Blood toxicity

by:

M.Sc. Nibras Jamal

TOXIC RESPONSES OF THE BLOOD

BLOOD AS A TARGET ORGAN

- Blood ranks with liver and kidney as one of the most important considerations in the risk assessment of individual patient populations exposed to potential toxicants in the environment, workplace, and medicine cabinet.

- **Hematotoxicology** is the study of adverse effects of drugs, nontherapeutic chemicals and other agents in our environment on blood and blood-forming tissues.

- The various blood cells (erythrocytes, granulocytes, and platelets) are each produced at a rate of approximately 1–3 million per second in a healthy adult and up to several times that rate in conditions where demand for these cells is high, as in hemolytic anemia or inflammation.

- Hematotoxicity may be regarded as:

✓ primary, where one or more blood components are directly affected.

✓ or secondary, where the toxic effect is a consequence of other tissue injury or systemic disturbances.

HEMATOPOIESIS

- Hematopoiesis, the production of blood cells, is a highly regulated sequence of events by which blood cell precursors proliferate and differentiate to meet the needs of oxygen transport, host defense and repair, hemostasis, and other vital functions.

- The bone marrow is the principal site of hematopoiesis in humans and animals.

- The spleen has a little function in blood cell production in healthy human, but plays a critical role in the clearance of defective or senescent cells, as well in host defense.

TOXICOLOGY OF THE ERYTHRON

The Erythrocyte

- Erythrocytes (red blood cells or RBCs) make 40–45% of the circulating blood volume and serve as the principal vehicle of transportation of oxygen from the lungs to the peripheral tissues, and transport of carbon dioxide from tissues to the lung.

- Xenobiotics may affect the production, function and/or survival of erythrocytes, and these effects are most frequently manifest as a change in the circulating red cell mass, usually resulting in a decrease (anemia).

- There are two general mechanisms that lead to anemia, either
  - decreased production
  - or increased erythrocyte destruction.

- Evaluation of a peripheral blood sample can provide evidence for the underlying mechanism of anemia.

- The usual parameters of a complete blood count (CBC), including
  - ✓ the red blood cell (RBC) count
  - ✓ hemoglobin concentration (Hbg)
  - ✓ and hematocrit (also referred to as packed cell volume, or PCV) can establish the presence of anemia.

Alterations in Red Cell Production

- Erythrocyte production is a continuous process that is dependent on frequent cell division and a high rate of hemoglobin synthesis.

- Adult hemoglobin (hemoglobin A), the major constituent of the erythrocyte cytoplasm, is a tetramer composed of two α- and two β-globin chains, each with a heme residue.

- An imbalance between α- and β-chain production is the basis of congenital **thalassemia** syndromes and results in decreased hemoglobin production and **microcytosis**.

- Xenobiotics can affect globin-chain synthesis and alter the composition of hemoglobin within erythrocytes.

➢ **Iron deficiency anemia** is usually the result of dietary deficiency or increased blood loss.

- Any drug that contributes to blood loss, such as nonsteroidal anti-inflammatory drugs, with their increased risk of gastrointestinal ulceration and bleeding, may potentiate the risk of developing iron deficiency anemia.

➢ Hematopoiesis requires active DNA synthesis and frequent mitoses.

- Folate and vitamin B12 are necessary to maintain synthesis of thymidine for incorporation into DNA. Deficiency of folate and/or vitamin B12 results in **megaloblastic anemia**.