Regressive lesions – 1

11- Pulmonary emphysema

12 - Osteoporosis

13 - Lipomatous atrophy of pancreas

15 - Renal amyloidosis

16 - Hepatic amyloidosis

Atrophy

Atrophy of any organ is defined as *shrinkage in the size of the cell by the loss of cell substance*.

Frequently, this condition is manifested by shrinkage (reduced size) of affected organ.
However, shrinking parenchymal cells are in some cases replaced by connective or fat tissue the dimension of atrophic organ remaining unchanged

Atrophy depends on the underlying cause and can be **local** or **generalized**

The common causes of atrophy are the following:
- diminished blood supply
- decreased workload (atrophy of disuse)
- inadequate nutrition
- loss of endocrine stimulation
- pressure
- loss of innervation (denervation atrophy)

Atrophy- morphologic classification

- Reference to **cells** (e.g. simple atrophy)
- Reference to **stroma**
  - **normal** stroma (e.g. simple atrophy)
  - **increased** stroma (e.g. due to excess of collagen- „fibrous a.", due to accumulation lymphocytes)
- Reference to an entire **organ**
  - **concentric**: diminution of an organ
  - **eccentric** atrophy: diminished mass of an organ while its size is normal or even increased (pulmonary emphysema, hydronephrosis, osteoporosis, lipomatous atrophy of the pancreas)

11 – Pulmonary emphysema
(Emphysema pulmonum essentiale)

The designation „pulmonary emphysema" is applied to a condition characterized by abnormal distention of air spaces distal to the terminal bronchioles with destruction of interalveolar septa.

The term „overinflation" refers to dilatation of air spaces which is not accompanied by destruction of their walls.

Emphysema (besides chronic bronchitis and small airways disease) is included in a group of pulmonary disorders, referred to as
Chronic **O**bstructive **P**ulmonary **D**isease (COPD).

11 – Pulmonary emphysema
(Emphysema pulmonum essentiale)

The most important factors contributing to development of pulmonary emphysema:
- **smoking**,
- inherited susceptibility and
- frequent respiratory tract infections (especially in childhood)

Clinically, **dyspnea** is the presenting symptom.
It results from loss of elastic recoil properties and reduction of gas-exchanging surface.

11 – Pulmonary emphysema
(Emphysema pulmonum essentiale)

MORHOLOGICALLY, emphysema is classified according to the distribution of changes within pulmonary acini.
• **Centrilobular (centriacinar) –** proximal acinar, involving respiratory bronchioles – result of cigarette smoking!
• **Paraseptal**- distal acinar, involving alveoli and alveolar ducts
• **Panacinar**- panlobular, involving pulmonary acini uniformly

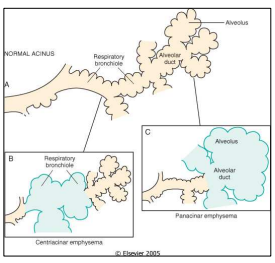


Diagram of normal structures within the acinus, the fundamental unit of the lung. A terminal bronchiole (not shown) is immediately proximal to the respiratory bronchiole.
B. **Centriacinar emphysema** with dilation that initially affects the respiratory bronchioles.
C. **Panacinar emphysema** with initial distention of the peripheral structures (i.e., the alveolus and alveolar duct); the disease later extends to affect the respiratory bronchioles.

11– Pulmonary emphysema
(Emphysema pulmonum essentiale)

- **Centriacinar (centrilobular) – result of cigarette smoking !**
  - Distal alveoli are spared and respiratory bronchioles are involved (both distended and normal airspaces are present)
  - upper lobes
  - spaces that exceed 1 cm in size – „bullae"
- **Panacinar – inherited alpha –1 antitrypsin deficiency**
  - Develops usually early in life (third decade)
  - respiratory bronchioles and terminal alveoli are involved
  - lower lobes

11 – Pulmonary emphysema - pathogenesis

1. The protease-antiprotease imbalance

The destructive effect of high protease activity (cellular proteases from neutrophils) in subjects with low antiprotease activity (low levels of serum α1-antitrypsin)-------elastic tissue destruction is unchecked and emphysema results.

2. The oxidant-antioxidant imbalance

Normally, the lung contains a healthy complement of **antioxidants** that keep oxidative damage to a minimum.
Tobacco smoke contains abundant reactive oxygen species (**free radicals**), which deplete these antioxidant mechanisms, thereby inciting tissue damage. A secondary consequence of oxidative injury is **inactivation of native antiproteases**, resulting in "functional" α1-antitrypsin deficiency even in patients without enzyme deficiency.

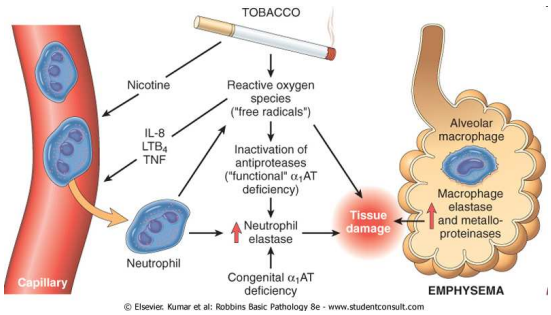
11 – Pulmonary emphysema - pathogenesis

- Neutrophils and macrophages accumulate in alveoli (in smokers, in chronic inflammation) – they release proteases (elastase) –
- or free radicals (present in tobacco smoke) –TNF and IL-8 – activation of neutrophils

Tissue damage due to: free radicals, neutrophil elastase, macrophage elastase

- „functional" or congenital alpha-1 antitrypsin (major inhibitor of proteases) deficiency

Pulmonary emphysema - pathogenesis



The protease-antiprotease imbalance and oxidant-antioxidant imbalance are additive in their effects and contribute to tissue damage. α1-Antitrypsin (α1AT) deficiency can be either congenital or "functional" as a result of oxidative inactivation.
IL-8, interleukin 8; LTB4, leukotriene B4; TNF, tumor necrosis factor.

3 – Pulmonary emphysema
(Emphysema pulmonum essentiale)

MA: emphysematous lung is enlarged, the pleural surface as well as cut surface appear pale, and pulmonary parenchyma is dry because of the loss and compression of small blood vessels. On palpation, the lung substance is plastic, doughy, with the large emphysematous bullae

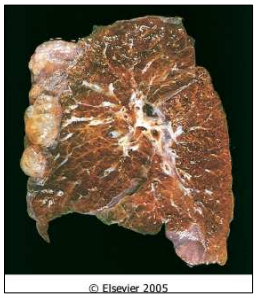
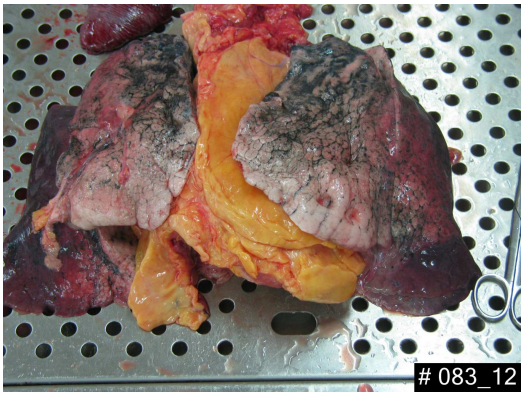


Figure. Bullous emphysema with large subpleural bullae (upper left).

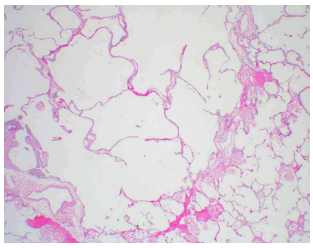
3 – Pulmonary emphysema



11 – Pulmonary emphysema

(Emphysema pulmonum essentiale)

MI: in presented slides histological examination reveals panacinar emphysema. It is characterized by disorganisation of whole pulmonary acini with replacement of alveoli by air-filled spaces considerably larger than the normal alveoli.The spaces originate from coalescence of alveoli after destruction of interalveolar septa. Walls of the spaces are **atrophic**, **thin** and **ripped.** Tapering remainders of interalveolar septa project into air-spaces. Capillaries are compressed



12 – Osteoporosis

Osteoporosis –is a disease characterized by increased porosity of the skeleton resulting from reduced bone mass. It is associated with an increase in bone fragility and susceptibility to fractures.

Primary osteoporosis (the most common form)

- **Type 1-** occurs in postmenopausal women within 10 years following menopause, is due to an absolute increase in osteoclasts activity and is a direct result of estrogen withdrawal (estrogen mediates osteoclasts activity)
- **Type 2** – *senile* in patients both sexes, older than 70 years of age, is caused by attenuated osteoblast function

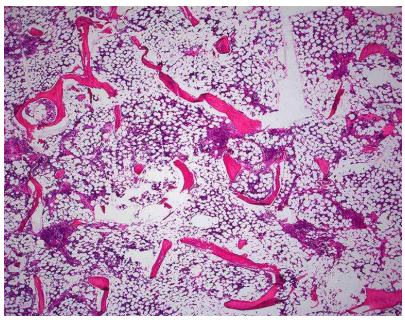
Causes: genetic factors, calcium nutritional state, physical activity, hormonal influences.

12 - Osteoporosis

- *Secondary osteoporosis* due to:
  - Corticosteroids (inhibit osteoblasts)
  - Hyperthyroidism and hyperparathyroidism (due to adenomas or hyperplasia): both increase osteoclastic activity
  - Malabsorption: gastrointestinal or hepatic disease
  - Alcoholism: direct inhibitor of osteoblasts
  - Hematological malignancies: multiple myeloma secrete osteoclast-activating factor

12 – Osteoporosis

MI: Irregular and very thin bone trabeculae; plenty of adipose bone marrow. Osteoclastic activity is present. The mineral content of the remaining bone is normal and thus there is no alteration in the ratio of minerals to protein matrix.



13 – Pancreatic lipomatous atrophy

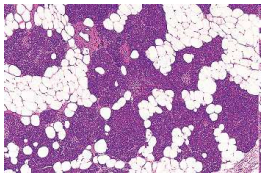
(Atrophia lipomatosa pancreatis)

The term **„pancreatic lipomatous atrophy"** refers to a condition in which the majority of exocrine pancreas is replaced by fatty tissue.

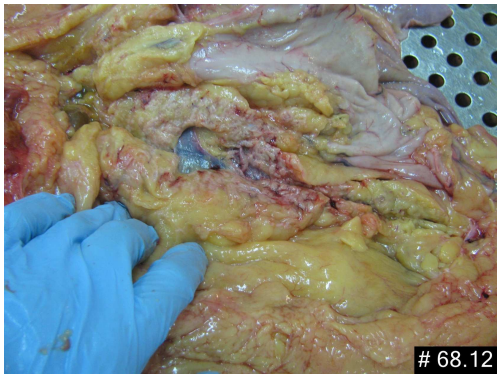
It predominantly occurs in elderly obese persons and is not necessarily associated with diabetes mellitus.

MA: the pancreas is of normal size or even enlarged („lipomatous pseudohypertrophy")

MI: fatty replacement of atrophic pancreatic tissue is visible, with no other particular features present



13 – Pancreatic lipomatous atrophy



Degeneration

- ✓ **excessive intra- or extracellular accumulation of substances which under normal conditions are there in very small quantities or are absent**
- ✓ **abnormality of chemical composition of substances**
- ✓ **deficiency of certain tissue components (e.g. calcium in rachitic bones)**

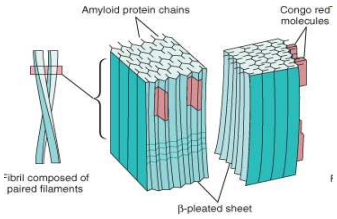
Amyloidosis

Amyloidosis is a general term designating a group of diseases displaying extracellular deposition of pathologic material (**amyloid**) which has no specific chemical composition but shows specific staining properties and characteristic appearance under polarized light.

Amyloidosis serves as an example of extracellular degeneration.

Amyloid is not a structurally homogenous protein, although it always has the same morphologic appearance.

Physical Nature of Amyloid. By electron microscopy all amyloid deposits are composed of nonbranching fibrils, 7.5 to 10 nm in diameter, each formed characteristic cross-β-pleated sheet conformation. This conformation is seen regardless of the clinical setting or chemical composition and **is responsible for the distinctive staining and birefringence of Congo red-stained amyloid**.



Structure of an amyloid fibril, depicting the β-pleated sheet structure and binding sites for the Congo red dye, which is used for diagnosis of amyloidosis

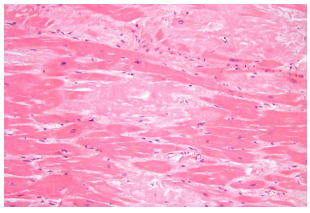
Chemical Nature of Amyloid. Approximately 95% of the amyloid material consists of fibril proteins, the remaining 5% being the P component and other glycoproteins. Of the more than 20 biochemically distinct forms of amyloid proteins that have been identified, **three are most common:**

1. The **AL (amyloid light chain)** is derived from Ig light chains and/or their amino-terminal fragments produced in plasma cells; The deposition of amyloid fibril protein of the AL type is associated with some form of monoclonal B-cell proliferation (e.g. multiple myeloma).
2. The **AA (amyloid-associated)** fibril is a unique non-Ig protein derived from a larger serum precursor called SAA (serum amyloid-associated) protein that is synthesized in the liver. The production of this protein is increased in inflammatory states as part of the "acute phase response"; therefore this form of amyloidosis is associated with chronic inflammatory disorders.
3. **Aβ amyloid** is produced from β amyloid precursor protein (APP) and is found in the cerebral lesions of Alzheimer disease

AMYLOID

Amyloid is deposited in various tissues and organs of the body in a wide variety of clinical settings.
Because amyloid deposition appears insidiously its clinical recognition ultimately depends on morphologic identification of this distinctive substance in appropriate biopsy specimens.

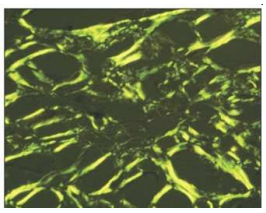
With the **light microscope** and H&E stains, amyloid appears as an **amorphous**, **eosinophilic (red or pink)**, **hyaline**, **extracellular substance** that, with progressive accumulation produces pressure atrophy of adjacent cells.

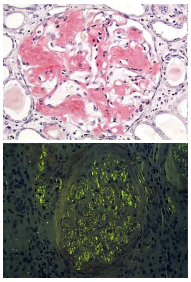


AMYLOID

To differentiate amyloid from other hyaline deposits (e.g., collagen, fibrin), a variety of histochemical techniques are used.

The most widely used is the **Congo red stain**, which under ordinary light imparts a **pink or red color** to tissue deposits, but far more striking and specific is the **green birefringence** of the stained amyloid when observed by polarizing microscopy





Amyloidosis- classification

According to distribution of amyloid deposits, the condition can be categorized as:

- **systemic / generalized** amyloidosis (involving several organ systems) or
- **localized** (involving one organ)
  - heart (senile cardiac a.)
  - brain (e.g. Alzheimer disease)
  - pancreas-islets of Langerhans (in diabetes mellitus)
  - endocrine tumors (e.g. thyroid medullary carcinoma)

Amyloidosis- classification

On clinical grounds, the systemic, or generalized, pattern is subclassified into:

- ***primary amyloidosis***, when associated with some immunocyte dyscrasia, or
- ***secondary amyloidosis***, when it occurs as a complication of an underlying chronic inflammatory or tissue destructive process.

Hereditary or *familial amyloidosis* constitutes a separate, albeit heterogeneous group, with several distinctive patterns of organ involvement.

15 – Renal amyloidosis

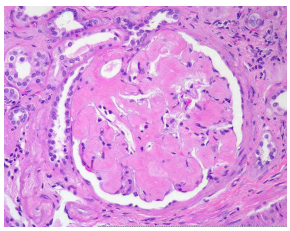
Amyloidosis of the kidney is the most common and potentially the most serious form of organ involvement.

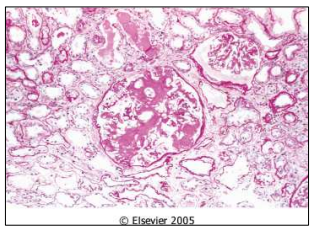
It affects all glomeruli of both kidneys, starting from small deposits which gradually enlarge and eventually occupy entire glomeruli.
This reflects the clinical course starting from slight **proteinuria**, through **nephrotic syndrome** to **chronic renal failure** and **uraemia**.
Unfortunately, amyloidosis affects also a transplanted kidney.

Grossly, the kidneys may be of normal size and color, or, in advanced cases, they may be shrunken because of ischemia caused by vascular narrowing induced by the deposition of amyloid within arterial and arteriolar walls.
Macroscopical examination of kidneys may reveal what is called „large white kidney". This is a non-specific picture testifying to an increased glomerular permeability for proteins of any cause. In this instance, kidney is enlarged, pale and firm.

15 - Renal amyloidosis

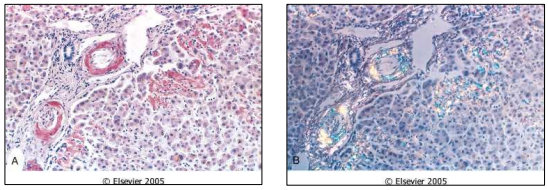
MI: in kidneys amyloidosis primarily affects the glomeruli which show abundant amorphous acellular eosinophilic material in mesangium. Glomerular capillaries are narrowed. Amyloid may be shown both in stroma and extraglomerular vessels.





16 - Hepatic amyloidosis

MI: in liver, amyloid is laid down in Disse spaces (the spaces between sinus endothelium and hepatocytes) and sinusoidal walls, primarily in the midzonal lobular region. There are numerous atrophic hepatocytes separated from sinusoids by abundant eosinophilic material as well as preserved apparently normal ones.



Amyloidosis. A. A section of the liver stained with Congo red reveals pink-red deposits of amyloid in the walls of blood vessels and along sinusoids. B. The yellow-green birefringence of the deposits when observed by polarizing microscope.

Hepatic amyloidosis