Color changes of tissues and organs associated with disease

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Introduction
• Acute observation is critical skill of physicians, veterinarians and animal caretakers
• Changes in tissue coloration is an important marker of disease
• Most common examples of tissue color changes that occur are related to hemoglobin
• Even with careful clinical observation specific alterations are usually detectable only when changes are moderate to severe [minor changes are only detectable by laboratory testing]

Lecture Outline
• Red blood cell synthesis
• Hemoglobin: synthesis and degradation
• Anemia and hemorrhage
• Jaundice
• Miscellaneous color changes
Erythropoiesis

Erythropoiesis = red cell synthesis

Erythropoiesis
- Occurs in bone marrow – multiple bones throughout the body
- Requires protein signal from kidney (erythropoietin) – promotes survival of red cell precursors
- Require significant amounts of iron and other molecular building blocks

Erythropoiesis

With differentiation towards erythrocyte (RBC)
- More hemoglobin is synthesized
- Nucleus shrinks and is finally removed
- Reticulocytes are released into the blood
- Reticulocytes mature into erythrocytes in about 24 hours
- Erythrocytes live about 4 months in circulation

Structure of hemoglobin

Hemoglobin

Heme
Pathway for synthesis of hemoglobin

Normal pathway for the degradation of hemoglobin

Anemia – An abnormality characterized by deficiency in the oxygen-carrying component of the blood

- Anemia
  - Decreased red blood cell concentration
  - Decreased hemoglobin concentration of red cells
  - Decreased size of red blood cells

- Consequences
  - Decreased oxygen carrying capacity of blood
  - Weakness, collapse, hypoxic organ damage
  - Some adaptation occurs to chronic anemia
Important causes of anemia in animals and man

• **Blood loss**
  – Internal hemorrhage
  – External hemorrhage

• **Decreased production of red cells or hemoglobin**
  – Chronic kidney disease – decreased erythropoietin
  – Iron deficiency
  – Bone marrow damage – many causes

• **Increased destruction of blood cells**
  – Autoimmune hemolytic anemia
  – Red cell protozoans e.g. Malaria, Babesia

External hemorrhage as a cause of anemia

– External trauma
– Gastrointestinal tract disease
– Acute – hemorrhagic shock
– Chronic – loss of protein and iron

Iron deficiency as a consequence of chronic external hemorrhage

• Iron loss due to hemorrhage
• Iron essential for hemoglobin synthesis
• Iron deficiency results in decreased hemoglobin content with erythrocytes
  – Anemia is hypochromic

• Questions
  – Do males and females have different iron requirements? Why? Why not?
  – How else may iron deficiency anemia occur?
**Internal hemorrhage**

- Hemorrhage into body cavities and tissues
- Usually acute, can be chronic

**Hemoperitoneum**
**Hemorrhage resulting in a collapsed lung**

*Would you expect to see secondary iron deficiency with internal hemorrhage?*

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**Hemoglobin degradation occurs locally in areas of contusion**

- Early
  - Pink
  - Red
  - Purple

- Late
  - Yellow
  - Green

**Hemoglobin – red**

**Biliverdin - green**

**Bilirubin - yellow**

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**Resolution of a bruise**

**Hemoglobin** ➔ **Globin (protein component)**

**Heme**

**Iron**

**Biliverdin**

**Non-conjugated bilirubin**

**Conjugated bilirubin [conjugation occurs in liver]**

**Excretion by liver into bile [released into small intestine]**

**Degraded to stercobilin (mainly responsible for normal fecal color)**
Icterus = jaundice

Hyperbilirubinemia = increased bilirubin in blood

Causes of elevated bilirubin = hyperbilirubinemia

- **Pre-hepatic** = increased degradation of hemoglobin
- **Hepatic** = Decreased conversion of non-conjugated to conjugated bilirubin
- **Post-hepatic** = Obstruction of flow of bile

Pathways to icterus I

Hemoglobin $\rightarrow$ Globin (protein component)

Heme $\rightarrow$ Iron $\rightarrow$ Biliverdin $\rightarrow$ Non-conjugated bilirubin $\rightarrow$ Conjugated bilirubin (conjugation occurs in liver) $\rightarrow$ Excretion by liver into bile (released into small intestine) $\rightarrow$ Degraded to stercobilin (mainly responsible for normal fecal color)
Pathways to icterus II

Failure of bilirubin conjugation indicates liver disease (hepatocellular)
Failure of excretion indicates obstruction of bile flow
- Intra-hepatic = liver disease
- Extra-hepatic e.g. bile duct cancer

Porphyrsins in tissues – associated with disease or normal pigmentation in some species

Porphyrsins are colored intermediates in the pathway to heme synthesis e.g. Uroporphyrinogen. [Porphura is greek for purple].

Purple moorhen
Tear staining
Discolored teeth
Rat - chromodacryorrhea
Produced by Harderian gland next to eye

How do porphyrin levels accumulate in tissues? Consequences of defects of heme synthesis pathway

- Most porphyrsins are genetic in origin
- single gene inheritance
- autosomal dominant or recessive
- Manifestations vary according to gene involved
Consequences of porphyria
Porphyrins, at high levels, are toxic

- UV LIGHT
- Photosensitivity
- Elevated porphyrins
- Excretion in urine
- Damage to liver and nervous system

Other color changes in tissues
- Fat accumulation - pale swollen liver
- Melanoma – neoplasm of melanin producing cells

Example questions
- What is icterus?
- Why is icterus often present with hepatic disease?
- Where are aged red cells normally degraded?
- Provide two basic causes of iron deficiency anemia?
- Why is anemia often present in animals and people with chronic renal disease?
- Explain what is meant by the term ‘autosomal recessive disease’

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