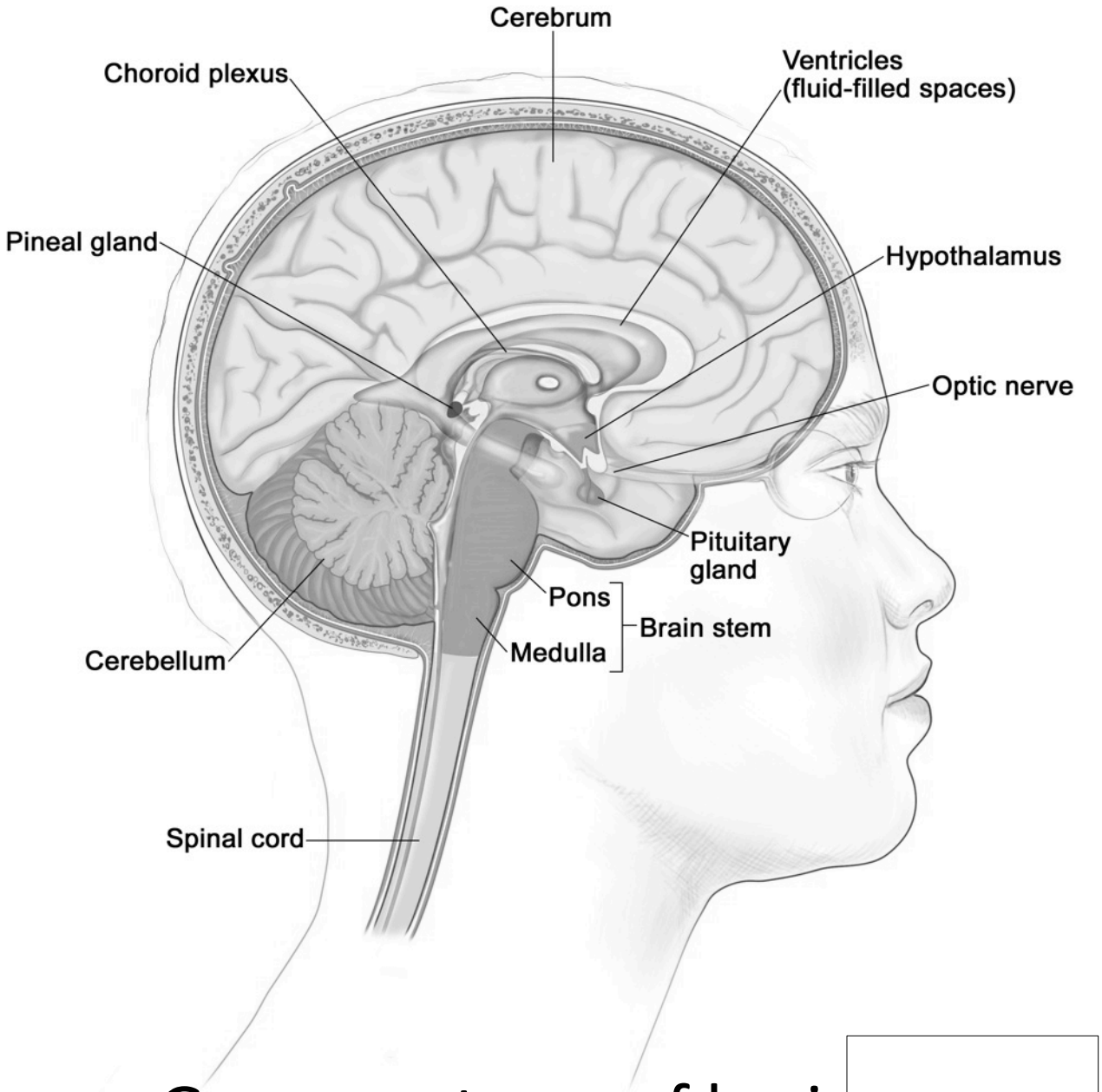
Quiz 6 Review

Kristine Krafts, M.D.

CNS Outline

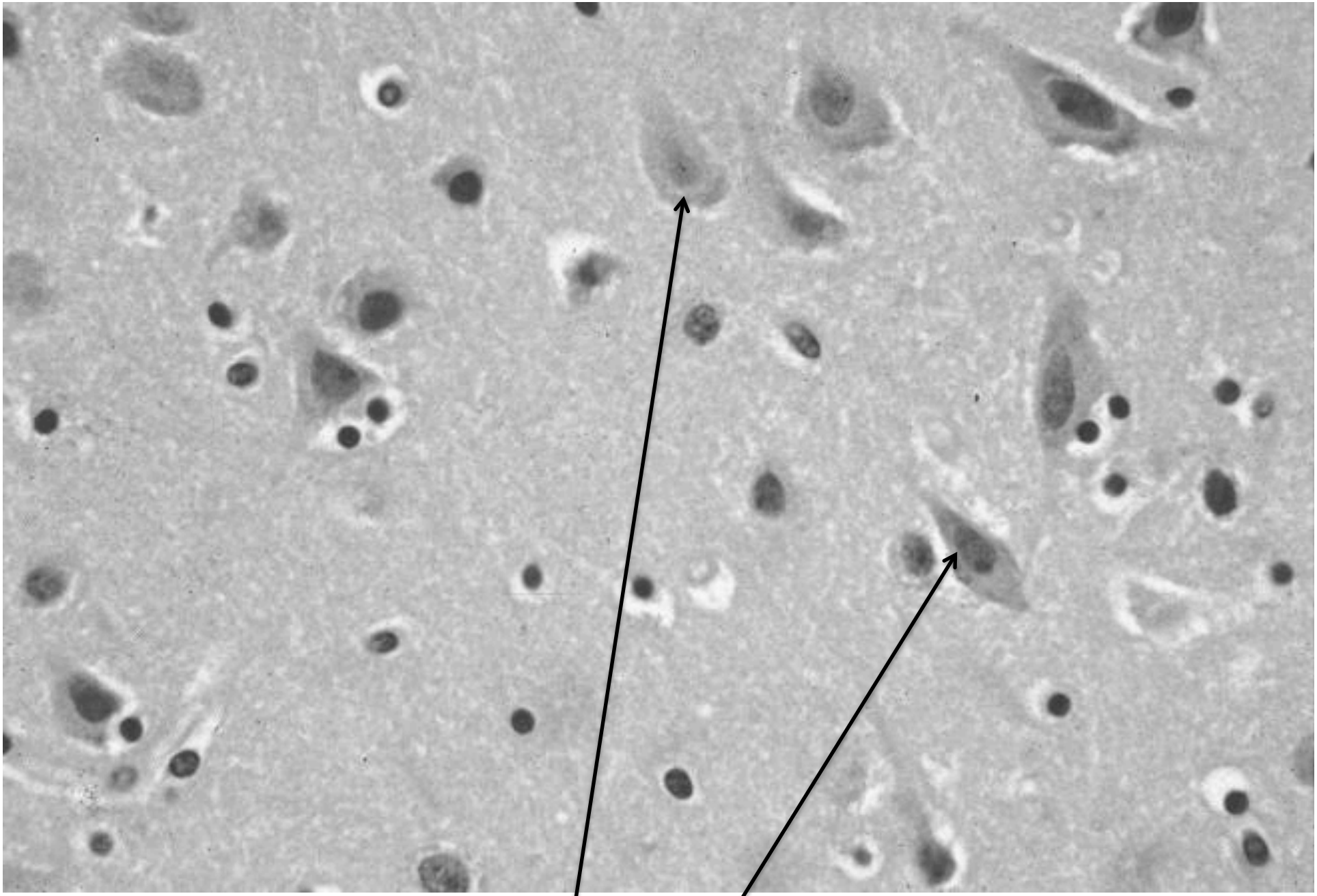
- Introduction

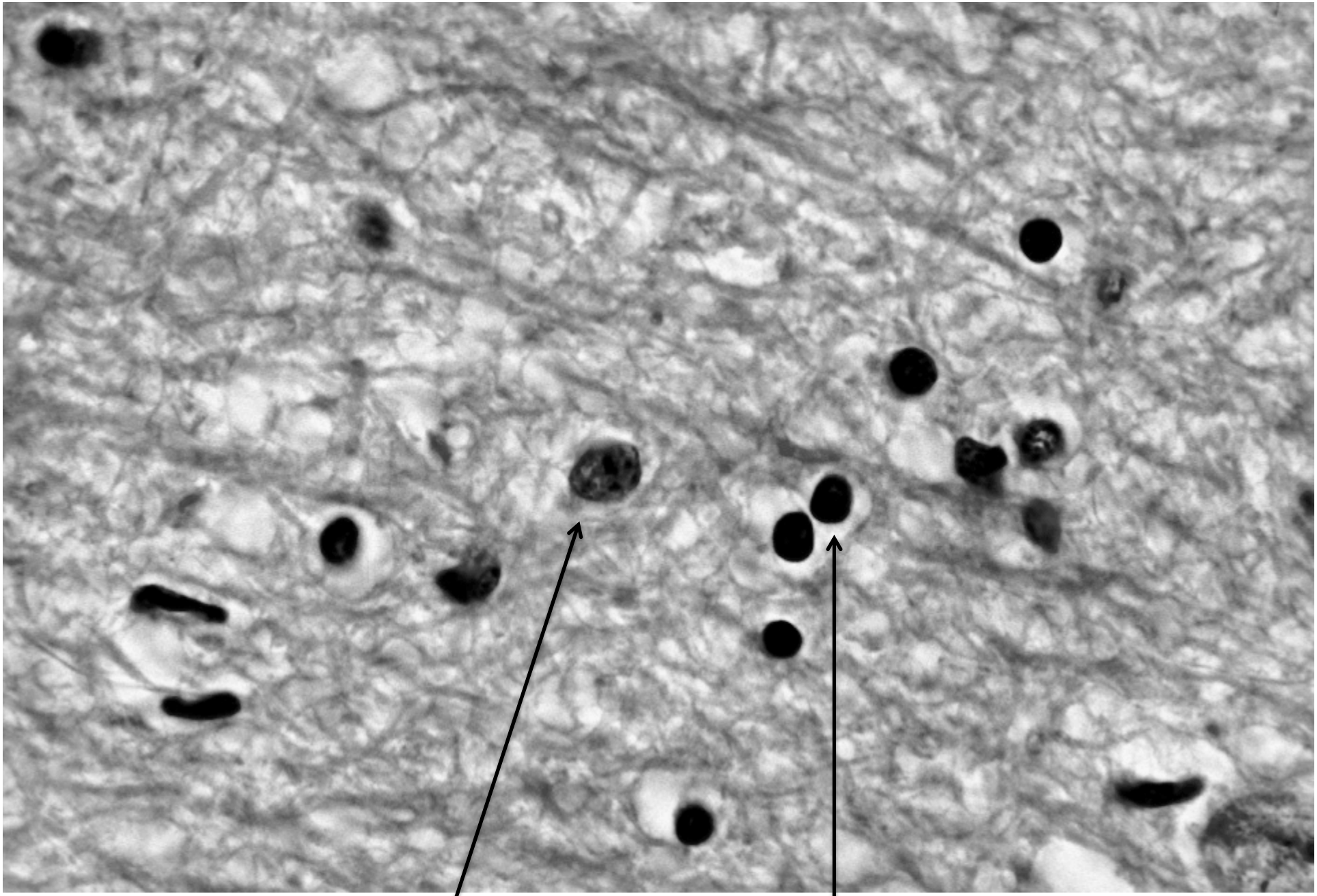


Gross anatomy of brain

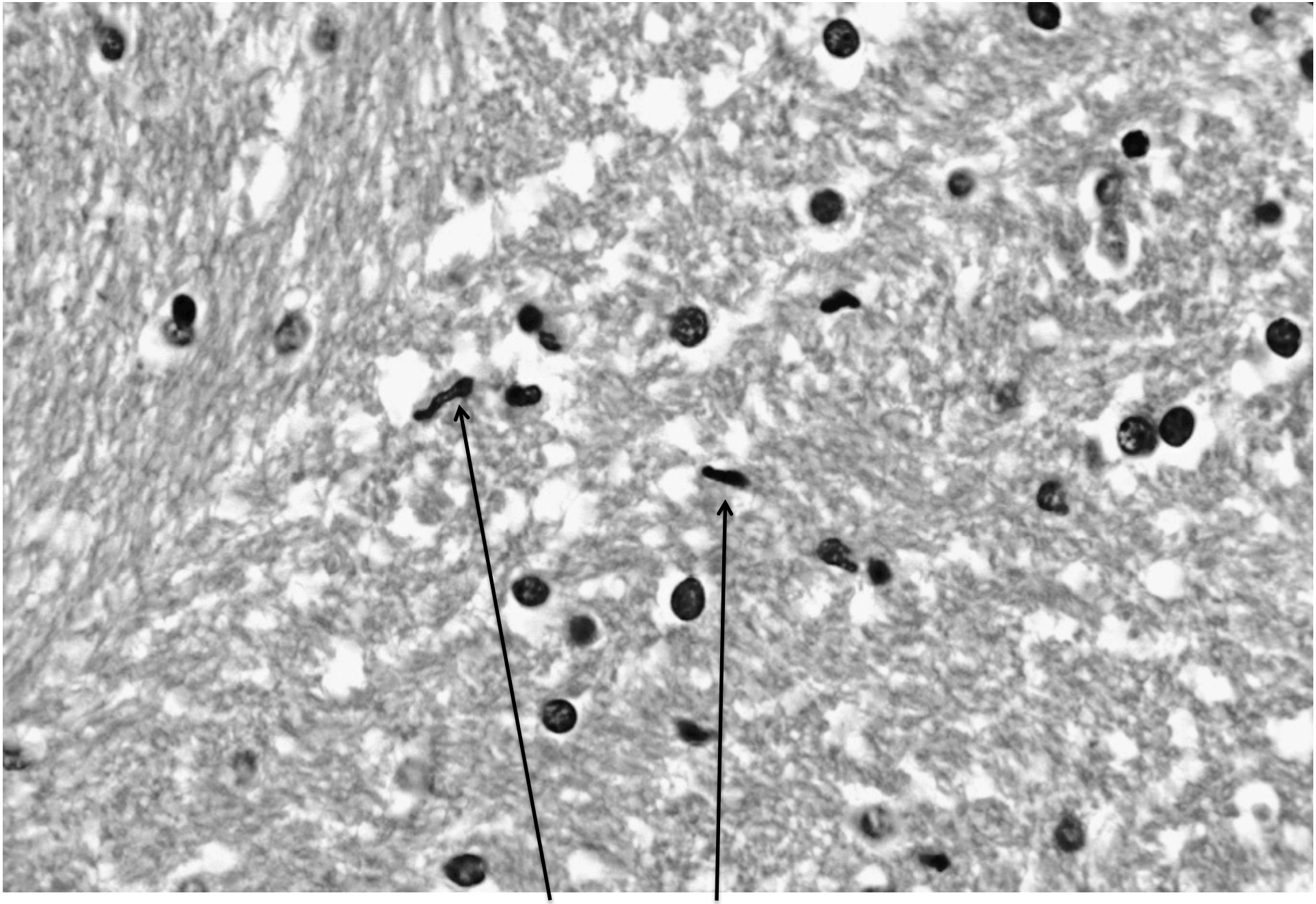
Cells of the CNS

- Neurons – transmit impulses
- Astrocytes – part of blood brain barrier
- Oligodendrocytes – produce myelin
- Microglia – phagocytose intruders
- Ependymal cells – line ventricles


Neurons



Astrocytes and oligodendrocytes


Microglial cells

Ependymal cells

Reactions of Cells to Injury

- Neurons: become “red” and degenerate
- Astrocytes: undergo hypertrophy, hyperplasia
- Microglia: proliferate
- Oligodendrocytes and ependymal cells don’t react much

CNS Outline

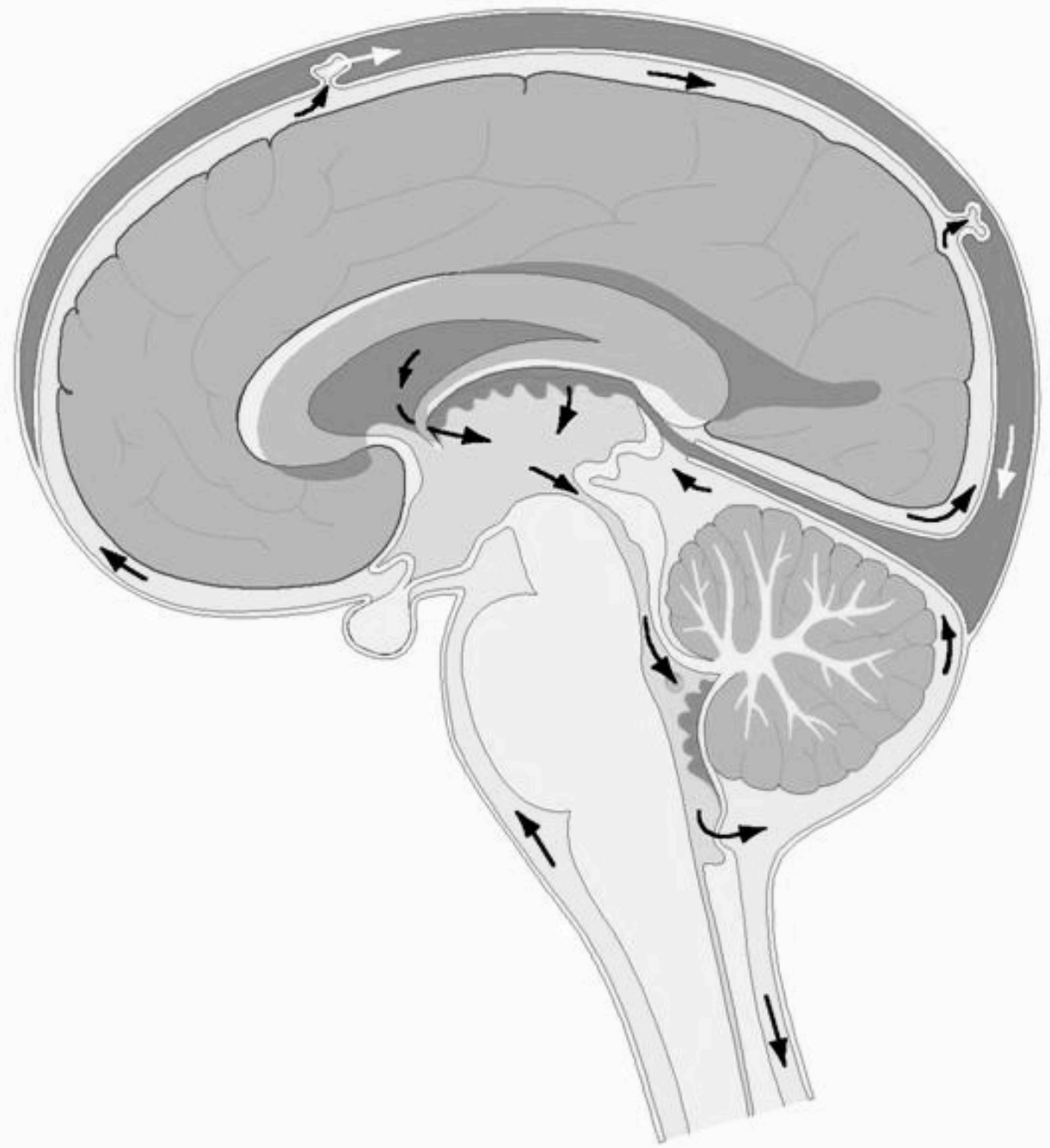
- Introduction
- Increased intracranial pressure

Causes of Increased ICP

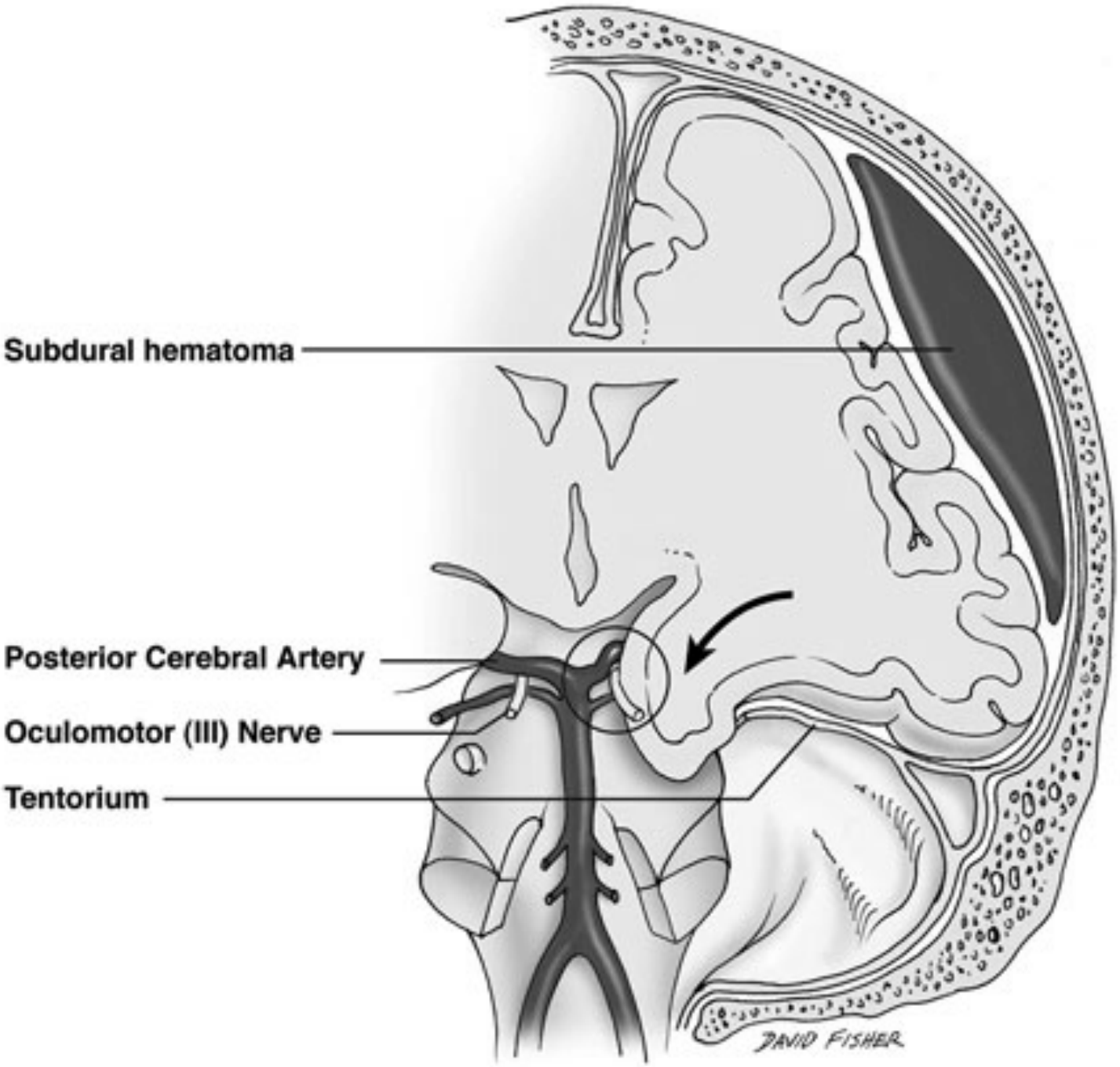
- Cerebral edema
  - Generalized (diffuse insult, like hypoxia, toxin exposure, encephalitis, trauma)
  - Focal (around focal lesions, like acute infarcts, contusions, penetrating injuries, mass lesions)
- Increased CSF volume (hydrocephalus)
- Expanding mass lesions

Hydrocephalus

- Definition: accumulation of excessive CSF within the ventricular system
- Usually due to impaired flow and resorption of CSF (rarely due to overproduction of CSF)
- If occurs in infancy, head enlarges
- If after infancy, ventricles expand, ICP increases



CSF circulation

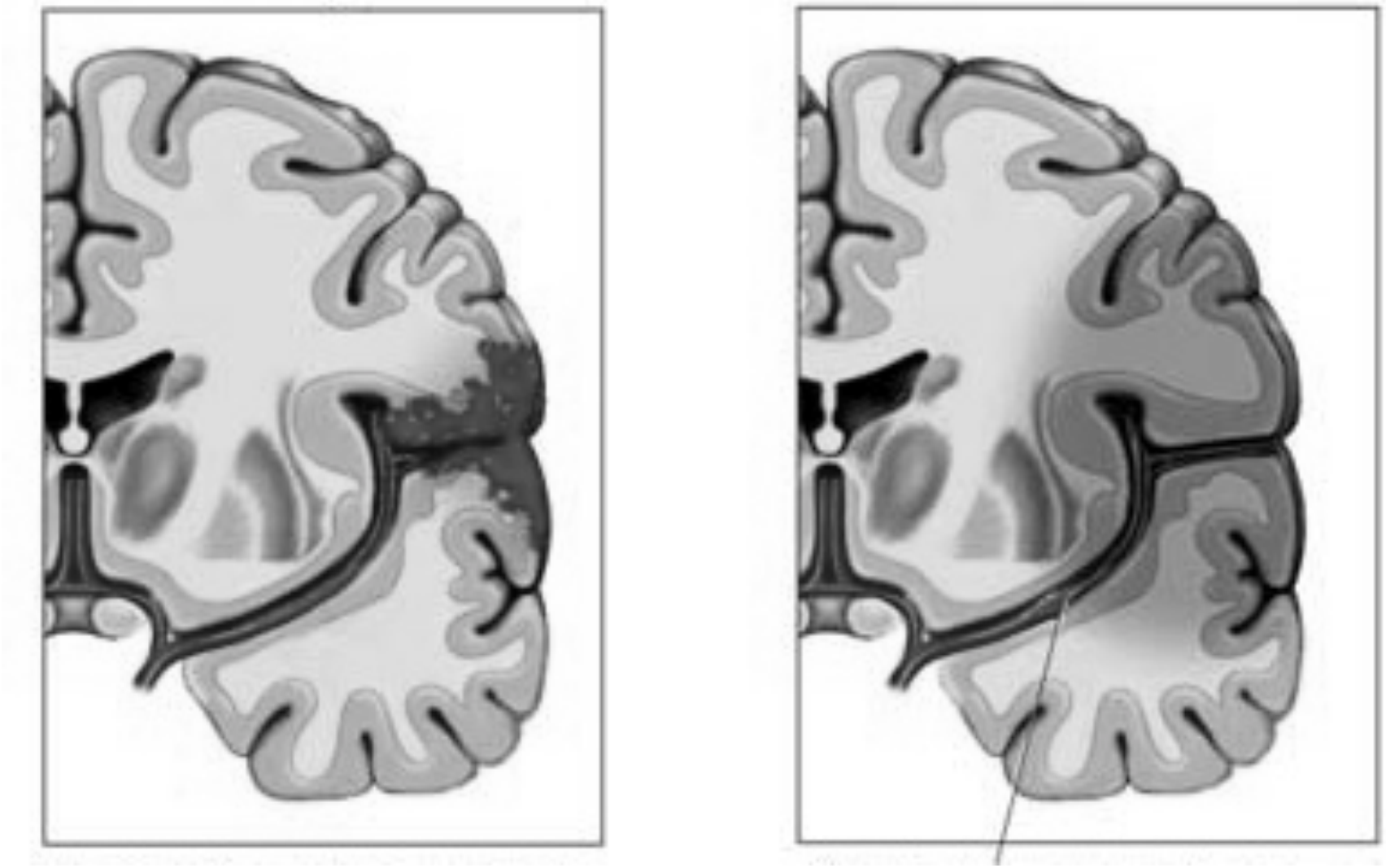

Subdural hematoma
Posterior Cerebral Artery
Oculomotor (III) Nerve
Tentorium
DAVID FISHER

CNS Outline

- Introduction
- Increased intracranial pressure
- Vascular disorders (“strokes”)

Focal Cerebral Ischemia

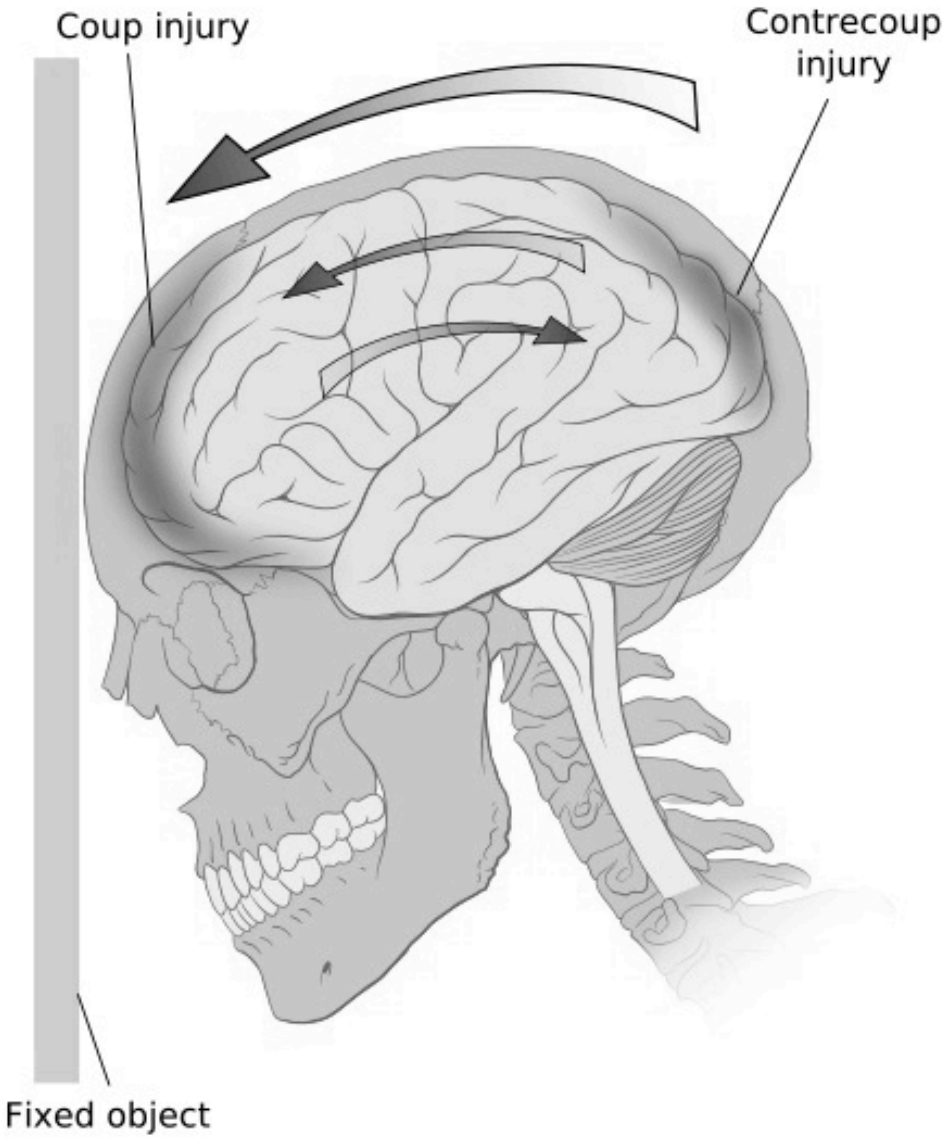
- Due to obstruction of blood flow
- Hemorrhagic (red) infarcts
  - due to emboli + reperfusion
  - often arise from heart
- Ischemic (pale) infarcts
  - due to thrombi
  - often arise from atherosclerotic plaques
- Transient ischemic attacks (TIAs) are often harbingers



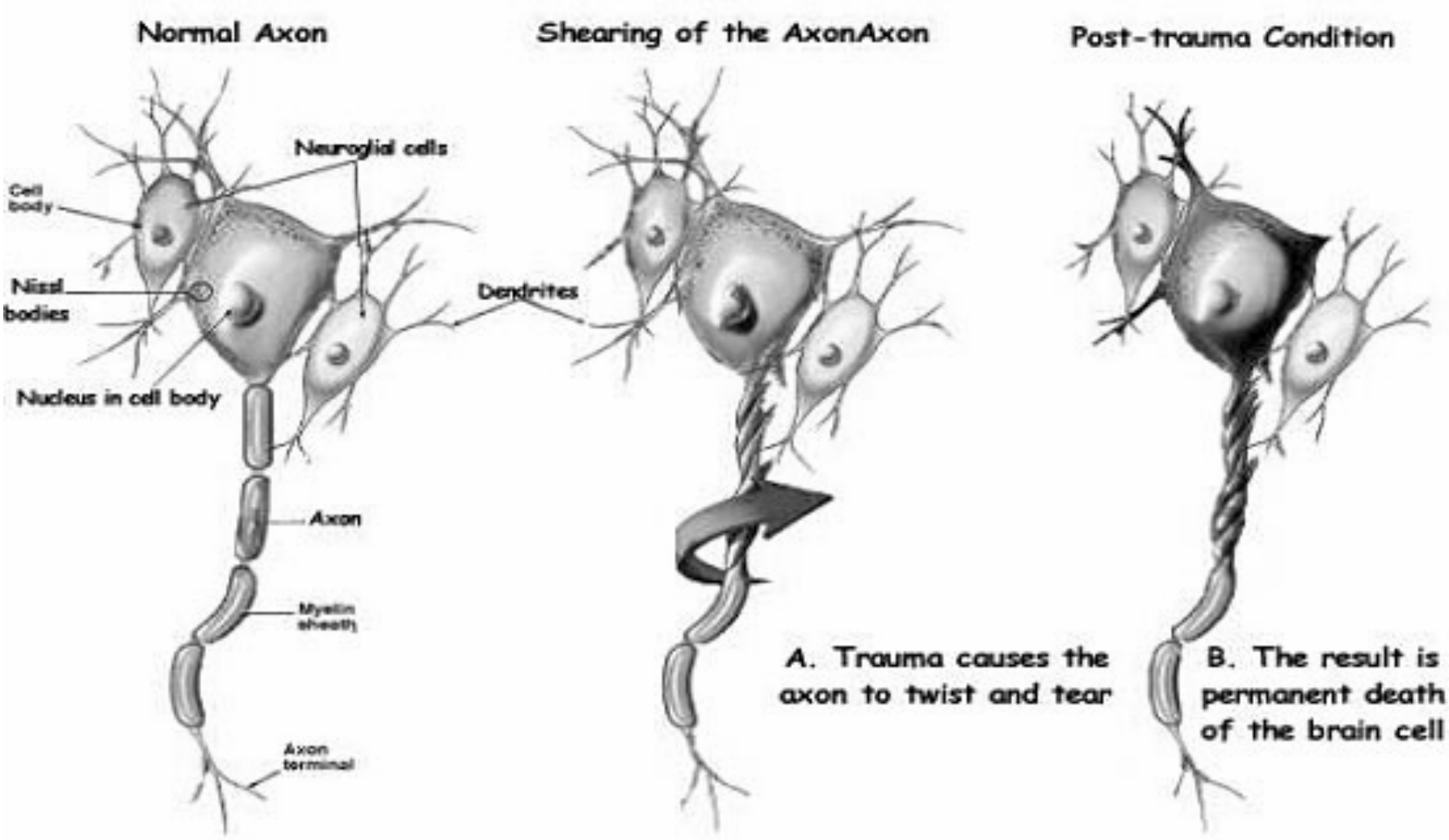
Hemorrhagic (L) vs. ischemic (R) infarction

CNS Outline

- Introduction
- Increased intracranial pressure
- Vascular disorders (“strokes”)
- Trauma



Coup vs. contrecoup injury



Axonal shearing

Traumatic Vascular Injury

Epidural hemorrhage

- Blood above dura
- Tear in middle meningeal artery
- Neurosurgical emergency

Subdural hemorrhage

- Blood between dura and arachnoid
- Shearing of bridging veins
- Acute (hours) or chronic (months)

Subarachnoid hemorrhage

- Blood in subarachnoid space
- Contusions, ruptured berry aneurysms
- Neurosurgical emergency

CNS Outline

- Introduction
- Increased intracranial pressure
- Vascular disorders (“strokes”)
- Trauma
- Infections

Meningitis

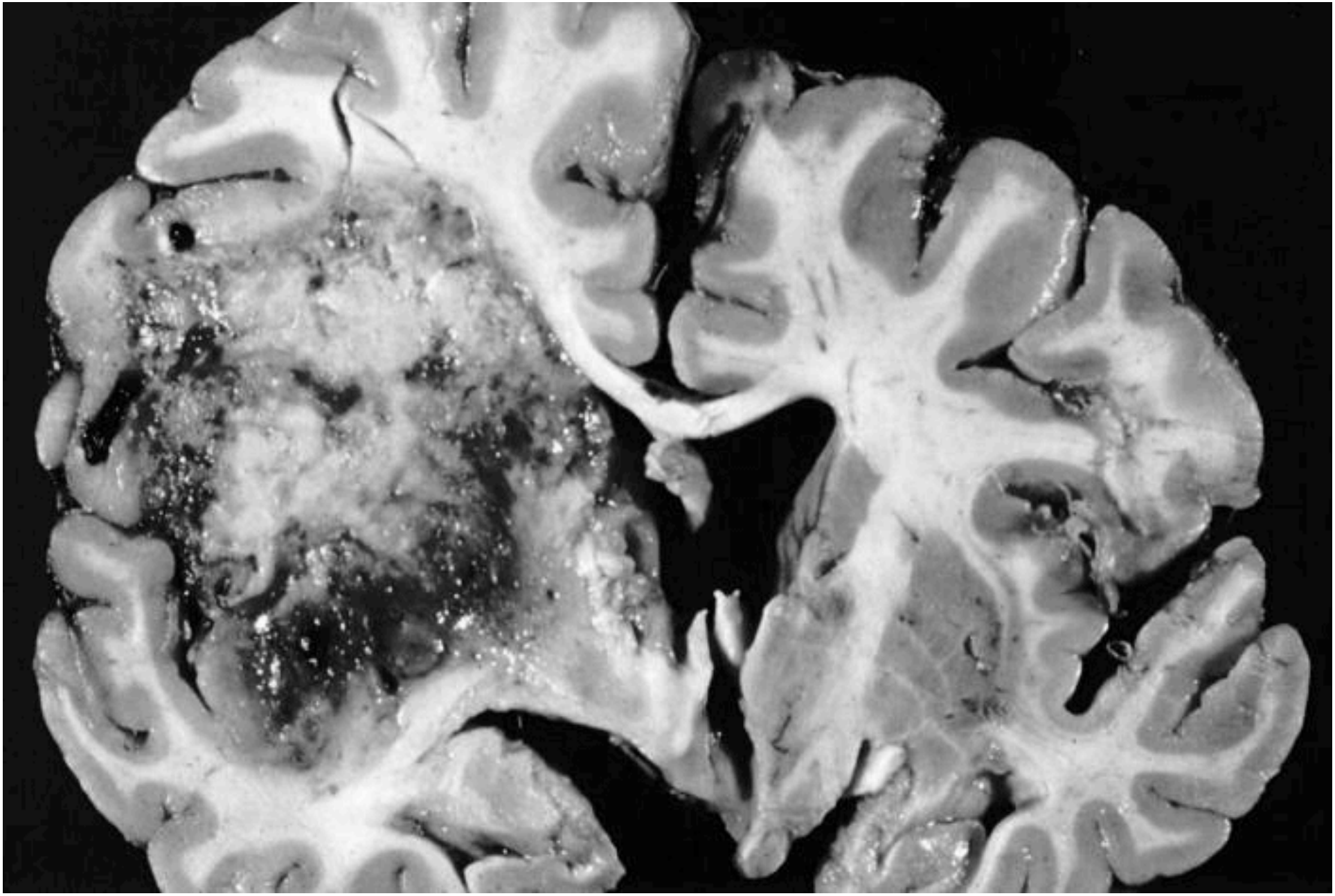
- Inflammation of the meninges
- Symptoms: Fever, headache, stiff neck.
- Without treatment: Loss of consciousness, coma, death.
- Infectious causes:
  - Bacteria (newborns: E. coli, S. agalactiae; young adults: N. meningitidis; elderly: S. pneumoniae)
  - Viruses (Coxsackie, ECHO, mumps)
  - Tuberculosis, rarely

CNS Outline

- Introduction
- Increased intracranial pressure
- Vascular disorders (“strokes”)
- Trauma
- Infections
- Tumors

Gliomas

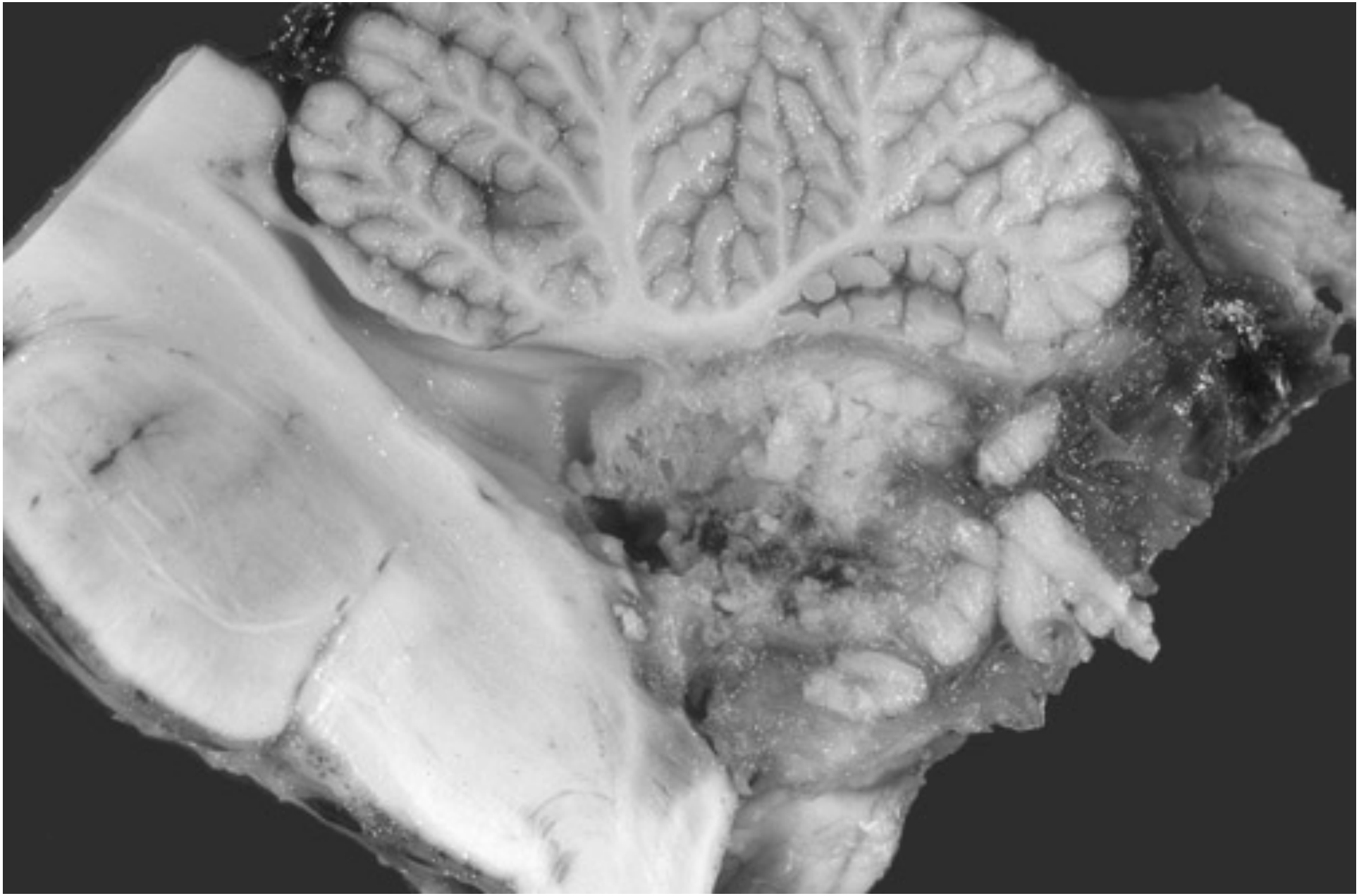
- Arise from astrocytes, oligodendrocytes, ependymal cells
- Often fatal (location and infiltrative borders prevent complete excision)
- Glioblastoma (highest-grade astrocytoma) is most malignant



Glioblastoma multiforme (high-grade astrocytoma)

Medulloblastoma

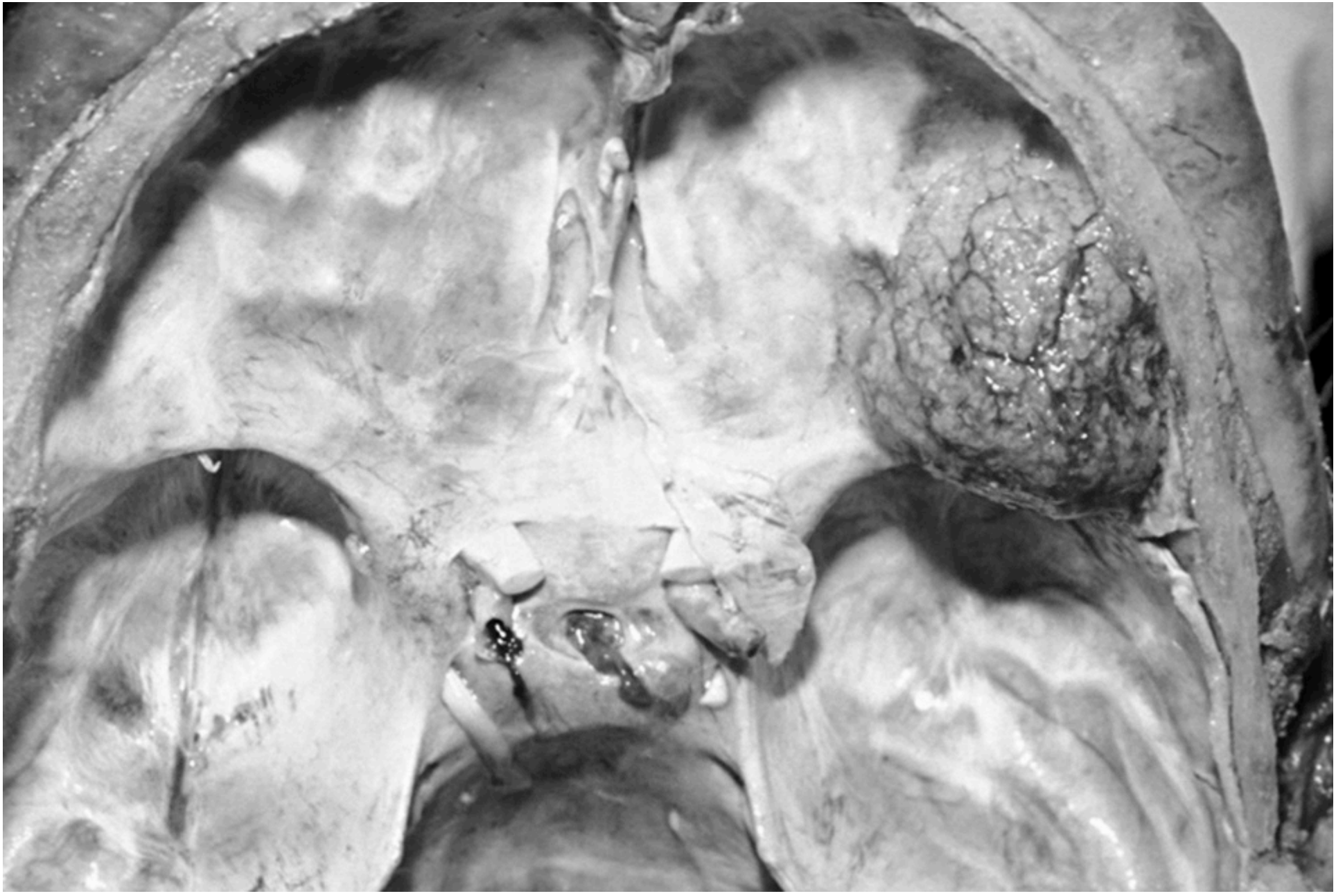
- Tumor of primitive neurons
- Cerebellum
- Children
- Very radiosensitive!



Medulloblastoma

Meningioma

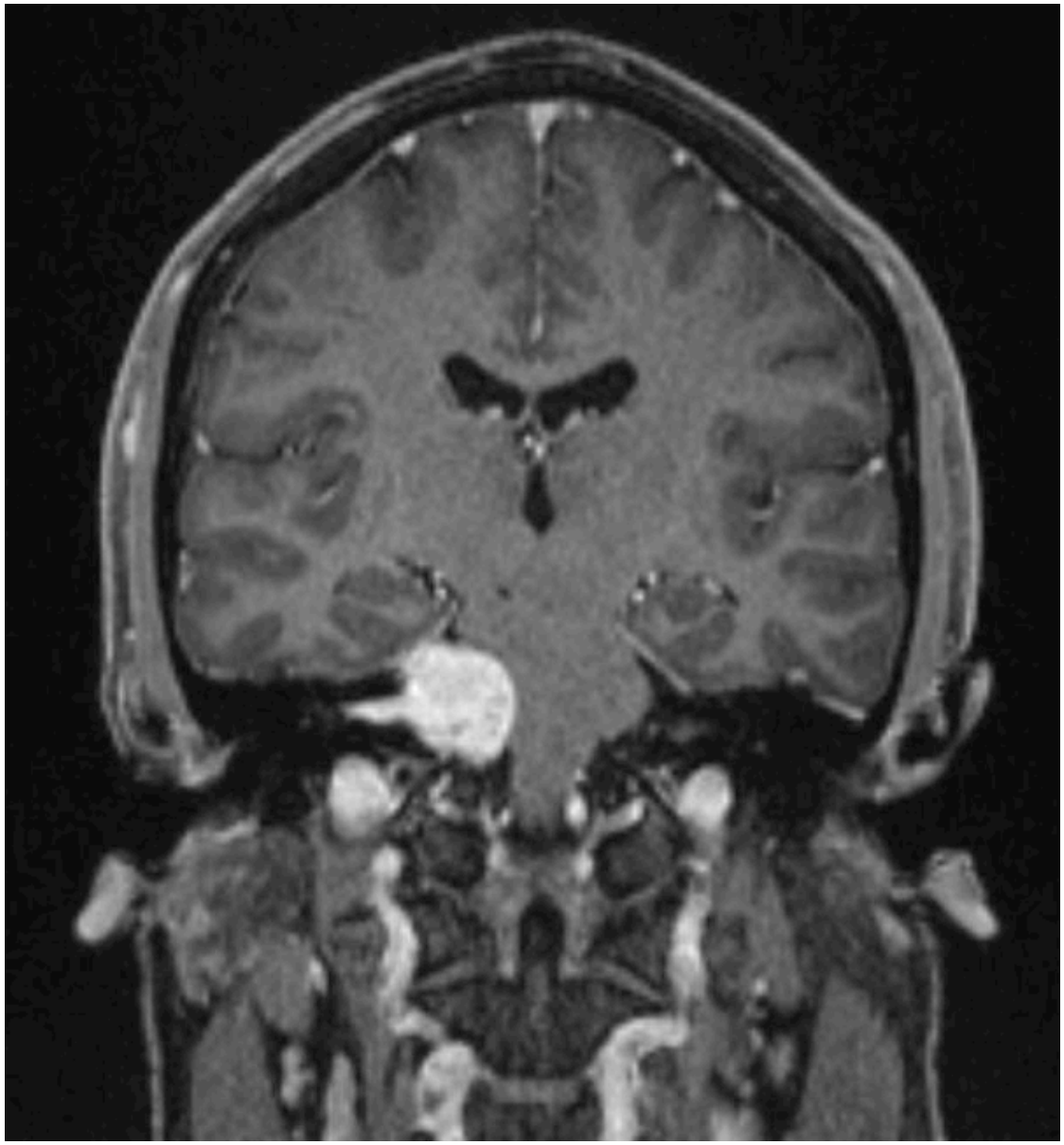
- Encapsulated, benign tumor
- Surface of brain (no invasion)
- Symptoms caused by compression
- Cured by resection



Meningioma

Nerve Sheath Tumors

- Arise from cranial (esp. VIII) and spinal nerve roots, and peripheral nerves
- Derived from support cells of nerve
- Benign but may compress nerve
- Schwannoma ("acoustic neuroma" if involving VIII), neurofibroma



“Acoustic neuroma” (schwannoma)

CNS Outline

- Introduction
- Increased intracranial pressure
- Vascular disorders (“strokes”)
- Trauma
- Infections
- Tumors
- Demyelinating diseases

Multiple Sclerosis

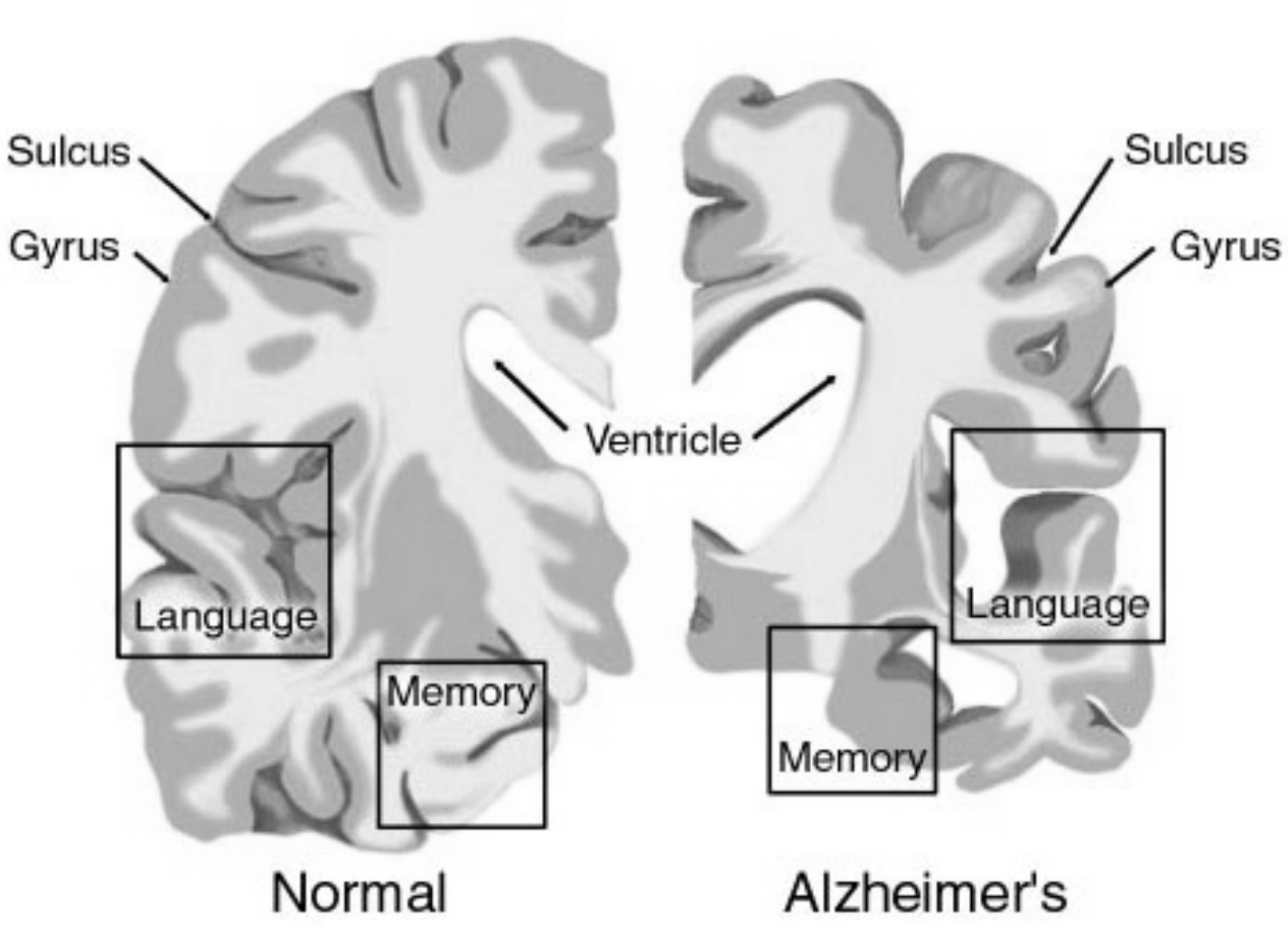
- Most common demyelinating disorder
- Etiology unknown; related to autoimmunity
- Variety of motor and sensory symptoms
- Relapsing-remitting course
- Plaques (areas of demyelination) in brain, cord

CNS Outline

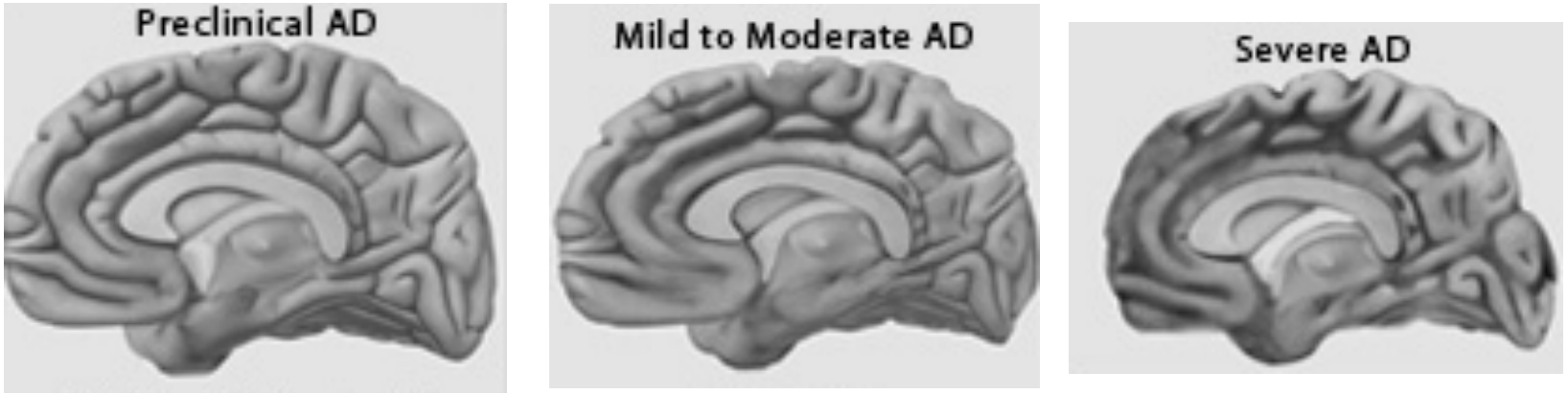
- Introduction
- Increased intracranial pressure
- Vascular disorders (“strokes”)
- Trauma
- Infections
- Tumors
- Demyelinating diseases
- Degenerative diseases

Alzheimer Disease

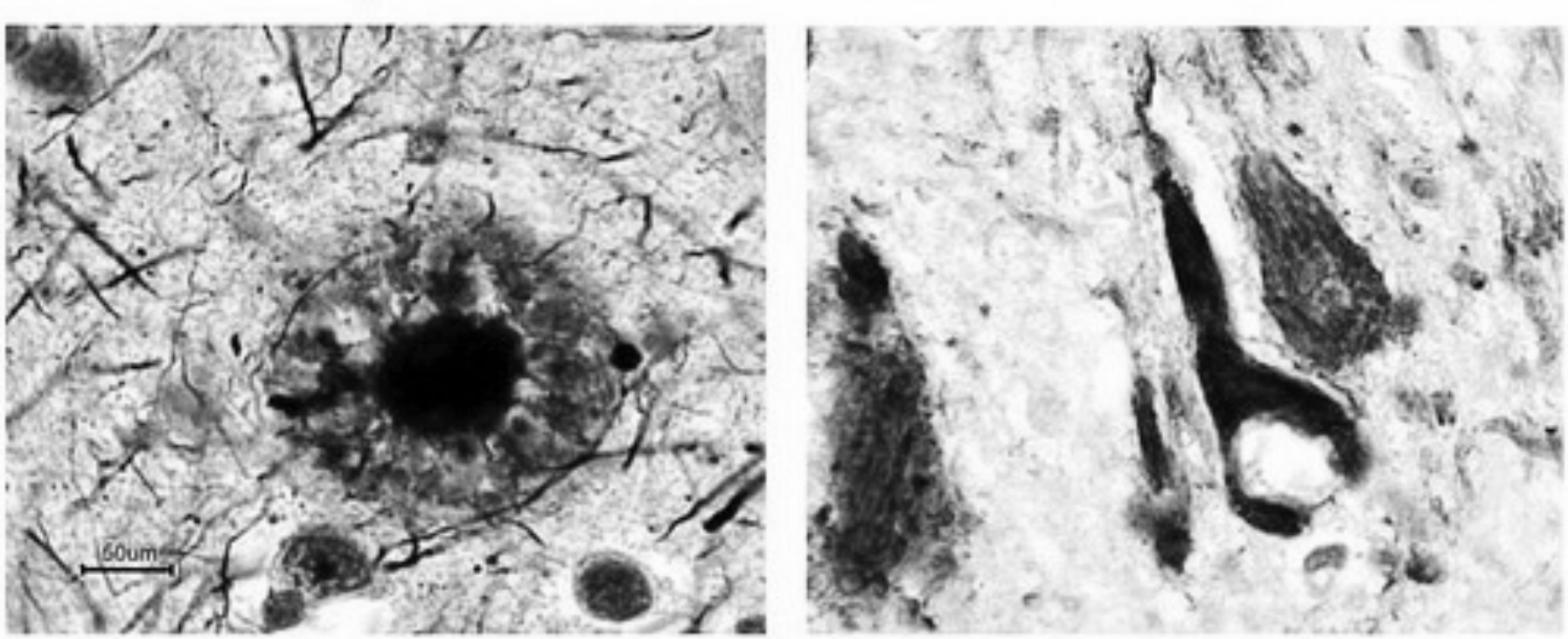
- Most common cause of dementia in the elderly
- Symptoms:
  - Early on: forgetfulness, memory disturbances
  - Language deficits, loss of learned motor skills, alterations in mood/behavior, disorientation
  - Finally, patient becomes profoundly disabled, mute, immobile
- Gross: Cortical atrophy, neuronal loss
- Microscopic: neurofibrillary tangles, neuritic plaques



Alzheimer disease: brain atrophy



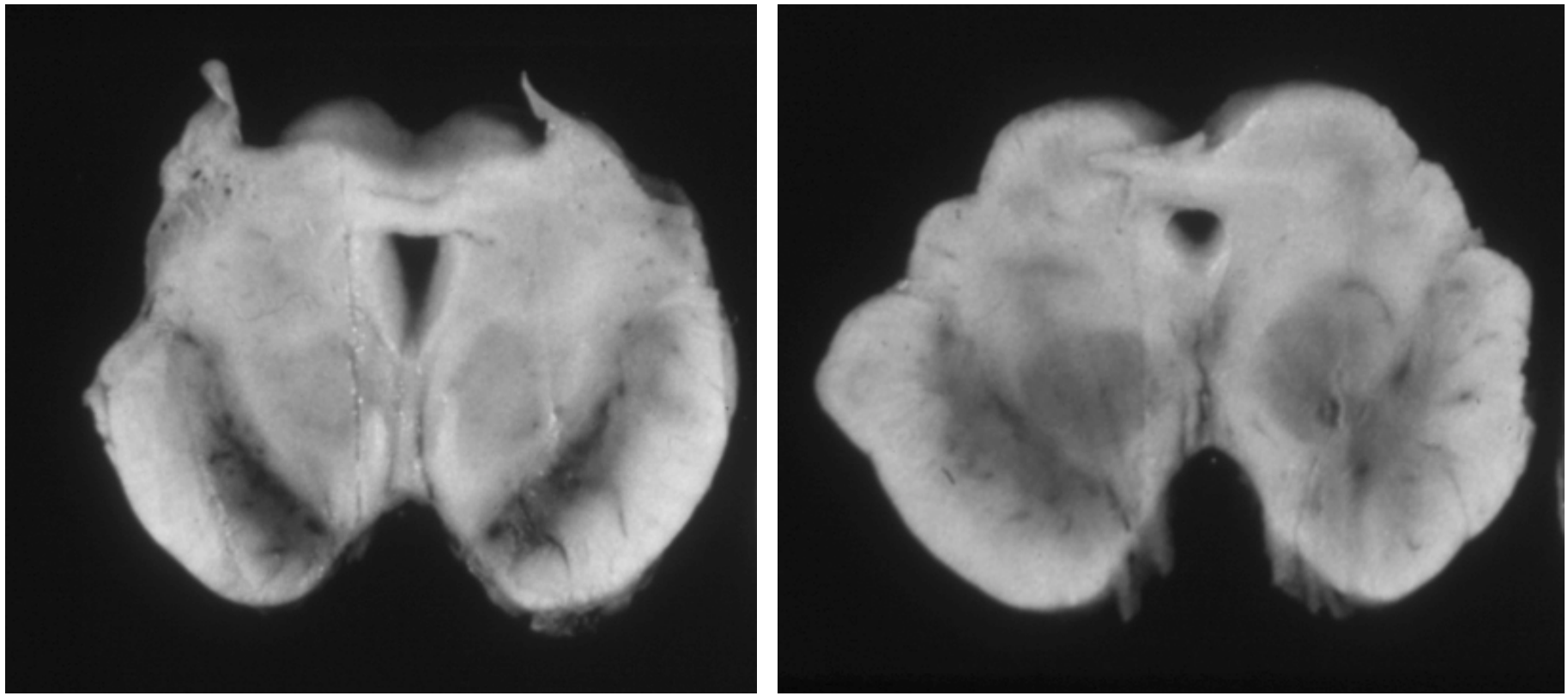
Alzheimer disease: progression



Alzheimer disease: plaques (L) and tangles (R)

Parkinson Disease

- Degeneration of pigmented neurons (containing dopamine) in the substantia nigra
- Cause unknown
- Early symptoms: tremor, rigidity, slow movement
- Later: cognitive problems, dementia, dyskinesia
- Gross: atrophy of substantia nigra
- Microscopic: Lewy bodies (inclusions in neurons)



Parkinson disease (R) : atrophy of substantia nigra

Huntington Disease

- Degeneration of basal ganglia and cerebral cortex
- Early symptoms: lack of coordination, unsteady gait
- Later: chorea (involuntary writhing), psychiatric symptoms, dementia
- Autosomal dominant mutation
- Begins in 30s-40s; slow progression over 10-20 years

Amyotrophic Lateral Sclerosis

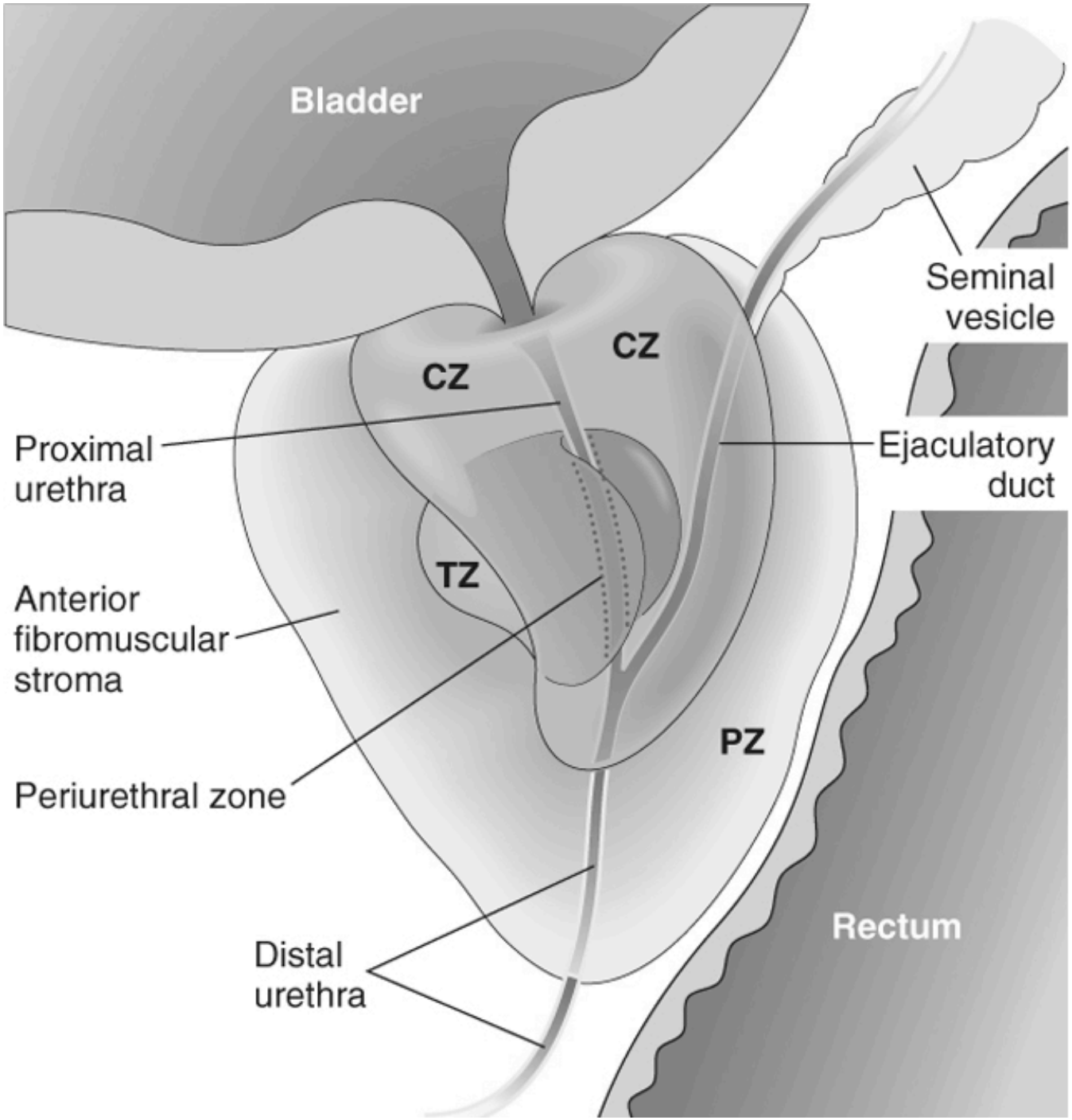
- Degeneration of neurons involved in motor control
- Rapidly progressive weakness, muscle atrophy, spasticity, dysphagia
- Early symptoms: muscle weakness in an arm or leg, twitching, slurred speech
- Death within 2-3 years due to respiratory compromise
- Sensory and cognitive function are unaffected

Clinical Features of Testicular Cancer

- Common in men between 15-35
- Firm, painless enlargement of the testis
- Some present with metastases
- Treatable – curable! - if detected early

Testicular Cancer Classification

- Seminoma
- Non-seminoma
  - Embryonal carcinoma
  - Yolk sac tumor
  - Choriocarcinoma
  - Teratoma


Bladder
CZ
CZ
Seminal vesicle
Proximal urethra
Ejaculatory duct
TZ
Anterior fibromuscular stroma
PZ
Periurethral zone
Rectum
Distal urethra

Nodular Hyperplasia

- Very common! 90% of men have it by their 70s.
- Big prostate
- Usually affects central zone of the prostate
- Symptoms (in 10% of patients): hesitancy, urgency, nocturia, poor urinary stream.
- Cause: excessive androgen stimulation

Clinical Features of Prostate Cancer

- Most common, 2nd deadliest cancer in men
- Peak incidence: 65-75
- Cause: androgens + genetics + ?environment
- Symptoms: asymptomatic, then palpable nodule, then local pain/obstruction

Female Reproductive System Outline

- Cervix
- Uterus
- Ovaries
- Breast

Cervical Intraepithelial Neoplasia (CIN)

- Precursor to carcinoma
- Almost all carcinomas arise in CIN; but not all cases of CIN progress to carcinoma!
- Three grades:
  - CIN I: mild dysplasia (half regress, 20% progress)
  - CIN II: moderate dysplasia
  - CIN III: severe dysplasia (30% regress, 70% progress)
- The higher the grade, the more likely the lesion will progress to carcinoma

Cervical Carcinoma Risk Factors

- Early age at first intercourse
- Multiple sexual partners
- A male partner with multiple previous partners
- Persistent infection with high-risk HPV
- Smoking
- Immunodeficiency

Cervical Carcinoma and HPV

- HPV is detectable in almost all CIN and cancer.
- "High-risk" types:
  - 16, 18, 45, 31
  - Found in carcinomas
  - Integrate into genome, inactivate p53, RB
- "Low-risk" types:
  - 6, 11
  - Found in condylomas (benign lesions)
  - Do not integrate into genome

Invasive Cervical Carcinoma

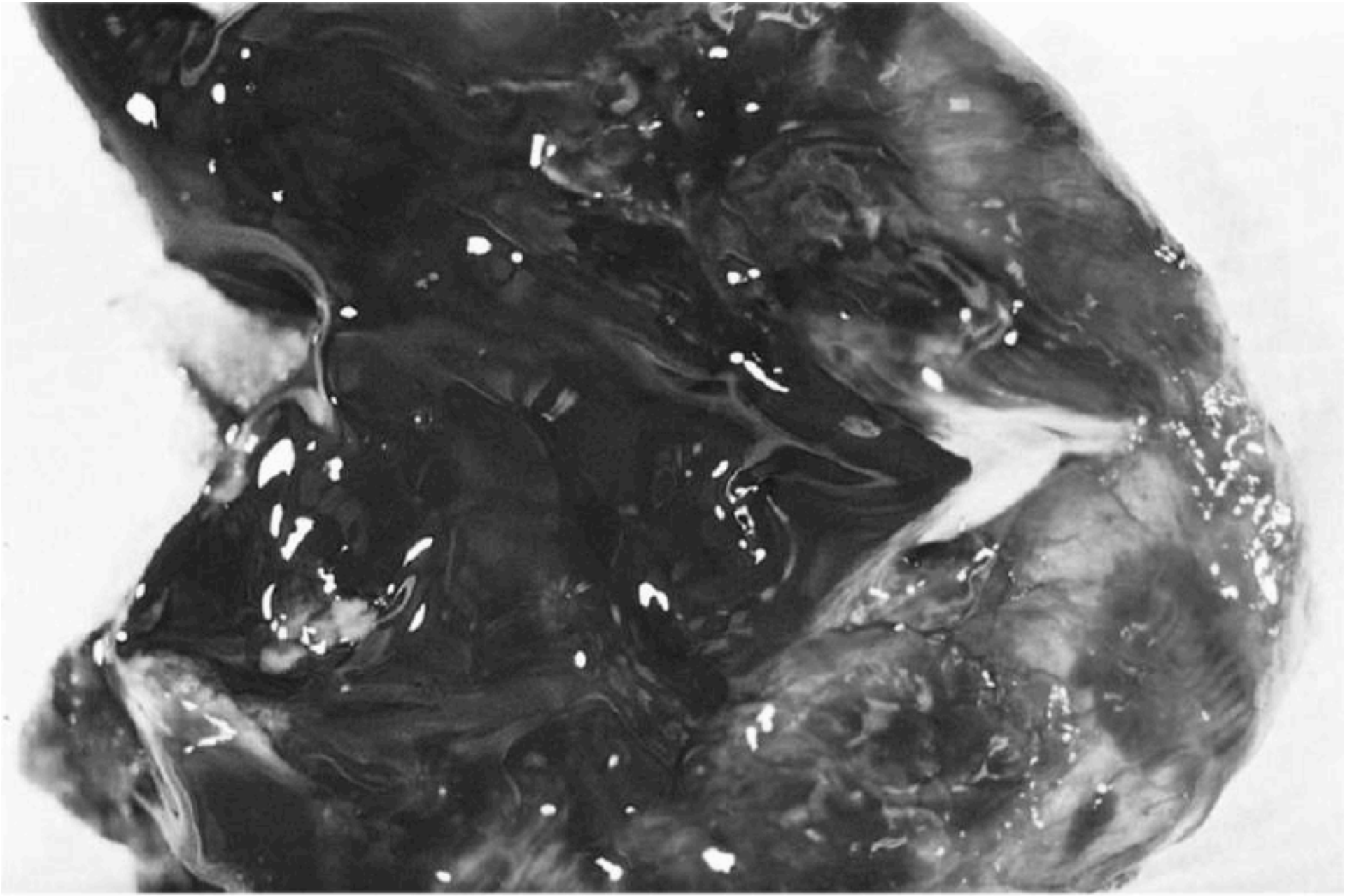
- Most cases are squamous, arising from CIN
- Small number are adenocarcinomas
- Peak age: 45 (10-15 years after CIN develops!)
- Spreads slowly
- Most cases are diagnosed early
- Mortality is related to stage
  - Stage 0 (preinvasive): 100% 5 year survival
  - Stage 4: 10% 5 year survival

Female Reproductive System Outline

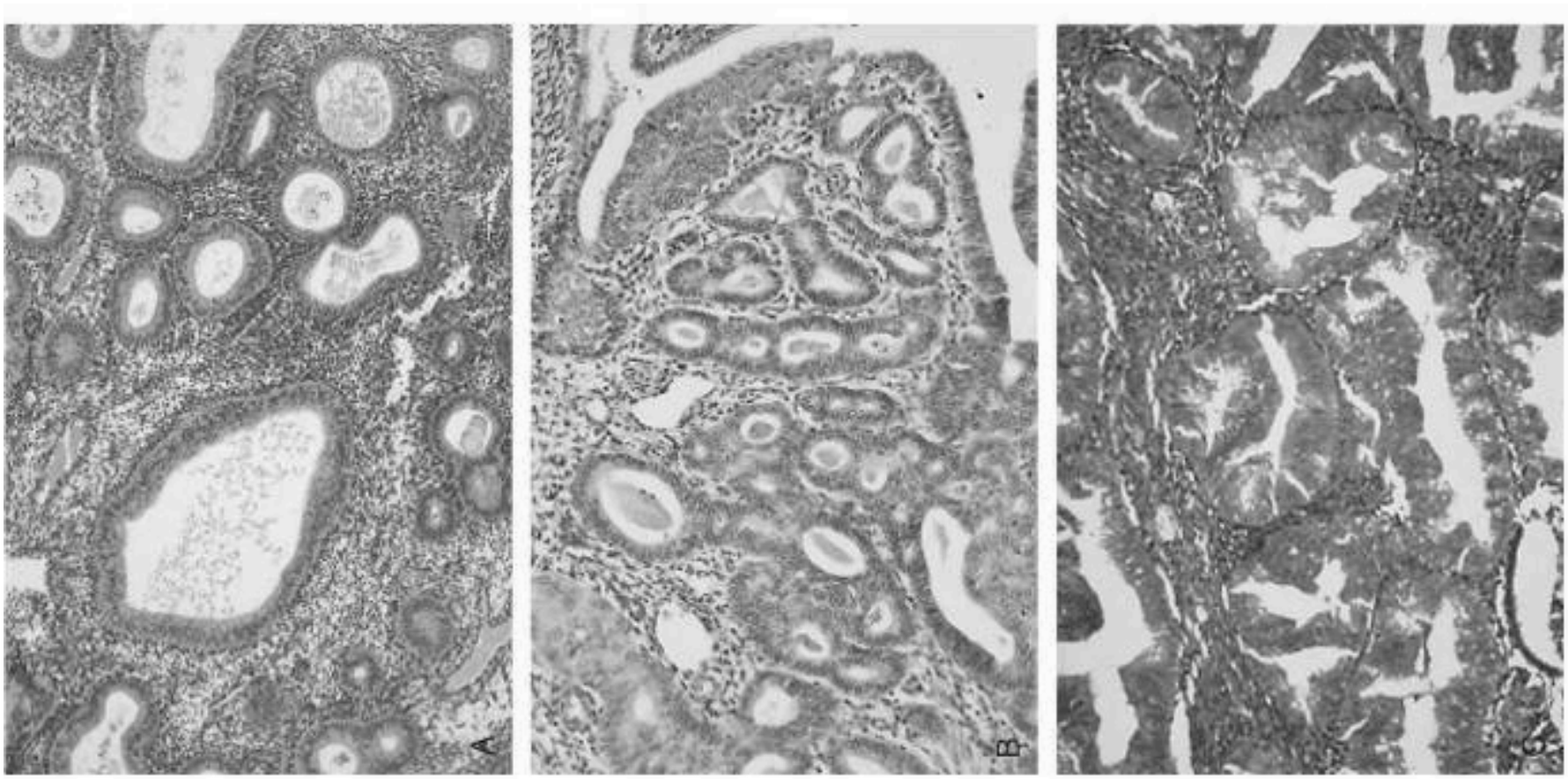
- Cervix
- Uterus
  - Endometriosis
  - Endometrial hyperplasia
  - Tumors

Endometriosis

- Location of endometrial glands outside uterus
- Usually peritoneum, rarely lymph nodes
- Endometrium undergoes cyclic bleeding
- Causes scarring, pain, sometimes sterility
- How does endometrium get out?



Endometriosis in ovary (“chocolate cyst”)



Simple Complex Atypical

Endometrial hyperplasia

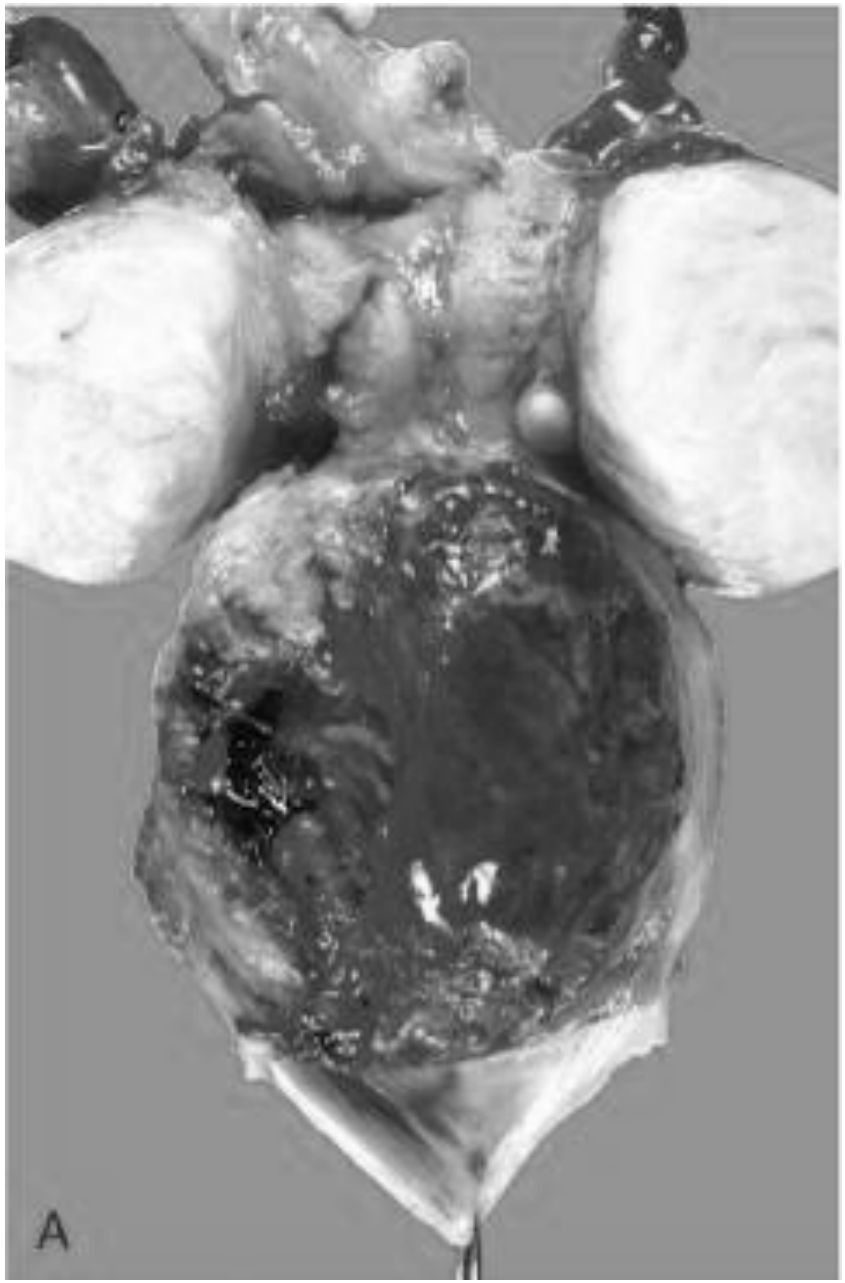
Leiomyoma

- “Fibroid”
- Benign tumor of smooth muscle
- Common!
- Stimulated by estrogen
- Menorrhagia, metrorrhagia, or asymptomatic

Leiomyosarcoma

- Malignant tumor of smooth muscle
- Necrotic, with atypical cells and lots of mitoses
- Often recur after surgery
- Many metastasize, especially to lungs
- 5 year survival = 40%

Leiomyoma



Leiomyosarcoma

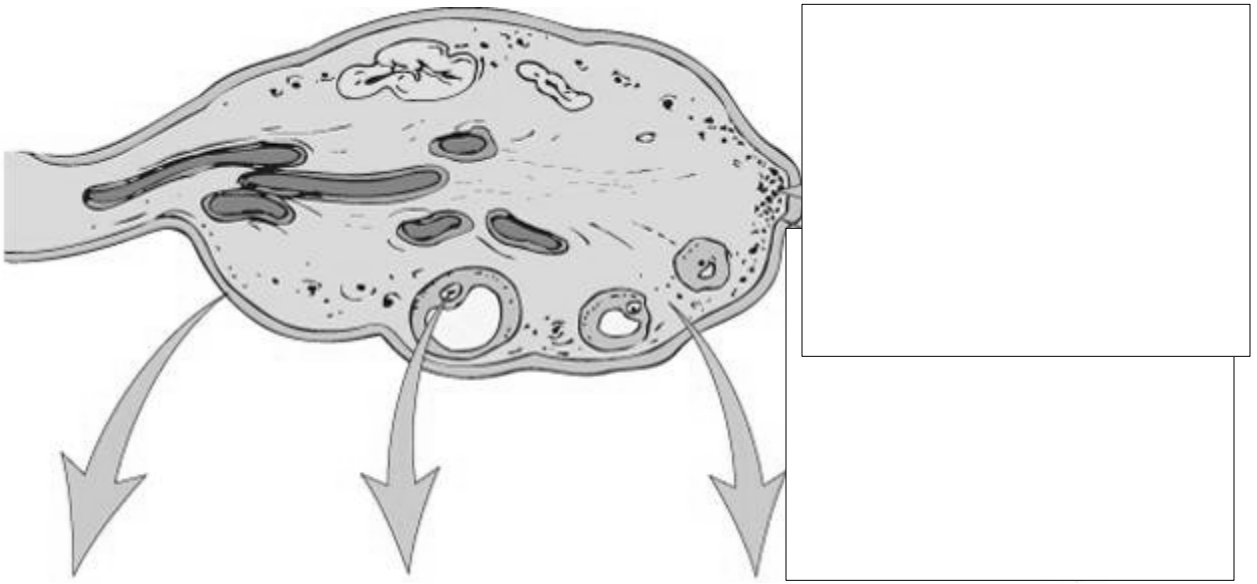
Endometrial Carcinoma

- Peak age: 55-65 (not before 40)
- Frequently arises in endometrial hyperplasia
- Risk factors: obesity, nulliparity, estrogen replacement
- Symptoms: leukorrhea, irregular bleeding
- Metastasizes late

Female Reproductive System Outline

- Cervix
- Uterus
- Ovaries
  - Tumors

Origin of Ovarian Tumors



Surface epithelial tumors

- Cystadenoma
- Cystadenocarcinoma

Germ cell tumors

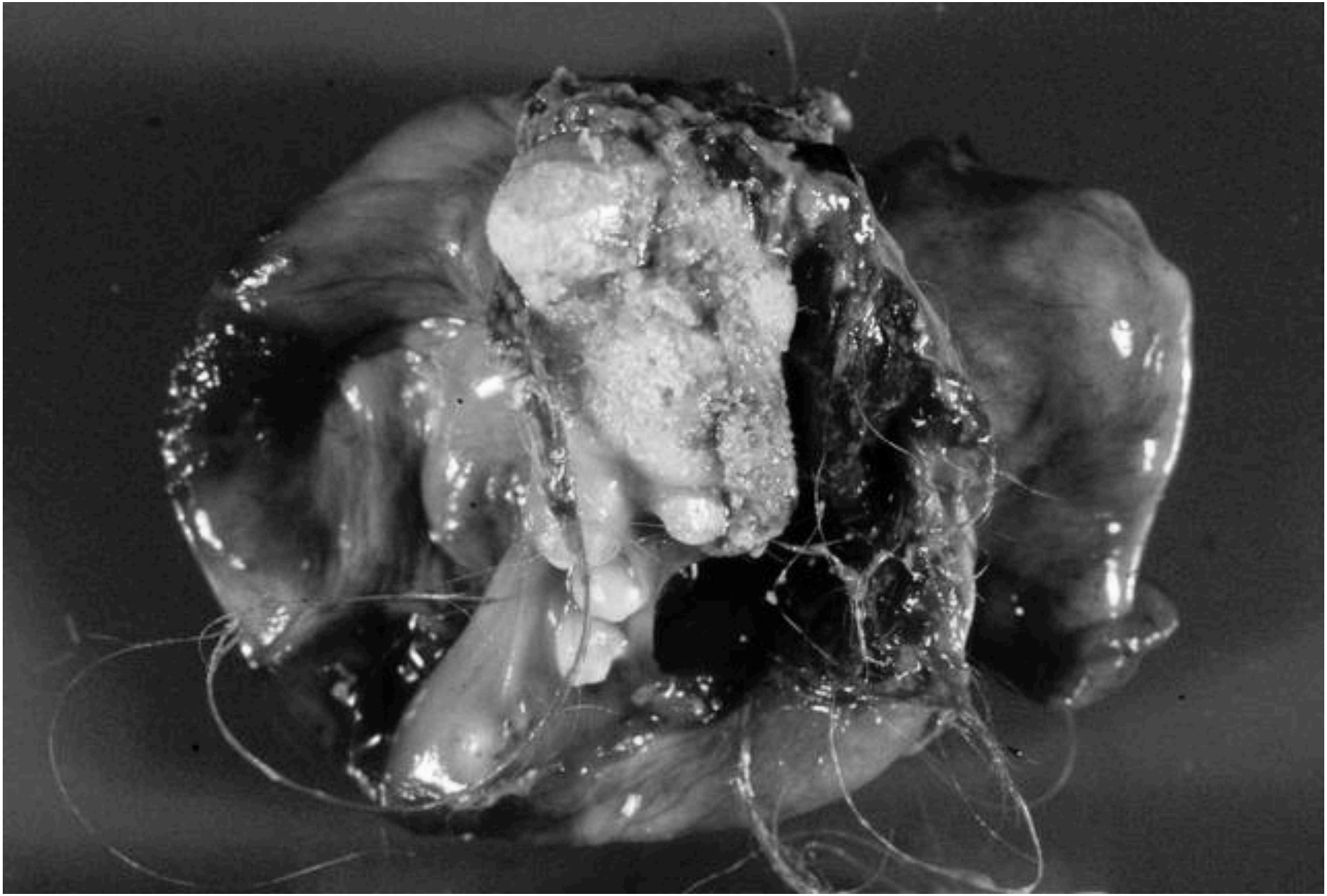
- Teratoma
- Dysgerminoma
- Yolk sac tumor
- Choriocarcinoma

Sex cord-stromal tumors

- Granulosa-theca cell tumor
- Sertoli-Leydig cell tumor

Teratoma

- Benign tumor with differentiation along all three germ cell layers (ectoderm, endoderm, mesoderm)
- Usually cystic, with skin inside ("dermoid cyst")
- Sebaceous material, matted hair, teeth, bone…
- Malignant variant has immature tissues



Teratoma

Ovarian Cancer

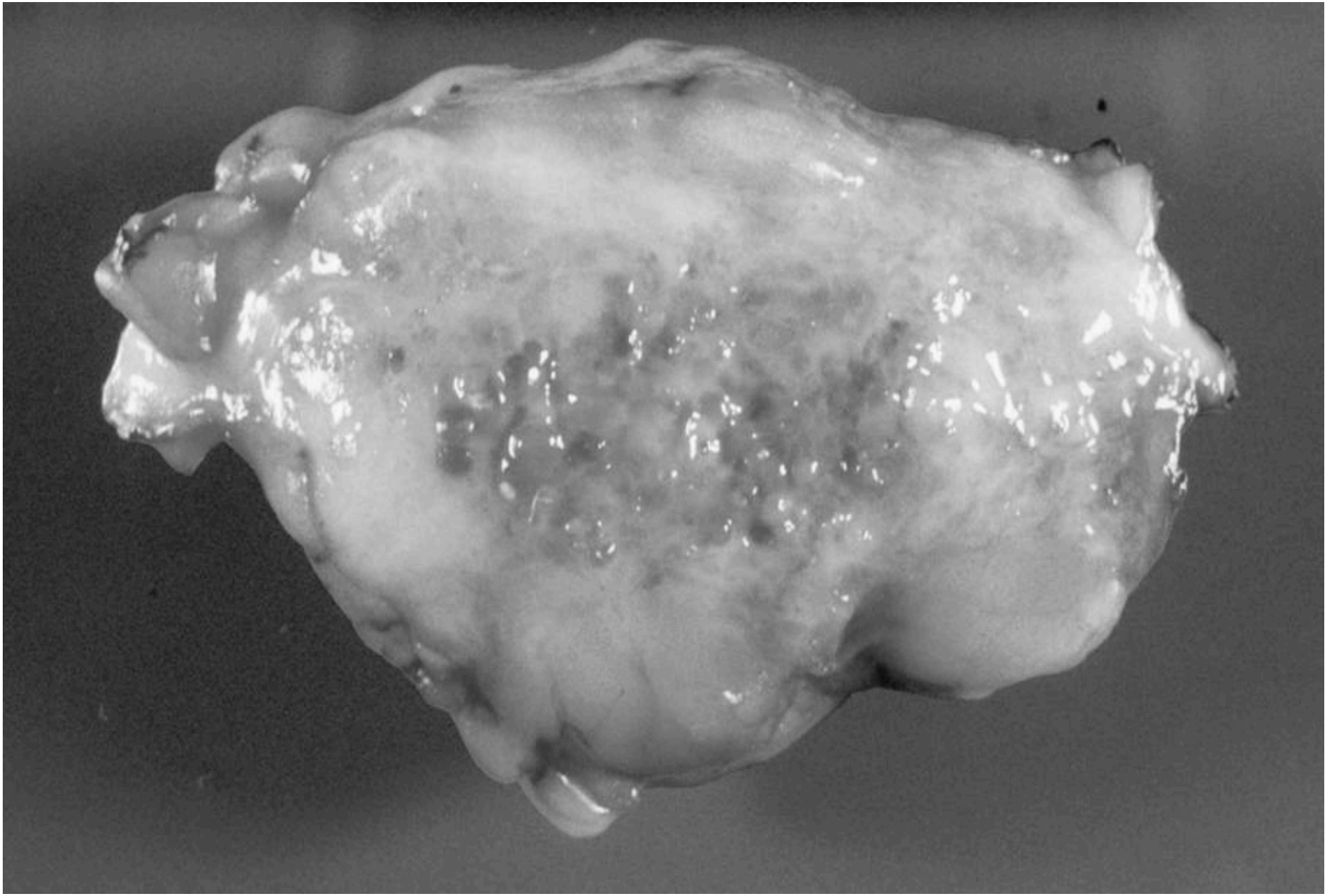
- 22,000 new cases / 14,000 deaths in 2014
- 5th commonest, 5th most deadly cancer in women
- Danger: no definitive signs until advanced
- Peak age: 50
- Most are cystadenocarcinomas

Female Reproductive System Outline

- Cervix
- Uterus
- Ovaries
- Breast
  - Fibrocystic change
  - Tumors

Fibrocystic Change

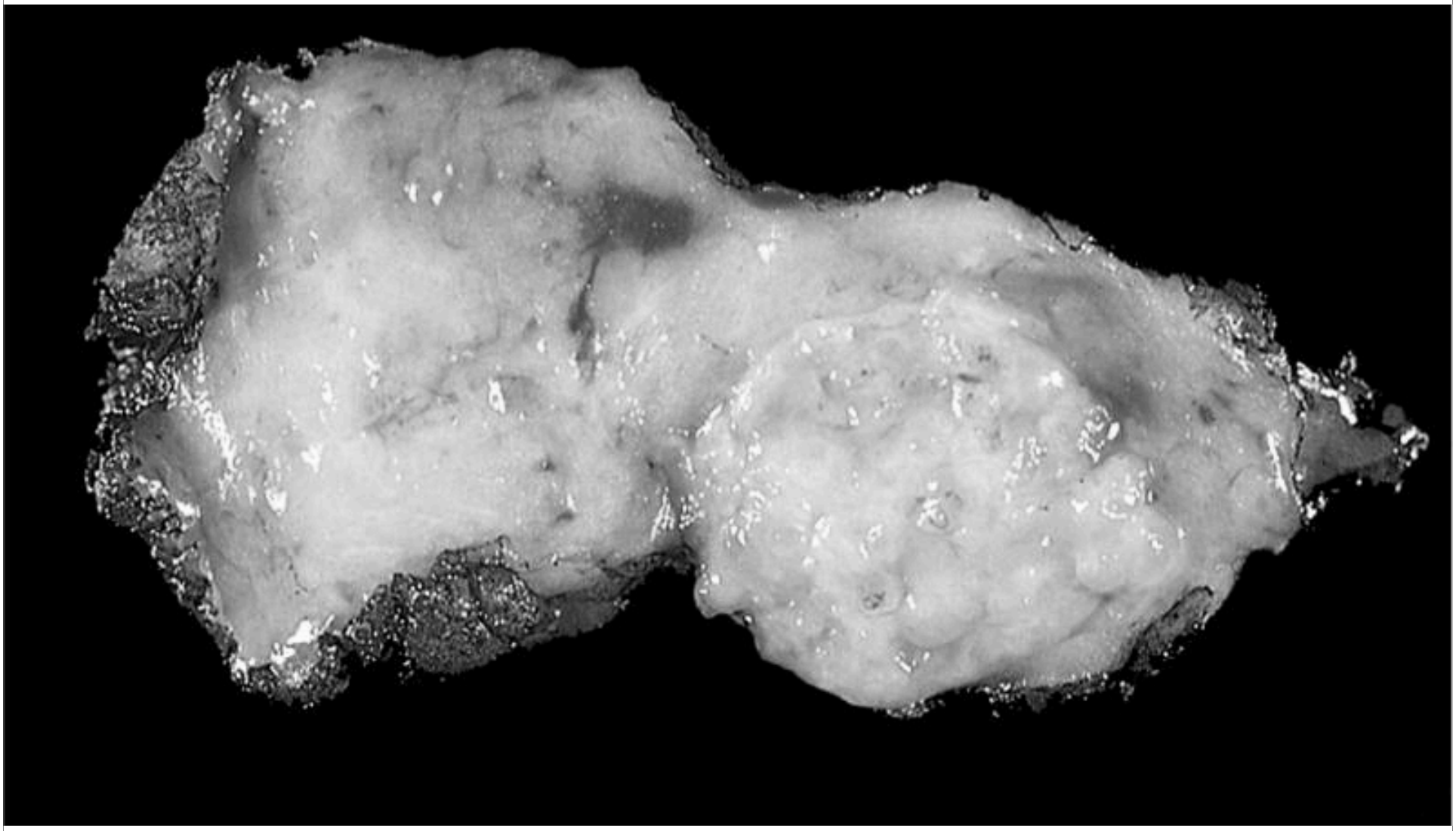
- Two kinds: nonproliferative and proliferative change
- Cause: exaggeration of normal breast cycles
- Rarely associated with increased cancer risk
- Very common (present in most women at autopsy)
- Called fibrocystic *change*, not fibrocystic *disease*



Fibrocystic change

Fibroadenoma

- Most common benign breast tumor
- Stimulated by estrogen
- Peak incidence in 20s
- Solitary, discrete, moveable mass
- Fibrous tissue with compressed ducts and lobules



Fibroadenoma

Breast Carcinoma

- 233,000 new cases / 40,000 deaths in 2014
- Most common, 2nd deadliest cancer in women
- Lifetime risk: 1 in 8
- 75% of patients are >50
- Rate was increasing but now stable

Breast Carcinoma Risk Factors

- Age
- Family history
- Increased estrogen exposure
- Obesity
- Alcohol consumption
- High-fat diet

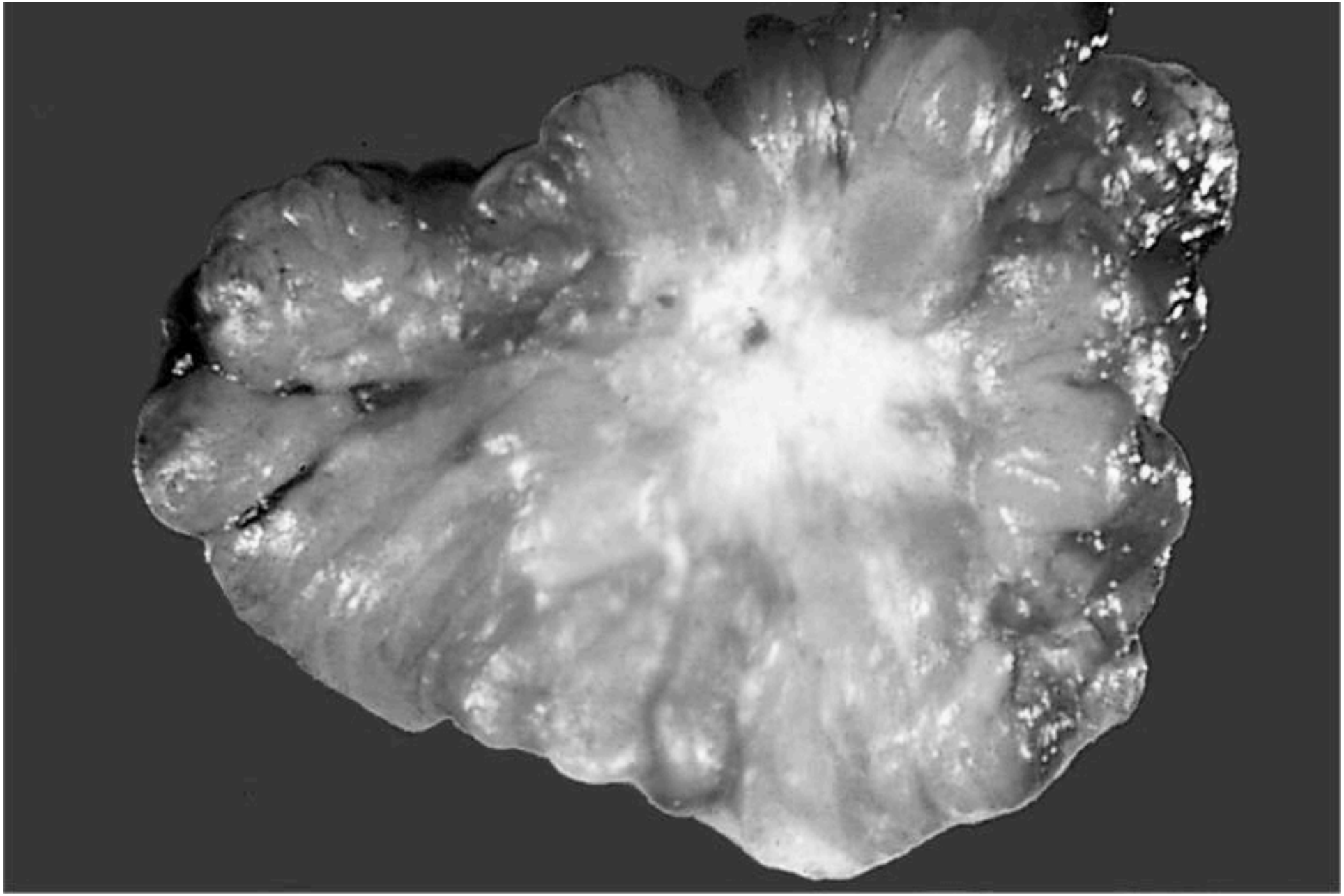
Breast Carcinoma Histologic Types

Non-invasive

- Ductal carcinoma in situ (DCIS)
- Lobular carcinoma in situ (LCIS)

Invasive

- Ductal
- Lobular
- Inflammatory
- Others



Invasive breast carcinoma