



Hematology



WHAT IS HEMATOLOGY?

The study (morphology, physiology, and pathology) of blood and blood-forming organs and the diseases thereof

- Uses:
 - As part of a routine medical exam to assess overall health
 - Diagnosis (e.g., an infection, anemia, leukemia)
 - Monitoring of a condition and its treatment

HEMATOPOIESIS/HEMOPOIESIS

The formation of blood cells and platelets. In a fetus, formation starts in the yolk sac, moves to the liver and spleen, and then moves to the bone marrow. In an infant, formation occurs in bone marrow, which is present in almost all bones. In an adult, formation of blood cells (red and most white) and platelets occurs in the marrow of the proximal ends of the femur, pelvis, sacrum, vertebrae, ribs, sternum, and skull.

- **Hemopoietic growth factors:** Erythropoietin (EPO), FLT3 ligand (FLT3-L), granulocyte colony-stimulating factor (G-CSF), granulocyte-macrophage-CSF (GM-CSF), interleukin-1 (IL-1), IL-3, IL-5, IL-6, macrophage-CSF (M-CSF), stem cell factor (SCF), thrombopoietin (TPO), tumor necrosis factor (TNF), vascular endothelial growth factor (VEGF). Effects are mediated by binding receptors on cell surfaces.
- **Hemopoietic stem cell:** Pluripotent, rare (frequency is 1 per 20 million nucleated cells in bone marrow) CD34⁺CD38⁻Lin⁻ phenotype. Gives rise to more than 10⁶ mature cells after 20 cell divisions and can self-renew by asymmetric cell division.
- **Hemopoietic progenitor cell:** Multipotent.
- **Erythropoiesis:** Formation of red blood cells (RBCs); regulated by EPO, which is secreted by the kidneys in response to hypoxia (oxygen tension, the partial pressure of oxygen).
 - Stem cell → progenitor cell → colony-forming unit (CFU) granulocyte, erythroid, monocyte, and megakaryocyte (GEMM) (CFU_{GEMM}) → burst-forming unit (BFU) erythroid (BFU-E) (CFU_E) → proerythroblast → series of normoblasts in marrow that decrease in size, increase in hemoglobin (Hb) content, lose RNA; protein synthesis apparatus, and increase chromatin condensation → reticulocyte (nucleus extruded; nuclear DNA loss), which contains some ribosomal RNA (rRNA) and synthesizes Hb → mature erythrocyte (RBC) (red), which is a non-nucleated, bi-concave disc (i.e., cell-like).
 - Assays by Hb level, reticulocyte count, and bone marrow exam.
 - **Total erythropoiesis** assessed by the cellularity of marrow and myeloid/erythroid ratio.
 - **Effective erythropoiesis** assessed by reticulocyte count.
 - **Ineffective erythropoiesis:** 50–15% of erythroblasts die in bone marrow; increases in some chronic anemias; associated with increased unconjugated bilirubin (derived from the breakdown of Hb) and lactate dehydrogenase LDH (derived from breakdown of cells) in serum.
- **Extramedullary hematopoiesis (EH):** Formation and development of blood cells outside bone marrow in response to the failure of erythropoiesis in bone marrow.
- **Granulopoiesis:** Formation of granulocytes.
 - Stem cell → CFU → CFU granulocyte progenitor (CFU_G) → basophil
 - Stem cell → CFU → CFU granulocyte monocyte neutrophil (CFU_{GMN}) → CFU eosinophil progenitor (CFU_E) → eosinophil (acidophil)
 - Mast cell (mastocyte or basophil)
 - Stem cell → CFU → CFU → CFU granulocyte monocyte progenitor (CFU_{GMP}) → CFU-G → neutrophil
- **Lymphopoiesis:** Formation of lymphocytes and natural killer (NK) cells.
 - Stem cell → common lymphoid progenitor → B-lymphocyte (B cell)
 - Stem cell → common lymphoid progenitor → thymus → T lymphocyte (T cell)
 - Stem cell → common lymphoid progenitor → natural killer cell (NK cell)
- **Myelopoiesis:** Formation of blood marrow and all blood cells in marrow.
 - Monocyte formation
 - Stem cell → CFU → CFU → CFU → CFU-M → monocyte
- **Thrombopoiesis:** Formation of thrombocytes, or platelets, in about 10 days; regulated by TPO (95% from the liver; 50% constitutively produced and 50% produced in response to platelet destruction). As the platelet ages, it loses cell-surface sialic acid, exposing galactose residues that attach to the Achewell-Morell receptor in the liver, signaling for TPO production.
 - Stem cell → CFU → CFU megakaryocyte progenitor (CFU_M) → platelet (fragment of cytoplasm of megakaryocyte)
 - TPO binds to the c-MPL receptor on megakaryocytes and platelets, so plasma TPO is low in patients with excess platelets and high in patients with thrombocytopenia.

ORGANS OF THE LYMPHATIC SYSTEM

- **Bone marrow:** Modified connective tissue in bone cavities that is soft, fatty, and vascular.
 - **Red marrow:** Where blood cells are formed.
 - **Yellow marrow:** Mostly fat.
- **Lymph nodes:** Small, widespread organs of the lymphatic system, connected by lymphatic vessels. They filter lymph, form lymphocytes, become inflamed/enlarged with infection, disease, and injury, and are used to stage cancer.
- **Thymus gland:** Lymphoid organ behind the sternum where T cells are produced and mature; mature T cells migrate to lymph nodes throughout the body. This gland decreases in size with the onset of puberty and is replaced with fat.
 - **Thymosin:** Hormone produced by the thymus gland; stimulates T cell development.
- **Tonsils:** Pair of masses of lymphoid tissue located at the root of the tongue in the throat; M cells on the surface take up antigens (Ag) produced by pathogens and stimulate B cells and T cells; they also produce T cells.
- **Spleen:** Largest organ of the lymphatic system, located in the upper left quadrant of the abdomen. It filters blood, including old and damaged red blood cells, and produces lymphocytes.

BLOOD

Delivers oxygen, nutrients, and hormones to tissues; delivers carbon dioxide to lungs and other waste products to kidneys for removal; blood that leaves the heart returns in 20–30 seconds; there are 5–6 quarts of blood in the human body.

COMPONENTS

Red Blood Cells (RBCs)

- Also called **erythrocytes**, they are non-nucleated, bi-concave discs when mature. They contain Hb, have a 120-day lifespan, and are 6–8 µm diameter (avg).
- **Hemoglobin (Hb):** 4 polypeptide (globin) chains: 96–98% Hb-A (α₂β₂), 1.5–1.2% Hb-A₂ (α₂β₂), and 0.5–0.8% Hb-F (α₂γ₂), wherein each polypeptide chain (α, β, γ, and δ) contains an iron atom bound to protoporphyrin to form a heme; it transports oxygen from lungs to body tissues and carbon dioxide from body tissues to lungs.

White Blood Cells (WBCs)

Also called **leukocytes**, they defend the body against infection. There is ~1 WBC for every 500–700 RBCs.

GRANULOCYTES

- Also called **myelocytes**, they are immune cells containing granules that release enzymes.
- **Basophil:** Cell's granules release enzymes during an allergic reaction, asthma, and infection. It can be stained by basic dye, is phagocytic, and has a lifespan of a few hours to a few days.
- **Eosinophil (acidophil):** Cell's granules release enzymes during an allergic reaction, asthma, and an infection with parasites. It can be stained by acidic dye, is phagocytic, and has a lifespan of 8 to 12 days.
- **Neutrophil (polymorph):** Most numerous WBC; characterized by a dense, multi-lobed nucleus (2–5 lobes) and a pale cytoplasm with an irregular outline and fine azurophilic granules, which are predominantly secondary (specific) granules (see **myelocyte** below). Has a 6–50 hour lifespan.
 - These precursors, located in bone marrow, rarely occur in normal peripheral blood other than the band, stab, and juvenile forms.
- **Myeloblast:** Also called **myelomonoblast**, it is the earliest recognizable precursor; characterized by a large nucleus with fine chromatin and 2–5 nucleoli, and a cytoplasm with no granules. It varies in size, is capable of cell division, and it gives rise to promyelocytes. Bone marrow comprises less than 5% myeloblasts and it is difficult to distinguish from monoblasts, promonocytes, and monocytes (see **monocyte** below).
- **Promyelocyte:** Slightly larger than myeloblasts, can distinguish commitment to basophilic, eosinophilic, and neutrophilic lineages using electron microscopy (EM). Cytoplasm contains primary granules (of lysosomal origin) containing myeloperoxidase (MPO) and other acid hydrolases. It is capable of cell division, and gives rise to myelocytes.
- **Myelocyte:** Can distinguish morphological commitment to basophilic, eosinophilic, and neutrophilic lineages. The nuclear chromatin is more condensed, nucleoli are not visible, and the cytoplasm contains secondary (specific) granules of lysosomal origin containing lactoferrin, lysozyme, and other enzymes. It is capable of cell division and gives rise to metamyelocyte.
- **Metamyelocyte:** Non-dividing cell. The nucleus is indented or band-shaped and the cytoplasm contains primary and secondary granules.
- **Band, stab, or juvenile:** Forms of neutrophil between metamyelocyte and mature neutrophil. They are distinguishable from mature neutrophil by the absence of clear, fine filaments between nuclear lobes.
- **Functions:**
 - **Chemotaxis:** Cell is mobilized and migrates to a foreign material (e.g., bacterium, fungus, debris) or a site of inflammation by chemotactic substances released by damaged tissue, cytokines, and by the interaction of leukocyte adhesion molecules with ligands on damaged tissue.
 - **Phagocytosis:** Ingestion of bacteria, fungi, foreign debris, and dead or damaged host cells.
 - **Cling and digestion:**
 - **Oxygen-dependent:** Superoxide, hydrogen peroxide, and other activated oxygen species are generated from oxygen and reduced nicotinamide adenine dinucleotide phosphate (NADPH). Bacteria are killed when hydrogen peroxide reacts with halide and myeloperoxidase; process may also involve activated oxygen species.
 - **Oxygen-independent:** Proteins, such as cathelicin C, lysozyme (with hydrogen peroxide), or elastase (with hydrogen peroxide) kill bacteria; may also act with a decrease in pH inside a phagocytic vacuole containing lysosomal enzymes. Lactoferrin binds iron, thereby depriving bacteria of iron and generating free radicals (bactericidal).

Hematology Fellow Study Guide

**Francis P. Worden, Rami N.
Khoriaty, Kathleen A. Cooney, Michael
Deininger**

Hematology Fellow Study Guide:

Hematology Board Review Rami N. Khoriaty, Morgan Jones, Francis P. Worden, 2023-12-27 Now in its second edition Hematology Board Review has been thoroughly revised and updated to contain the latest information that fellows and clinicians need to successfully prepare for the Hematology Certification Exam administered by the American Board of Internal Medicine ABIM The new edition now contains even more high yield board study content and review questions For the hematology oncology fellow hematologist medical oncologist or internist looking to review a given disease or blueprint category prior to their examination this extremely practical study guide provides the pertinent points of emphasis that are often highlighted on the exam Chapters on blood disorders and disease sites cover epidemiology etiology and risk factors staging signs and symptoms diagnostic criteria indications for treatment prognostic factors treatment recommendations and special considerations Clinical pearls on other major subspecialty areas found on the exam include hematologic emergencies and supportive care transfusion medicine stem cell biology and hematopoiesis cellular therapy management of hematologic disease complications after cellular therapy and biostatistics With 240 practice questions detailed rationales and a convenient print digital package Hematology Board Review gives you the tools to study your way and the confidence to pass the first time Key Features Aligns with the latest Hematology Certification Exam ABIM blueprint Provides a comprehensive yet concise review of all hematologic malignancies blood disorders transfusion medicine cellular therapy standard treatment regimens and biostatistics Revised to include new treatment recommendations and FDA approvals Includes end of chapter assessment questions with detailed rationales a total of 240 questions

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Hematology Board Review Francis P. Worden, Rami N. Khoriaty, Kathleen A. Cooney, Michael Deininger, 2018 Note to Readers Publisher does not guarantee quality or access to any included digital components if book is purchased through a third party seller Now with a free mobile web app with print purchase Hematology Board Review Blueprint Study Guide and Q A is a concise outline based study guide covering all topics that appear on the Hematology Certification Exam The book includes all topics listed in the American Board of Internal Medicine ABIM blueprint as essential material for the exam and highlights topic areas that are often found on the test For hematology and oncology fellows as well as practicing clinicians needing a refresher before taking MOC this handy study guide which comes with a mobile optimized App provides succinct overviews of all blood disorders syndromes and diseases with practice questions on the go Each disorder or disease based chapter provides the same structure for ease of use beginning with the epidemiology and followed by the etiology and risk factors signs and symptoms diagnostic criteria indications for treatment prognostic factors treatment recommendations and special considerations The authors provide the most accurate and up to date information including well established treatment regimens for a variety of blood disorders including iron disorders bone marrow failure syndromes platelet and megakaryocytic disorders hemostasis thrombosis and hematologic malignancies Later chapters review other major subspecialty areas found on the exam including transfusion medicine and hematopoietic cell transplantation With 200 board style questions and answers with detailed rationales Hematology Board Review is the go to quick review for any trainee preparing for initial certification and for hematologists or oncologists preparing for recertification Key Features Includes 200 board style questions and answers with rationales Provides key point summaries of each topic area for quick study and easy recall Thorough coverage of hematologic malignancies blood disorders transfusion medicine hematopoietic cell transplantation and standard treatment regimens Tables providing key data and information related to staging treatment options and disease classifications Includes free access to mobile and online app track and sync your progress on up to three devices **Oncology Board Review, Third Edition** Francis P. Worden, Rami N. Khoriaty, Erin Cobain, 2021-11-10 Now in

its third edition Oncology Board Review Blueprint Study Guide and Q A is designed to help you prepare for the American Board of Internal Medicine ABIM Medical Oncology Certification Exam This comprehensive digital resource has been revised to include new treatment regimens clinical guidelines and other advancements impacting the field as well as updated board style Q A Dedicated sections cover hematological malignancies and solid tumors with a templated chapter approach highlighting epidemiology etiology and risk factors diagnostic criteria staging signs and symptoms of the disease prognostic factors indications for treatment and special considerations Later sections address other topics found on the exam including cancer genetics and tumor biology supportive and palliative care bone marrow transplantation and biostatistics With more than 240 practice questions and detailed rationales Oncology Board Review gives you the tools to study your way and the confidence to pass the first time Key Features Aligns with the latest ABIM Medical Oncology Certification Exam blueprint Provides a comprehensive yet concise review of all hematologic malignancies and solid tumors Covers anticancer therapies clinical research methodology survivorship and palliative care and more areas found on the exam Revised to include new treatment recommendations and FDA approvals Includes end of chapter assessment questions with detailed rationales a total of more than 240 questions throughout **Oncology Board Review, Second Edition** Francis P. Worden,Rami N.

Khoriaty,Erin Cobain,Alexander T. Pearson,2017-05-08 Print version of the book includes free access to the app web iOS and Android which offers interactive Q A review plus the entire text of the print book Please note the app is included with print purchase only Oncology Board Review Blueprint Study Guide and Q A is a concise outline based study guide covering the topics that appear on the Medical Oncology Certification Exam This second edition has been thoroughly revised to include new treatment regimens clinical guidelines and other updates impacting the field and reflected on the test The book includes all topics listed in the American Board of Internal Medicine ABIM blueprint as essential material for the Medical Oncology Certification Exam The coverage spans all hematologic malignancies and solid tumors beginning with the epidemiology and followed by the etiology and risk factors of the disease staging signs and symptoms diagnostic criteria indications for treatment prognostic factors treatment recommendations and special considerations Later chapters review other major subspecialty areas found on the exam including cancer genetics and tumor biology supportive and palliative care bone marrow transplantation and biostatistics Each chapter includes key points summarized in digestible bullets for easy recall and self assessment And now containing over 230 board style questions with answers and detailed rationales Oncology Board Review Second Edition is the go to quick review for any trainee preparing for initial certification and for oncologists preparing for recertification New to this Edition Includes over 230 board style questions and answers with rationales New chapter on Bone Marrow Transplantation Thoroughly updated and revised chapters with all new treatment recommendations and FDA approvals for solid tumors and hematologic malignancies included **Clinical Informatics Study Guide** John T. Finnell,Brian E. Dixon,2022-04-22 This completely updated study guide textbook is written to support the formal training

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Cancer Pharmacology and Pharmacotherapy Review Anthony J. Perissinotti, Bernard L. Marini, 2016-03-14 Cancer Pharmacology and Pharmacotherapy Review is the first book devoted entirely to providing the must know facts on each cancer agent including their pharmacokinetics FDA approved indications toxicity interactions and other important information that is commonly found on board examinations and essential for any clinician or practitioner to review The authors an oncologist and two pharmacists have developed a handy question and answer format to present the material in digestible bursts As the pharmacology section continues to represent a major portion of the medical oncology exam and a key component on oncology MOC exams this portable study guide will help prepare anyone looking to fine tune their knowledge on cancer drugs before the test Not to mention with recent advancements in the field of cancer treatment it has become more cumbersome to recall and maintain essential knowledge of every cancer therapeutic making this book not only an exam resource but also a handy quick reference for oncologists and pharmacists alike **KEY FEATURES** Conveniently organized and arranged by drug class and subtypes for easier recall and classification Includes proper dosage adjustments to account for liver and kidney dysfunction Features tables throughout that provide quick reference regarding FDA approved medications Simplified diagrams and illustrations facilitate the pharmacokinetic processes *Study Guide for The Human Body in Health and Illness - E-Book* Barbara Herlihy, 2017-10-28 Use this practical review to get the most out of your A P textbook Corresponding to the chapters in The Human Body in Health and Illness 6th Edition by Barbara Herlihy this study guide makes it easy to understand and remember basic Anatomy Physiology Engaging exercises activities and quizzes help you memorize A P terms and master the key concepts relating to A P and disease of the human body Even if you find science intimidating this review tool can help you succeed in A P Textbook page references are included with the questions to make it easier to find and review A P topics Objectives at the beginning of each chapter reinforce the goals of the textbook and set a

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