REKAP DAFTAR HADIR KULIAH PAKAR BLOK 20/GERONTOLOGI

SEMESTER GASAL TAHUN AKADEMIK 2020/2021

PERIODE : 21 NOVEMBER - 4 DESEMBER 2020

NO	NAMA DOSEN	DEPARTEMEN	JLH JAM RENCANA	BLOK 20/GERONTOLOGI								REALISASI KP
				NOVEMBER				DESEMBER				
				24	25	26	27	1	2	3	4	
1	dr. Agus Yudha Wijaya, SpS M.Si.Med.	Neurologi	4	4	-	-	-	-	-	-	-	4
2	dr. Bellinda J. L. Latumente, Sp.KFR	Bedah	4	4	-	-	-	-	-	-	-	4
3	dr. Nia Reviani, MAPS	Kedokteran Komunitas	4	4	-	-	-	-	-	-	-	4
4	dr. Kurniyanto, SpPD	Ilmu Penyakit Dalam	4	-	4	-	-	-	-	-	-	4
5	Dr. dr. Ago Harlim, SpKK, M.Sc., MARS	Ilmu Kes. Kulit & Kelamin	4	-	-	4	-	-	-	-	-	4
6	dr. Veronica N. K. Dewi Kalay, M.Biomed.	Mikrobiologi	4	-	-	-	4	-	-	-	-	4
7	Dr.med. Dr. Abraham Simatupang, M.Kes.	Farmakologi Terapi	4	-	-	-	-	4	-	-	-	4
8	dr. Ruyandi Hutasoit, SpBU	Bedah	4	-	-	-	-	4	-	-	-	4
9	dr. Dwi Karlina, SpKJ	Psikiatri	4	-	-	-	-	4	-	-	-	4
10	dr. Hildebrand Hanoch Victor W, SpPD	Ilmu Penyakit Dalam	4	-	-	-	-	-	-	4	-	4
11	dr. Tiroy Sari Bumi Simanjuntak, SpPD	Ilmu Penyakit Dalam	4	-	-	-	-	-	4	-	-	4
12	dr. Fajar L. Gultom, SpPA	Pato. Anatomi	4	-	-	-	-	-	-	-	4	4
Total			48									48
PERSENTASI KEHADIRAN KULIAH PAKAR BLOK 20			100%									

Jakarta, 6 Desember 2020

Mengetahui
Manager P2SK,

Dra. Lusia Sri Sunarti, MS

Koordinator Blok 20,

Dr. dr. Forman Erwin Siagian, M.Biomed.

Universitas Kristen Indonesia
Fakultas Kedokteran

SURAT KEPUTUSAN
No. : 165/UKI.F5.D/HKP.3.5.6/2020
tentang

PENUGASAN TENAGA AKADEMIK DALAM MEMBERIKAN KULIAH PAKAR PIMPINAN FAKULTAS KEDOKTERAN UNIVERSITAS KRISTEN INDONESIA

MENIMBANG : Bahwa untuk kelancaran proses belajar mengajar dan meningkatkan mutu pendidikan di FKUKI diperlukan penugasan tenaga akademik FKUKI untuk memberikan Kuliah Pakar

MENGINGAT :
1. Peraturan Pemerintah No. 60 tahun 1999 tentang Pendidikan Tinggi
2. Surat Keputusan Dekan FKUKI No. 53/SK/FKUKI/11.2006 tanggal 21 November 2006 tentang Pemberlakuan Kurikulum Berbasis Kompetensi (KBK) di FKUKI
3. Surat Keputusan Rektor UKI No. 90/UKI.R/SK/SDM.8/2018 tentang pengangkatan Dekan Fakultas Kedokteran UKI
4. Surat keputusan pengangkatan sebagai tenaga akademik

MEMUTUSKAN

MENETAPKAN :
1. Penugasan dalam memberikan Kuliah Pakar :

Nama	dr. Fajar Gultom, SpPA
Departemen	Patologi Anatomi
Blok	20 (Gerontologi)
Judul Materi	Gambaran Patologi Anatomi pada Lanjut Usia
Semester	gasal 2020/2021
Kelas	A : 0,21 SKS
	B : 0,21 SKS
SKS	0,42 SKS

2. Apabila dikemudian hari ternyata terdapat kekeliruan dalam Surat Keputusan ini akan diperbaiki sebagaimana mestinya

Asli Surat Keputusan ini disampaikan kepada yang bersangkutan untuk diketahui

Ditetapkan di : Jakarta
Pada tanggal : 10 September 2020
Dekan,

Dr. dr. Robert Hotman Sirait, Sp.An.
NIP. UKI. 051 545

Tembusan:
1. Rektor UKI
2. Wakil Dekan Bidang Akademik FKUKI

Jl. Mayjen Sutoyo no.2 Cawang - Jakarta 13630 INDONESIA Tel. 021.29362033,Tel. Langsung 021.29362038, Faks. 021.29362036 E-mail: fk-uki@uki.ac.id http://www.uki.ac.id

“Cellular Aging”

Fajar L. Gultom
Patologi Anatomik
Fakultas Kedokteran
Universitas Kristen Indonesia
Desember 2020

Aging

Definition

Starting at what is commonly called middle age, operations of the human body begin to be more vulnerable to daily wear and tear; there is a general decline in physical, and possibly mental, functioning. In the Western countries, the length of life is often into the 70s. The upward limit of the life span, however, can be as high as 120 years. During the latter half of life, an individual is more prone to have problems with the various functions of the body and to develop any number of chronic or fatal diseases. The cardiovascular, digestive, excretory, nervous, reproductive and urinary systems are particularly affected. The most common diseases of aging include Alzheimer's, arthritis, **cancer**, diabetes, depression, and heart disease.

http://medical-dictionary.thefreedictionary.com/aging

Aging:

Perubahan struktural bertahap yang terjadi seiring berjalannya waktu, bukan diakibatkan oleh penyakit/ kecelakaan, dan akhirnya menyebabkan kematian.

-Kamus Saku Kedokteran Dorland ed 29, 2015-

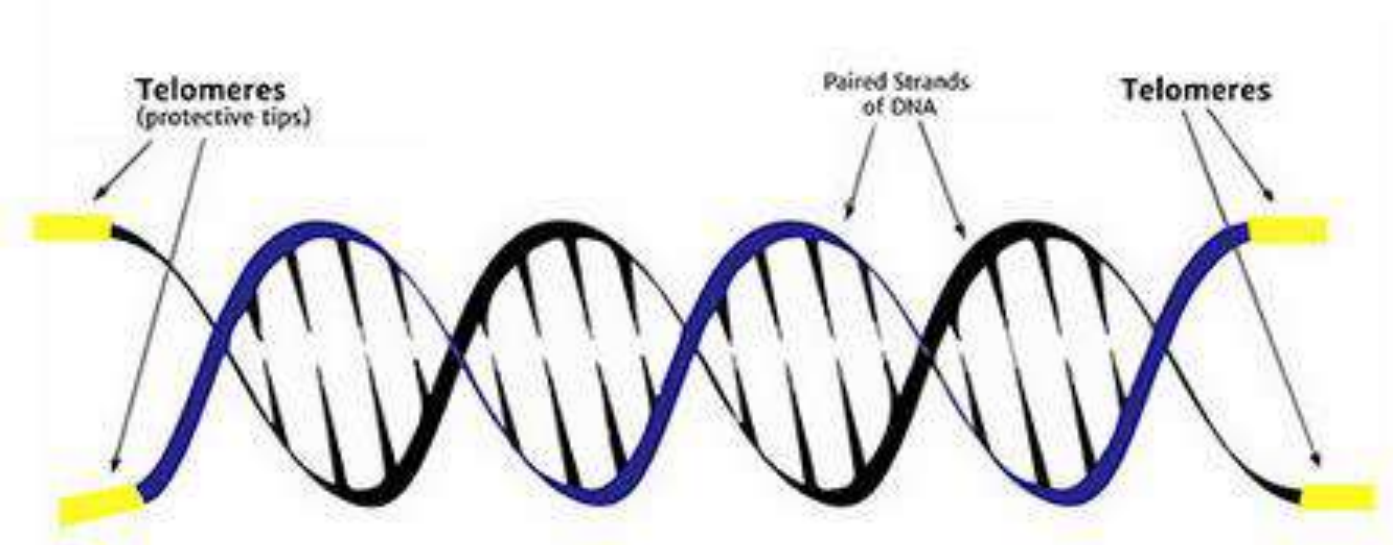
Cellular aging

- Individuals age → cells age
- Public focus → cosmetic only…→ **Elixir of youth**
- Age → **INDEPENDENT RISK FACTOR**: cancer, alzheimer, ischemic heart disease
- Progressive decline: life span and functional capacity of cells

Cellular aging

Several mechanisms:

- DNA damage → DNA repair enzymes ↓
- Decreased cellular replication
- Defective protein homeostasis



https://www.tasciences.com/what-is-a-telomere/

DNA damage

- Exogenous agents (physical, chemical, biologic) & Endogenous agents: ROS
- Threaten integrity nuclear and mitochondrial DNA
- DNA damage → DNA repair → some persist and accumulate
- Next Generation Sequencing (NGS) study→ hematopoietic stem cell suffers 14 mutation per year

Cellular Senescence

- All normal cells have limited capacity for replication
- Non dividing state → Replicative senescence
- Telomeres:
  - Sequences DNA → ends of chromosome
  - Ensuring complete replication → protecting from fusion and degradation
- Progressive shortening telomeres → ends of chromosome cannot be protected → cell cycle arrest
- Telomerase → maintained telomere length

Cellular Senescence

- Telomerase:
  - Germ cells: **expressed**
  - Stem cell: **low level**
  - Somatic cell: **absent**
  - Cancer cells: **Reactivated**
- Activation tumor suppressor gene: CDKN2A

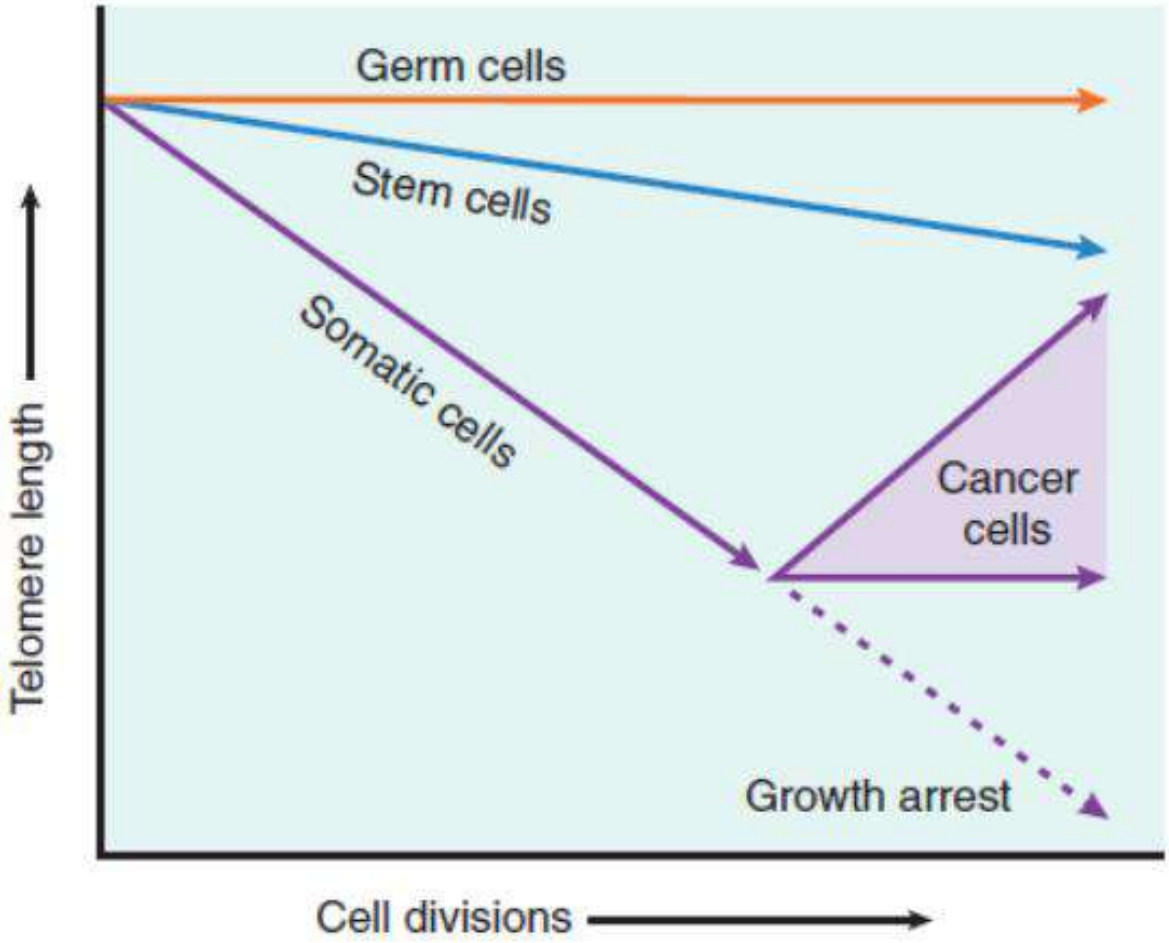


Figure 1–30 The role of telomeres and telomerase in replicative senescence of cells. Telomere length is plotted against the number of cell divisions. In most normal somatic cells there is no telomerase activity, and telomeres progressively shorten with increasing cell divisions until growth arrest, or senescence, occurs. Germ cells and stem cells both contain active telomerase, but only the germ cells have sufficient levels of the enzyme to stabilize telomere length completely. In cancer cells, telomerase is often reactivated.

Robbins basic pathology 9th ed, 2015

Cellular Aging Mechanism and Counteract

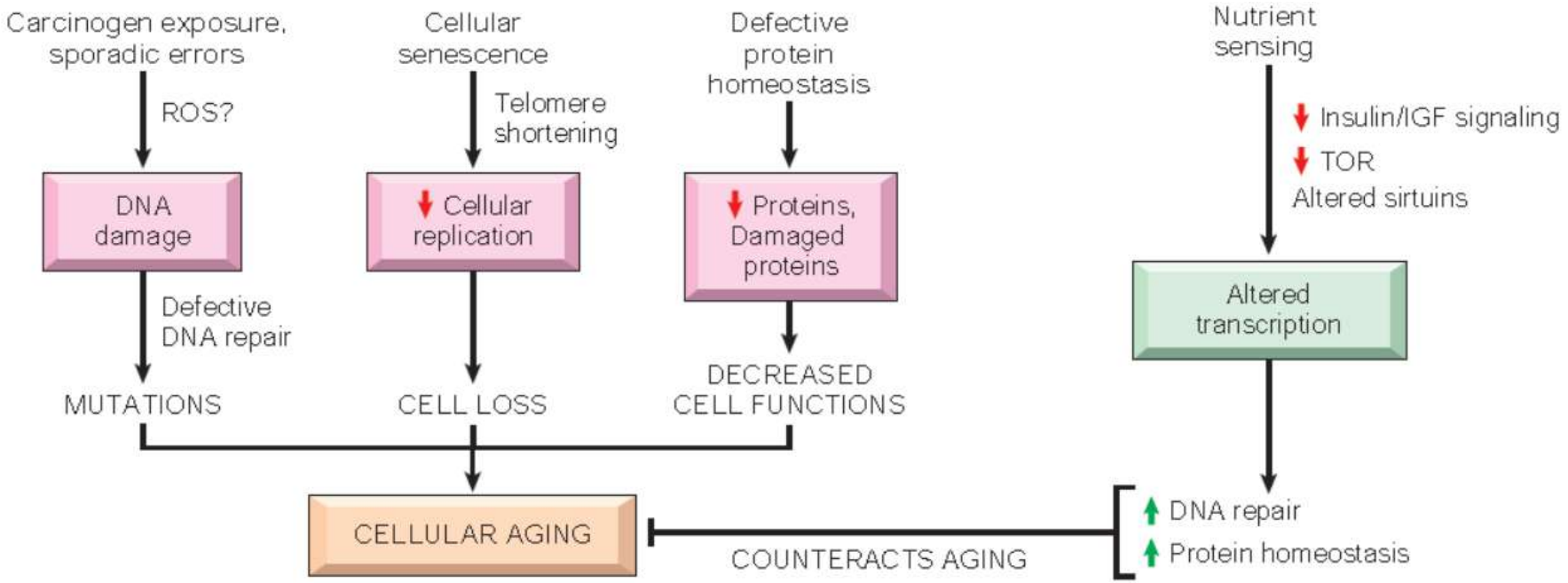


Figure 2-35 Mechanisms that cause and counteract cellular aging. DNA damage, replicative senescence, and decreased and misfolded proteins are among the best described mechanisms of cellular aging. Nutrient sensing exemplified by calorie restriction, counteracts aging by activating various signaling pathways and transcription factors. IG, Insulin-like growth factor; TOR, target of rapamycin.

Robbins basic pathology 9th ed, 2015

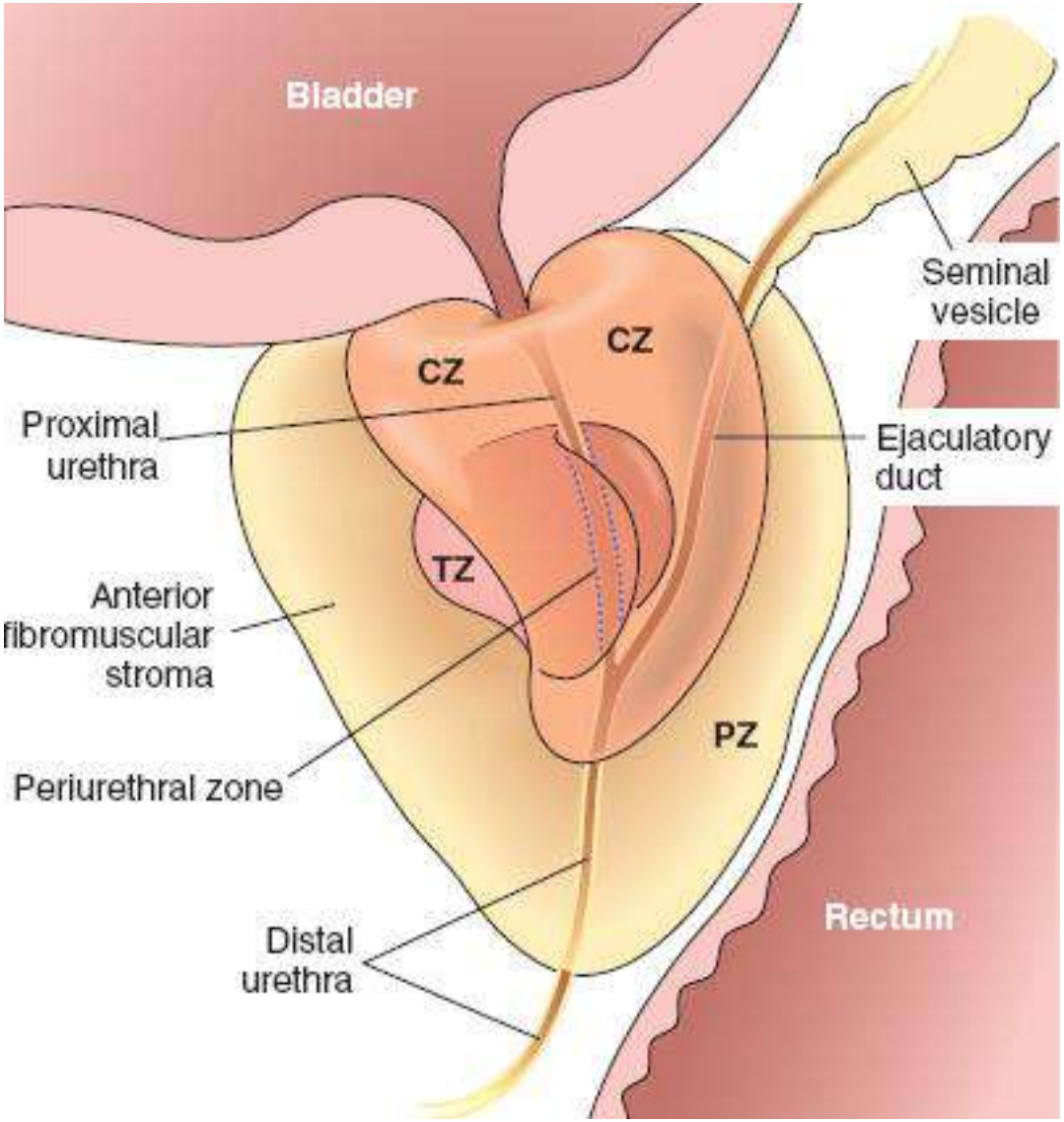
BPH

- Men > 50 yrs (50%)
- Urinary obstruction – LUTS
- Hesitancy, intermitten interruption, urgency, frequency, nocturia - UTI
- **Central zone different with Prostate Ca (peripheral zone)**

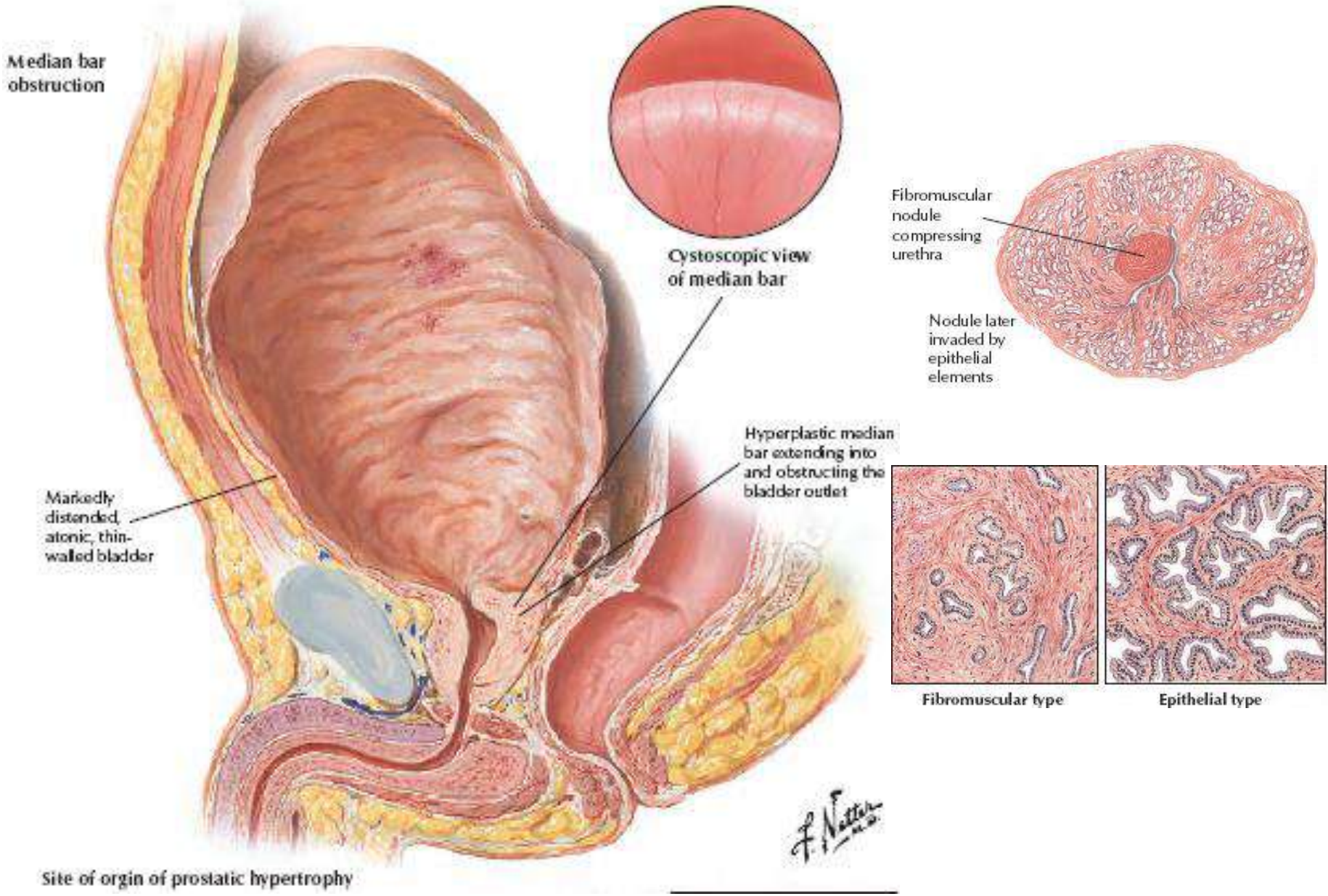
BPH

- Androgen dependent growth – castrated before puberty ≠ BPH
- Testosterone (T) → Dihydrotestosterone (DHT) → proliferation of stromal cell n glands
- Proliferation of glands and stromal → compress urethra
- Th/
  - Inhibit DHT formation (≠ enzyme 5 αR1, 2): dutasteride, finasteride
  - - α blocker
- Surgery (Radical prostatectomy) or **T**rans**U**rethral **R**esection **P**rostate (TUR-P)

BPH

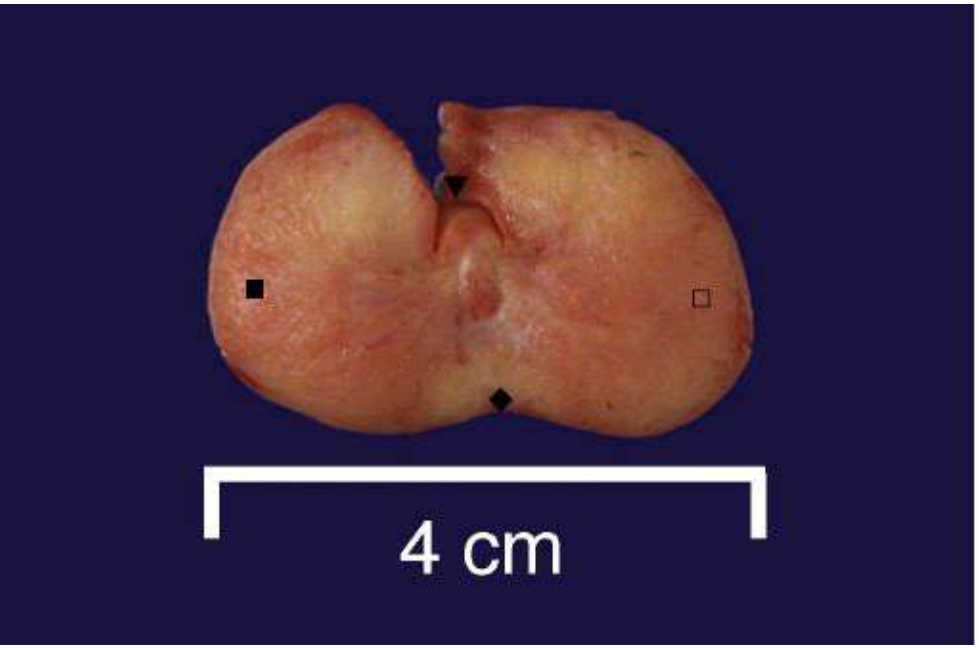


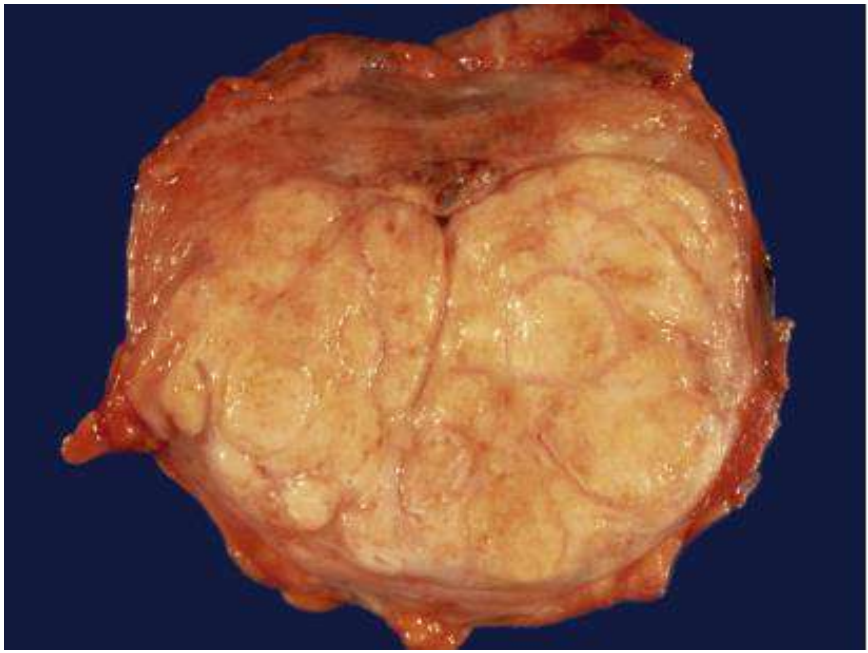
Robbins basic pathology 9th ed, 2013



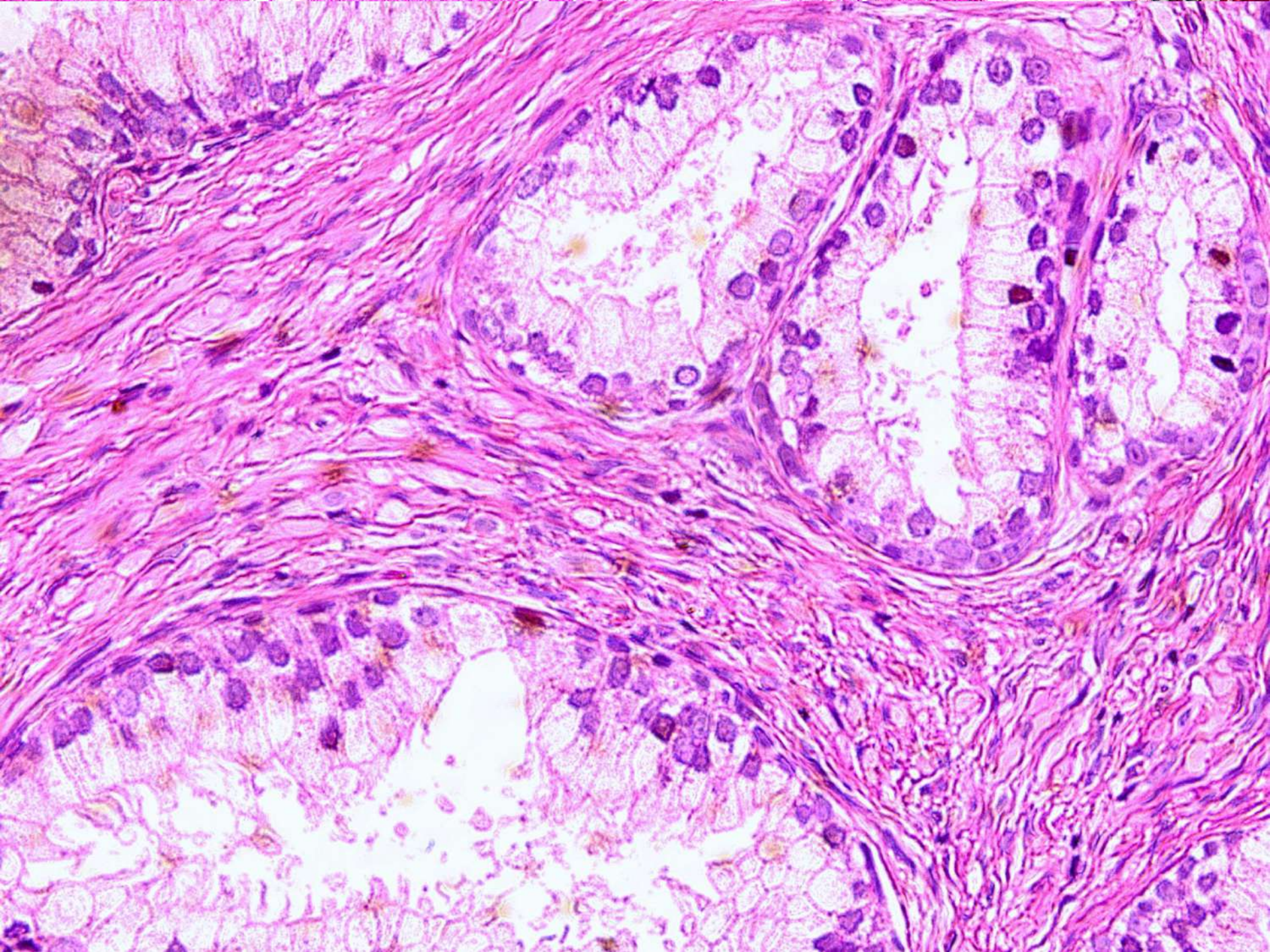
Netter's Illustrated human pathology. 2014

BPH





BPH VS normal ??



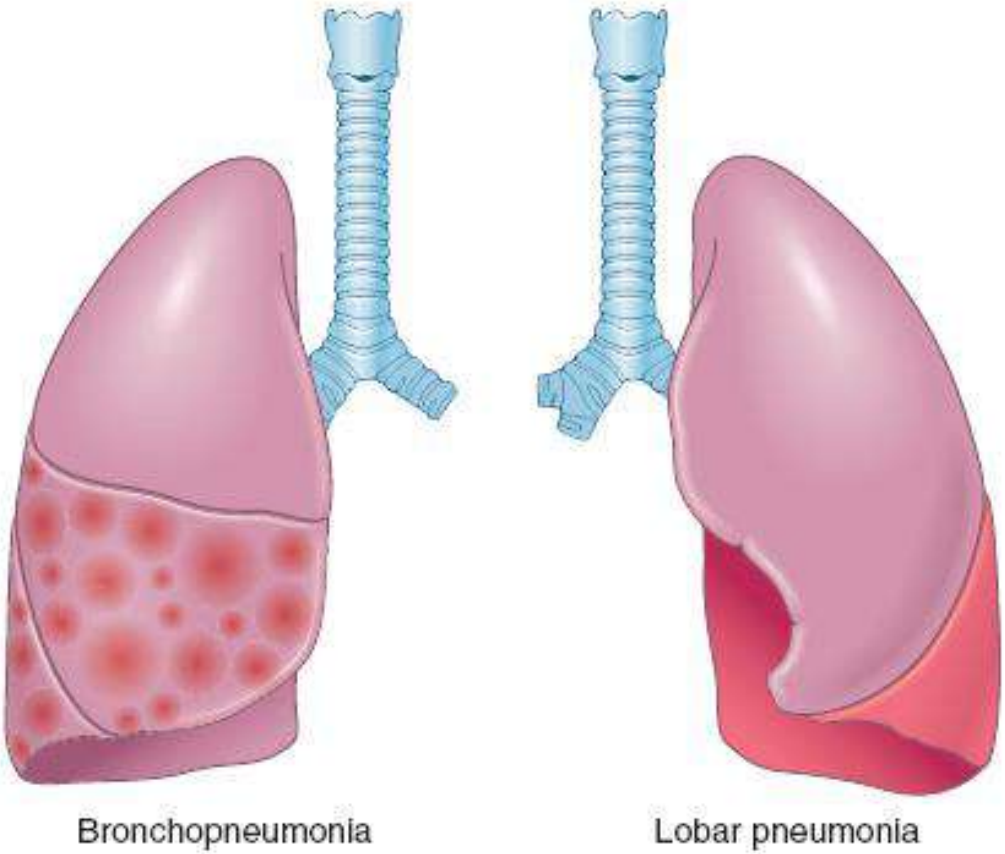
Pulmonary infection

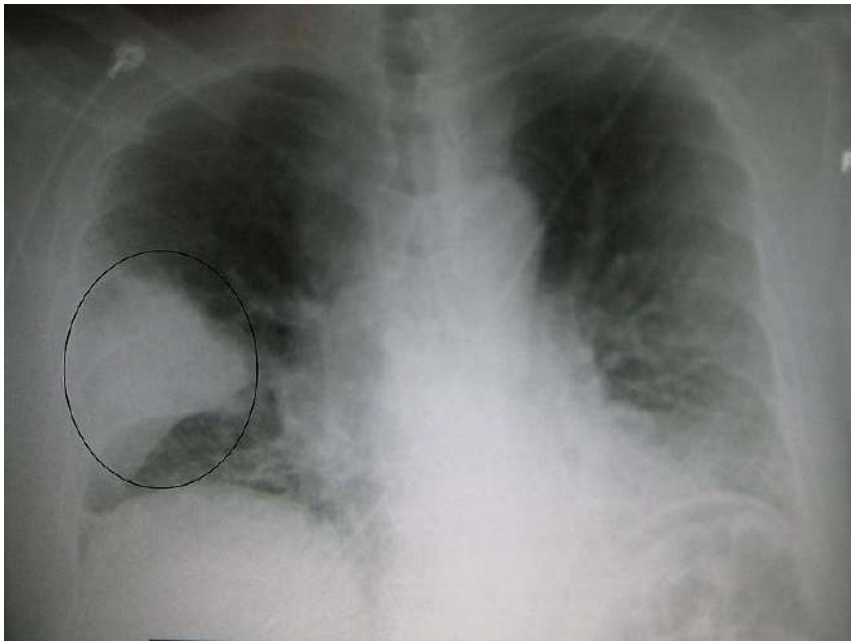
- **PNEUMONIA**
- 1/6 all deaths in US
- Streptococcus pneumonia > 90%
- Bronchopneumonia – lobar pneumonia
- Anatomic n radiologic

Pneumonia

“Radang paru-paru yang disertai eksudasi dan konsolidasi, biasanya disebabkan oleh mikroorganisme seperti bakteri, jamur, virus dan parasite”

Dorland, 2014





BLURRY…..

Classify – etiology or clinical settings

Pneumonia

- **Community-acquired pneumonia**
- **Health care-associated pneumonia**
- **Hospital-associated pneumonia**
- Aspiration pneumonia
- Chronic pneumonia
- Necrotizing pneumonia and lung abscess
- Pneumonia in compromised host

CAP - HAP

- Community acquired pneumonia (CAP)

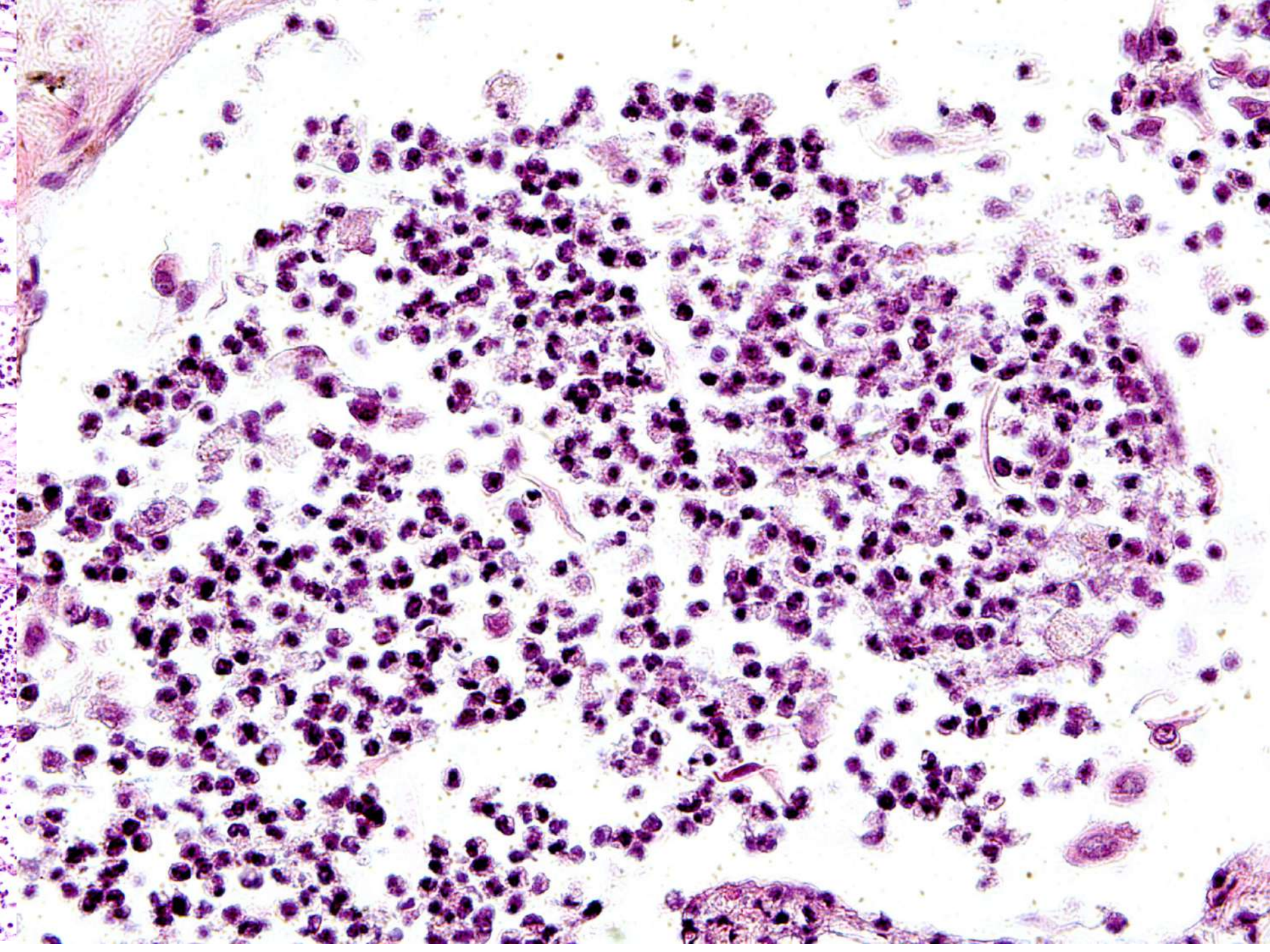
  S. pneumonia, H. influenzae,….

- Health care-associated pneumonia

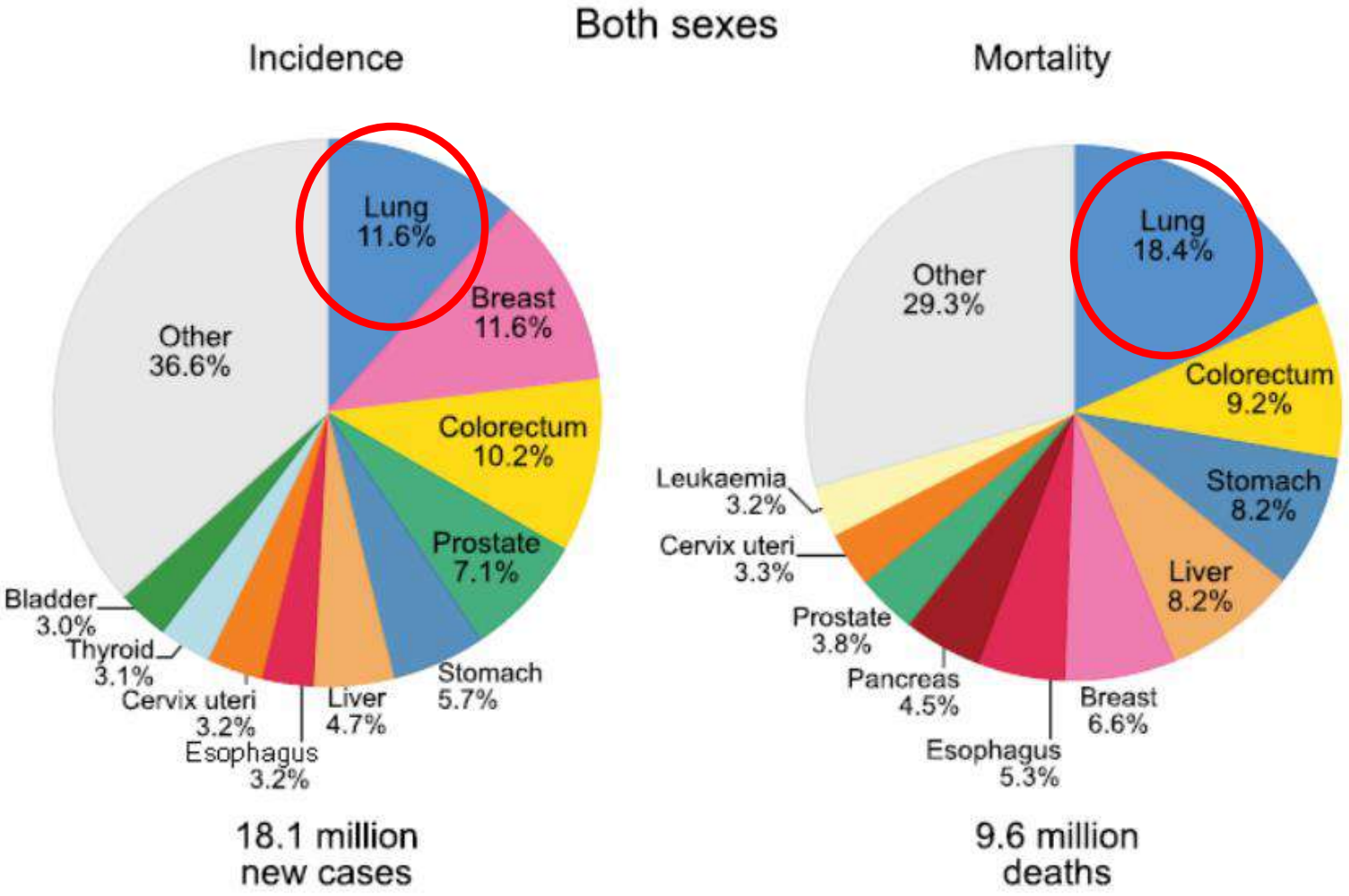
  S. aureus, Pseudomonas

- Hospital acquired pneumonia (HAP)

  Gram negative rods, enterobactericeae (Klebsiella, E. coli)….



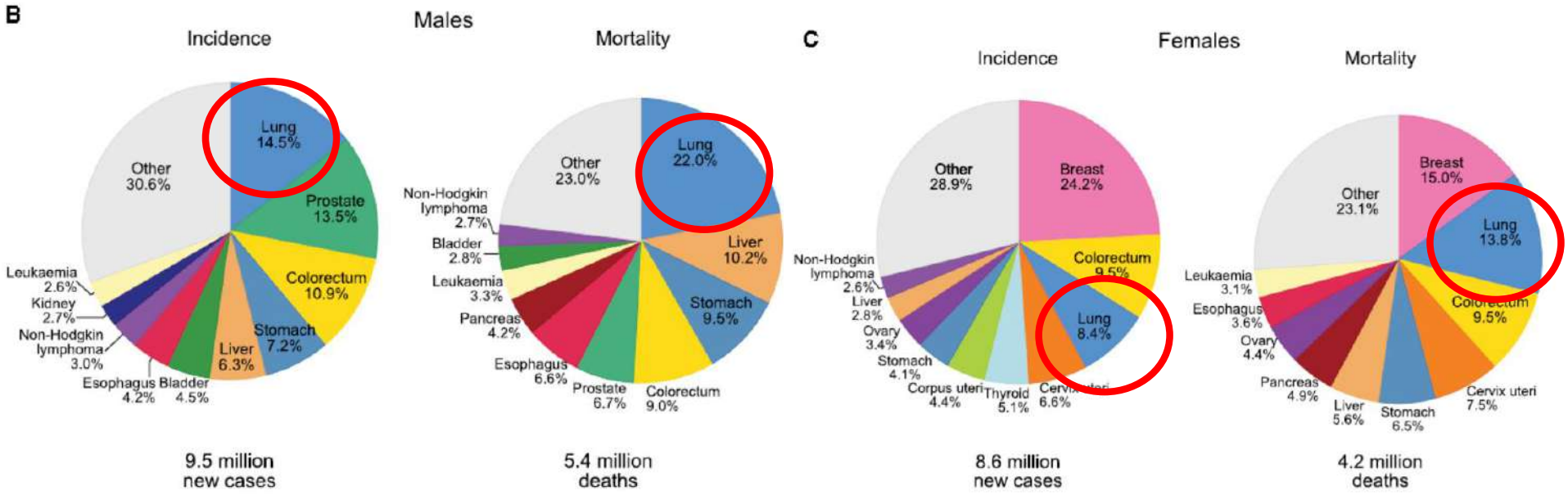
Lung Tumors



Lung cancer: 1st most frequently diagnosed and 1st leading cause of death

GLOBOCAN, 2018

Lung Tumors



GLOBOCAN, 2018

WHO, 2004

Table 1.06
Stage of lung carcinoma at presentation by histologic subtype. SEER data 1983-1987.
Modified, from reference {192}.

Stage	Squamous	Adenocarcinoma	Small cell	Large cell
Localized	21.5%	22.2%	8.2%	15.2%
Regional	38.5%	33.1%	26.1%	31.5%
Distant	25.2%	35.9%	52.8%	40.3%
Unstaged	14.8%	8.8%	12.8%	12.9%

60 – 70%

Poor prognosis…

Lung tumors

- Benign - malignant, epithelial – mesenchymal
- 90-95 % → carcinoma
- 5-10%: carcinoids, lymphoma
- **SMOKING RELATED…TOBACCO EPIDEMIC !!! polycyclic aromatic hydrocarbons, such as benzopyrene, anthracenes, radioactive isotopes**
- EGFR – KRAS mutation → personalized therapy

Lung tumors

TOBACCO EPIDEMIC !!!

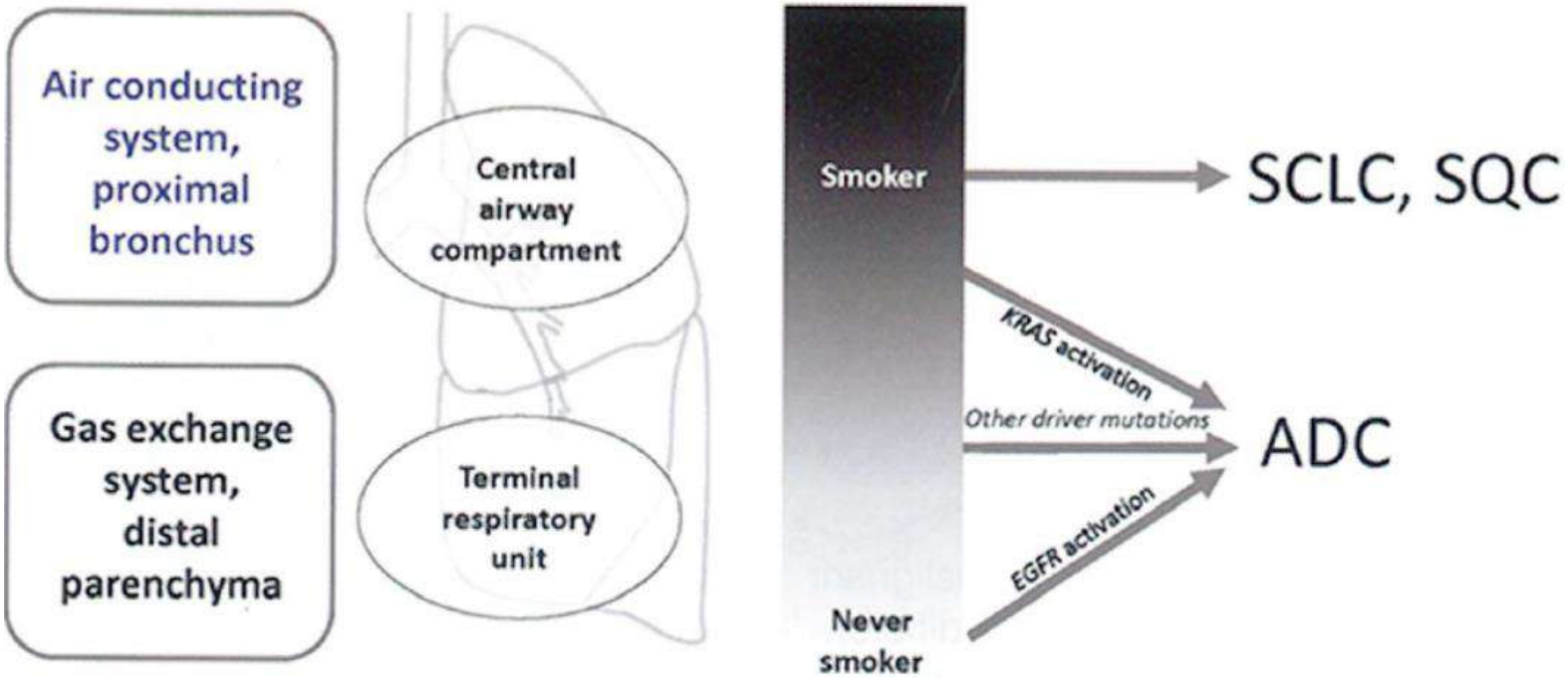
Lung cancer is one of the most preventable cancers. Most lung cancers could be avoided by eliminating smoking initiation and increasing smoking cessation among current smokers. This requires a comprehensive tobacco control program that includes raising the price of tobacco products through excise taxes, banning smoking in public places and tobacco sales to minors, restricting tobacco advertising and promotion, counteradvertising, and providing treatment and counseling for tobacco dependence. In the United States, comprehensive tobacco control programs in many states, including California and New York, have markedly decreased smoking rates and accelerated the reduction in

Lung tumors

- Small cell lung cancer (SCLC)
- Non-small cell lung cancer (NSCLC)
  - Adenocarcinoma
  - Squamous cell carcinoma
  - Large cell carcinoma

- Why?? **Management…**

Concept Two Compartment Model in Molecular Pathogenesis Lung Cancer



Travis et al. WHO Lung, thymus and heart. 2015

Prior WHO 2004 classification

- Tumors other than small cell carcinoma (SCLC) lumped together → non-small cell carcinoma (NSCLC)
- No theurapetic implication for subtyping
- Light microscopy → only H&E stained

WHO Lung, Thymus and Heart (2015)

Non small cell lung cancer:

- **Adenocarcinoma**
- **Squamous cell carcinoma**
- Large cell neuroendocrine (NE) carcinoma
- Neuroendocrine/ Carcinoid tumor: Typical and Atypical
- Adenosquamous carcinoma
- Pleomorphic carcinoma
- Spindle cell carcinoma
- ……..

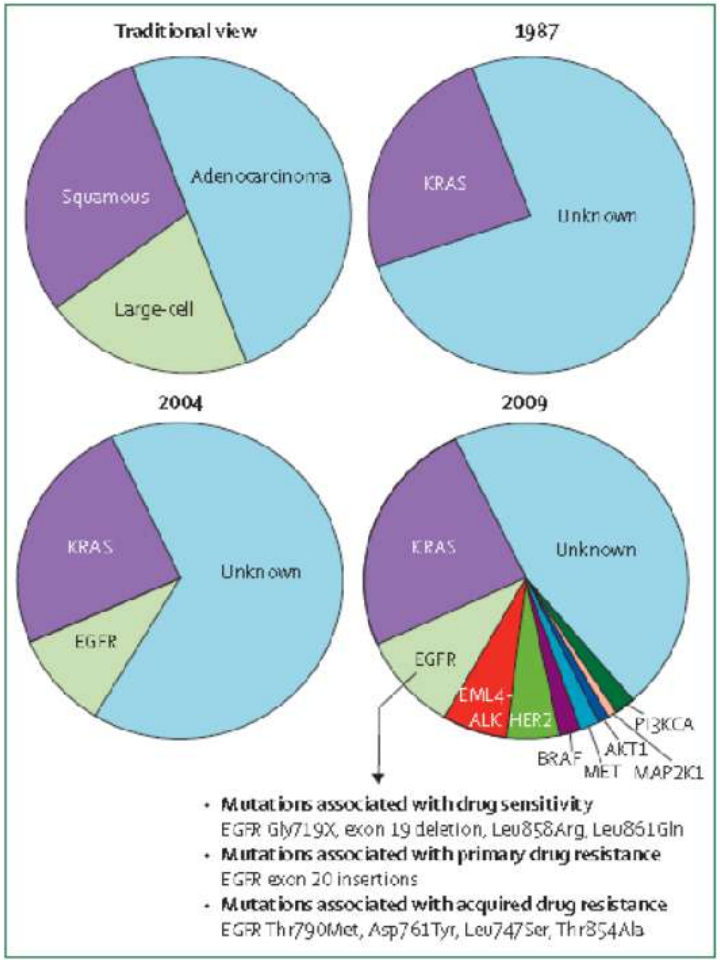
WHO Lung, Thymus and Heart (2015)

- Molecular biology and patient treatment
- EGFR gene mutation in lung adenocarcinoma → targeted therapy (gefitinib, erlotinib) → Significant response
- ALK inhibitor → crizotinib → adenocarcinoma with ALK fusion
- Molecular testing for treatment selection in lung cancer

- Bell DW et al. Epidermal growth factor receptor mutations and gene amplification innsclc. Molecular analysis of the IDEAL/INTACT gefitinib trials. J Clin Oncol. 2005
- Eberhard DA. Mutations in the egfr and in kras are predictive and prognostic indicators in nsclc treated with chemotherapy alone and in combination with erlotinib. J Clin Oncol 2005
- Kwak LE et al. Anaplastic lymphoma kinase inhibition innsclc. NEJM. 2010

Major Genetic Changes in Lung Cancer
"Oncogene Addiction"

Alterations	Small cell carcinoma (%)	Adenocarcinoma (%)	Squamous cell carcinoma (%)
Mutation			
BRAF	0	< 5	0
EGFR Caucasian	< 1	10–20	< 1
Asian	< 5	35–45	< 5
ERBB2/HER2	0	< 5	0
KRAS Caucasian	< 1	15–35	< 5
Asian	< 1	5–10	< 5
PIK3CA	< 5	< 5	5–15
RB	> 90	5–15	5–15
TP53	> 90	30–40	50–80
Amplification			
EGFR	< 1	5–10	10
ERBB2/HER2	< 1	< 5	< 1
MET	< 1	< 5	< 5
MYC	20–30	5–10	5–10
FGFR1	< 1	< 5	15–25
Gene rearrangement			
ALK	0	5	< 1
RET	0	1–2	0
ROS1	0	1–2	0
NTRK1	0	< 1	0
NRG1	0	< 1	0



- Travis et al. WHO Lung, thymus and heart. 2015.
- Pao W. New driver mutations in non-small lung cancer. Lancet Oncol. 2011

Adenocarcinoma

- Def: malignant epithelial tumor with glandular differentiation, mucin production or pneumocyte marker expression.
- Incidence → Lung cancer trends by histologic type
- Changes in design and characteristic of manufactured cigarretes
- Clinical features: variety of symptoms/ no symptoms at all. Progressive shortness of breath, cough, chest pain/ pressure, hoarseness, loss of voice, hemoptysis.
- Localization: **lung periphery**
- Adeno markers: TTF1, Napsin A

- Lewis et al. U.S. Lung cancer trends by histologic type. Cancer.2014

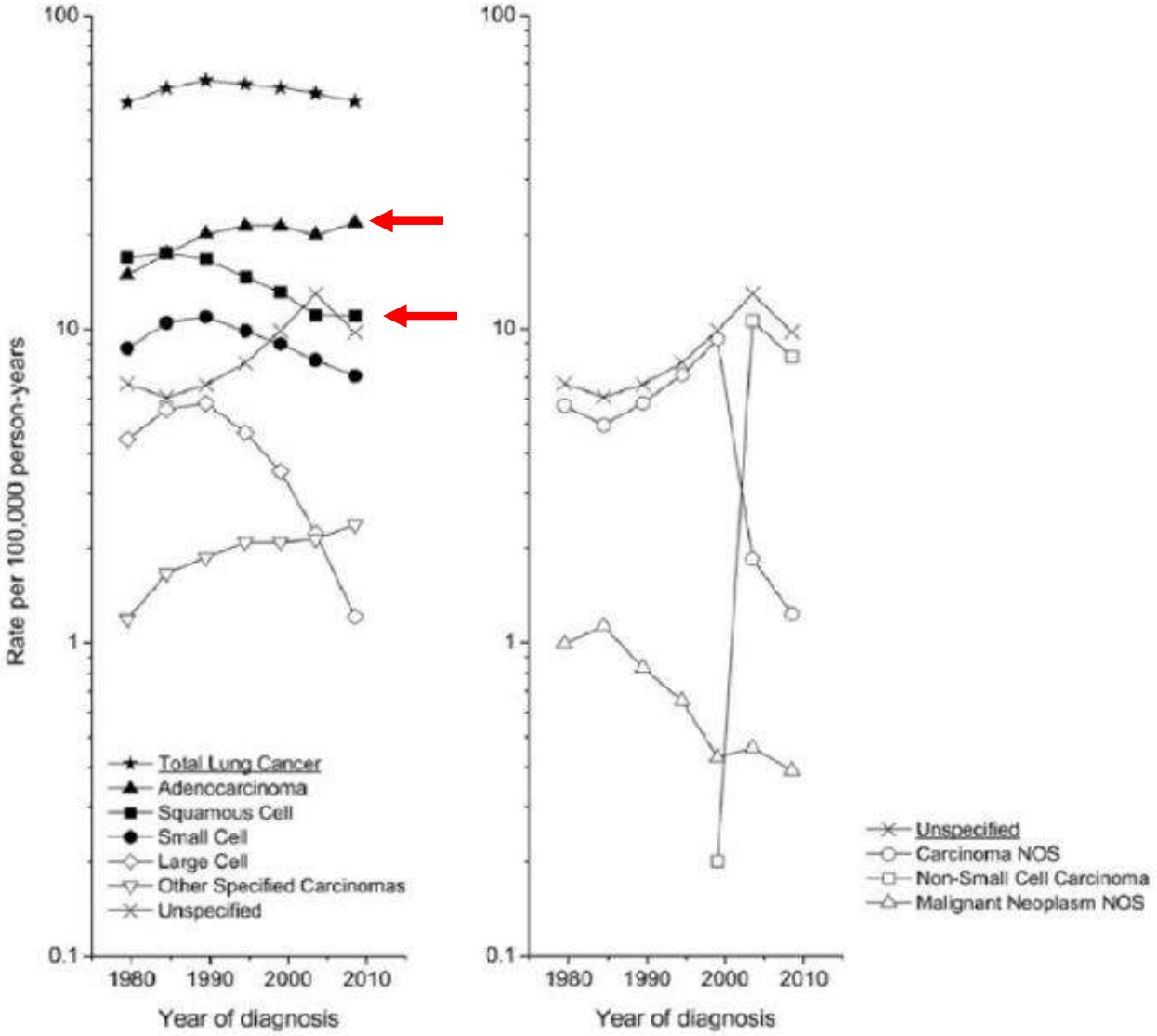
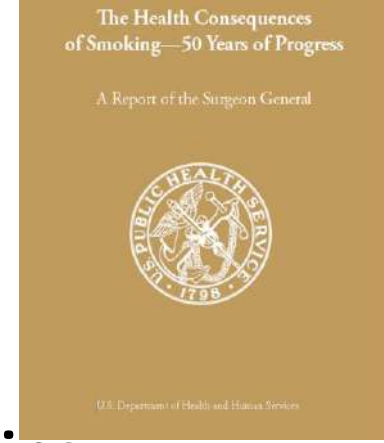


Figure 1.

Trends in lung cancer incidence rates (age-adjusted 2000 US standard) from 1977 to 1981 through 2006 to 2010 in the SEER 9 registries by histologic type.

- Lewis et al. U.S. Lung cancer trends by histologic type. Cancer.2014



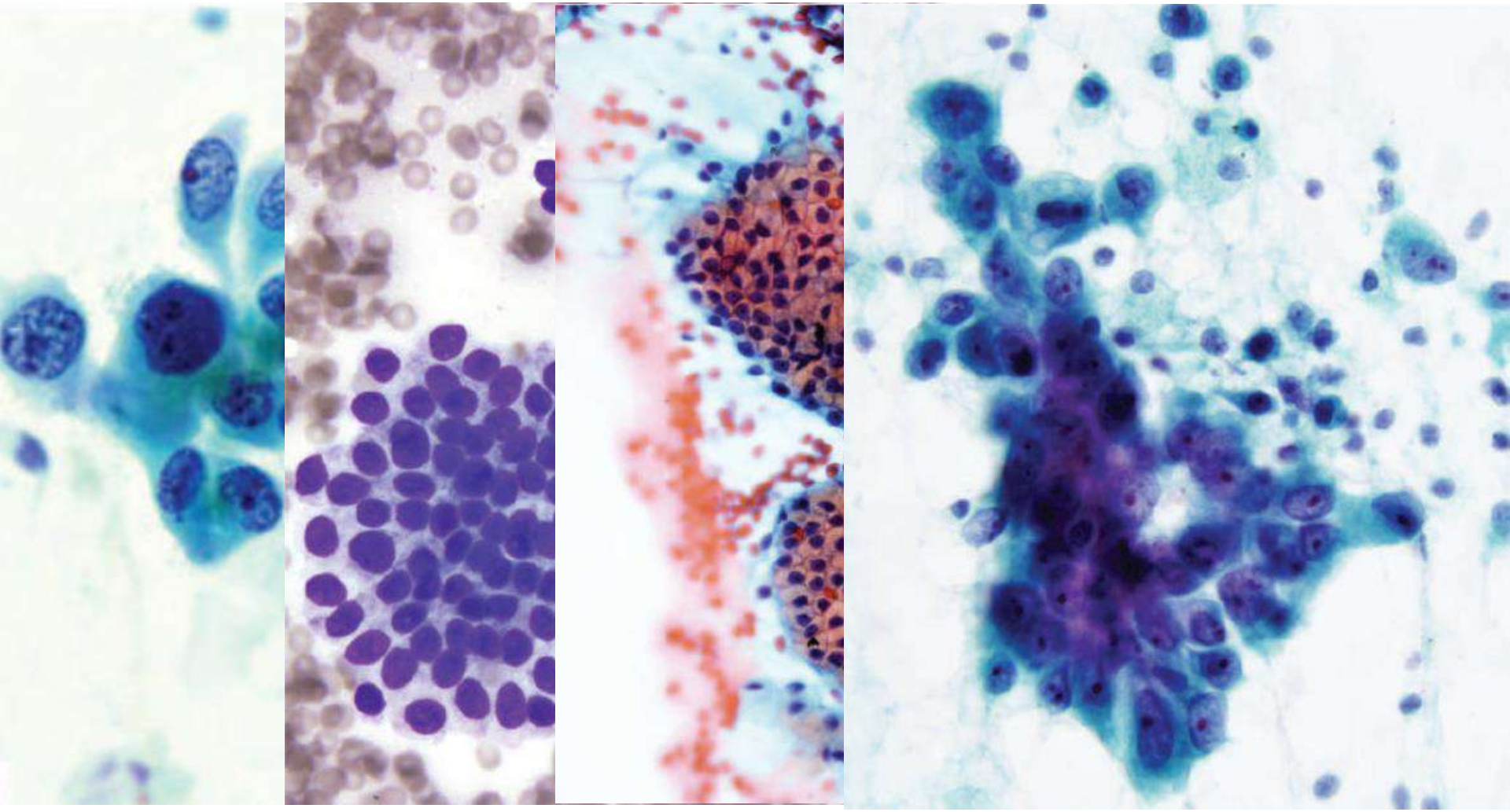
Adenocarcinoma

US Surgeon General's 2014 report:

1. The evidence is sufficient that the **risk of developing adenocarcinoma** of the lung from cigarette smoking has **increased since 1960s**
2. The evidence is sufficient that the **risk of adenocarcinoma in smokers** results from **changes in the design and composition of cigarettes since the 1950s**
3. The evidence is not sufficient to specify which design changes are responsible, **suggestive ventilated filters and increased levels of tobacco specific nitrosamines**
4. The evidence shows that the **decline of squamous cell carcinoma follows the trend of declining smoking prevalence**

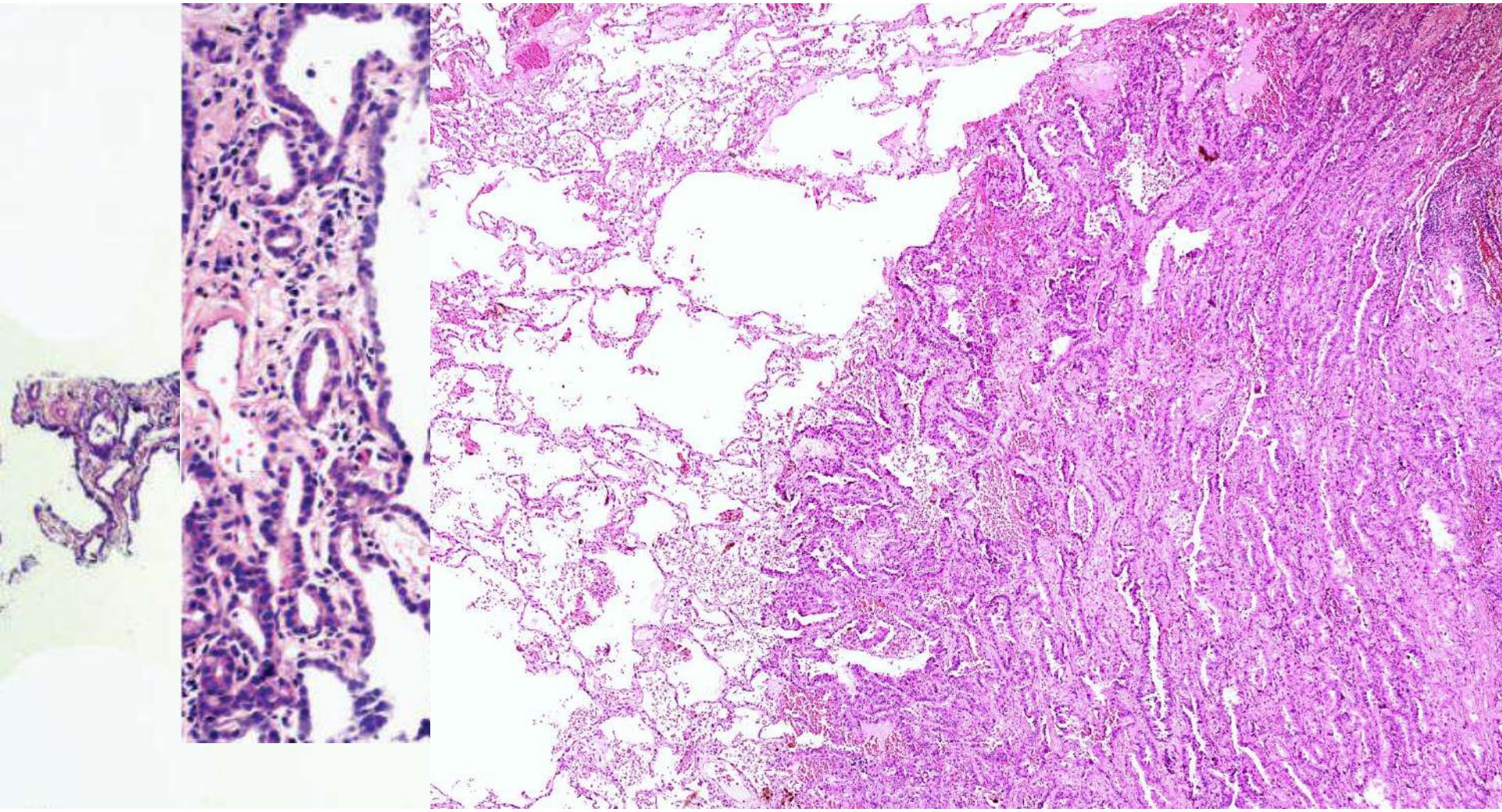
- US public health service office of the surgeon general and national center for chronic disease prevention and health promotion. The health consequences of smoking – 50 years of progress. 2014

Adenocarcinoma Cytology



- Travis WD. Diagnosis of lung cancer in small biopsies and cytology. Implications of the 2011 international association for study of lung cancer/ American thoracic society/ European respiratory society classification. Arch pathol lab med. 2013

Adenocarcinoma Histopatology



- Travis WD. Diagnosis of lung cancer in small biopsies and cytology. Implications of the 2011 international association for study of lung cancer/ American thoracic society/ European respiratory society classification. Arch pathol lab med. 2013

Osteoporosis

- Acquired condition → reduction of bone mass
- Osteopenia → osteoporosis
- Bone fragility – fracture
- US – 1,5 mil/ yr osteoporosis related fracture
- Primary or secondary
- Most common ???
- Senile osteoporosis – postmenopausal

Table 20–1 Categories of Generalized Osteoporosis

Primary
Postmenopausal
Senile
Secondary
Endocrine Disorders
Hyperparathyroidism
Hypo or hyperthyroidism
Hypogonadism
Pituitary tumors
Diabetes, type 1
Addison disease
Neoplasia
Drugs
Anticoagulants
Chemotherapy
Corticosteroids
Anticonvulsants
Alcohol
Miscellaneous
Osteogenesis imperfecta
Immobilization
Pulmonary disease
Homocystinuria
Anemia

Primary

Postmenopausal

Senile

Robbins basic pathology 9th ed, 2013

Osteoporosis

- Bone mass peak – young adulthood
- 3^{rd} – 4^{th} decade → bone resorption
- Bone loss – 0,5% per year → **inevitable**
- Abundant trabecular bone – spine, head of femur

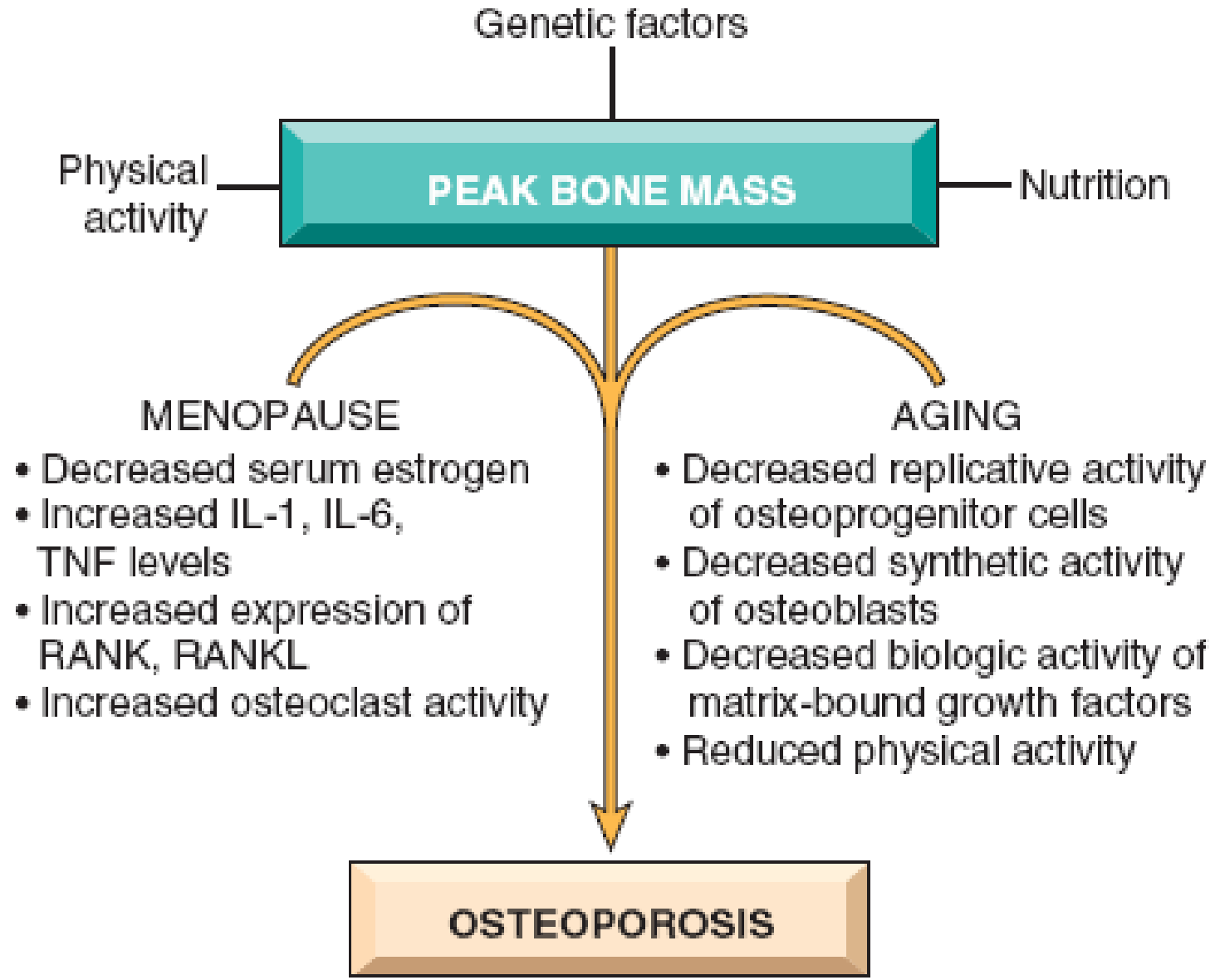


Figure 20–4 Pathophysiology of postmenopausal and senile osteoporosis (see text).

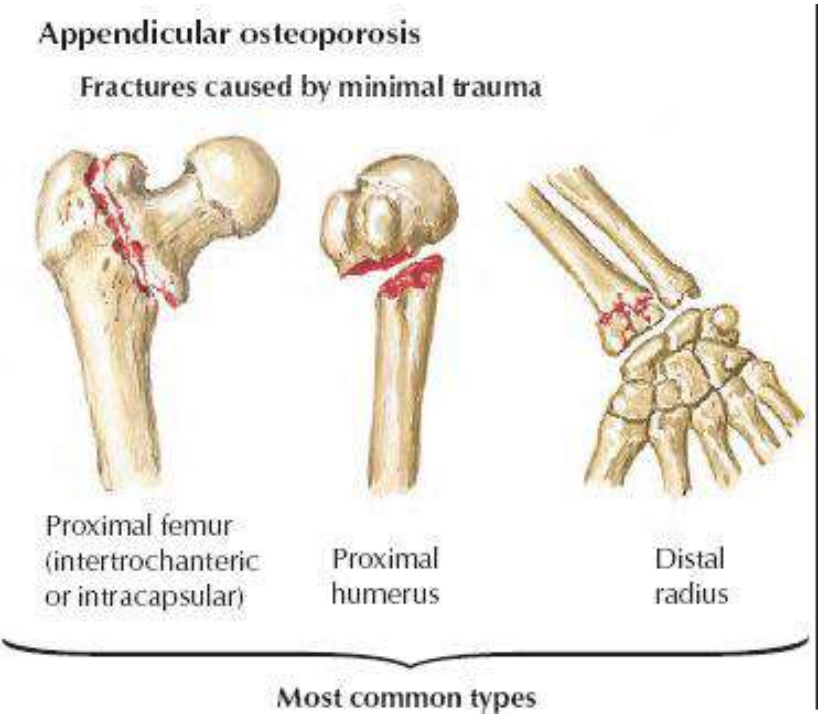
Robbins basic pathology 9th ed, 2015

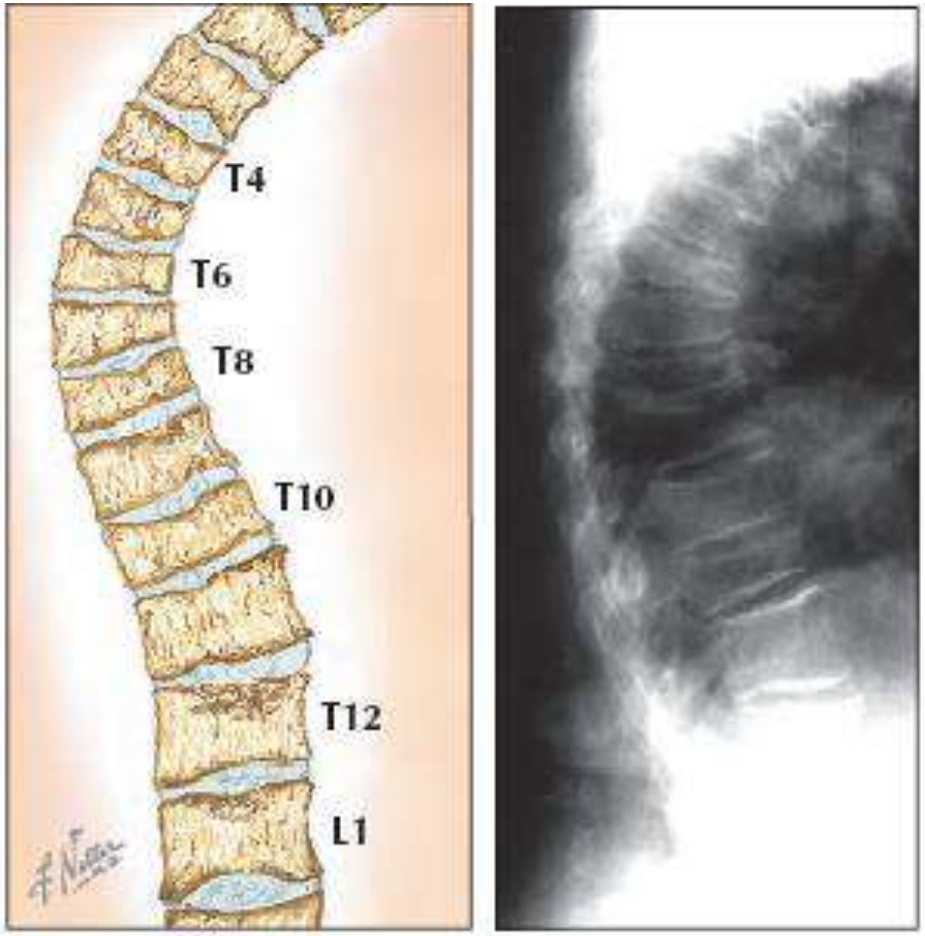
Pathogenesis

- Age-related change:

  Osteoblast <<, osteoclast N
- Hormonal influences: estrogen
- Physical activity
- Genetic factor
- Calcium nutritional state
- Secondary causes

Osteoporosis

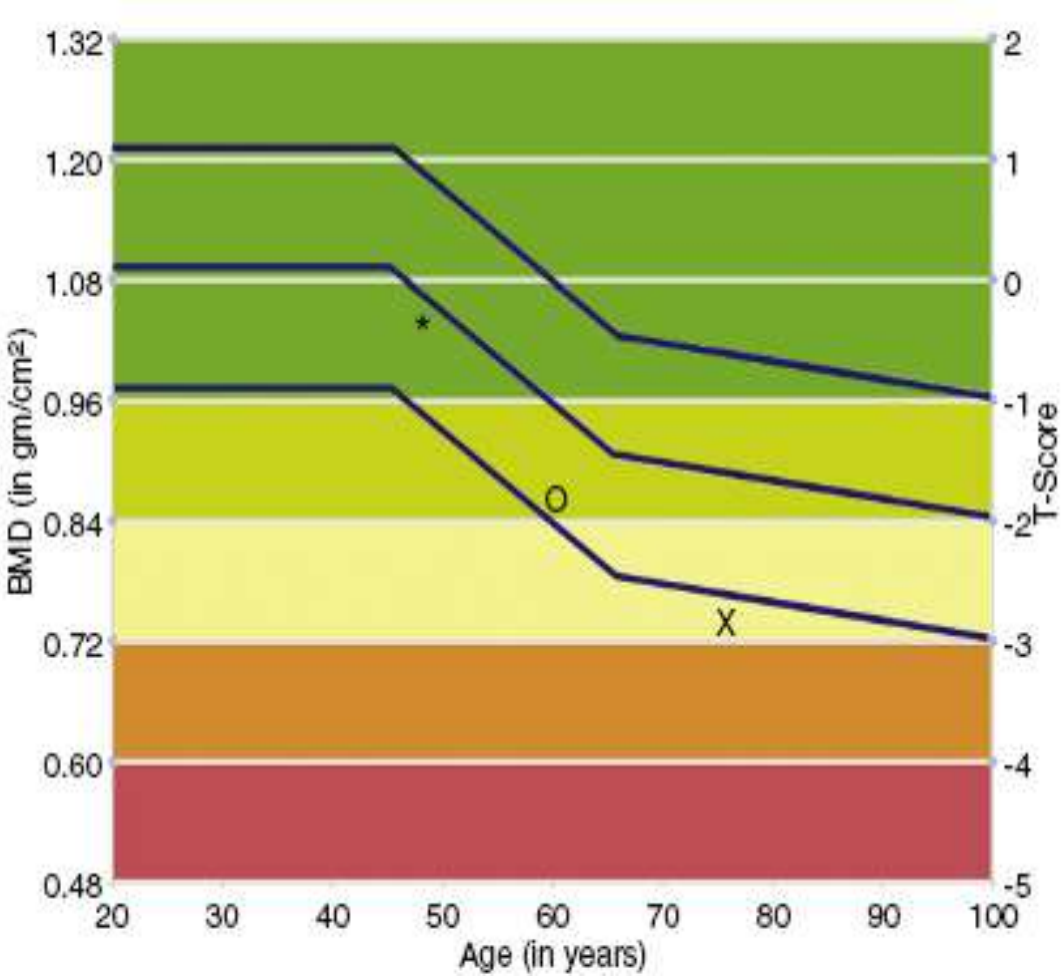




Multiple grade 3 compression fractures are evident in the thoracic vertebral bodies, resulting in marked kyphosis.

Netter's Illustrated human pathology. 2014

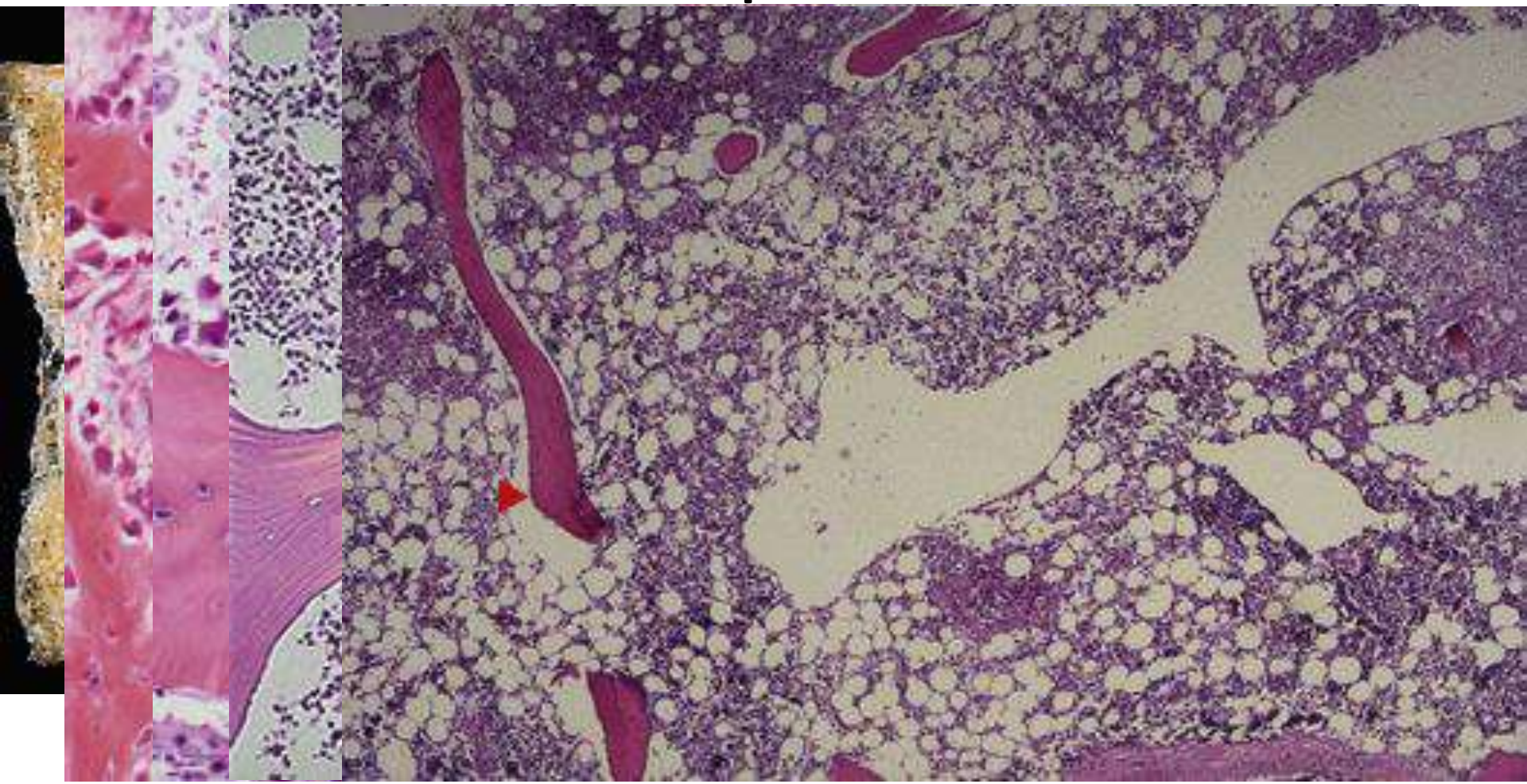
Osteoporosis



- BMD (bone mineral density)
- DEXA chart (Dual energy X ray absorptiometry)
- Osteopenia (-1 - -2,5)
- Osteoporosis (> -2,5)

Robbins and Cotrans atlas pathology 3th ed, 2015

Osteoporosis



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Osteoporosis Prevention

- Adequate dietary calcium intake.
- Vit D supplementation.
- Regular exercise regimen.
- Before age of 30.

Osteoarthritis

- Degenerative joint disease
- Frequent, aging > 65 yrs
- Inflammation? → degeneration articular cartilage
- Chondrocytes respon biomechanic n biologic stress → breakdown matrix
- Hands, knees, hips and spines
- Heberden nodes in finger
- Deep, pain exacerbated by use, morning stiffness, crepitus, limitation ROM

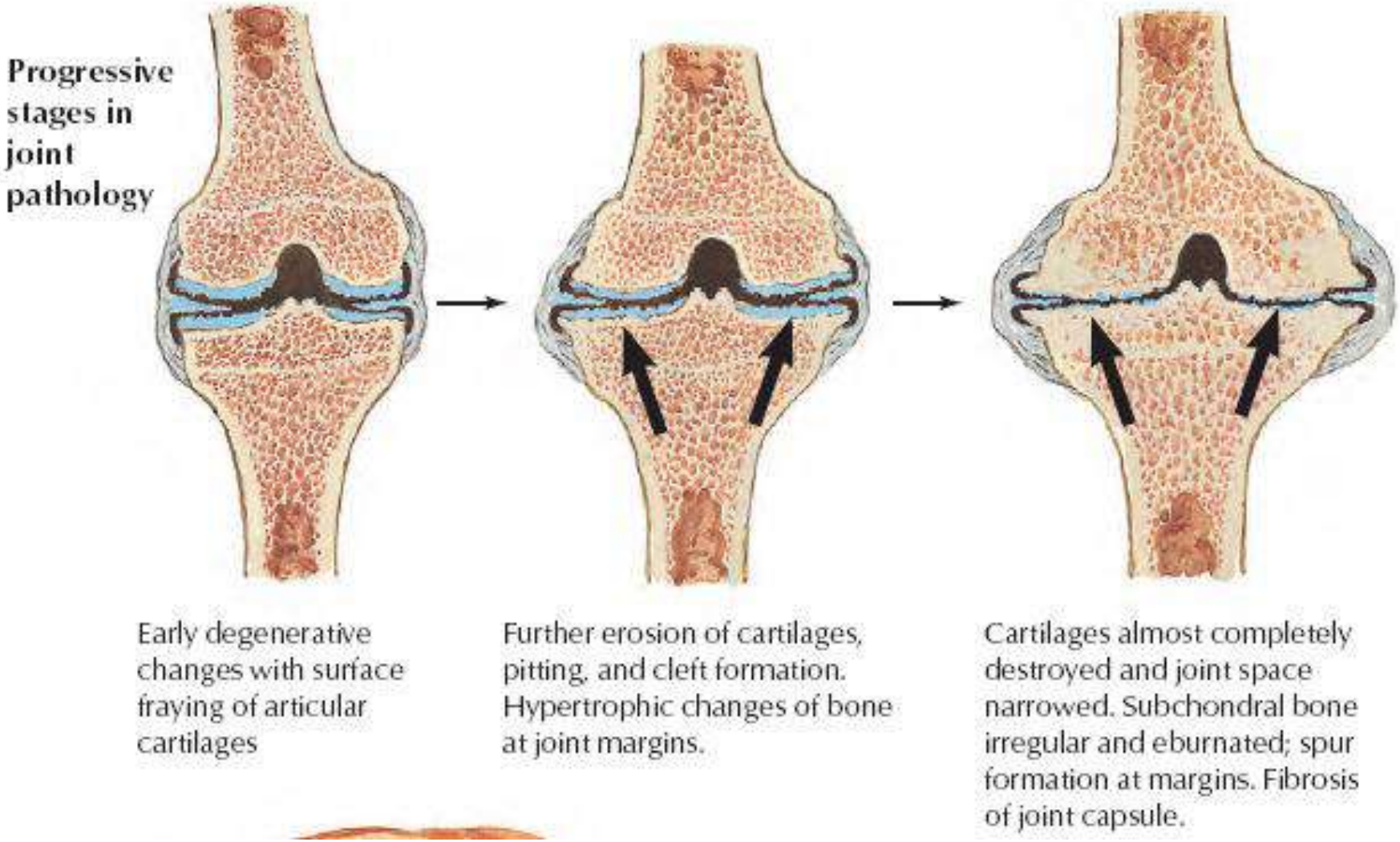
Osteoarthritis

Normal articular cartilago function:

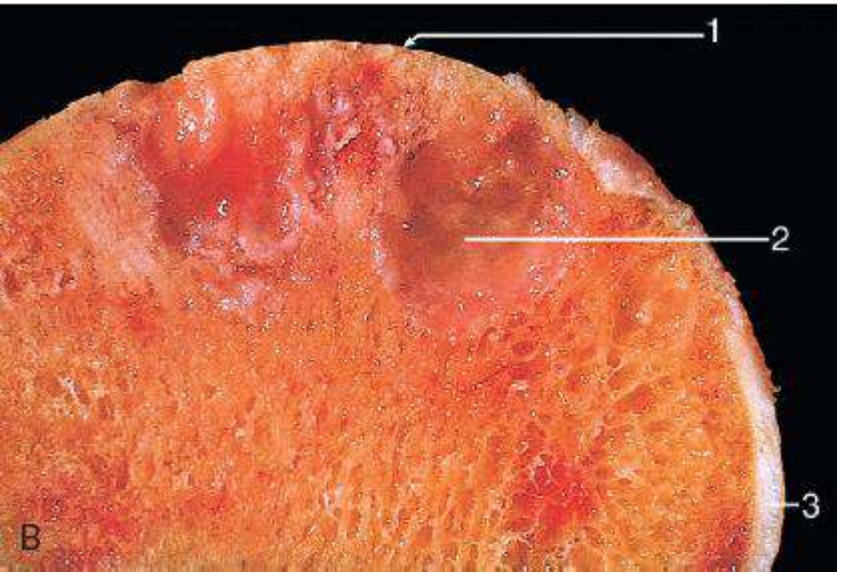
- Frictionless movement → provide resistance and tension
- Chondrocyte: proteoglycan + type II collagen

(Early) Chondrocyte injury – chondrocytes proliferate, secrete inflammatory mediator

(Late)Degradation exceeds synthesize



Netter's Illustrated human pathology. 2014



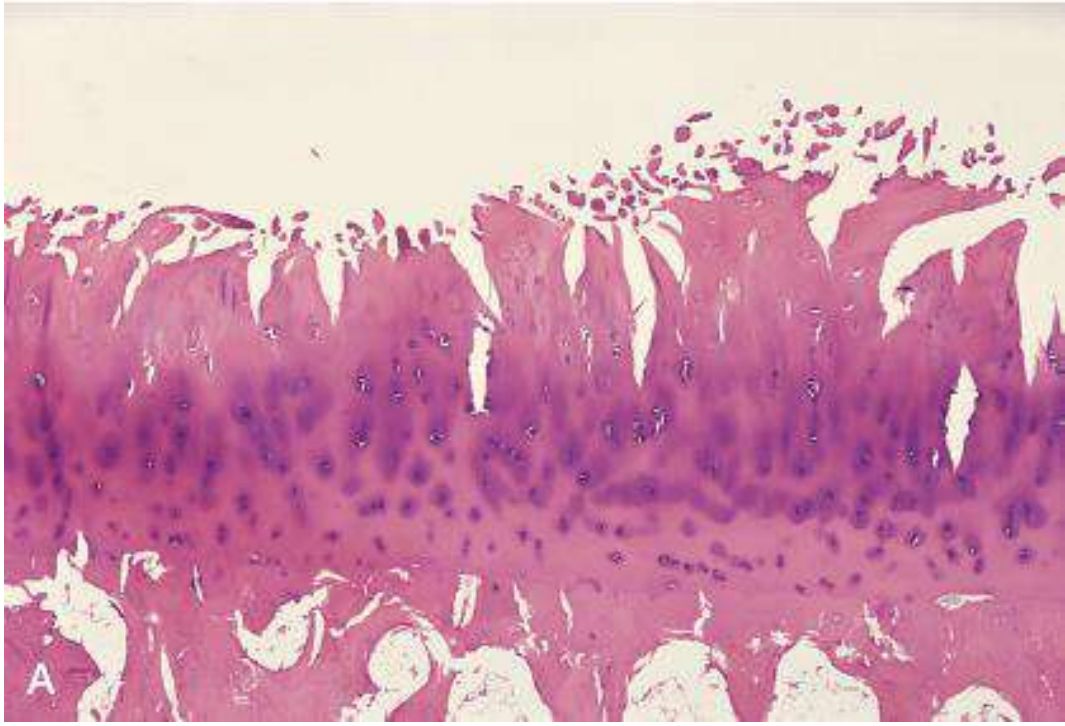


Figure 26-39 Osteoarthritis. **A,** Histologic demonstration of the characteristic fibrillation of the articular cartilage. **B,** Eburnated articular surface exposing subchondral bone (1), subchondral cyst (2) and residual articular cartilage (3).

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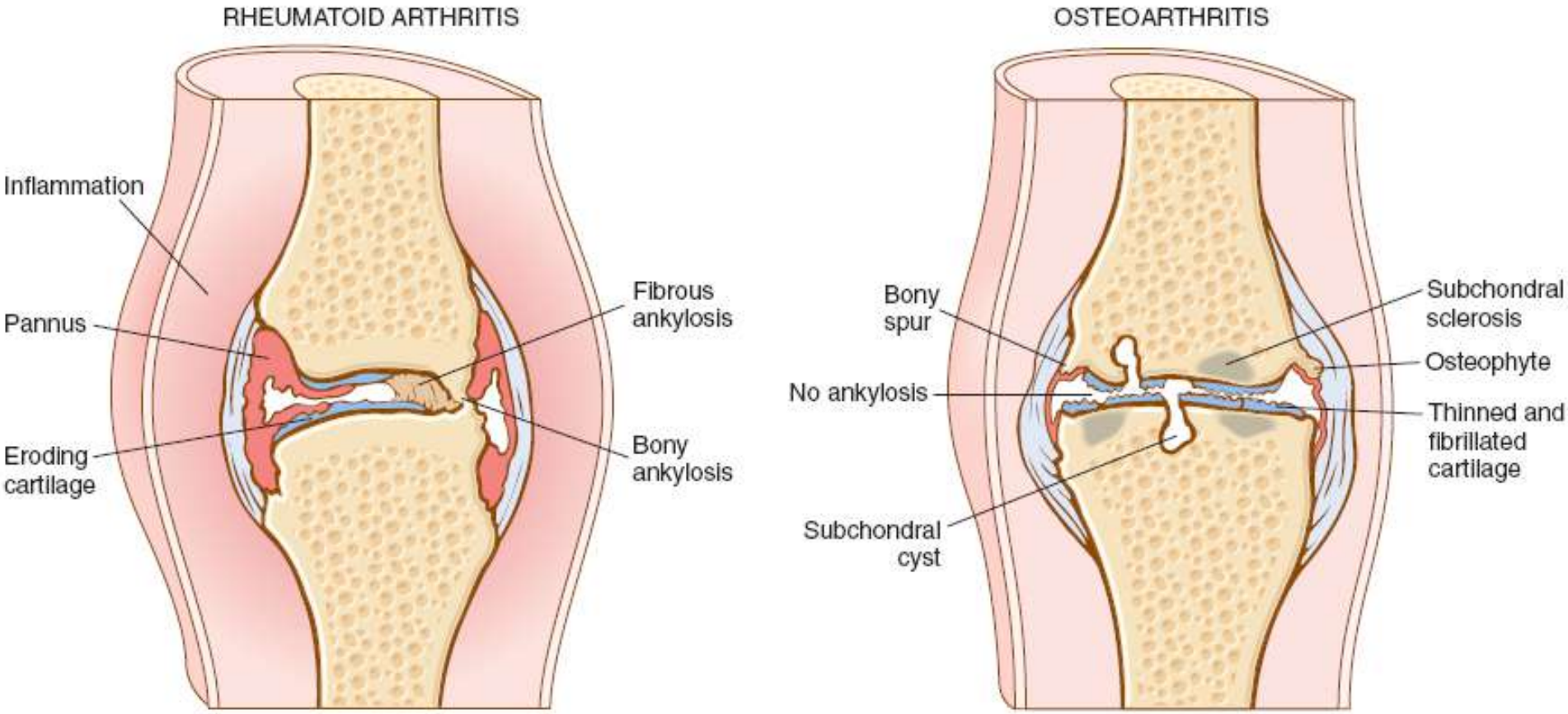

Figure 20–17 Comparison of the morphologic features of rheumatoid arthritis (RA) and osteoarthritis.

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Gout Arthritis

- Transient acute arthritis → crystallization of monosodium urate (MSU) within and around joints
- Primary Gout (90%) or secondary Gout (10%)

Table 26-7 Classification of Gout

Clinical Category	Uric Acid Production	Uric Acid Excretion
Primary Gout (90%)		
Unknown enzyme defects (85%-90%)	↑ (majority) ↑↑ (minority) Normal	Normal ↑ ↓
Known enzyme defects (e.g., partial HGPRT deficiency)	↑	Normal
Secondary Gout (10%)		
Increased nucleic acid turnover (e.g., leukemia)	↑↑	↑
Chronic renal disease	Normal	↓
Congenital (e.g., Lesch-Nyhan syndrome HGPRT deficiency)	↑↑	↑

HGPRT, Hypoxanthine guanine phosphoribosyl transferase.

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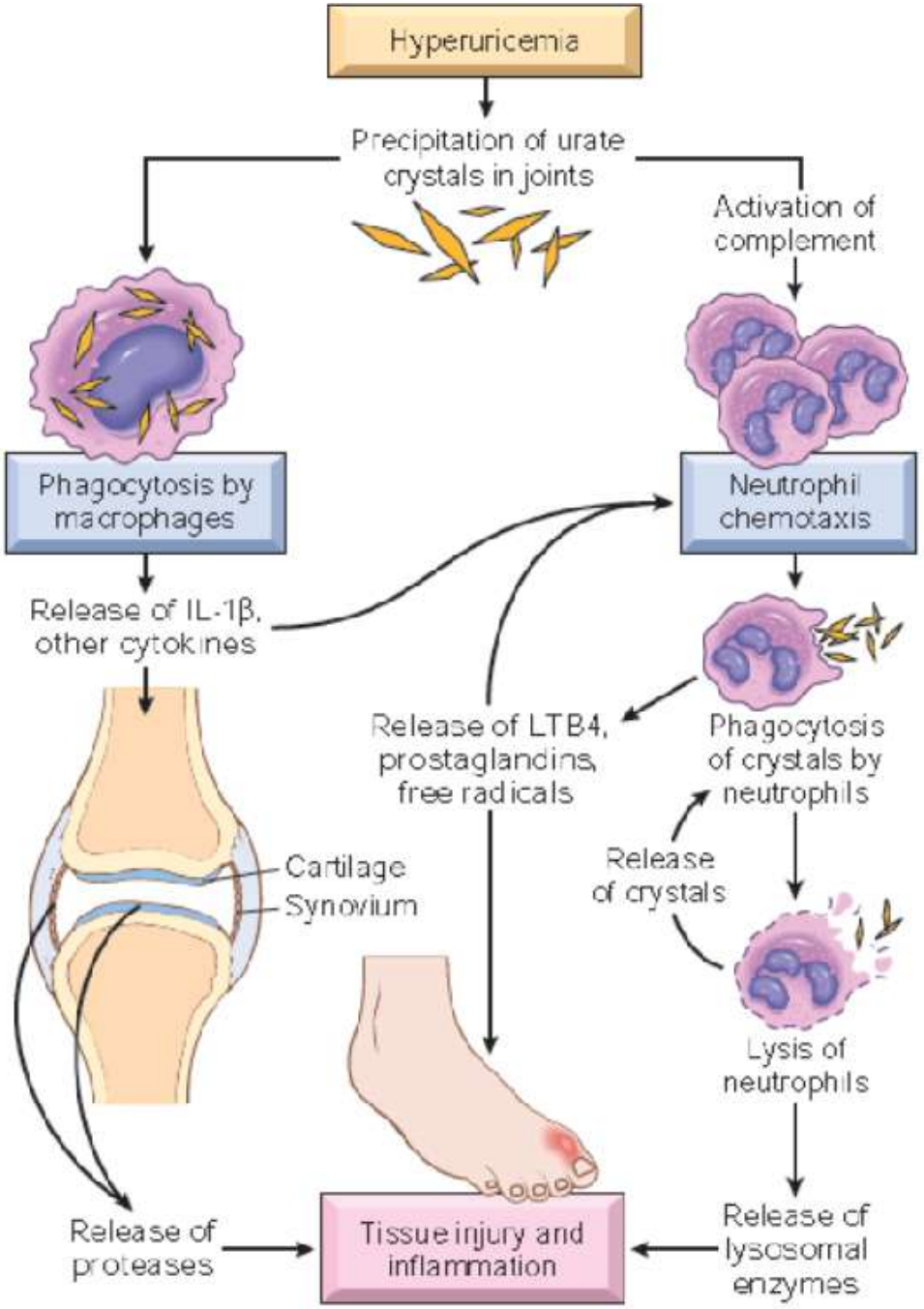

Figure 26-46 Pathogenesis of acute gouty arthritis. LTB4, Leukotriene B4; IL-1β, interleukin 1β.

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