percentage of cells falling into a defined morphological category, positivity for a certain cytochemical reaction, or the presence of a certain immunological marker. An ideal classification of acute leukaemia must be biologically relevant. If it is to be useful to the clinical haematologist, as well as to the research scientist, it should also be readily reproducible and easily and widely applicable. Rapid categorization should be possible so that therapeutic decisions can be based on the classification. The classification should be widely acceptable and should change as little as possible over time so that valid comparisons can be made between different groups of patients. Ideal classifications of acute leukaemia do not yet exist, although many have been proposed.

The development of the French–American–British (FAB) classification of acute leukaemia by a collaborating group of French, American and British haematologists [3–7] was a major advance in leukaemia classification, permitting a uniform classification of these diseases over two decades. It appears likely that the WHO classification, published in its definitive form in 2001 [8], will gradually take the place of the FAB classification. However, since application of the WHO classification requires knowledge of the results of cytogenetic analysis it appears equally likely that haematologists will make an initial diagnosis in FAB terms, pending the availability of results of cytogenetic or molecular genetic analysis. It is important that FAB designations (which have a precise, carefully defined meaning) are not applied to WHO categories for which the diagnostic criteria differ. For maximum clarity, all publications relating to acute leukaemia and the myelodysplastic syndromes (MDS) should state which classification is being used and should adhere strictly to the criteria of the relevant classification.

The FAB group both established diagnostic criteria for acute leukaemia and proposed a system of classification. There is usually no difficulty in recognizing that a patient with ALL is suffering from acute leukaemia, although arbitrary criteria are necessary to distinguish ALL from the closely related lymphoblastic lymphomas. In the case of AML, more difficulty can arise because of the necessity to distinguish between acute leukaemia and MDS. The latter term indicates a group of related conditions, characterized by an acquired intrinsic defect in the maturation of myeloid cells, which has been designated myelodysplasia or dysmyelopoiesis. MDS is a clonal, neoplastic disorder, which is closely related to, and in some patients precedes, acute leukaemia. In other patients MDS persists unchanged for many years or leads to death from the complications of bone marrow failure without the development of acute leukaemia; it is therefore justifiable to regard the myelodysplastic syndromes as diseases in their own right rather than merely as preludes to acute leukaemia. As the prognosis of MDS is generally better than that of acute leukaemia, and because therapeutic implications differ, it is necessary to make a distinction between acute leukaemia (with or without coexisting myelodysplasia or a preceding MDS) and cases of MDS in which acute leukaemia has not supervened. The FAB group proposed criteria for making the distinction between acute leukaemia and MDS, and for further categorizing these two groups of disorders. The distinction between AML and MDS will be discussed in this chapter and the further categorization of MDS in Chapter 3.

The FAB classification

The FAB classification of acute leukaemia was first published in 1976 and was subsequently expanded, modified and clarified [3–7]. It deals with both diagnosis and classification.

Diagnosing acute leukaemia

The diagnosis of acute leukaemia usually starts from a clinical suspicion. It is uncommon for this diagnosis to be incidental, resulting from the performance of a blood count for a quite different reason. Clinical features leading to suspicion of acute leukaemia include pallor, fever consequent on infection, pharyngitis, petechiae and other haemorrhagic manifestations, bone pain, hepatomegaly, splenomegaly, lymphadenopathy, gum hypertrophy and skin infiltration. A suspicion of acute leukaemia generally leads to a blood count being performed and, if this shows a relevant abnormality, to a bone marrow aspiration. The diagnosis then rests on an assessment of the peripheral blood and bone marrow.

The FAB classification requires that peripheral blood and bone marrow films be examined and that differential counts be performed on both. In the case of the bone marrow, a 500-cell differential count is required. Acute leukaemia is diagnosed if:

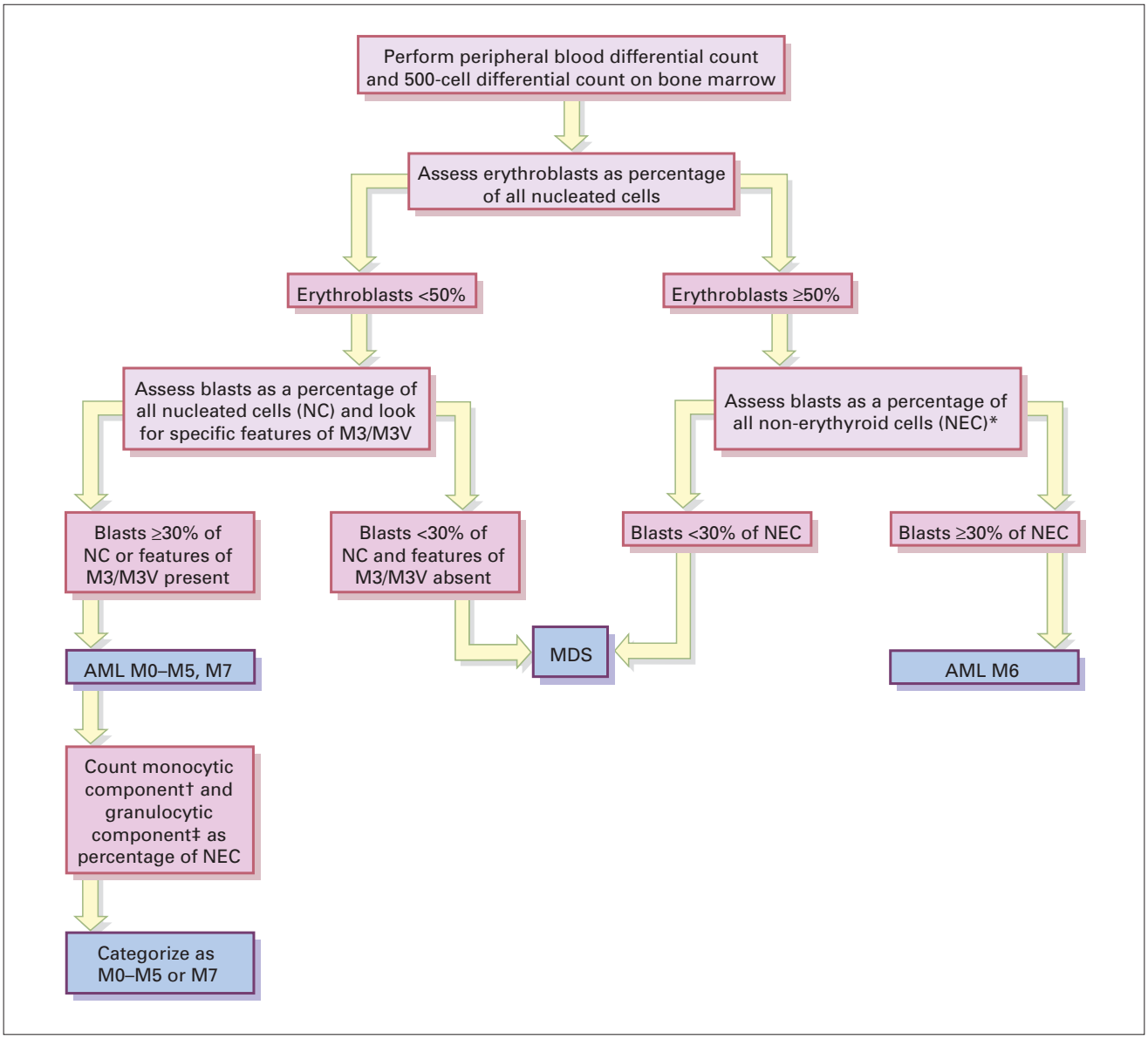

Fig. 1.1 A procedure for diagnosing acute myeloid leukaemia (AML) and for distinguishing it from the myelodysplastic syndromes [6]. *Excludes also lymphocytes, plasma cells, mast cells and macrophages. †Monoblasts to monocytes. ‡Myeloblasts to polymorphonuclear leucocytes.

1 at least 30%* of the total nucleated cells in the bone marrow are blast cells; or
2 if the bone marrow shows erythroid predominance (erythroblasts ≥50% of total nucleated cells) and at least 30% of non-erythroid cells are blast cells (lymphocytes, plasma cells and macrophages also being excluded from the differential count of non-erythroid cells); or
3 if the characteristic morphological features of acute promyelocytic leukaemia (see page 16) are present (Fig. 1.1).

Cases of ALL will be diagnosed on the first criterion since erythroid hyperplasia does not occur in this condition, but the diagnosis of all cases of AML requires application also of the second and third criteria. The bone marrow in acute leukaemia is usually hypercellular, or at least normocellular, but this is not necessarily so since some cases meet

*It should be noted that the criterion of at least 30% blast cells has been altered, in the WHO classification, to at least 20% blast cells (see page 127).

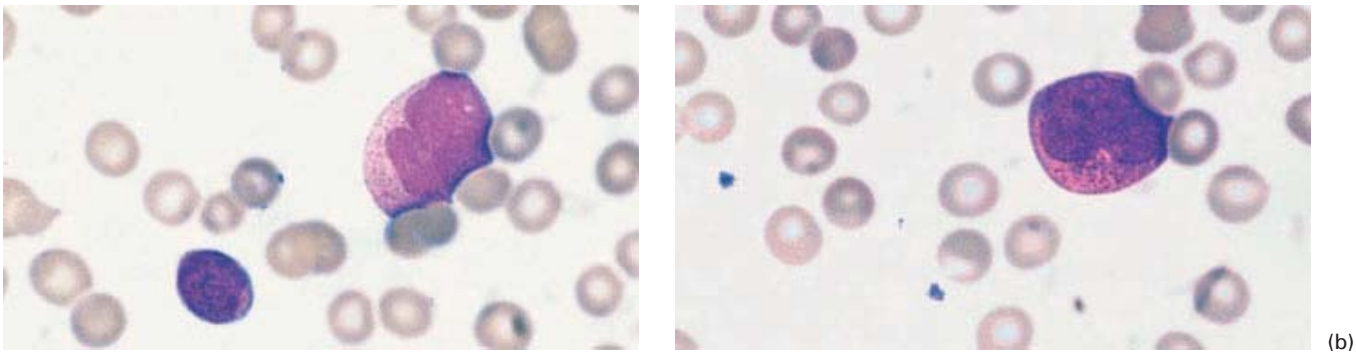

Fig. 1.2 The peripheral blood (PB) film of a patient with AML showing: (a) a type II blast with scanty azurophilic granules; (b) a promyelocyte with more numerous granules and a Golgi zone in the indentation of the nucleus. May–Grünwald–Giemsa (MGG) × 870.

the above criteria when the bone marrow is hypocellular.

Defining a blast cell

The enumeration of blasts in the bone marrow is crucial in the diagnosis of acute leukaemia and the definition of a blast cell is therefore important. Whether immature myeloid cells containing small numbers of granules are classified as blasts is a matter of convention. The FAB group chose to classify such cells as myeloblasts rather than promyelocytes. They recognized two types of myeloblast [9]. Type I blasts lack granules and have uncondensed chromatin, a high nucleocytoplasmic ratio and usually prominent nucleoli. Type II blasts resemble type I blasts except for the presence of a few azurophilic granules and a somewhat lower nucleocytoplasmic ratio. Cells are categorized as promyelocytes rather than type II blasts when they develop an eccentric nucleus, a Golgi zone, chromatin condensation (but with the retention of a nucleolus), numerous granules and a lower nucleocytoplasmic ratio. The cytoplasm, except in the pale Golgi zone, remains basophilic. Cells that have few or no granules, but that show the other characteristics of promyelocytes, are regarded as hypogranular or agranular promyelocytes rather than as blasts. Examples of cells classified as type II myeloblasts and promyelocytes, respectively, are shown in Figs 1.2 and 1.3. The great majority of lymphoblasts lack granules and are therefore type I blasts; they resemble myeloblasts but are often

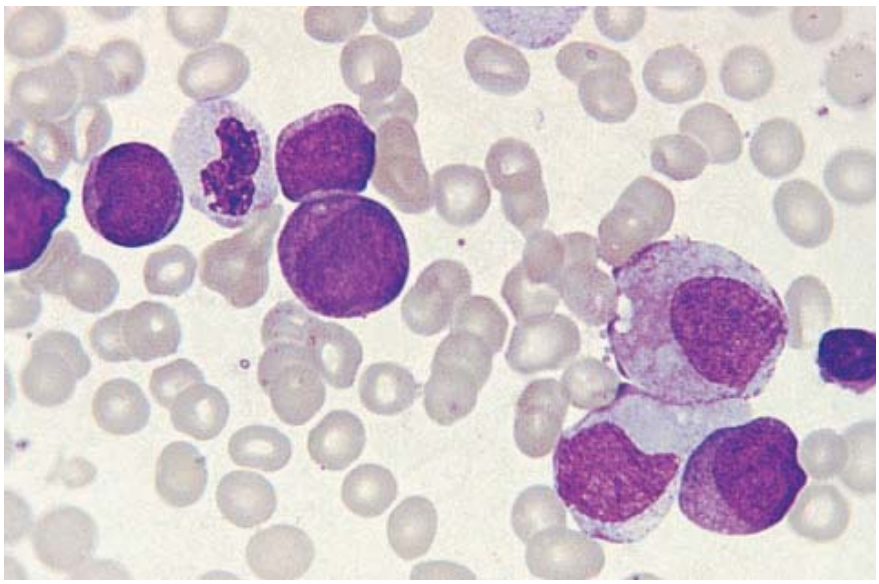

Fig. 1.3 Bone marrow (BM) of a patient with AML (M2/t(8;21)) showing a cell that lacks granules but nevertheless would be classified as a promyelocyte rather than a blast because of its low nucleocytoplasmic ratio; defective granulation of a myelocyte and a neutrophil is also apparent. Type I and type II blasts are also present. MGG × 870.