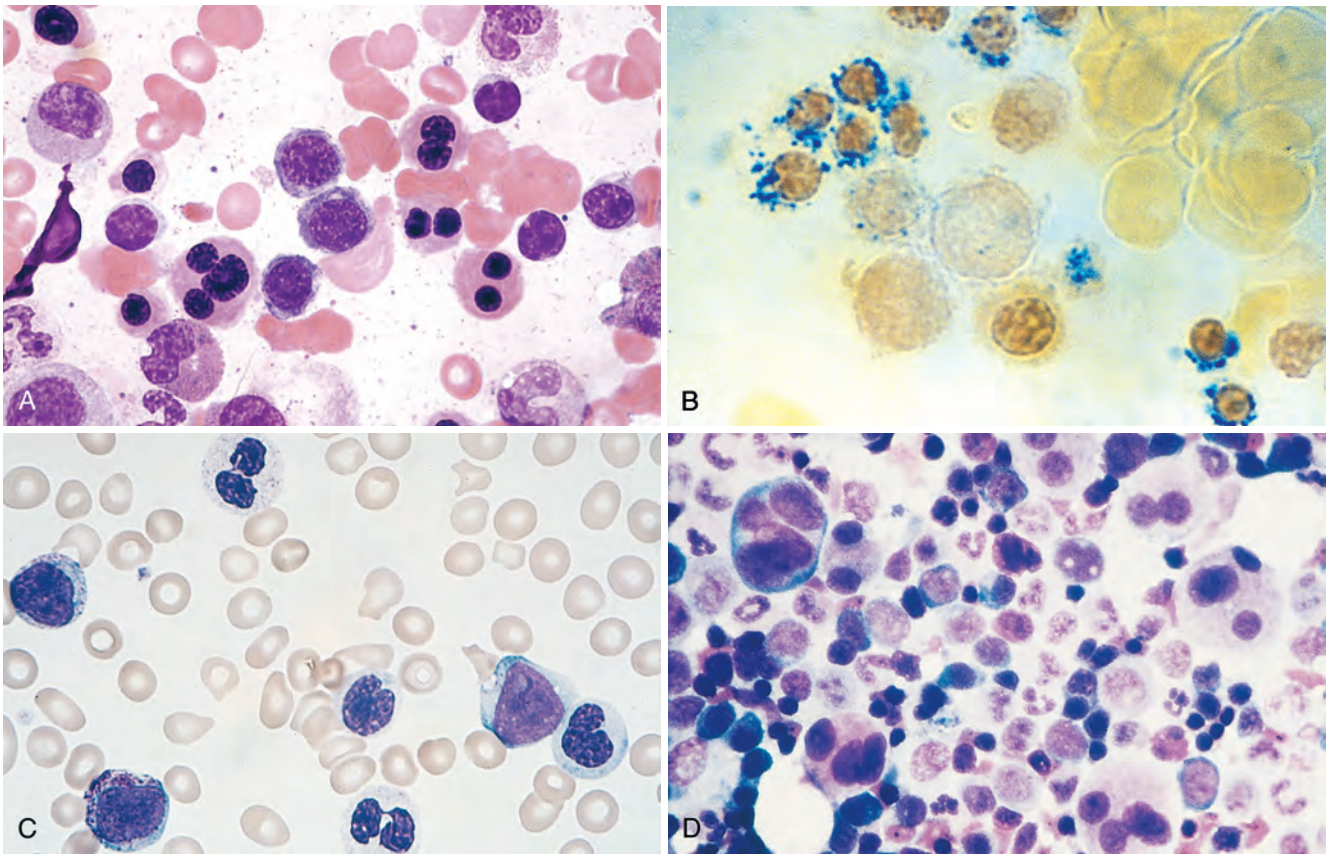

Figure 13-31 Myelodysplasia. Characteristic forms of dysplasia are shown. **A,** Nucleated red cell progenitors with multilobated or multiple nuclei. **B,** Ringed sideroblasts, erythroid progenitors with iron-laden mitochondria seen as blue perinuclear granules (Prussian blue stain). **C,** Pseudo-Pelger-Hüet cells, neutrophils with only two nuclear lobes instead of the normal three to four, are observed at the top and bottom of this field. **D,** Megakaryocytes with multiple nuclei instead of the normal single multilobated nucleus. (**A, B, D,** Marrow aspirates; **C,** peripheral blood smear.)

chromosomal abnormalities, including monosomies 5 and 7, deletions of 5q, 7q, and 20q, and trisomy 8.

As with aneuploidy in other cancers, it is not known how these aberrations contribute to MDS. One idea with some experimental support is that the gain or loss of single copies of key genes is sufficient to give cells a growth advantage, and that aneuploidy is one way to achieve this result. For example, subtle increases in the notorious oncoprotein MYC is sufficient to stimulate cell growth. Notably, the *MYC* gene is located on chromosome 8, and trisomy 8 is one of the most common forms of aneuploidy in a wide range of myeloid tumors. Similarly, the region that is commonly lost on chromosome 5q contains a gene encoding the ribosomal protein RPS14. In experimental systems, loss of one copy of RPS14 produces ineffective erythropoiesis, one of the hallmarks of MDS.

MORPHOLOGY

Although the marrow is usually hypercellular at diagnosis, it is sometimes normocellular or, less commonly, hypocellular. The most characteristic finding is disordered (dysplastic) differentiation affecting the erythroid, granulocytic, monocytic, and megakaryocytic lineages to varying degrees (Fig. 13-31). Within the erythroid series, common abnormalities include **ring sideroblasts**, erythroblasts with iron-laden mitochondria visible as perinuclear granules in Prussian blue-stained aspirates or biopsies; **megaloblastoid maturation**, resembling that seen in vitamin B_{12} and folate deficiency (Chapter 14); and **nuclear budding abnormalities**, recognized as nuclei with misshapen, often polyploid, outlines. Neutrophils frequently contain decreased numbers of secondary granules, toxic granulations, and/or Döhle bodies. **Pseudo-Pelger-Hüet cells**, neutrophils with only two nuclear lobes, are commonly observed, and neutrophils are seen occasionally that completely lack nuclear segmentation. Megakaryocytes with single nuclear lobes or multiple separate nuclei (**pawn ball megakaryocytes**) are also characteristic. **Myeloid blasts** may be increased but make up less than 20% of the overall marrow cellularity. The blood often contains pseudo-Pelger-Hüet cells, giant platelets, macrocytes, and poikilocytes, accompanied by a relative or absolute monocytosis. Myeloid blasts usually make up less than 10% of the leukocytes in the blood.

Clinical Features. Primary MDS is predominantly a disease of older adults; the mean age of onset is 70 years. In up to half of the cases, it is discovered incidentally on routine blood testing. When symptomatic, it presents with weakness, infections, and hemorrhages, all due to pancytopenia.

Primary MDS is divided into eight categories based on morphologic and cytogenetic features in the WHO