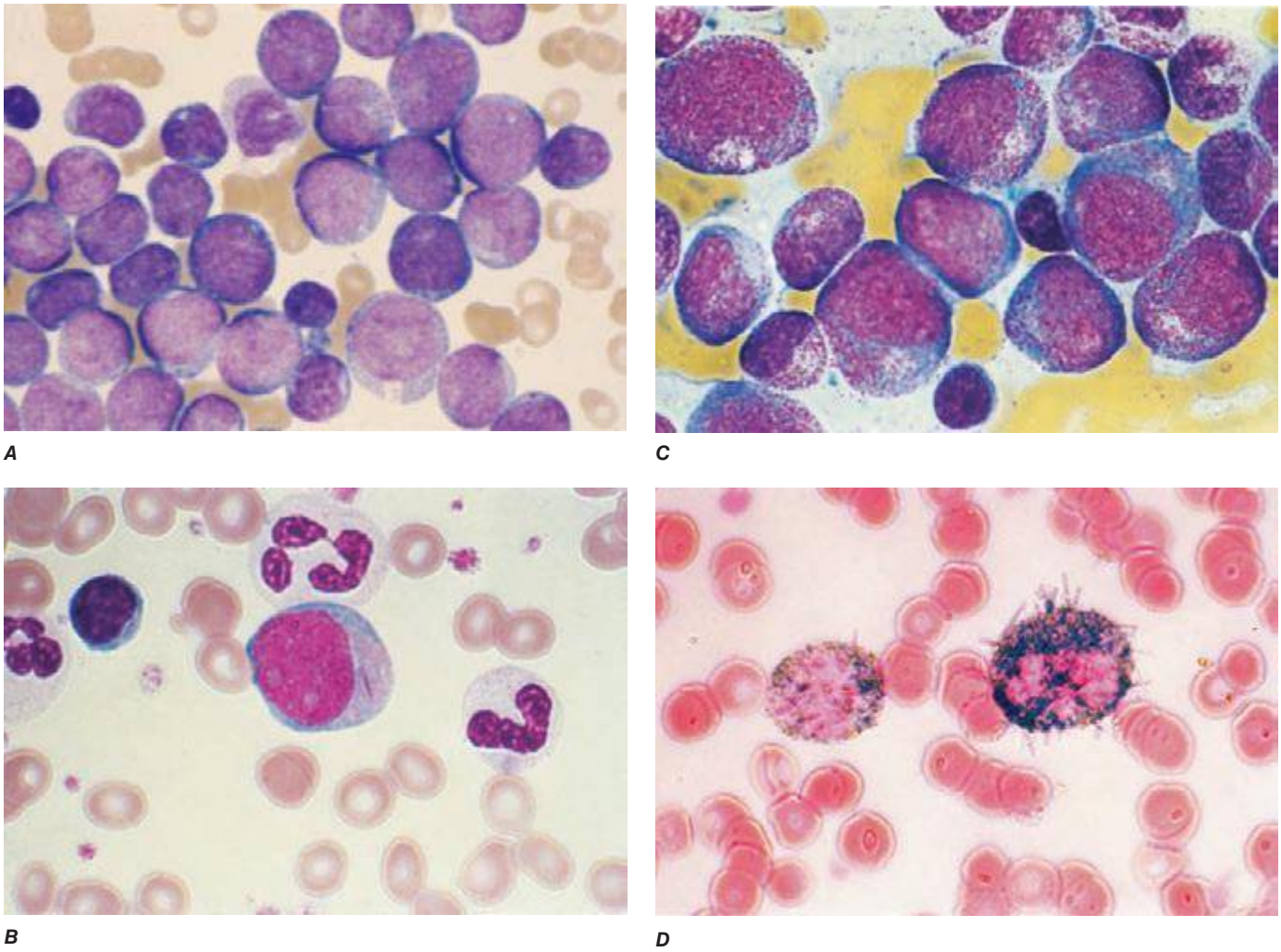

**FIGURE 132-1** **Morphology of acute myeloid leukemia (AML) cells.** ***A.*** Uniform population of primitive myeloblasts with immature chromatin, nucleoli in some cells, and primary cytoplasmic granules. ***B.*** Leukemic myeloblast containing an Auer rod. ***C.*** Promyelocytic leukemia cells with prominent cytoplasmic primary granules. ***D.*** Peroxidase stain shows dark blue color characteristic of peroxidase in granules in AML.

uric oxidase) is also useful for treating uric acid nephropathy and often can normalize the serum uric acid level within hours with a single dose of treatment. The presence of high concentrations of lysozyme, a marker for monocytic differentiation, may be etiologic in renal tubular dysfunction, which could worsen other renal problems that arise during the initial phases of therapy.

## TREATMENT ACUTE MYELOID LEUKEMIA

Treatment of the newly diagnosed patient with AML is usually divided into two phases, induction and postremission management (Fig. 132-2). The initial goal is to induce CR. Once CR is obtained, further therapy must be used to prolong survival and achieve cure. The initial induction treatment and subsequent postremission therapy are often chosen based on the patient's age. Intensifying therapy with traditional chemotherapy agents such as cytarabine and anthracyclines in younger patients (<60 years) appears to increase the cure rate of AML. In older patients, the benefit of intensive therapy is controversial; novel approaches for selecting patients predicted to be responsive to treatment and new therapies are being pursued.

### INDUCTION CHEMOTHERAPY

The most commonly used CR induction regimens (for patients other than those with APL) consist of combination chemotherapy with cytarabine and an anthracycline (e.g., daunorubicin, idarubicin, mitoxantrone). Cytarabine is a cell cycle S-phase–specific antimetabolite that becomes phosphorylated intracellularly to an active triphosphate form that interferes with DNA synthesis. Anthracyclines are DNA intercalators. Their primary mode of action is thought to be inhibition of topoisomerase II, leading to DNA breaks.

In younger adults (age <60 years), cytarabine is used either at standard dose (100–200 mg/m$^2$) administered as a continuous intravenous infusion for 7 days or higher dose (2 g/m$^2$) administered intravenously every 12 h for 6 days. With standard-dose cytarabine, anthracycline therapy generally consists of daunorubicin (60–90 mg/m$^2$) or idarubicin (12 mg/m$^2$) intravenously on days 1, 2, and 3 (the 7 and 3 regimen). Other agents can be added (i.e., cladribine) when 60 mg/m$^2$ of daunorubicin is used.

High-dose cytarabine-based regimens have also been shown to induce high CR rates. When given in high doses, higher intracellular levels of cytarabine may be achieved, thereby saturating the cytarabine-inactivating enzymes and increasing the intracellular levels of 1-β-D-arabinofuranylcytosine-triphosphate, the active metabolite incorporated into DNA. Thus, higher doses of cytarabine may increase the inhibition of DNA synthesis and thereby overcome resistance to standard-dose cytarabine. With high-dose cytarabine, daunorubicin 60 mg/m$^2$ or idarubicin 12 mg/m$^2$ is generally used.

The hematologic toxicity of high-dose cytarabine-based induction regimens has typically been greater than that associated with 7 and 3 regimens. Toxicity with high-dose cytarabine also includes pulmonary toxicity and significant and occasionally irreversible