

morphologic aberrations are associated with functional defects.

Other causes of acquired neutrophil hypersegmentation include vitamin B<sub>12</sub> or folate deficiency, occasional drug treatments, iron deficiency, and renal insufficiency (see [t22.2](#)). Acquired Pelger-Huët change also is associated with certain drug exposures, notably colchicine, sulfonamide, and valproic acid therapy. This nuclear segmentation defect can be found in patients with mycoplasma infection, HIV-1 infection, and (rarely) in bone marrow transplant recipients. Likewise, several morphologic abnormalities of neutrophils, including pseudo-Pelger-Huët nuclear hyposegmentation, giant neutrophils, and neutrophils with Howell-Jolly-like cytoplasmic inclusions, have been described in patients with AIDS. Similar nuclear remnants (pseudo Howell-Jolly bodies) have been described within the cytoplasm of iatrogenically immunosuppressed patients. Prominent cytoplasmic inclusions are seen in neutrophils and monocytes in patients with cryoglobulinemia. Copper deficiency is associated with distinct cytoplasmic vacuoles in granulocytic and erythroid precursors, as well as in some maturing forms. Finally, mild dysplastic features have been noted in bone marrow specimens from healthy adults, especially elderly patients.

## 22.1 Pathophysiology

The pathophysiology of hereditary granulocytic disorders is linked to the underlying genetic defect. The cause of acquired neutrophil abnormalities is not always clear-cut. In patients with vitamin B<sub>12</sub> or folate deficiency, the basic defect is an inability to undergo cell division (see Chapter 5), whereas the various nuclear and cytoplasmic abnormalities identified in patients with hematologic neoplasms are the consequence of an acquired clonal genetic defect. The cause of medication- or infection-associated morphologic abnormalities of neutrophils is generally unknown, but these changes should regress following successful treatment of the infection or cessation of the drug treatment.

## 22.2 Clinical Findings

Associated clinical findings in patients with hereditary neutrophil disorders are listed in [t22.1](#). The clinical findings in patients with acquired neutrophil disorders are associated with the specific underlying disorder. Patients with hematologic neoplasms often experience fatigue, malaise, and fever if secondary infection has occurred. Likewise, splenomegaly and hepatomegaly may be evident in some of these patients.

## 22.3 Diagnostic Approach

When a morphologic neutrophilic abnormality is encountered, it is essential to determine whether it is a hereditary or an acquired defect. The cause of acquired defects, either neoplastic or non-neoplastic, also must be determined. The integration of clinical findings, other hematologic parameters, medical history, and the physical examination generally allow for these distinctions. The evaluation of a patient with neutrophil morphologic abnormalities generally includes the following steps:

1. A complete blood count (CBC) with differential.
2. A morphologic review of neutrophils and other lineages.
3. A family history and possible evaluation of other family members.
4. An evaluation for evidence of underlying infection.
5. An evaluation for evidence of bleeding.
6. An evaluation for evidence of a hematologic neoplasm.

7. An assessment for drug treatments and other conditions linked to specific morphologic abnormalities of neutrophils.
8. An evaluation for phenotypic abnormalities that occur in constitutional neutrophil disorders.
9. An evaluation for possible secondary lymphoproliferative disorders or infection-associated hemophagocytic syndrome in selected patients with genetic disorders, especially Chédiak-Higashi syndrome.

## 22.4 Hematologic Findings

### 22.4.1 Blood Cell Measurements

Several of the hereditary and acquired granulocytic disorders with abnormal morphology are associated with cytopenias, most notably neutropenia and/or thrombocytopenia. Anemia also may be evident in patients with recurrent chronic infections and in patients with underlying hematologic malignancies.

### 22.4.2 Peripheral Blood Smear Morphology

The various morphologic abnormalities of neutrophil nuclei and cytoplasm in patients with either hereditary or acquired granulocytic disorders are delineated in [t22.1](#) and [t22.2](#) ([i22.1–i22.6](#)). In addition, enlarged platelets characterize May-Hegglin anomaly; cytoplasmic abnormalities of other granulated cells or lymphocytes/natural killer cells may be encountered in patients with May-Hegglin anomaly, Chédiak-Higashi syndrome, and Alder-Reilly anomaly (see [t22.1](#)). In patients with acquired neutrophil abnormalities, other blood findings suggestive of myeloid neoplasms may be evident; multilineage abnormalities also are evident in megaloblastic anemia [i22.2](#), [i22.3](#), [i22.5](#).

#### i22.1 Morphologic abnormalities

Blood smears illustrating morphologic abnormalities in **a** Pelger-Huët anomaly, **b** May-Hegglin anomaly, and **c** Chédiak-Higashi syndrome. (Wright stain) (image **c** courtesy P Ward, MD)

