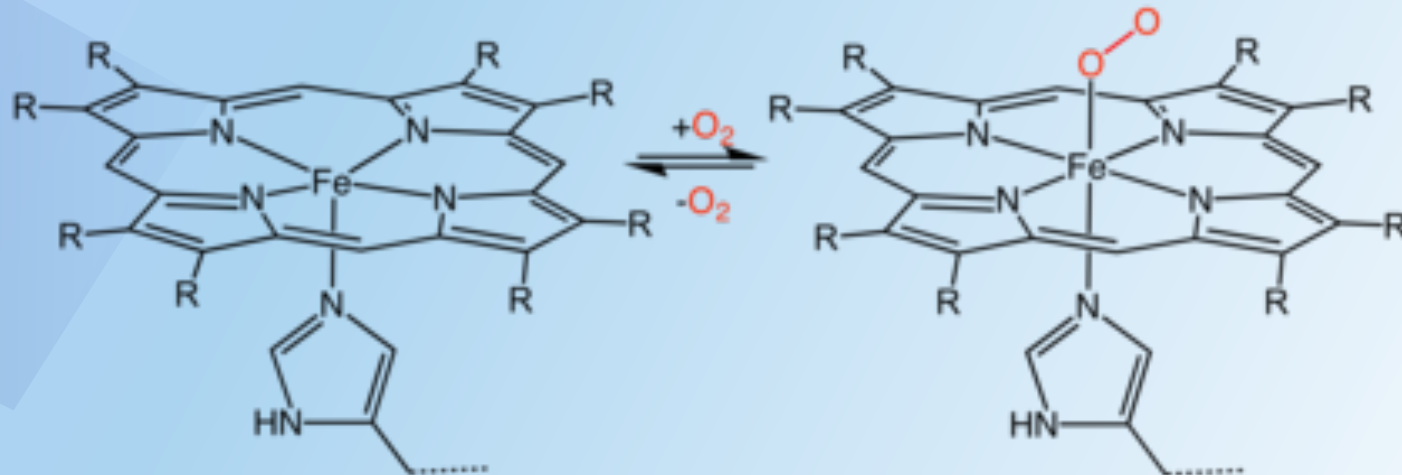


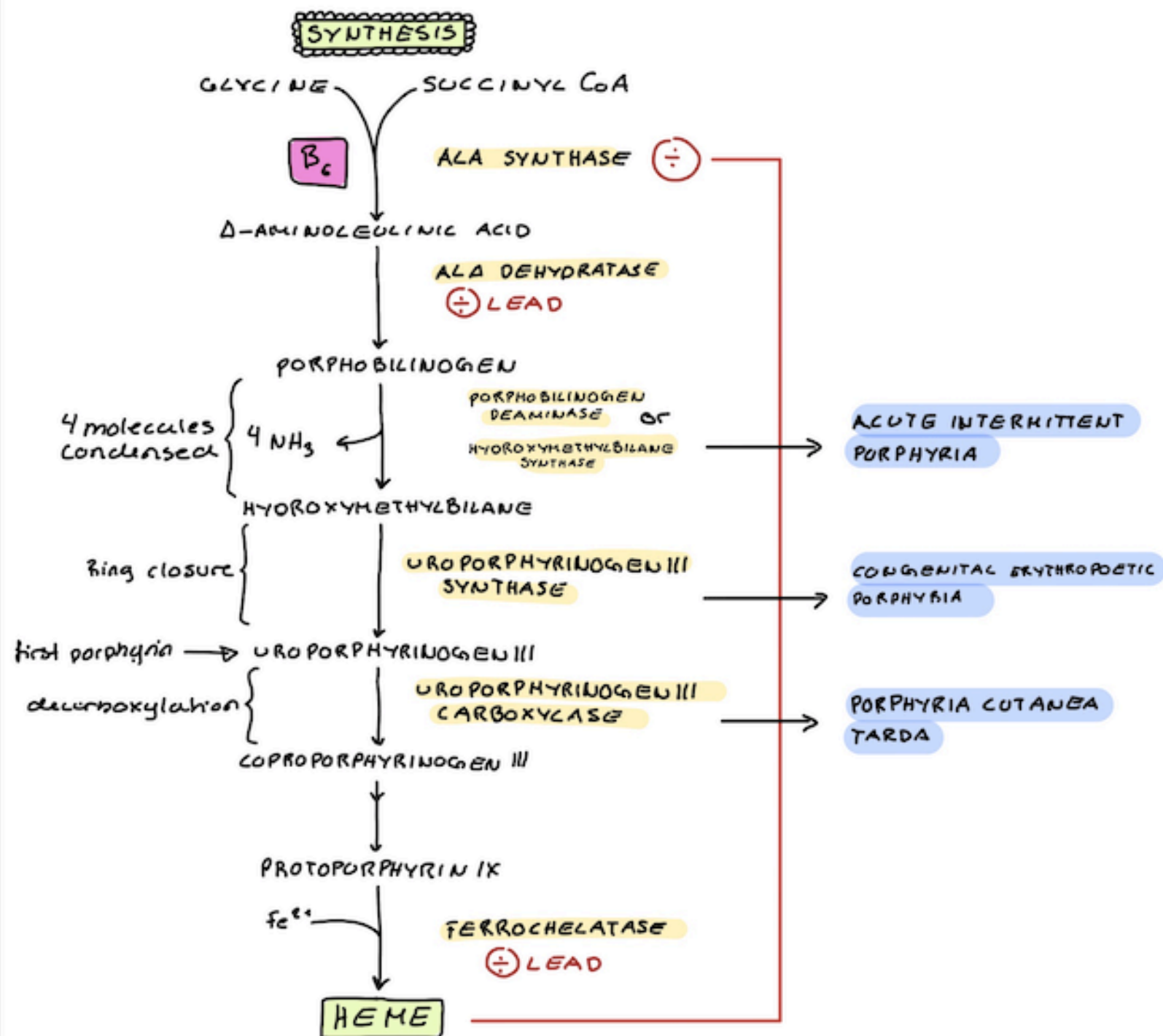
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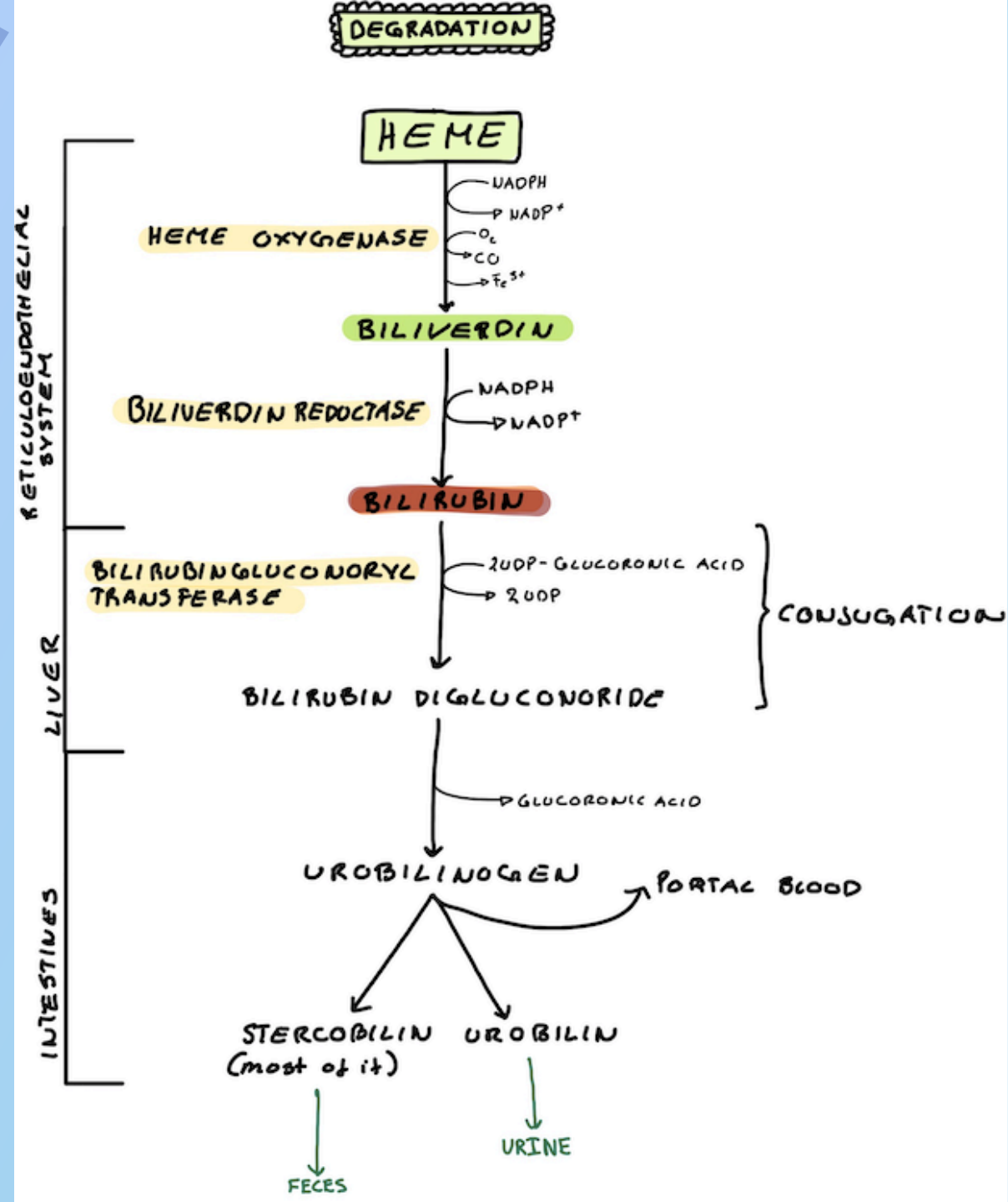
Heme Metabolism and ROS

What is heme?

- heme is a coordination complex consisting of an iron ion coordinated to a porphyrin
- hemes are most commonly recognized as components of **hemoglobin**, but they are also found in a number of other hemoproteins such as myoglobin, **cytochromes**, and catalase
- heme is most synthesized in the **liver** and **bone marrow**





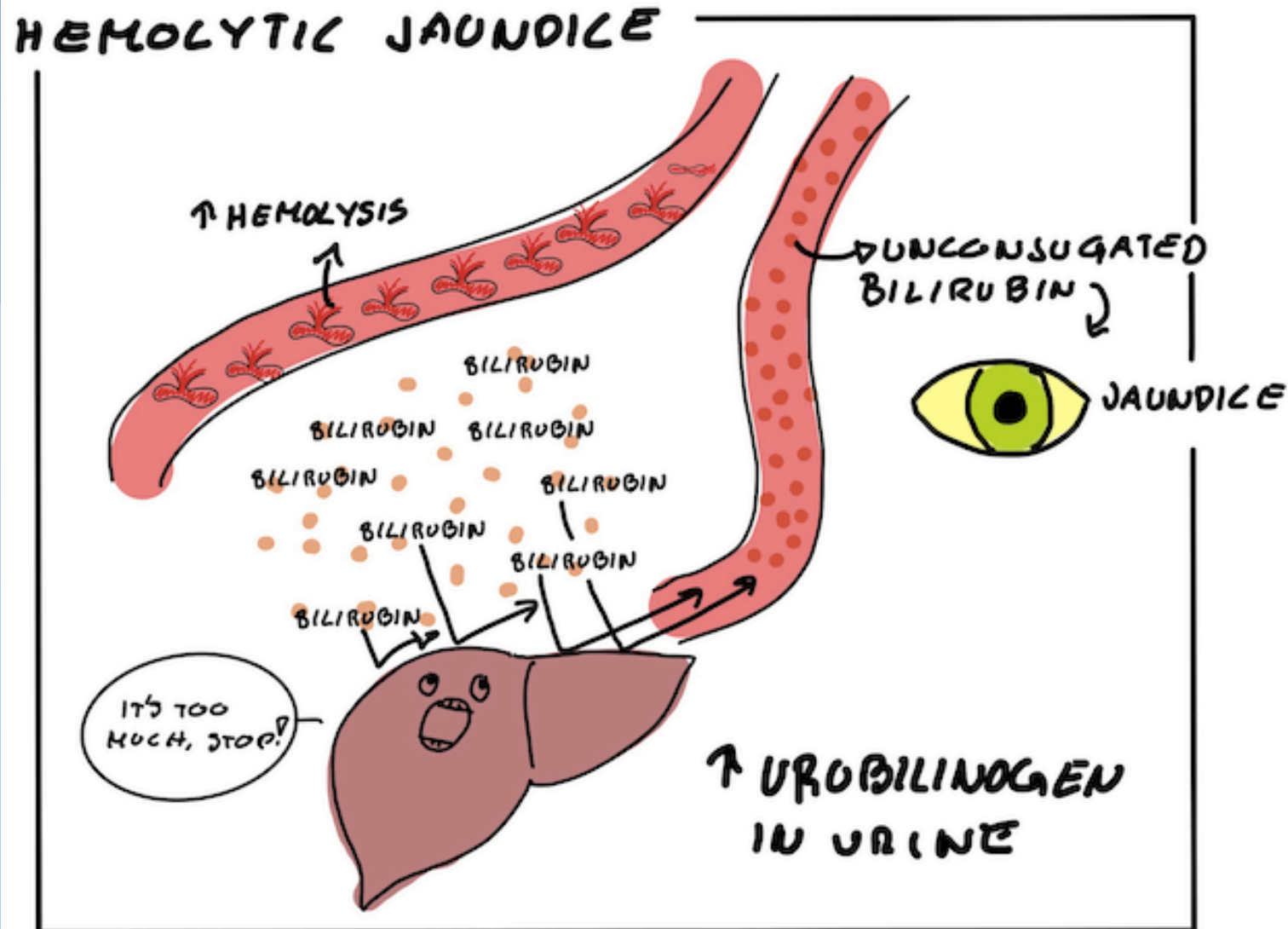


Types of Jaundice

- Yellow discoloration of the skin, earliest sign is scleral icterus
- Due to **increase in bilirubin**

Category	Definition
Pre-hepatic/hemolytic	The pathology is occurring prior to the liver , due to either: A. Intrinsic defects in red blood cells B. Extrinsic causes external to red blood cells
Hepatic/hepatocellular	The pathology is located within the liver caused due to disease of parenchymal cells of liver.
Post-hepatic/cholestatic	The pathology is located after the conjugation of bilirubin in the liver caused due to obstruction of biliary passage. ^[15]

Pre-hepatic/Hemolytic Jaundice



↑ Unconjugated Bilirubin in serum

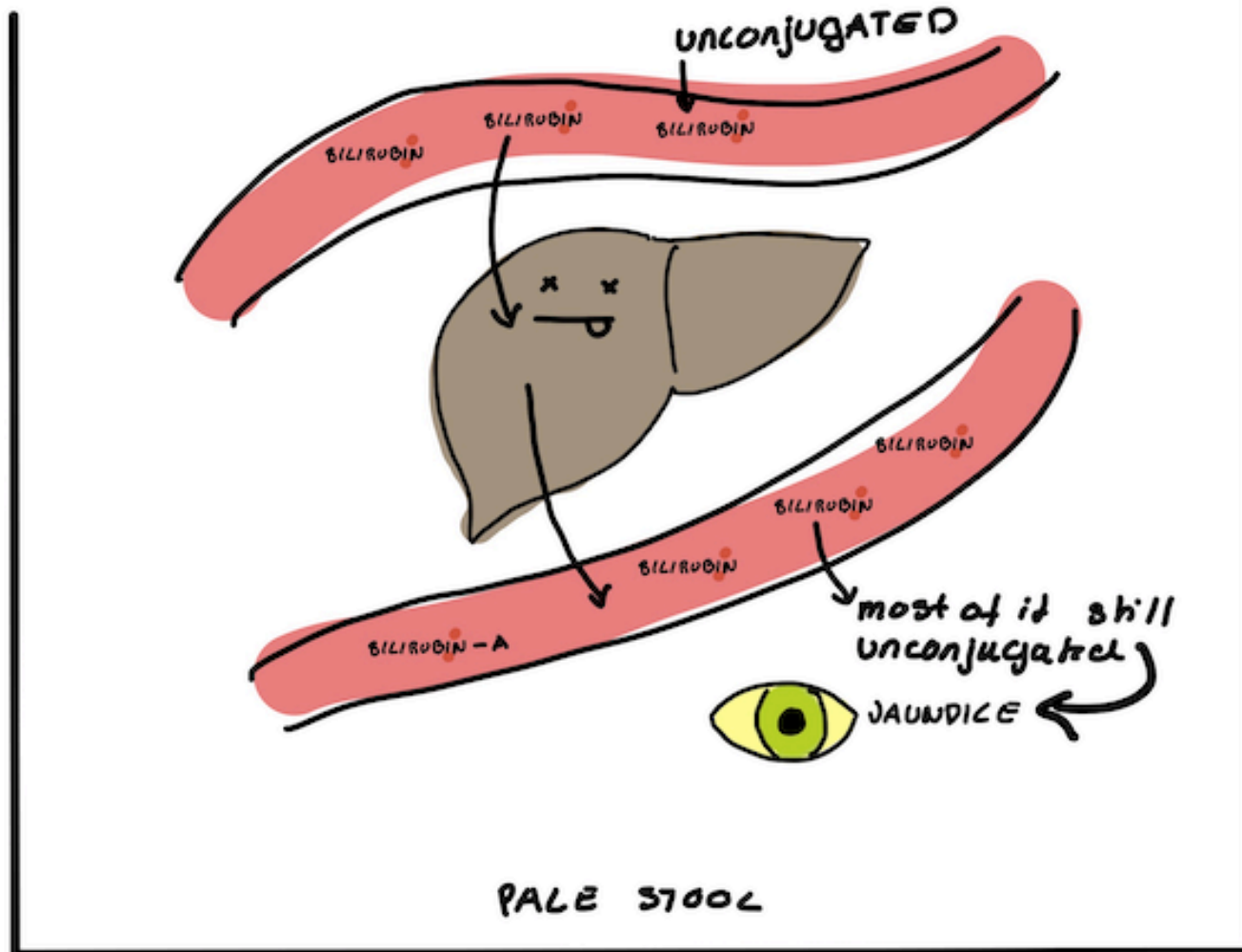
↑ Urine Urobilinogen

Dark urine due to increase in urine urobilinogen
Will there be unconjugated bilirubin in the urine?

↑ Risk for bilirubin gallstones

Hepatic/Hepatocellular Jaundice

HEPATOCELLULAR JAUNDICE



↑ In both Conjugated Bilirubin and Unconjugated Bilirubin in the serum

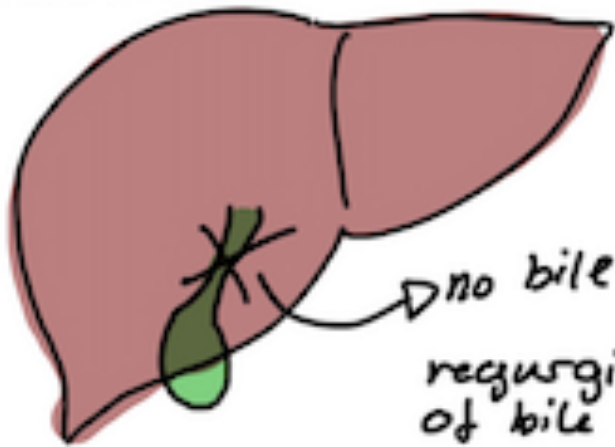
↔ or ↓ Urine Urobilinogen

Dark urine due to increased conjugated bilirubin

Post-hepatic/Cholestatic Jaundice

OBSTRUCTIVE JAUNDICE

- GI PAIN, NAUSEA
- PALE STOOLS
- DARK URIN
- NO UROBILINOGEN IN URIN



no bile enters blood
regurgitation
of bile into blood



↑
Conjugated Bilirubin in serum

↓
Urine Urobilinogen

Pale stools

Increase in alkaline phosphatase

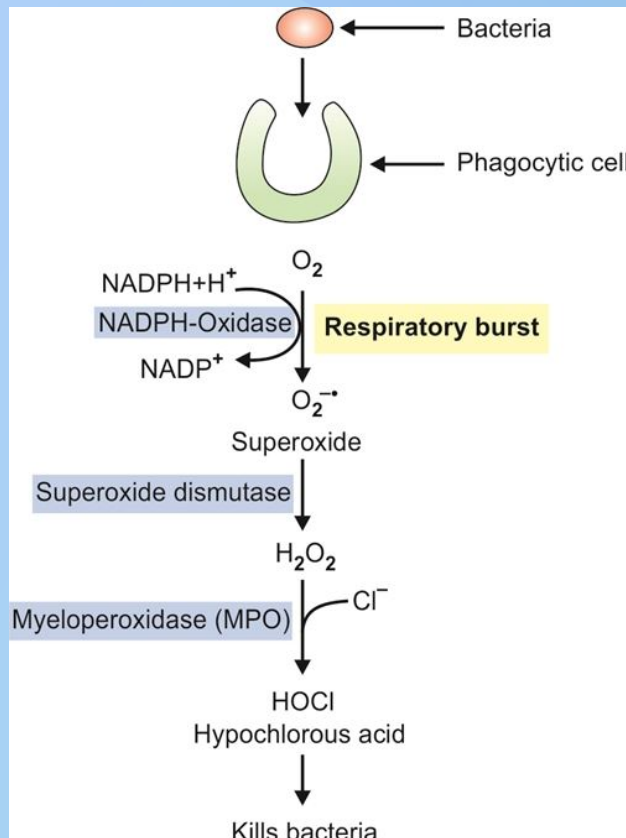
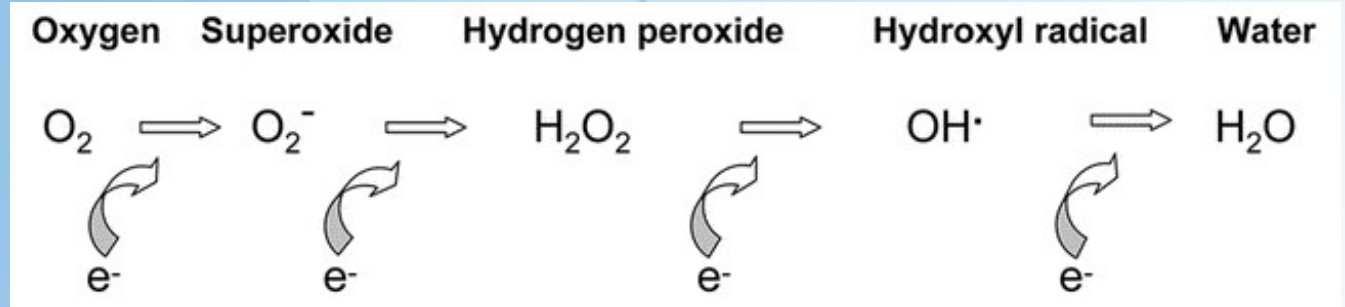
ROS

Reactive Oxygen Species

(free radicals)

Physiological Generation

- occurs during oxidative phosphorylation
 - Coenzyme Q is a major site of superoxide formation
 - Complex IV can partially reduce O₂

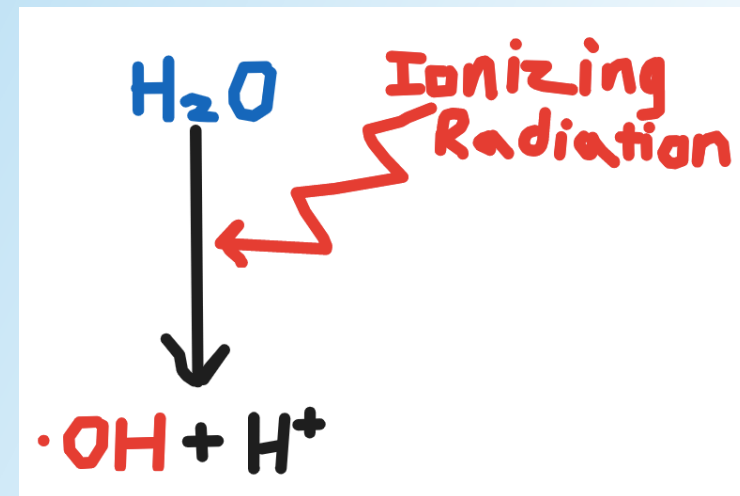
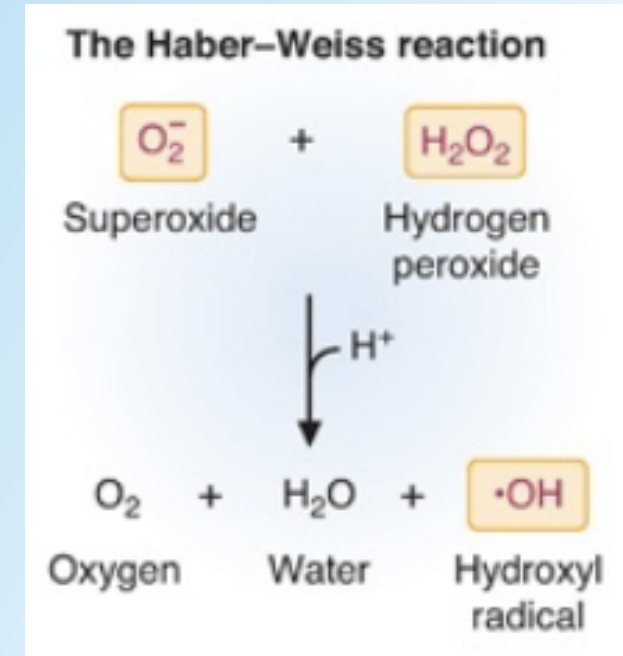
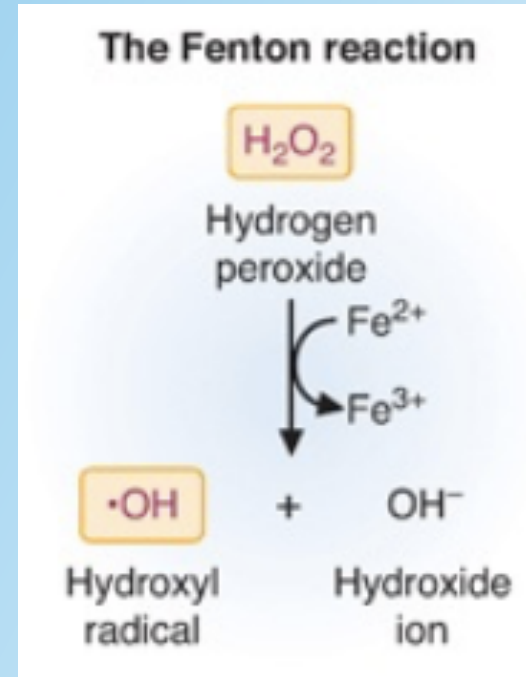


• OXIDATIVE BURST

- NADPH oxidase generates superoxide ions during oxygen-dependent killing
- *Chronic Granulomatous Disease (CDG)* is characterized by poor O₂⁻ dependent killing
- *NADPH oxidase defect*

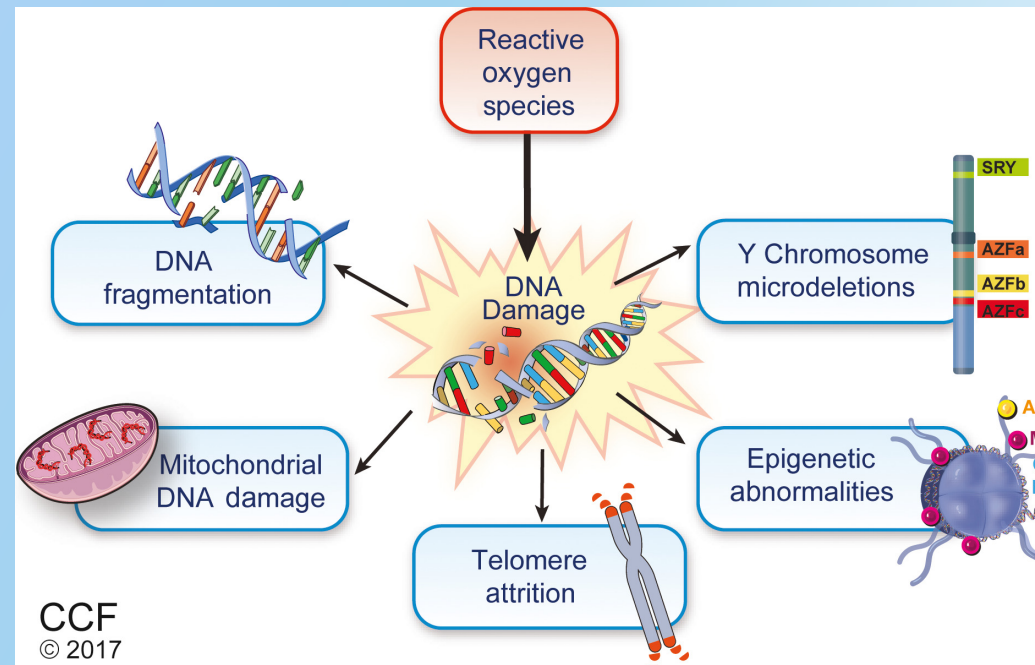
Pathological Generation

- Ionizing Radiation - water is hydrolyzed to hydroxyl free radical
- Inflammation
- Metals (i.e., *iron*, copper) - Fe²⁺ generates hydroxyl free radicals via the *Fenton Reaction*
- Drugs and chemicals - P450 system of liver metabolizes drugs (acetaminophen)



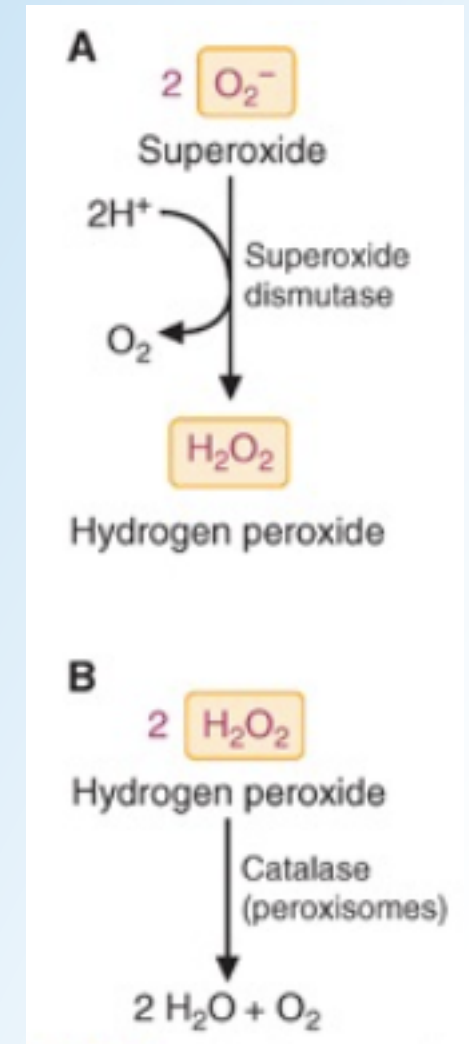
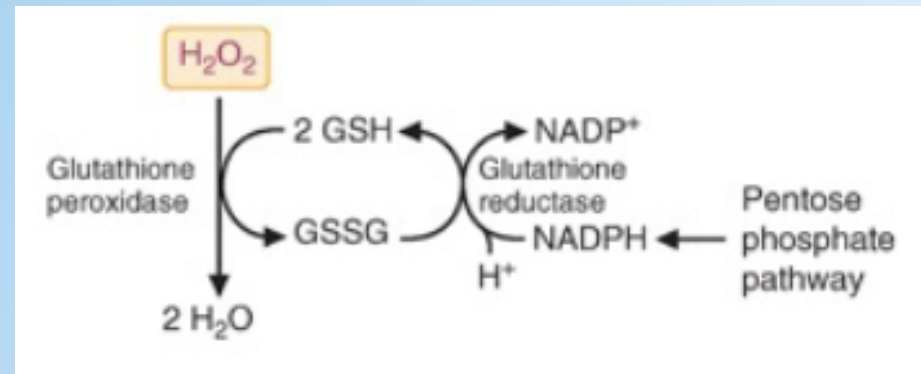
Damage

- cause cellular injury via
 - *peroxidation of lipids*
 - oxidation of proteins and DNA (oncogenesis and aging)



Elimination

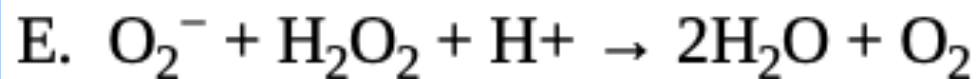
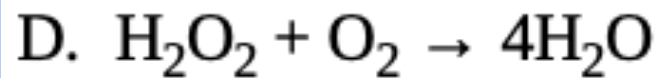
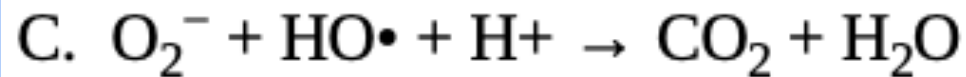
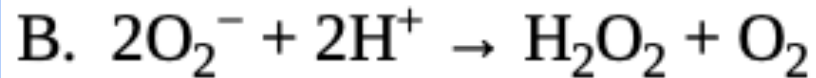
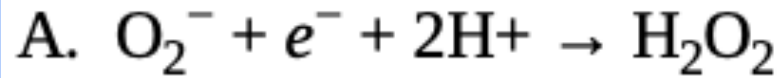
- antioxidants (*glutathione* and vitamins A, C, and E)
- metal carrier proteins (transferrin, ceruloplasmin)
- protective enzymes
 - superoxide dismutase
 - glutathione peroxidase
 - catalase (peroxisomes)



Reperfusion Injury

- return of blood flow to ischemic tissue results in production of O₂-derived free radicals -> further damages tissue
- leads to a continued rise in cardiac enzymes (troponin)

SOD is one of the body's primary defense mechanisms against oxidative stress. The enzyme catalyzes which one of the following reactions?



A patient with chronic granulomatous disease, who is complaining of fever, dermatitis, and diarrhea, is seen in your clinic. The genetic form of this disease results in the inability to generate, primarily, which one of the following?

- A. Superoxide
 - B. Hydrogen peroxide
-
- C. Reduced glutathione
 - D. Hypochlorous acid
 - E. Nitric oxide