TABLE 80-4 INHERITED DISORDERS OF PHAGOCYTE FUNCTION: DIFFERENTIAL FEATURES

Clinical Manifestations	Cellular or Molecular Defects	Diagnosis
Chronic Granulomatous Diseases (70% X-Linked, 30% Autosomal Recessive)		
Severe infections of skin, ears, lungs, liver, and bone with catalase-positive microorganisms such as *Staphylococcus aureus, Burkholderia cepacia* complex, *Aspergillus* spp., *Chromobacterium violaceum*; often hard to culture organism; excessive inflammation with granulomas, frequent lymph node suppuration; granulomas can obstruct GI or GU tracts; gingivitis, aphthous ulcers, seborrheic dermatitis	No respiratory burst due to the lack of one of five NADPH oxidase subunits in neutrophils, monocytes, and eosinophils	DHR or NBT test; no superoxide and H_2O_2 production by neutrophils; immunoblot for NADPH oxidase components; genetic detection
Chédiak-Higashi Syndrome (Autosomal Recessive)		
Recurrent pyogenic infections, especially with *S. aureus*; many patients get lymphoma-like illness during adolescence; periodontal disease; partial oculocutaneous albinism, nystagmus, progressive peripheral neuropathy, mental retardation in some patients	Reduced chemotaxis and phagolysosome fusion, increased respiratory burst activity, defective egress from marrow, abnormal skin window; defect in *CHS1*	Giant primary granules in neutrophils and other granule-bearing cells (Wright's stain); genetic detection
Specific Granule Deficiency (Autosomal Recessive and Dominant)		
Recurrent infections of skin, ears, and sinopulmonary tract; delayed wound healing; decreased inflammation; bleeding diathesis	Abnormal chemotaxis, impaired respiratory burst and bacterial killing, failure to upregulate chemotactic and adhesion receptors with stimulation, defect in transcription of granule proteins; defect in *CEBPE*	Lack of secondary (specific) granules in neutrophils (Wright's stain), no neutrophil-specific granule contents (i.e., lactoferrin), no defensins, platelet α granule abnormality; genetic detection
Myeloperoxidase Deficiency (Autosomal Recessive)		
Clinically normal except in patients with underlying disease such as diabetes mellitus; then candidiasis or other fungal infections	No myeloperoxidase due to pre- and posttranslational defects in myeloperoxidase deficiency	No peroxidase in neutrophils; genetic detection
Leukocyte Adhesion Deficiency		
Type 1: Delayed separation of umbilical cord, sustained neutrophilia, recurrent infections of skin and mucosa, gingivitis, periodontal disease	Impaired phagocyte adherence, aggregation, spreading, chemotaxis, phagocytosis of C3bi-coated particles; defective production of CD18 subunit common to leukocyte integrins	Reduced phagocyte surface expression of the CD18-containing integrins with monoclonal antibodies against LFA-1 (CD18/CD11a), Mac-1 or CR3 (CD18/CD11b), p150,95 (CD18/CD11c); genetic detection
Type 2: Mental retardation, short stature, Bombay (hh) blood phenotype, recurrent infections, neutrophilia	Impaired phagocyte rolling along endothelium; due to defects in fucose transporter	Reduced phagocyte surface expression of Sialyl-Lewis^x, with monoclonal antibodies against CD15s; genetic detection
Type 3: Petechial hemorrhage, recurrent infections	Impaired signaling for integrin activation resulting in impaired adhesion due to mutation in *FERMT3*	Reduced signaling for adhesion through integrins; genetic detection
Phagocyte Activation Defects (X-Linked and Autosomal Recessive)		
NEMO deficiency: mild hypohidrotic ectodermal dysplasia; broad-based immune defect: pyogenic and encapsulated bacteria, viruses, *Pneumocystis*, mycobacteria; X-linked	Impaired phagocyte activation by IL-1, IL-18, TLR, CD40L, TNF-α leading to problems with inflammation and antibody production	Poor in vitro response to endotoxin; impaired NF-κB activation; genetic detection
IRAK4 and MyD88 deficiency: susceptibility to pyogenic bacteria such as staphylococci, streptococci, clostridia; resistant to *Candida*; autosomal recessive	Impaired phagocyte activation by endotoxin through TLR and other pathways; TNF-α signaling preserved	Poor in vitro response to endotoxin; lack of NF-κB activation by endotoxin; genetic detection
Hyper IgE–Recurrent Infection Syndrome (Autosomal Dominant) (Job's Syndrome)		
Eczematoid or pruritic dermatitis, "cold" skin abscesses, recurrent pneumonias with *S. aureus* with bronchopleural fistulae and cyst formation, mild eosinophilia, mucocutaneous candidiasis, characteristic facies, restrictive lung disease, scoliosis, delayed primary dental deciduation	Reduced chemotaxis in some patients, reduced memory T and B cells; mutation in *STAT3*	Somatic and immune features involving lungs, skeleton, and immune system; serum IgE >2000 IU/mL; genetic testing
DOCK8 deficiency (autosomal recessive), severe eczema, atopic dermatitis, cutaneous abscesses, HSV, HPV, and molluscum infections, severe allergies, cancer	Impaired T cell proliferation to mitogens; mutation in *DOCK8*	Severe allergies, viral infections, high IgE, eosinophilia, low IgM, progressive lymphopenia, genetic detection
Mycobacteria Susceptibility (Autosomal Dominant and Recessive Forms)		
Severe extrapulmonary or disseminated infections with bacille Calmette-Guérin (BCG), nontuberculous mycobacteria, salmonella, histoplasmosis, coccidioidomycosis, poor granuloma formation	Inability to kill intracellular organisms due to low IFN-γ production or response; mutations in IFN-γ receptors, IL-12 receptors, IL-12 p40, *STAT1*, *NEMO*, *ISG15*, *GATA2*	Abnormally low or very high levels of IFN-γ receptor 1; functional assays of cytokine production and response; genetic detection
GATA2 Deficiency (Autosomal Dominant)		
Persistent or disseminated warts, disseminated mycobacterial disease, low monocytes, NK cells, B cells; hypoplastic myelodysplasia, leukemia, cytogenetic abnormalities, pulmonary alveolar proteinosis	Impaired macrophage activity, cytopenias; mutations in *GATA2*	Profound circulating monocytopenia, NK and B cell cytopenias; genetic detection

Abbreviations: C/EBPε, CCAAT/enhancer binding protein-ε; DHR, dihydrorhodamine (oxidation test); DOCK8, dedicator of cytokinesis 8; GI, gastrointestinal; GU, genitourinary; HPV, human papilloma virus; HSV, herpes simplex virus; IFN, interferon; IL, interleukin; IRAK4, IL-1 receptor–associated kinase 4; LFA-1, leukocyte function–associated antigen 1; MyD88, myeloid differentiation primary response gene 88; NADPH, nicotinamide–adenine dinueleotide phosphate; NBT, nitroblue tetrazolium (dye test); NEMO, NF-κB essential modulator; NF-κB, nuclear factor-κB; NK, natural killer; STAT1–3, signal transducer and activator of transcription 1–3; TLR, Toll-like receptor; TNF, tumor necrosis factor.