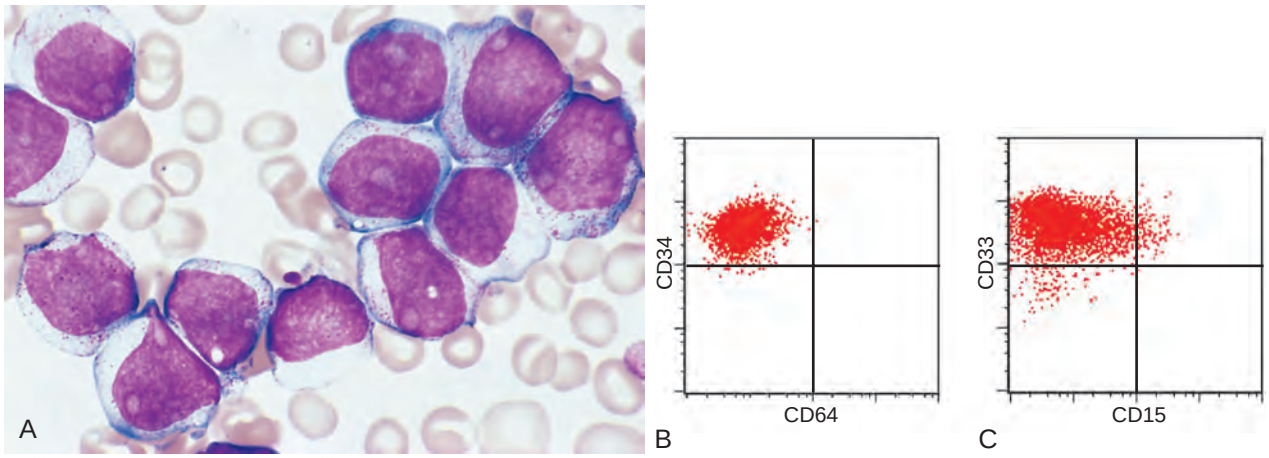

Figure 13-29 **A,** Acute myeloid leukemia without maturation (FAB M1 subtype). Myeloblasts have delicate nuclear chromatin, prominent nucleoli, and fine azurophilic granules in the cytoplasm. **B,** In the flow cytometric analysis shown, the myeloid blasts, represented by the red dots, express CD34, a marker of multipotent stem cells, but do not express CD64, a marker of mature myeloid cells. **C,** The same myeloid blasts express CD33, a marker of immature myeloid cells, and a subset express CD15, a marker of more mature myeloid cells. Thus, these blasts are myeloid cells showing limited maturation. (**A,** Courtesy Dr. Robert W. McKenna Department of Pathology, University of Texas Southwestern Medical School, Dallas, Tex; **B** and **C,** courtesy Dr. Louis Picker, Oregon Health Science Center, Portland, Ore.)

Gene expression is regulated by two types of epigenetic modifications, DNA methylation and posttranslational modifications of histones (e.g., acetylation, methylation, phosphorylation). Some of the most commonly mutated genes in AML encode factors that influence DNA methylation or histone modifications. Another 15% of tumors have mutations involving genes encoding components of the cohesin complex, proteins that regulate the three-dimensional structure of chromatin. The precise mechanism by which these mutations contribute to the development of AML remains to be determined and is a "hot" area of current research.

MORPHOLOGY

The diagnosis of AML is based on the presence of at least 20% myeloid blasts in the bone marrow. Several types of myeloid blasts are recognized, and individual tumors may have more than one type of blast or blasts with hybrid features.

Myeloblasts have delicate nuclear chromatin, two to four nucleoli, and more voluminous cytoplasm than lymphoblasts (Fig. 13-29*A*). The cytoplasm often contains fine, peroxidase-positive azurophilic granules. **Auer rods**, distinctive needle-like azurophilic granules, are present in many cases; they are particularly numerous in AML with the t(15;17) (acute promyelocytic leukemia) (Fig. 13-30*A*). **Monoblasts** (Fig. 13-30*B*) have folded or lobulated nuclei, lack Auer rods, and are nonspecific esterase-positive. In some AMLs, blasts show megakaryocytic differentiation, which is often accompanied by marrow fibrosis caused by the release of fibrogenic cytokines. Rarely, the blasts of AML show erythroid differentiation.

The number of leukemic cells in the blood is highly variable. Blasts may be more than 100,000/mm^3, but are under 10,000/mm^3 in about 50% of patients. **Occasionally, blasts are entirely absent from the blood (aleukemic leukemia).** For this reason, a bone marrow examination is essential to exclude acute leukemia in pancytopenic patients.

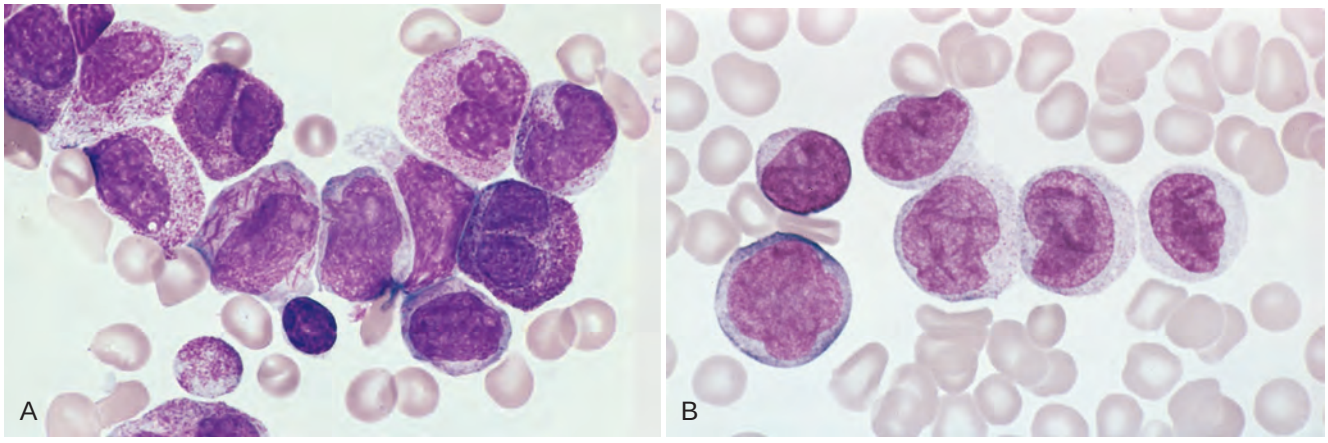

Figure 13-30 Acute myeloid leukemia subtypes. **A,** Acute promyelocytic leukemia with the t(15;17) (FAB M3 subtype). Bone marrow aspirate shows neoplastic promyelocytes with abnormally coarse and numerous azurophilic granules. Other characteristic findings include the presence of several cells with bilobed nuclei and a cell in the center of the field that contains multiple needle-like Auer rods. **B,** Acute myeloid leukemia with monocytic differentiation (FAB M5b subtype). Peripheral smear shows one monoblast and five promonocytes with folded nuclear membranes. (Courtesy Dr. Robert W. McKenna, Department of Pathology, University of Texas Southwestern Medical School, Dallas, Tex.)