New illustrated guide to bone marrow based on PT

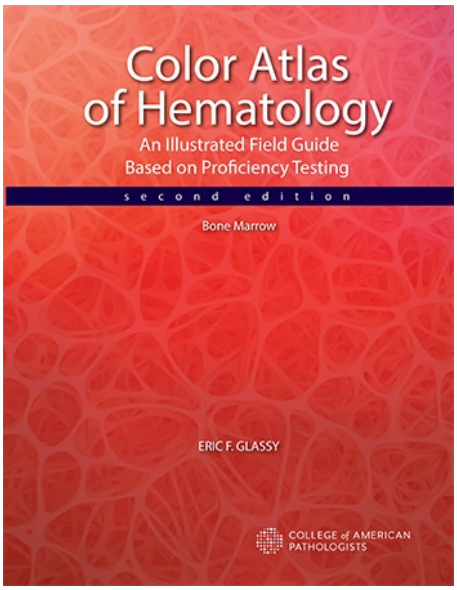
March 2022—*CAP Publications will release this spring volume two of the second edition of the* Color Atlas of Hematology*—on bone marrow. It continues in the tradition of its predecessor on peripheral blood cells (volume one, 2018): morphologic identification of cells based on proficiency testing. The senior and associate editors have organized the various components of volume two into "an eminently readable, practical, and in many respects entertaining resource for anyone interested in bone marrow morphology, physiology, and pathophysiology," Donald S. Karcher, MD, of George Washington University, writes in the foreword.*

CAP TODAY *asked Eric F. Glassy, MD, senior editor of the atlas and medical director of Affiliated Pathologists Medical Group, Rancho Dominguez, Calif., about the newest volume. Here is what he told us. A brief section from the atlas appears below.*

Tell us about the book's content and how it's organized and why Donald Karcher, MD, wrote in the foreword that the book is "more than a mere atlas."

Like its predecessor, volume two of the second edition of the *Color Atlas of Hematology* is based on proficiency testing challenges. That is its origin story. Volume one focused on peripheral blood and volume two on bone marrow. After an introduction containing sections on bone marrow sampling, marrow environment, smear differentials, and artificial intelligence, the main chapters deal with nucleated red cells, granulocytes and monocytes, megakaryocytic cells, blasts, lymphocytes and plasma cells, and miscellaneous bone marrow cells. Each identification has vital statistics, illustrations highlighting pertinent morphologic features, a discussion, and proficiency testing photomicrographs. Sections called "A Closer Look At . . ." provide a deeper dive into important concepts. But there is so much more.

Dr. Karcher rightly points out that this book is not just an atlas. Of course there are plenty of static images (937) and illustrations (274). More importantly, there are 125 virtual bone marrow smear links that can be navigated using the CAP's DigitalScope whole slide image viewer. These virtual smears provide as close to a real glass slide and analog microscope experience as possible, in keeping with one of the key tenets of proficiency testing. Finally, authors recorded 16 video vignettes of topics they were passionate about. This supplements the text quite nicely and follows the success of the CAP's Virtual Lecture series.



The images of bone marrow elements in the new book are taken from photographs used over many years in the CAP proficiency testing challenges. And you write in the preface that the "collective observations and wisdom of thousands of laboratorians are used to define truth." Why is this one of the book's strengths?

Morphology is still foundational for hematology. It provides diagnoses well before sophisticated testing can be performed, such as flow cytometry, cytogenetics, and FISH. But experts can disagree. The CAP Hematology/Clinical Microscopy Committee—the group that selects the proficiency testing challenges—does not always have a consensus for cell identification. Blood cells are dynamic—morphologic features blend from one stage to another. So how do you determine true north? What is the correct answer? The committee has always believed in the power of the laboratory—the collective wisdom of pathologists and technologists. The final answer is built on a crowdsourced response to an unknown cell. That is how proficiency testing is graded—80 percent of labs are

needed for consensus.

The section on artificial intelligence in the introduction envisions a future world where digital pathology coupled with artificial intelligence transform the practice of hematopathology. Can you tell us a bit more?

This section in the introductory chapter was written by a good friend, Mohamed Salama, MD. He predicts that artificial intelligence will dramatically change the practice of hematology over the next five to 10 years. Algorithms combined with digital pathology will soon outperform traditional microscopy. Multiple studies using machine learning for diagnosis, classification, and differentiation of neoplastic hematologic conditions and their precursors have confirmed the utility of AI in the diagnostic workflow. This will most likely change how proficiency testing is performed, and if that is the case, I am sure the next edition of this *Color Atlas* will have a greatly expanded discussion of hematologic algorithms.

What should potential readers of the atlas know about your associate editors, David Blomberg, MD, and Katherine Galagan, MD, and many contributors and the role of the CAP Hematology/Clinical Microscopy Committee over years?

My two fellow editors once again need special recognition—Drs. Katherine Galagan and David Blomberg. Each brings unique skills to this publishing endeavor. They share senior editorship with me and were always available for inspiration. This book would never have been published without their unflagging assistance. I am proud of our contributions to pathology literature—now having collaborated on four CAP color atlases. We make a good team.

The 18 contributing authors are members or were members of the Hematology/Clinical Microscopy Committee—all experts in their field. I also want to single out Patrick Ward, MB, BCh, who is one of the world's best morphologists. He has an amazing collection of hematology images, perhaps the largest in the world, and they are all pristinely photographed. He generously shared his photomicrographs with us.

You've worked on six atlases for the CAP so far. Will there be a seventh?

Dr. Galagan, Dr. Blomberg, and I just received the green light from the CAP Publications Committee to begin work on the second edition of the body fluids atlas. The CAP now has virtual body fluid proficiency testing, and those whole slide scans will be the centerpiece of this new and expanded atlas. I hope we can visit again when that book is published.

Following is the section on neutrophil necrobiosis (degenerated neutrophil) from the chapter on granulocytes and monocytes.

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Neutrophil Necrobiosis (Degenerated Neutrophil)

Degenerated neutrophils are generally easily identified since they resemble normal segmented neutrophils. The major distinguishing feature is karyorrhexis and/or pyknosis of the nucleus. These changes are appreciated when a cell with neutrophilic granules (pale pink cytoplasm with fine lilac granules) contains multiple, unconnected nuclear lobes (karyorrhexis) or a single, dark, round to oval nucleus (pyknosis). The chromatin is dense and homogeneous without visible parachromatin or nucleoli. The nuclear outlines may become indistinct and blurred. The nuclear lobes may also fragment into numerous small particles of varying sizes that resemble microorganisms such as bacteria or fungi. The degenerating cell may also contain real fungi or bacteria; special stains may be needed to confirm the diagnosis.

As the cellular degeneration continues, the cytoplasm will become hypogranulated and then agranular. The cytoplasmic borders may become frayed and indistinct. Sometimes, the cells will contain scattered larger azurophilic or dark blue granules (toxic granulation). Vacuolization is frequent.

Other cells that may resemble degenerated neutrophils are nucleated red cells in the blood and orthochromatophilic normoblasts in the bone marrow. These cell types have pinkish orange, agranular cytoplasm and have a single, often eccentric nucleus with dense chromatin and very little to no parachromatin. The nuclear-to-cytoplasmic ratio is about 1:2, and the nuclear and cytoplasmic borders are sharp and distinct.

If a cell is too degenerated to recognize it as a neutrophil, one should identify it as a basket/smudge cell. Basket/smudge cells have no identifiable characteristics and consist of smeared nuclear material without distinguishable cytoplasm.

SYNONYMS
Degenerated leukocyte

VITAL STATISTICS

Size	10 to 15 µm
N:C ratio	1:3 or less
Cell shape	usually round or oval
Nuclear shape	variable; multiple lobes that often vary in size and shape without connecting filaments; can be single; may appear fragmented and small, resembling organisms; nuclear margins may be blurred
Chromatin	pyknotic, dark, homogeneous and dense; parachromatin not visible
Nucleoli	none
Cytoplasm	abundant; generally pale pink with numerous fine, lilac granules; toxic granulation; can be hypogranular or agranular; often vacuolated; cytoplasm becomes frayed as cell degenerates; may contain ingested organisms

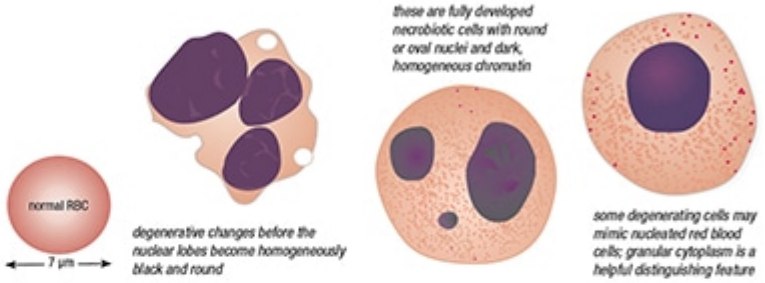
KEY DIFFERENTIATING FEATURES
- Abundant cytoplasm containing neutrophilic granules and multiple, unconnected nuclear lobes with dark, homogeneous chromatin
- Based on cytoplasmic appearance and nuclear characteristics can still be identified as neutrophils, rather than basket cells/smudge cells

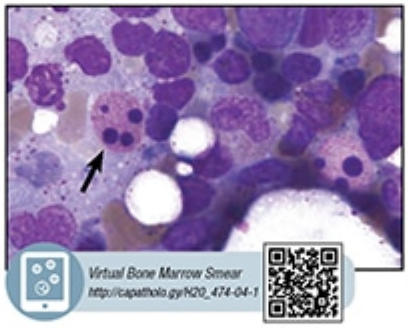
OTHER FINDINGS
- Signs of infection or inflammation such as neutrophilia, toxic granulation and/or vacuolization, and left-shifted myeloid maturation; may see ingested organisms (must be distinguished from small nuclear fragments)

POTENTIAL LOOK-ALIKES
- Orthochromatophilic normoblasts
- Neutrophils with toxic granulation and/or vacuolization
- Degenerated leukocytes

ASSOCIATED DISEASE STATES AND CONDITIONS
- Nonspecific and non-diagnostic finding
- Normal bone marrows
- Wide range of pathologic conditions including:
  - infections
  - inflammation
  - reactive disorders
  - malignancies

Necrobiotic Neutrophils



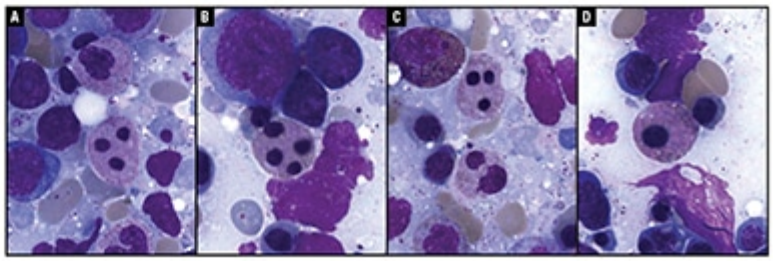


BMD-04, 2015 (Marrow, WG, X330)

Identification	Referee %	Participant %
Neutrophil necrobiosis	-	94.7
Neutrophil with dysplasia	-	3.5

The arrowed cell is an example of a neutrophil undergoing necrobiosis. The degenerated cell shows multiple unconnected nuclear lobes with dark, dense and homogeneous pyknotic nuclear material. A second similar cell on the far right is a necrobiotic neutrophil. The cytoplasm resembles the myelocyte in the center of the field, which has neutrophil granules present. In the peripheral blood this is a relatively common finding that can be seen in normal individuals as well as in a spectrum of medical conditions such as infections, chronic inflammatory disorders, and malignancies. This is a nonspecific finding but important to recognize, especially when there is only one single dark pyknotic nucleus, as the cell may be misidentified as a nucleated red cell or dysplastic cell.

Other Examples of Necrobiosis in Bone Marrow



*Photomicrographs all show necrobiotic neutrophils. Each of the degenerated cells in **A, B** and **C** contain unconnected lobes that are composed of dark pyknotic nuclear material. The central cell in photomicrograph **D** is unilobed. The cytoplasm of the necrobiotic cells contains neutrophilic granules which are similar to those seen in more viable adjacent neutrophils. A distinguishing feature of necrobiotic neutrophils is the presence of distinct, round, pyknotic lobes. It is important not to label these cells as dysplastic. Dysplastic nuclei retain a recognizable chromatin pattern unlike these cells. An example of a dysplastic neutrophil is in photomicrograph **C**. This is a pseudo-Pelger-Huët cell which is just beneath the necrobiotic one. The lobes are not round and chromatin material is visible.*