This complex origin, organisation, and timecourse means that abnormal development of any one system can impact upon the development of hearing.
Objectives

- Understanding of sensory placode development
- Understanding of inner, middle and external ear origins
- Understanding of timecourse of auditory development
- Understanding of abnormalities of auditory development
- Brief understanding of other (vision) sensory development

Also review your Head development lecture.

Lecture Resources

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Development Timing

- **Week 3** - otic placode, otic vesicle
- **Week 5** - cochlear part of otic vesicle elongates (humans 2.5 turns)
- **Week 9** - Mesenchyme surrounding membranous labryinth (otic capsule) chondrifies
- **Week 12-16** - Capsule adjacent to membranous labryinth undegoes vacuolization to form a cavity (perilymphatic space) around membranous labryinth and fills with perilymph
- **Week 16-24** - Centres of ossification appear in remaining cartilage of otic capsule form petrous portion of temporal bone. Continues to ossify to form mastoid process of temporal bone.
- **3rd Trimester** - Vibration acoustically of maternal abdominal wall
Embryonic Origin Overview

Adult hearing embryonic origins

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<td>• Middle Ear Ossicles</td>
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<td>• External Auditory Meatus - Pharyngeal Arch 1 groove or cleft (ectoderm)</td>
<td>• Malleus and incus - Pharyngeal Arch 1 cartilage Neural crest (ectoderm)</td>
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<tr>
<td>• Tympanic Membrane - Pharyngeal Arch 1 membrane (ectoderm, mesoderm, endoderm)</td>
<td>• Stapes - Pharyngeal Arch 2 cartilage Neural crest (ectoderm)</td>
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<tr>
<td></td>
<td>• Middle Ear Muscles</td>
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<tr>
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<td>• Tensor tympani - Pharyngeal Arch 1 (mesoderm)</td>
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<td>• Middle ear cavity -</td>
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induces startle response in fetus.
Sensory Placodes

**Week 4**

<table>
<thead>
<tr>
<th>Otic placodes (Stage 11 dorsal view)</th>
<th>Sensory placodes ((Stage 14 ventral view)</th>
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- week 4 a series of thickened surface ectodermal patches form in pairs in the head region.
  - Recent research suggests that all sensory placodes may arise from common panplacodal primordium origin around the neural plate, and then differentiate to eventually have different developmental
sensory placodes will later contribute key components of each of our special senses (vision, hearing and smell).

- Other species have a number of additional placodes which form other sensory structures (fish, lateral line receptor).
- Note that their initial position on the developing head is significantly different to their final position in the future sensory system.

**Otic Placode**

- stage 13/14 embryo (shown below) the otic placode has sunk from the surface ectoderm to form a hollow epithelial ball, the otocyst, which now lies beneath the surface surrounded by mesenchyme (mesoderm).
- The epithelia of this ball varies in thickness and has begun to distort, it will eventually form the inner ear membranous labyrinth.

**Lens Placode**

- lies on the surface, adjacent to the outpocketing of the nervous system (which will form the retina) and will form the lens.
Nasal Placode

- 2 large components (medial and lateral), will form the nasal olfactory epithelium.

- Note the extension of the (neural tube) diencephalon forming the optic stalk underlying the optic placode.

Inner Ear
Described in detail later in lecture.

Stage 13 Embryo
(week 5, 28-32 days, 30 somite pairs)

Stage 13 otocyst

Stage 22 Embryo
(week 8, 54-56 days, 23-28 mm)

Stage 22 ear
• The inner ear is derived from a pair of surface sensory placodes (otic placodes) in the head region.
• These placodes fold inwards forming a depression, then pinch off entirely from the surface forming a fluid-filled sac or vesicle (otic vesicle, otocyst).
• The vesicle sinks into the head mesenchyme some of which closely surrounds the otocyst forming the otic capsule.
• The otocyst finally lies close to the early developing hindbrain (rhombencephalon) and the developing vestibulo-cochlear-facial ganglion complex.

**Links:** [Inner Ear](#) | [Neuroscience - The Inner Ear](#)

### Middle Ear

• derived from first pharyngeal pouch and 1st and 2nd arch mesenchyme
• extends as tubotympanic recess - during week 5 recess contacts outer ear canal
• mesoderm between 2 canals forms tympanic membrane
• expands to form tympanic recess
• stalk of recess forms auditory tube(eustachian tube, pharyngotympanic tube)

### Ossicles

• The middle ear ossicles (bones) are derived from 1st and 2nd arch mesenchyme.
• The space in which these bones sit is derived from the 1st pharyngeal pouch.
  - remains connected to the oral cavity by the auditory tube.
• ossicles connected with tympanic cavity walls by ligaments (3 for the malleus, and 1 each for the incus and stapes).

![Pharyngeal arch cartilages](#)

### Tympanic Cavity

• tympanic cavity enlarges to
incorporate
- coats with epithelia
- first arch mesoderm - tensor tympani muscle
- second arch mesoderm - stapedius muscle

Cavities formed from the First Cleft

Middle Ear Genes - gooscloid, RARs, Prx1, Otx2, Hoxa1, Hoxb1, endothelial related molecules

Links: Middle Ear | Neuroscience - The Middle Ear

Outer Ear

- **External ear** is derived from 6 surface hillocks, 3 on each of pharyngeal arch 1 and 2.
  - structure completed during embryonic period.
- **External auditory meatus** is derived from the 1st pharyngeal cleft.
  - transiently blocked during development.
- The newborn external ear structure and position is an easily accessible diagnostic tool for potential abnormalities or further clinical screening.

Pinna- Auricle

Develops from six aural hillocks

- 3 on first arch
- 3 on second arch
- originally on neck, moves cranially during mandible development
<table>
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<tr>
<th>Pharyngeal Arch</th>
<th>Hillock</th>
<th>Auricle Component</th>
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<tr>
<td>Arch 1</td>
<td>1</td>
<td>tragus</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>helix</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>cymba concha</td>
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<tr>
<td>Arch 2</td>
<td>4</td>
<td>concha</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>antihelix</td>
</tr>
<tr>
<td></td>
<td>6</td>
<td>antitragus</td>
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Arch 1 and 2 hillocks
External ear stages 14-23 and adult (not to scale)

**External auditory meatus**

- derived from first pharyngeal cleft
- ectodermal diverticulum
- week 5 - extends inwards to pharynx
- until week 18 has ectodermal plug - plug forms stratified squamous epithelia of canal and outer eardrum

**Timeline**

- Embryonic Period - Ectodermal cells proliferate and fill the entire lumen forming a meatal plug
- 10 weeks - Meatal plug extends in a disc-like fashion. In the horizontal plane the meatus is boot-shaped with a narrow neck and the sole of the meatal plug spreading widely to form the future tympanic membrane medially. Proximal portion of the neck starts to be resorbed.
- 13 weeks - Disc-like plug innermost surface in contact with the primordial malleus, contributes to the formation of the tympanic membrane.
- 16.5 week - Meatus is fully patent throughout its length, lumen is still narrow and curved.
- 18 week - Meatus is already fully expanded to its complete form.

(EAM data - Nishimura, 1992 PMID 1441991)

**Links:** [Outer Ear](#) | [Neuroscience - The External Ear](#)

**Inner**
Otocyst

- week 3 otic placode forms on surface ectoderm
- otic placode sinks into mesoderm
- forms otocyst (otic vesicle)
- branches form and generate endolymphatic duct and sac
- forms vestibular (dorsal) and cochlear (ventral) regions
- differentiation of otic vesicle to membranous labyrinth

Vestibular Sac

- generates 3 expansions - form semicircular ducts
- remainder forms utricle
- epithelia lining generates - hair cells, ampullary cristae, utricular macula
- Vestibular - Otoconia, otoconin- inner ear biominerals

Cochlear sac
Carnegie Stage 13 otic vesicle

**Bony Labyrinth**

- formed from chondrified mesoderm
- Periotic Capsule
- mesenchyme within capsule degenerates to form space filled with perilymph

**Vestibulocochlear Nerve**

- forms beside otocyst
- from wall of otocyst and neural crest cells
- bipolar neurons
- vestibular neurons
  - outer end of internal acoustic meatus
  - innervate hair cells in membranous labyrinth
  - axons project to brain stem and synapse in vestibular nucleus
- cochlear neurons
- cell bodies lie in modiolus
- central pillar of cochlear
- innervate hair cells of spiral organ
- axons project to cochlear nucleus

Inner Ear Genes

- hindbrain segmentation occurs at same time placode arises
- otocyst adjacent to rhombomere 5
- may influence development
- Hoxa1, kreisler, Fgf3
- genes regulating neural crest cells (neural genes)
- Pax2 Ko affects cochlear and spiral ganglion, but not vestibular apparatus
- nerogenin 1 affects both ganglia

Semicircular canal

- Otx1- cochlear and vestibular normal
- Hmx3, Prx1, Prx2

Sensory Organs

- thyroid hormone receptor beta
- Zebrafish-mindbomb mutant has excess hair cells but not supporting cells, Notch-Delta signaling
- Gene Expression-inner ear
- Brn-3c and Hair cell development
- Supporting Cells- p27kip
- Thyroid Hormone
- Ganglion neurons require growth factors
- vestibular neurons- BDNF, NT3
  - survival not development
Postnatal Changes

Newborn to adult Eustachian (auditory, otopharyngeal or pharyngotympanic) tube.

- Connects middle ear cavity to nasopharynx portion of pharynx

Functions

- Ventilation - pressure equalization in the middle ear
- Clearance - allow fluid drainage from the middle ear. Tube is normally closed and opened by muscles

At birth

- shorter (17-18 mm), narrower and runs almost horizontal. Tube is opened by a single muscle, tensor palati muscle

Adult

- longer (twice as long), wider and runs at approximately 45 degrees to the horizontal. Tube is opened by two separate muscles, tensor palati and levator palati

Vision

Timeline

- **Weeks 3-4** - Eye Fields-Optic Vesicle
- **Weeks 5-6** - Optic Cup, Lens Vesicle, Choroid Fissure, Hyaloid Artery
- **Weeks 7-8** - Cornea, Anterior Chamber, Pupillary Membrane, Lens, Retina
- **Weeks 9-15** - Iris, Ciliary Body
- **Weeks 8-10** - Eyelids
Stage 13 (week 5)

**Lens**

Surface ectoderm -> lens placode (optic placode) -> lens pit -> lens vesicle -> lens fibres -> lens capsule and embryonic/fetal nucleus.

**Retina**

Neural plate ectoderm -> prosencephalon (forebrain) eye fields -> neural plate growth carries eye field region forward -> eye field invaginates forming optic grooves (sulci) -> diencephalon optic groove interacts with surface ectoderm (induces optic placode) -> optic stalk -> optic vesicle -> folds inward (optic cup) forming double layer -> inner neural retina, outer pigmented retina

Links: [Embryo Images - Eye Development](#)

**Neural Crest**

Eye connective tissue

**Abnormalities**

- Inner - common cavity, severe cochlear hypoplasia
Large vestibular aqueduct syndrome (LVAS) can be one of the common causes of hearing loss

- Middle - rare and can be part of first arch syndrome, Malleus, Incus and Stapes Fixation
- Cholesteatoma - Epithelium trapped within skull base in development, erosion of bones: temporal bone, middle ear, mastoid
- Outer - Several genetic effects and syndromes, Environmental Effects

Outer Ear Abnormalities

- Microtia - abnormally small external ear
- Preauricular sinus - occurs in 0.25% births, bilateral (hereditary) 25-50%, unilateral (mainly the left), duct runs inward can extend into the parotid gland, Postnatally sites for infection

Fetal Alcohol Syndrome

- Postion- Lower or uneven height, "railroad track" appearance, curve at top part of outer ear is under-developed, folded over parallel to curve beneath
**Fetal Alcohol Syndrome Face**

**Sensorineural** - cochlear or central auditory pathway

- Hereditary
- recessive- severe
- dominant- mild
  - can be associated with abnormal pigmentation (hair and irises)

- Acquired
  - rubella (German measles), maternal infection during 2nd month of pregnancy, vaccination of young girls
  - streptomycin
  - antibiotic
  - thalidomide

**Conductive** - disease of outer and middle ear

- produced by otitis media with effusion, is widespread in young children.
- temporary blockage of outer or middle ear

**Bionic Ear**

Cochlear Implant - Professor Graeme Clark (1960s, Australia)
Array of electrodes implanted within cochlea, direct electrical stimulation to auditory nerve fibres

**Conductive Hearing Loss**

- Conductive Hearing Loss Produces a Reversible Binaural Hearing
8704-8711
http://www.jneurosci.org/cgi/content/abstract/19/19/8704

- tested ferrets by lon-term plugging of ear canal
- Repeated testing during the 22 months after unplugging revealed a gradual return to normal levels of unmasking.
- Results show that a unilateral conductive hearing loss, in either infancy or adulthood, impairs binaural hearing both during and after the hearing loss.
- Show scant evidence for adaptation to the plug and demonstrate a recovery from the impairment that occurs over a period of several months after restoration of normal peripheral function.

References

Textbooks

- **Before We Are Born** (5th ed.) Moore and Persaud Chapter 20: p460-479
- **Essentials of Human Embryology**, Larson Chapter 12: p252-272

Online Textbooks


- **Neuroscience** Purves, Dale; Augustine, George J.; Fitzpatrick, David; Katz, Lawrence C.; LaMantia, Anthony-Samuel; McNamara, James O.; Williams, S. Mark. Sunderland (MA): Sinauer Associates, Inc.; c2001 The Auditory System | The Inner Ear | The Middle Ear |
The External Ear | Early Brain Development | Construction of Neural Circuits | Modification of Brain Circuits as a Result of Experience

- **Molecular Biology of the Cell** (4th Edn) Alberts, Bruce; Johnson, Alexander; Lewis, Julian; Raff, Martin; Roberts, Keith; Walter, Peter. New York: Garland Publishing; 2002. [Neural Development] | [The three phases of neural development]

- **Clinical Methods** 63. Cranial Nerves IX and X: The Glossopharyngeal and Vagus Nerves | The Tongue | 126. The Ear and Auditory System | An Overview of the Head and Neck - Ears and Hearing | Audiometry

- **Health Services/Technology Assessment Text (HSTAT)** Bethesda (MD): National Library of Medicine (US), 2003 Oct. [Developmental Disorders Associated with Failure to Thrive]

- **Eurekah Bioscience Collection** [Cranial Neural Crest and Development of the Head Skeleton]

Search

- **Bookshelf** hearing development

- **Pubmed** hearing development

External Links

*External Links Notice* - The dynamic nature of the internet may mean that some of these listed links may no longer function. If the link no longer works search the web with the link text or name. Links to any external commercial sites are provided for information purposes only and should never be considered an endorsement. UNSW *Embryology* is provided as an educational resource with no clinical information or commercial affiliation.

- NIDCD - [Balance Disorders]
Embryo Images Online
- **Eye Development** - Eye Development Unit | Eye Fields-Optic Vesicle (Weeks 3-4) | Optic Cup, Lens Vesicle, Choroid Fissure, Hyaloid Artery (Weeks 5-6) | Cornea, Anterior Chamber, Pupillary Membrane, Lens, Retina (Weeks 7-8) | Iris, Ciliary Body (Weeks 9-15) | Eyelids (Weeks 8-10)
- **Ear Development** - Ear Development Unit | Inner Ear | [http://www.med.unc.edu/embryo_images/unit-ear/ear_htms/ear012.htm Middle Ear | External Ear

**Terms**

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**2017 ANAT2341** - Timetable | Course Outline | Group Projects | Moodle | Tutorial 1 | Tutorial 2 | Tutorial 3

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