Pigments

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Intracellular accumulations

- There are four main pathways of abnormal intracellular accumulations:
- Inadequate removal of a normal substance, as in fatty change
- Accumulation of an abnormal endogenous substance as a result of genetic or acquired defects, as in hemosiderosis, amyloidosis
- Failure to degrade a metabolite due to inherited enzyme deficiencies, as in Gaucher's disease
- Deposition and accumulation of an abnormal exogenous substance when the cell has neither the enzymatic machinery to degrade it, as in anthracosis

Questions

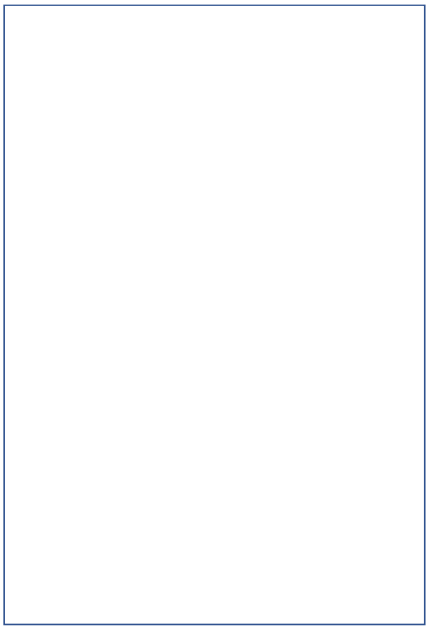
- Histochemical caracteristics of the different pigments. Exogenous pigments.
- Hemoglobinogenic pigments. Causes and forms of jaundice.
- Hemoglobinogenic pigments. Pathological forms of iron storage.
- **Endogenous non-hemoglobinogenic pigments: lipofuscin, melanin, homogentizic acid.**

Definition of pigments

Pigments are colored substances that are either exogenous, coming from outside the body, such as carbon, or endogenous, synthesized within the body itself, such as lipofuscin, melanin, and certain derivatives of hemoglobin.

Carbon

- The most common exogenous pigment is *carbon* (an example is coal dust), a ubiquitous air pollutant of urban life.
- When inhaled, it is phagocytosed by alveolar macrophages and transported through lymphatic channels to the regional tracheobronchial lymph nodes. Aggregates of the pigment blacken the draining lymph nodes and pulmonary parenchyma (*anthracosis*).



Lipofuscin

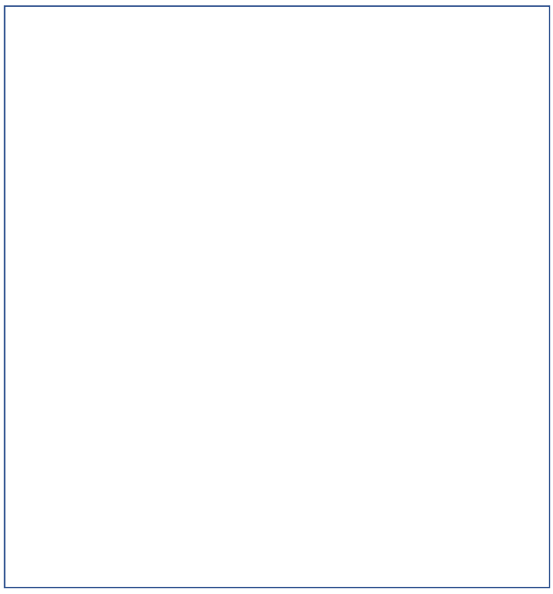
Lipofuscin, or "wear-and-tear pigment," is an insoluble brownish-yellow granular intracellular material that accumulates in a variety of tissues (particularly the heart, liver, and brain) as a function of age or atrophy.

Lipofuscin represents complexes of lipid and protein that derive from the free radical–catalyzed peroxidation of polyunsaturated lipids of subcellular membranes.

It is not injurious to the cell but is a marker of past *free radical* injury.

The brown pigment, when present in large amounts, imparts an appearance to the tissue that is called *brown atrophy*.

One of the most common endogenous pigments found in human tissues.



Melanin

Melanin is an endogenous, brown-black pigment that is synthesized by melanocytes located in the epidermis and acts as a screen against harmful ultraviolet radiation.

Although melanocytes are the only source of melanin, adjacent basal keratinocytes in the skin can accumulate the pigment (e.g., in freckles), as can dermal macrophages.

Hemosiderin

Hemosiderin is a hemoglobin-derived granular pigment that is golden yellow to brown and accumulates in tissues when there is a local or systemic excess of iron.

Iron is normally stored within cells in association with the protein apoferritin, forming ferritin micelles.

Hemosiderin pigment represents large aggregates of these ferritin micelles.

The iron can be identified by the Prussian blue histochemical reaction.

Although hemosiderin accumulation is usually pathologic, small amounts of this pigment are normal in the mononuclear phagocytes.

Excessive deposition of hemosiderin, called hemosiderosis, and more extensive accumulations of iron seen in hereditary hemochromatosis.

Bilirubin

- Bilirubin is the non-iron-containing, yellow-orange pigment that results from breakdown of porphyrin rings (mostly hemoglobin).
- Bilirubin by itself is insoluble in water and is carried on albumin to the liver, where hepatocytes conjugate it with glucuronic acid and pour it into the bile.
- Elevated levels of bilirubin in the blood mean jaundice.
- You may see bile plugs (bile in distended canaliculi; big ones that ruptured are "bile lakes") or intracellular bilirubin in the liver in obstructive jaundice.

Alkapton (homogentisic acid)

Patients with the hereditary alkaptonuria accumulate homogentisic acid, a breakdown product of tyrosine / phenylalanine, which polymerizes into black pigment in their cartilages (nose, ears) and joints.

The accumulation itself is called ochronosis.

Patients are asymptomatic as children or young adults, but their urine may turn brown or even inky black if collected and left exposed to open air. They develop arthritis symptoms later in life.

It is an autosomal recessive hereditary condition.

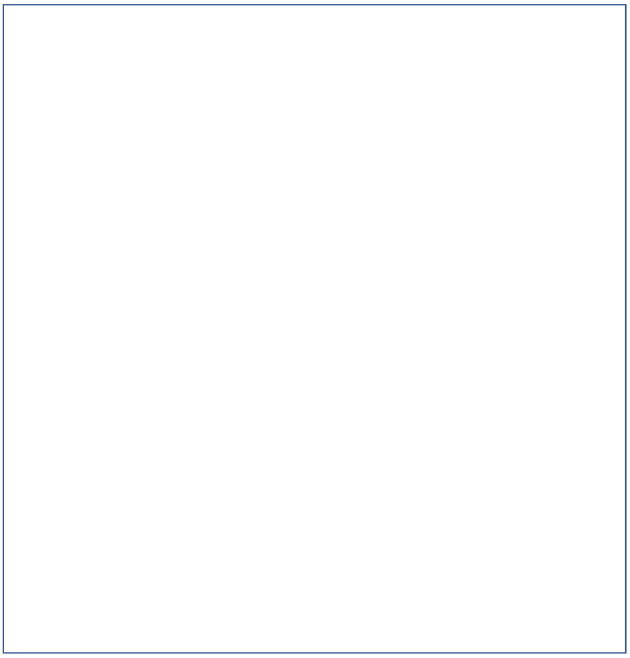
Exogenous vs. Endogenous pigments

Exogenous: inhaled or digested pigments or traumatic entry (injury, tattoo).

Endogenous:

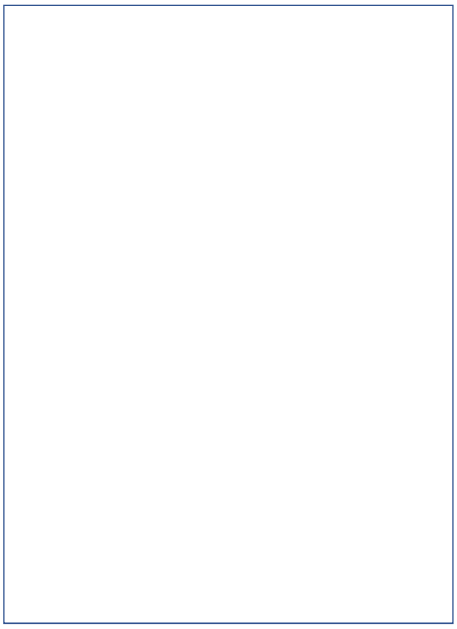
- Non-hemoglobinogenic pigments: melanin, lipofuscin, homogentisic acid
- Hemoglobinogenic pigments: hemosiderin and bilirubin

Hemoglobin is a complex protein made of heme and globin. During brakedown of scenecent erthrocytes, pigments are made.



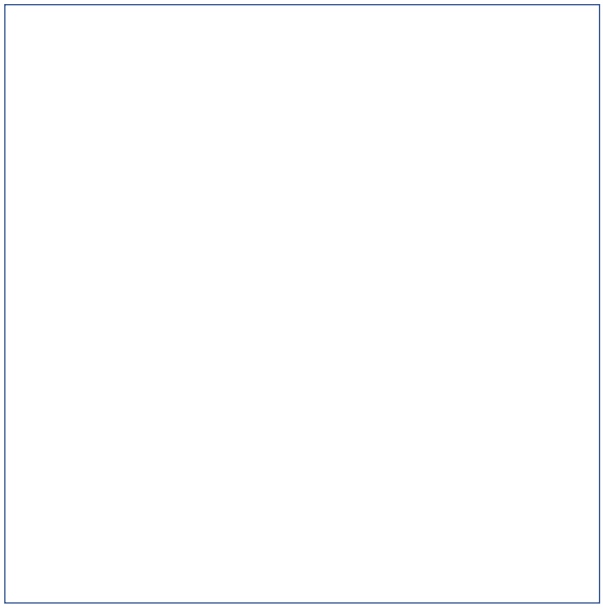
Histochemical characteristics

- Hemosiderin stains blue with Prussian Blue.
- Bleaching techniques remove melanin.They make use of a strong oxidizing agent such as potassium permanganate or hydrogen peroxide.
- Formaldehyde-induced fluorescence can be used to highlight melanin in tissues. Formalin fixation imparts a strong yellow autofluorescence to unstained tissues with these substances.
- Lipofuscin can be stained by Sudan black B and PAS.



Tattoo

Pigment (ink) is taken up by macrophages. Ink granules are not presented as antigens. The granules remain in the papillary dermis and are eventually engulfed by fibroblasts and macrophages which work to repair the damage from the needles by creating scar tissue. Once the scar is formed, the ink is permanently held in the epidermis.

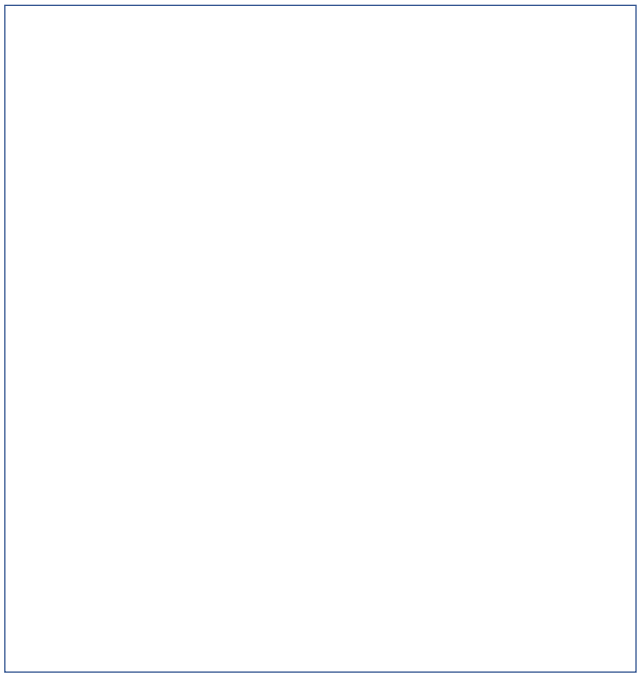


Pneumoconioses

Pneumoconiosis is a term originally coined to describe the non-neoplastic lung reaction to inhalation of mineral dusts.

The term has been broadened to include diseases induced by organic (sawdust) as well as inorganic (carbon) particulates.

The mineral dust pneumoconioses—the three most common of which result from exposure to coal dust, silica, and asbestos—nearly always result from exposure in the workplace.



Pathogenesis of anthracosis

The reaction of the lung to mineral dusts depends on many variables, including size, shape, solubility, and reactivity of the particles.
Particles greater than 5 to 10 μm are unlikely to reach distal airways. Particles smaller than 0.5 μm move into and out of alveoli, often without substantial deposition and injury.
Particles that are 1 to 5 μm in diameter are the most dangerous, because they get lodged in the distal airways.
Coal dust is relatively inert, and large amounts must be deposited in the lungs before lung disease is clinically detectable.
Silica and asbestos are more reactive than coal dust, resulting in fibrotic reactions.
The pulmonary alveolar macrophage is a key cellular element in lung injury and fibrosis.
Some of the inhaled particles reach the lymphatics within migrating macrophages and initiate an immune response.
Tobacco smoking worsens the effects of all inhaled mineral dusts.

Coal Worker's Pneumoconiosis

The spectrum of lung findings in coal workers is wide, ranging from asymptomatic anthracosis, in which pigment accumulates without cellular reaction, to simple coal worker's pneumoconiosis(CWP), in which accumulations of macrophages occur with fibrosis (scar tissue in the lungs).

CWP: complicated cases present with severe progressive fibrosis in the lungs. It is a rare disease.

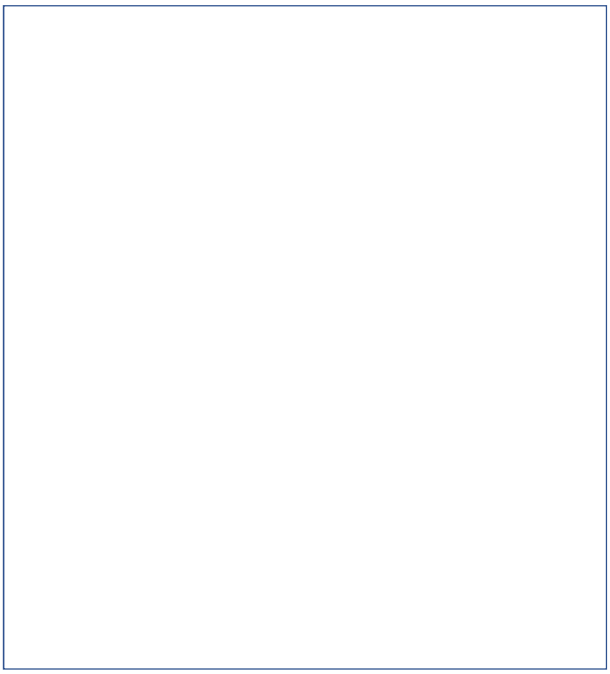
Silicosis és azbesztosis also can cause pulmonary fibrosis.

Morphology

Pulmonary anthracosis is the most common coal-induced pulmonary lesion in coal miners and also is commonly seen in all urban dwellers and tobacco smokers.

Inhaled carbon pigment is engulfed by alveolar or interstitial macrophages, which then accumulate in the connective tissue along the lymphatics, or in lymph nodes.

- **Simple CWP** is characterized by **coal macules** and the somewhat larger **coal nodule.** The coal macule consists of dust-laden macrophages; in addition, the nodule contains small amounts of collagen fibers as well.
  Although these lesions are scattered throughout the lung, the upper lobes are more involved. Later in the course **emphysema** can occur.
- **Complicated CWP** occurs on a background of simple CWP by coalescence of coal nodules and generally requires decades to develop.
  It is characterized by multiple, black scars, sometimes up to 10 cm in greatest diameter. On microscopic examination the lesions are seen to consist of dense collagen and the pigment.



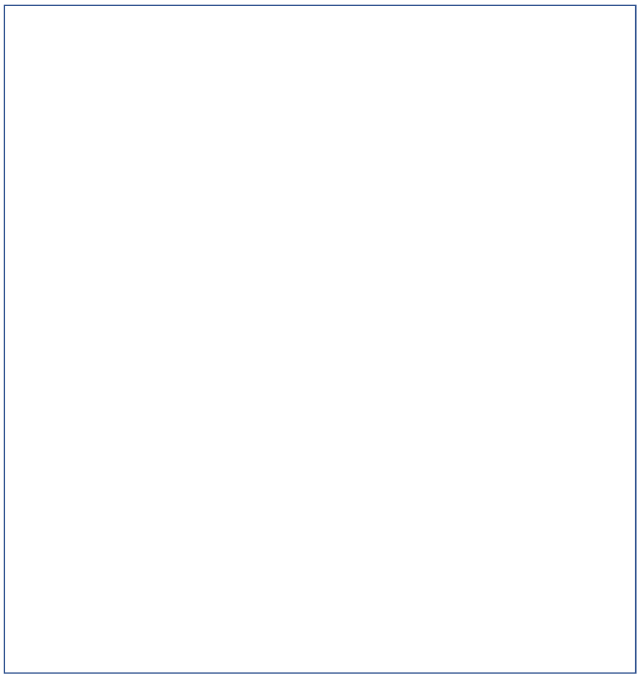
Clinical features

CWP is usually a benign disease that produces no decrement in lung function.

When fibrosis develops, there is increasing pulmonary dysfunction, pulmonary hypertension, and cor pulmonale (cardiac disease).

Unfortunately, PMF has a tendency to progress even in the absence of further exposure.

Once smoking-related risk has been taken into account, there is no increased frequency of lung carcinoma in coal miners, a feature that distinguishes CWP from both silica and asbestos exposures (discussed later in Pulmonary Pathology chapter).



Melanin

- Melanin is an endogenous, brown-black pigment that is synthesized by melanocytes located in the epidermis and acts as a screen against harmful ultraviolet radiation.
- FRECKLE: increase in pigment production by a local group of melanocytes.
- LENTIGO: a local hyperplasia of melanocytes, with hyperpigmentation.
- NEVUS: melanocytes cells pop up at the dermal-epidermal junction and/or the upper dermis.
- JUNCTIONAL NEVUS feature clumps of nevus cells along the dermoepidermal junction.
- DERMAL NEVUS: nevus cell nests in the dermis
- MALIGNANT MELANOMA: malignant tumor originating from melanocyes