Development of the Nervous System

- Neural tube derivatives
  - Spinal cord (alar vs. basal plate)
  - Brain vesicles
    - Brainstem nuclei
    - Cerebral cortex
- Neural crest derivatives
- Puituitary gland development
- Developmental pathology
  - Neural tube defects, craniopharyngioma, agenesis of corpus callosum
Development of Nervous System

Embryo of 18 days

- Neural plate
- Notochordal process
- Oropharyngeal membrane
- Primitive knot
- Primitive streak
- Cloacal membrane
- Neural plate
- Neural groove
- Neural fold
- Notochordal plate
- Amnion
- Wall of yolk sac
- Intraembryonic mesoderm
Neural fold development

- Extension of neural folds
- At Embryo of 22 days
  - Fusion at 4-6 somites
  - Open at both ends:
    - rostral neuropore
    - caudal neuropore
Embryo of 22 days

- Neural groove
- Neural fold
- **Neural tube**
  - Detachment from surface ectoderm
- **Neural crest**
  - Neuroectodermal cells between surface ectoderm and neural tube
Neurulation: Formation of neural tube

- at embryo of 22-23 days in 4-6 pairs of somites
  - Neural plate / tube: CNS
    - Cranial 2/3 (to 4\textsuperscript{th} somite): brain
    - Caudal 1/3: spinal cord
  - Neural crest: PNS and ANS, muscle/bone of head/neck
- Fusion of neural folds: rostral to caudal direction
  - Neural canal = lumen of neural tube; communicate with amnionic cavity
  - Rostral (Anterior) neuropore: close at 25\textsuperscript{th} day
  - Caudal (Posterior) neuropore: close at 27\textsuperscript{th} day
  - Neural tube defect (NTD)
Development of spinal cord

- Spinal cord: from neural tube caudal to 4th pair of somite
- **Ventricular zone** (ependymal layer): pseudostratified columnar neuroepithelium → neurons, glia
- **Marginal zone** → white matter of spinal cord
- **Intermediate zone** (mantle layer)
Development of spinal cord: 3 layers

23 days 9 weeks
Histogenesis of cells in CNS

- Neuroepithelium: Neuroblast, Glioblast, Ependyma
- Mesenchyme: Mesenchymal cells
Neuroblast

- Apolar neuroblast
- Bipolar neuroblast
- Unipolar neuroblast
- Neuron
Supporting cells

- Glioblast (spongioblast)
- Astroblast
- Protoplasmic astrocyte
- Fibrous astrocyte
- Oligodendroblast
- Oligodendrocyte
- Ependyma
- Epithelium of choroid plexus
- Mesenchymal cells
  - Microglial cells
- Origin of microglia: monocyte-macrophage lineage, enter CNS with blood vessels in fetal period
Differential growth of lateral wall of spinal cord
- Roof plate / Floor plate
- Sulcus limitans: shallow, longitudinal groove
- Dorsal alar plate (afferent); Ventral basal plate (efferent)
Differential growth of spinal cord

- Dorsal gray columns: cell bodies in alar plate
  - Dorsal (gray) horns
  - Dorsal roots
  - Dorsal septum or raphe
- Ventral / Lateral gray columns: from cell bodies in basal plate
  - Ventral (gray) horns / Lateral (gray) horns
  - Ventral roots
  - Ventral median septum → ventral median fissure
40 days

- Roof plate
- Alar plate
- Sulcus limitans
- Neuroepithelium
- Basal plate
- Floor plate
- Dorsal root of spinal nerve
- Central canal
- Spinal (dorsal root) ganglion
- Developing body of vertebra
- Ventral root of spinal nerve
Neural crest development: spinal ganglia / dorsal root ganglia (DRG)
50 days

- Dorsal septum
- Central canal
- Dorsal nerve root
- Ventricular zone
- Ventral median septum
- Ventral median fissure

- Dorsal (gray) horn
- Intermediate zone
- Marginal zone
- Ventral (gray) horn
- Spinal ganglion
- Developing centrum
Development of spinal meninges

- Primordial meninx (membrane): from mesenchyme surrounding neural tube
- External layer: dural mater
- Internal layer: pia-arachnoid (leptomeninges)
  - pia mater, arachnoid mater
  - participated by neural crest cells
  - Arachnoid trabeculae
  - Subarachnoid space with cerebrospinal fluid at 5th week
Spina bifida

Meningomyelocele

Myeloschisis

Meninges

Cyst

Spinal cord

Membranous sac

Dura mater

Displaced spinal cord

Roots of spinal nerve

Subarachnoid space

Spinal ganglion

Open spinal cord

Skin
Development of sympathetic nerves

- Post-ganglionic neurones: migration of Neural crest
  - Paravertebral ganglia
  - Preaortic ganglia (celiac, mesenteric ganglia)
- Sympathetic trunks
- Pre-ganglionic neurones: Neural tube (Intermediate cell column, lateral horn)
Development of parasympathetic nerves

- **Pre-ganglionic neurons**: nuclei in brainstem and spinal cord of sacral segments
  - **Brainstem nuclei**:
    - CN 3: Edinger-Westphal nucleus
    - CN 7: Salvatory nucleus (superior)
    - CN 9: Salvatory nucleus (inferior)
    - CN 10: Dorsal vagal nucleus
  - **Post-ganglionic neurons** in peripheral ganglia or in plexuses near/within structures being innervated
Brain vesicles

3 Primary vesicles
- Wall
- Cavity
- Forebrain (prosencephalon)
- Midbrain (mesencephalon)
- Hindbrain (rhombencephalon)

5 Secondary vesicles
- Telencephalon
- Diencephalon
- Mesencephalon
- Metencephalon
- Myelencephalon

Adult derivatives of walls:
- Cerebral hemispheres
- Thalami, etc.
- Midbrain
- Pons
- Medulla

Cavities:
- Lateral ventricles
- Third ventricle*
- Aqueduct
- Upper part of fourth ventricle
- Lower part of fourth ventricle

(4th week) (5th week)
Brain flexures

- Start from 4th weeks: ventral bending
  - Midbrain flexure
  - Cervical flexure
  - Pontine flexure
- Consequences: change in outline and position of gray/white matter
Gracile nuclei (medial) and Cuneate nuclei (lateral): neuroblasts from alar plates of myelencephalon migrate into marginal zone

Pyramids: in ventral area; corticospinal fibers from developing cortex
Myelencephalon (rostral): “open” medulla-1

- Effect of pontine flexure
  - thinning & stretching of roof
  - rhomboid cavity (Fourth ventricle)
  - lateral movement of walls
- Ventral movement of sulcus limitans
  - Alar plates: lateral to basal plates
  - Olivary nuclei: from alar plate
Embryo: NS

(alar plate)

Substantia gelatinosa [whole length]: touch, pressure, pain, temp.
Nucleus proprius [whole length]: con. proprioception, discrim. Touch, vibratory sens.
Nucleus dorsalis [C8→L3]: uncon. Proprioception,
Visceral afferent nucleus [T1→L3]: receiving visceral afferent information
Preganglionic sympathetic outflow
Medical / central / lateral group of neurons: innervate muscles, contain (α/skeletal muscles) & y efferents (intrafusal muscle fibres of muscle spindle)

(basal plate)

Tela choroidea
Choroid plexus

Special somatic afferent
General somatic afferent
Special visceral afferent
General visceral afferent
Olivary nucleus

General visceral efferent
Special visceral efferent
General somatic efferent
Myelencephalon (rostral): “open” medulla-2

- SSA: hearing
- GSA: from head/face
- SVA: taste
- GVA: from viscera

- GSE: hypoglossal nucleus
- SVE: muscles of pharyngeal arches
- GVE: nuclei of 9th and 10th CN
Pons: development of Metencephalon

- Pontine flexure: divergence of lateral walls of pons
- Gray matters: spread in floor of 4th ventricle
- Motor nuclei in ventral pons: pontine nuclei
Development of Cerebellum

- Cerebellum: thickening of dorsal part of alar plates
- Initially: project into 4th ventricle
- Later: enlarge & fuse in median plane
Development of Cerebellum

- Anterior lobe (paleocerebellum)
- Posterior lobe (neocerebellum)
- Flocculonodular lobe (archicerebellum)

Diagram showing primary fissure, capillary, cerebral aqueduct, dentate nucleus, pons, choroid plexus, and medulla.
Cerebellum: embryology and functions

- **Archicerebellum (floculonuclear lobe)**
  - phylogeny: oldest part
  - function: with vestibular system

- **Paleocerebellum (vermis & anterior lobe)**
  - phylogeny: intermediate
  - function: with sensory input from limbs

- **Neocerebellum (posterior lobe)**
  - phylogeny: the newest
  - function: with selective control of limb movements
Metencephalon: Alar and Basal plates

- Cerebellum: Cortex and Central (deep) nuclei
- Cochlear, Vestibular
- Pontine nuclei, 5th CN nuclei
Development of midbrain-1

- Neural canal → **cerebral aqueduct**
- Alar plate → **tectum** (colliculi); Basal plate → **tegmentum**
- Substantia nigra: from alar or basal plates
- Crus cerebri (Cerebral peduncles): corticobulbar, corticopontine, corticospinal fibers
**Development of midbrain-2**

- **Alar plate** → tectum (roof): superior & inferior colliculi; mesencephalic nucleus of CN V
- **Basal plate** → tegmentum: red nuclei; 3\textsuperscript{rd}, 4\textsuperscript{th} CN nuclei; reticular nuclei
Intermediate column (General Visceral Efferent)

Ventral horn (General somatic Efferent)
Formation of choroid plexus

- Tela choroid: ependyma + mesenchyme
- Choroid plexus: tela choroid + vessels
Development of forebrain

◆ Forebrain vesicles: upon closure of rostral neuropore,
  ◆ Optic vesicles: primodia of retinae, optic nerve
  ◆ Cerebral (telencephalic) vesicles: primodia of cerebral hemispheres, lateral ventricles
Development of diencephalon

- caudal part of forebrain:
  - Epithalamus, Thalamus, Hypothalamus
  - epithalamic sulcus, hypothalamic sulcus
- Interthalamic adhesion (mass intermedia)
Development of Epithalamus

- From roof & dorsal part of lateral wall of diencephalon
- **Pineal glands**: median diverticulum of caudal part of roof of diencephalon
Development of Pituitary gland

- Upgrowth from epidermal roof of stomodeum: hypophysial pouch or Rathke pouch at 4th week; constricted attachment at 5th week
- Downgrowth of neurohypophysial bud, neuroectoderm of diencephalon; contact of infundibulum with hypophysial pouch
Development of Adenohypophysis

- **Pars distalis**: anterior wall of hypophysial pouch
- **Pars tuberalis**: around infundibulum stem
- **Pars intermedia**: posterior wall of phypophysial pouch
- Regressing stalk of hypophysial pouch in developing sphenoid bone at 6th week
Development of Neurohypophysis

- **Infundibulum** give rise to **Median eminence**, **Infundibulum stem**, and **Pars nervosa**
- **Pituicytes** in posterior lobe of pituitary gland
Development of pituitary gland: Summary

Table 18-1 • Derivation and Terminology of the Pituitary Gland

**Oral Ectoderm**
(Hypophysial pouch from roof of stomodeum) → Adenohypophysis (glandular portion)

**Neuroectoderm**
(Neurohypophyseal bud from floor of diencephalon) → Neurohypophysis (nervous portion)

- Pars distalis
- Pars tuberalis
- Pars intermedia

- Pars nervosa
- Infundibular stem
- Median eminence

- Intraglandular cleft between pars distalis and pars intermedia
Craniopharyngioma

- Corpus callosum
- Thalamus
- Midbrain
- Cerebellum
- Craniopharyngioma
- Pons
Development of Telencephalon

- Cerebral vesicles: primordium of cerebral hemispheres
- Falx cerebri: mesenchyme in longitudinal fissure
- Cavity of median part: future 3rd ventricle
**Growth of cerebral hemisphere**

- **C-shaped curvature of cerebral hemisphere and ventricles**
- **Temporal lobe**: ventral and rostral turning with caudal end of cerebral hemisphere
- **Choroid fissure**: with temporal horn of lateral ventricle; formation of choroid plexus
Differential growth of cerebral cortex: Insula
Gyral formation during fetal period

24-25 weeks
Development of Basal ganglia

Corpus striatum: appear at 6th week, in floor of hemisphere
Development of Basal ganglia

- Divided by fibers (internal capsule) passing through corpus striatum:
- Caudate nucleus: inner
- Lentiform nucleus: outer
Development of cerebral commissural fibers

- **Lamina terminalis**: from roof plate of diencephalon to optic chiasm
- The first to form
  - **Anterior commissure**: connect olfactory bulb
  - **Hippocampal commissure**: connect hippocampal formation
- The largest: **corpus callosum**, connect neocortical areas

10 weeks
Agenesis of corpus callosum
Summary-1

- **Neural plate**: dorsal thickening of ectoderm at 3rd week, induced by underlying notochord & paraxial mesoderm
- **Neural groove**: infolding of neural plate, with neural folds on each side
- **Neural tube**: fusion of neural folds at 4th week
- **Neural crest**: neuroectodermal cells between neural tube & surface ectoderm
Summary-2

- Derivatives of neural tube
  - Forebrain: cerebral hemisphere, diencephalon
  - Embryonic midbrain: midbrain
  - Hindbrain: pons, medulla, cerebellum
  - Neural canal: ventricles, central canal
- Walls of neural tube: neurons and glia
  - Microglia: mesenchymal cells of blood vessels
Summary-3

- Pituitary gland
  - Ectodermal upgrowth from stomodeum: hypophysial pouch, become adenohypophysis
  - Neuroectoderm from diencephalon: neurohypophysial bud, become neurohypophysis

- Neural crest cells
  - Neurons in cranial, spinal & autonomic ganglia
  - Schwann cells
  - Chromaffin cells (adrenal medulla; cortex from mesoderm)