

**Fig. 6.1.** Schematic representation of the hemic cells that may be found in bone marrow of healthy mammals. The two major pools are cells of the neutrophil series in the granulocytic pool and cells of the erythroid pool. Eosinophils and basophils and their precursors are also components of the granulocytic pool. Monocytes are part of the myeloid pool but not the granulocytic pool. Megakaryocytes may be considered part of the myeloid pool or may be evaluated as a separate cell line and not included in the M : E ratio. Mast cells are terminally differentiated tissue cells rather than hematopoietic cells and are not included in the M : E ratio. Lymphocytes and plasma cells belong to the nonmyeloid lymphoid pool.

B, band neutrophil; CFU-E, colony-forming unit–erythroid; CFU-G, colony-forming unit–granulocyte; Mb, myeloblast; Mc, myelocyte; Mmc, meta-myelocyte; Mr, metarubricyte; Pg, progranulocyte; Pr, prorubricyte; Rb, rubriblast; Rc, rubricyte; and S, segmented neutrophil.

**Fig. 6.2.** The algorithm to use when hemic neoplasia is suspected because of an increased concentration of well-differentiated or atypical cells in blood or bone marrow:

- An increased concentration of well-differentiated erythrocytes, platelets, lymphocytes, monocytes, neutrophils, eosinophils, or basophils could be neoplastic or nonneoplastic.
  - ♦ Nonneoplastic disorders or conditions include appropriate or secondary inappropriate erythrocytosis, reactive thrombocytosis, or various types of inflammation.
  - ♦ Exclusion of nonneoplastic disorders or conditions incriminates one of the chronic myeloproliferative diseases (see Table 6.5), but confirmatory cytogenetic tests are currently unavailable.
- An increased population of nucleated cells with undifferentiated and immature features may be neoplastic or nonneoplastic. Neoplasia may or may not be obvious, depending mostly on the size of the population.
  - ♦ Nonneoplastic immature populations in blood or bone marrow may increase with reactive lymphocytosis, proliferation of immature granulocytes in a severe inflammatory reaction, reactive megakaryocytic hyperplasia, or markedly stimulated erythropoiesis in a severe regenerative anemia.
  - ♦ If findings do not support nonneoplastic disorders or conditions, hemic neoplasia should be characterized by immunophenotyping and possibly cytochemical staining of blood or bone marrow by means of panels of antibodies and stains.
    - If cells have a lymphoid phenotype, CD34 positivity supports ALL, whereas a CD34-negative population of lymphocytes may be chronic lymphocytic leukemia, lymphoma involving bone marrow and/or blood, or ALL of granular lymphocytes.
    - If atypical cells do not express identifying markers, that is evidence for an acute undifferentiated leukemia. Other rare acute leukemias of ambiguous origin include those consisting of more than one distinct atypical population (e.g., lymphoid blasts and myeloid blasts) or of one population of atypical cells expressing multiple phenotypes (e.g., lymphoid and myeloid markers).
    - If cells have a nonlymphoid phenotype, they may be identified as megakaryoblasts, rubriblasts, monoblasts, myeloblasts, or myelomonoblasts. Bone marrow analysis is needed to classify these proliferations.
- If erythroid cells are the minority of “all nucleated cells” and at least 30 % (or 20 % using the current human guideline) of “all nucleated cells” are “blasts,” then the patient has an acute myeloid leukemia other than erythroleukemia.
- If the erythroid cells are the minority of “all nucleated cells” and less than 30 % (20 %) of “all nucleated cells” are “blasts,” one should consider MDS or a chronic myeloid leukemia. Prominent dysplasia and ineffective hematopoiesis support MDS. A left-shifted granulocyte series with effective granulopoiesis would support chronic myeloid leukemia.
- When erythroid cells are at least half of “all nucleated cells,” either the percentage of nonerythroid cells that are “blasts” or the percentage of “all nucleated cells” that are “blasts” plus rubriblasts is used to determine whether there is erythroleukemia, erythroleukemia with erythroid predominance, or MDS with erythroid predominance.
- If the atypical cells are clearly plasma cells, reactive plasmacytosis must be differentiated from a plasma cell myeloma.
- If the cells are clearly mast cells, reactive mastocytosis must be differentiated from metastatic mast cell neoplasia and mast cell leukemia.
- If dysplasia is prominent and the cells do not fulfill criteria for acute myeloid leukemia or one of the chronic myeloproliferative diseases, then a MDS or myelodysplastic/myeloproliferative disease (e.g., CMMoL) should be considered.

*All nucleated cells* includes granulocytic, erythroid, and megakaryocytic cells, and excludes lymphocytes, plasma cells, monocytes, macrophages, and mast cells. *Nonerythroid cells* means “all nucleated cells” that are not nucleated erythroid cells, and *blasts* means myeloblasts, megakaryoblasts, monoblasts ± promonocytes, and atypical promyelocytes but not rubriblasts and lymphoblasts. ALL, acute lymphocytic leukemia; CLL, chronic lymphocytic leukemia; MDS, myelodysplastic syndrome; and CMMoL, chronic myelomonocytic leukemia, classified by the WHO system for hemic neoplasia as a myelodysplastic/myeloproliferative disease rather than MDS or one of the chronic myeloproliferative diseases.

**Fig. 6.3.** Schematic examples of the interpretation of CBC and bone marrow biopsy results. Reference intervals and other expected results for healthy dogs are provided in the *right column*. The number of marrow megakaryocytes is represented by the number and size of schematic megakaryocytes. Granulocytic and erythroid pools are represented by pool diagrams that are miniatures of those shown in Chapters 2 and 3. G : E ratios were calculated from the number of cells illustrated in the granulocytic and erythroid pools:

- Dog 1: Decreased fragment hematopoietic cellularity and an increased G : E ratio indicate erythroid hypoplasia. CBC results of a nonregenerative anemia without abnormal platelet or neutrophil concentrations support that it is selective erythroid hypoplasia.
- Dog 2: Increased fragment hematopoietic cellularity and a decreased G : E ratio indicate erythroid hyperplasia. CBC data indicate it is associated with a regenerative anemia; therefore, it is probably caused by blood loss or hemolysis. If CBC data indicated a persistent nonregenerative anemia, one would have to consider causes of ineffective erythropoiesis (see the text).
- Dog 3: Decreased fragment hematopoietic cellularity, a G : E ratio within the reference interval, and decreased megakaryocytes indicate generalized marrow hypoplasia. CBC data support the presence of an aplastic anemia (aplastic pancytopenia).
- Dog 4: Increased fragment hematopoietic cellularity with a decreased G : E ratio indicates erythroid hyperplasia. Increased density of megakaryocytes indicates megakaryocytic hyperplasia. CBC data further indicate effective erythropoiesis (reticulocytosis) and a stimulus for megakaryocytic hyperplasia (thrombocytopenia). Neutrophilia is evidence for myeloid hyperplasia despite a decreased G : E ratio; the granulocytic series is expanded, but the erythroid series is expanded more. The regenerative anemia is probably caused by blood loss or hemolysis, the neutrophilia is caused by an inflammatory process, and the thrombocytopenia is caused by decreased platelet survival. This dog’s inflammatory neutrophilia could be associated with an immune-mediated anemia and immune-mediated thrombocytopenia.
- Dog 5: Increased fragment hematopoietic cellularity and an increased G : E ratio with a predominance of atypical immature granulocytic cells indicates granulocytic neoplasia. A paucity of megakaryocytes and erythroid cells suggests the possibility of myelophthisic megakaryocytic and erythroid hypoplasia. CBC findings of thrombocytopenia and nonregenerative anemia further support this interpretation. Neutropenia is caused by defective neutropoiesis (neoplasia).

Hct, hematocrit.