

Index

- ABO antigen system, 134–5, 136–7, 143–4, 161, 329, 341–2
- abruptio placentae, 402–3
- acute intertwin transfusion, 402, 405
- acute lymphoblastic leukemia (ALL), 367–9
- acute myeloid leukemia (AML), 369–70
- evaluation of suspected, 368, 370
- Shwachman–Diamond syndrome
- risk for, 52–3
- acute myeloid leukemia of Down Syndrome (ML-DS), 371–2, 374, 375–7
- ADA deficiency. *See* adenosine deaminase deficiency
- adaptive immunity
- development of, 25, 26, 31–5
- evolution of, 26
- neonatal immaturity of, 63–6
- adenosine deaminase (ADA)
- deficiency, 71, 83, 97, 105–6.
- See also* deficiency of adenosine deaminase 2
- adrenal hemorrhage, 385
- adrenal masses, 383–5
- afibrinogenemia, 296, 297
- AGM. *See* aorta–gonad–mesonephros region
- AIDS. *See* human immunodeficiency virus
- AIN. *See* autoimmune neutropenia
- AIT. *See* alloimmune thrombocytopenia
- ALL. *See* acute lymphoblastic leukemia
- allergic transfusion reactions (ATRs), 346
- alloimmune hemolysis, 157. *See also* hemolytic disease of fetus and newborn
- alloimmune thrombocytopenia (AIT), 223, 235–6
- clinical presentation of, 228
- diagnosis of, 229–30
- alloantibody testing, 230
- antigen testing, 230
- genotyping, 230
- patient selection for testing, 230
- screening programs, 231
- incidence of, 223
- intracranial hemorrhage in, 228–9, 231, 232, 233–5
- management of, 231, 339–40, 341, 342
- antenatal therapy, 231–2
- efficacy of, 232–3
- future modalities for, 235
- in newborn, 235
- risk stratification and specific strategies for, 233–5
- special considerations, 235
- pathogenesis of, 223
- allo-antibody mediated thrombocytopenia, 227–8
- alloimmunization, 224–7
- human platelet-specific antigens, 223–4, 225, 226
- prognostic factors of, 229
- alpha₂-antiplasmin deficiency, 301
- alpha thalassemia, 169,
- alpha thalassemia trait, 170
- hemoglobin Constant Spring syndromes, 170, 172
- hemoglobin H disease, 170–1
- hemolysis due to, 170–2
- homozygous alpha thalassemia, 3, 170, 171–2
- newborn screening for, 96, 99–101
- silent carrier state, 170
- American Academy of Pediatrics, ix
- AML. *See* acute myeloid leukemia
- amniocentesis
- hemolytic disease of fetus and newborn monitoring with, 140–1
- for homozygous alpha thalassemia, 171–2
- amotosalen, 355
- amphotericin B, 345
- anemia, 113. *See also* congenital anemias; Fanconi anemia; hemolysis
- diagnosis of, 113–15
- erythrocyte transfusions for, 121, 329–30
- fetomaternal unit disorders causing, 117, 401–7
- identification of causes
- underlying, 115–16
- hemolysis, 117–18
- hemorrhage, 115, 116–17
- hypoproliferative, 118
- physiologic, 6–7, 156, 329–30
- in pregnancy, 414–17
- anemia of prematurity (AOP), 120, 126
- historical review of, 6–7
- physiology of, 120
- therapy for
- blood loss minimization, 120–1
- delayed umbilical cord clamping, 121
- erythrocyte transfusions, 121, 329–30
- erythropoietin, 121–4
- angiomas, 391
- aniline dyes, 175
- antibodies. *See also* maternal antibodies
- development of, 33–4
- measurement of function of, 82
- neonatal, 34, 65–6
- normal plasma levels of, 65
- antibody deficiency, 67, 68–70
- clinical manifestations of, 74–5
- diagnostic approach to, 82
- management of infants with, 84–5
- management of mothers with, 84–5
- secondary immune disorders associated with, 75
- anticoagulant-preservative (AP) solutions, 331–2
- anticoagulation therapy, 318–21
- anticonvulsants, 413
- anti-D antigen immune globulin, 5, 139–40, 141, 146, 341–2
- anti-erythrocyte antibodies. *See* maternal antibodies
- antigens, 31–2. *See also* blood group antigens
- cluster of differentiation, 18–19, 32–3, 34, 80–1
- human platelet, 223–4, 225, 226, 230
- T-cell recognition of, 33

- antiphospholipid antibody syndrome, 411–12
 antiretroviral therapy, 79, 426
 antithrombin, 315, 319
 antithrombin concentrates, for extracorporeal membrane oxygenation, 345
 antithrombin III (AT-III), 193
 AOP. *See* anemia of prematurity
 aorta–gonad–mesonephros region (AGM), 18, 27–8
 AP solutions. *See* anticoagulant–preservative solutions
 apheresis platelets, 341–2
 arterial thromboembolism
 iatrogenic/spontaneous, 315–16, 317–18
 management of, 317–18
 perinatal arterial ischemic stroke, 315, 317–18
 asphyxia. *See* perinatal asphyxia
 ataxia–telangiectasia (AT), 68–70, 72
 AT-III. *See* antithrombin III
 ATRs. *See* allergic transfusion reactions
 atypical teratoid rhabdoid tumor (ATRT), 388
 autoimmune neonatal
 thrombocytopenia, secondary to maternal immune thrombocytopenic purpura, 213–14
 autoimmune neutropenia (AIN), 267, 268
 autoimmune syndromes, fetomaternal unit disorders of, 157, 411–12
 autologous transfusion, 336–7
 AZT. *See* zidovudine
 babesiosis, 354
 barriers, immune system, 25, 62–3
 B-cells, 31–2,
 complement system role in memory of, 31
 deficiencies of, 66–7
 severe combined immunodeficiency disease, 67–71, 80, 81, 83–4, 95, 96–7, 105–6
 development of, 29, 33–4
 evolution of, 26
 flow cytometry enumeration of, 80–1
 innate like atypical, 26–7
 neonatal immaturity of, 63, 64, 65–6
 normal ranges of, 64
 Bernard–Soulier syndrome (BSS), 249–50
 beta thalassemia, 169
 beta thalassemia trait, 172
 hemoglobin E with, 173
 hemolysis due to, 172–3
 homozygous beta thalassemia, 172–3
 newborn screening for, 96, 98–102
 sickle, 174
 betamethasone, 414
 BFU-E. *See* erythroid burst-forming unit
 bilirubin. *See* hyperbilirubinemia
 Bizzozero, Giulio, 10, 1–2
 bleeding disorders, 293
 acquired, 301,
 disseminated intravascular coagulation (*See* disseminated intravascular coagulation)
 liver disease, 304–5
 vitamin K deficiency, 301–3
 clinical presentation of, 293–4
 congenital hemorrhagic disorders
 factor deficiencies, 296–301
 familial multiple factor deficiencies, 300
 hemostatic proteins in, 295, 296
 inheritance of, 295–6
 developmental hemostasis and, 293
 laboratory investigations of, 294–5
 bleeding time, 461–2
 bleeds, fetomaternal, 403
 blood cells. *See* hematopoietic cells
 blood flow. *See* hemodynamics
 blood group antigens, 135–6,
 ABO antigen system, 134–5, 136–7, 143–4, 161, 329, 341–2
 Duffy, 138
 Kell, 137–8, 140
 Kidd, 138–9
 maternal antibodies to, 133, 134–5, 157,
 mechanisms for development of, 134–5, 136
 perinatal communication of, 142–3
 screening of, 139–40, 141, 143, 144
 surveillance of, 140–1
 MNS blood group, 139
 Rhesus, 4, 133, 134–5, 137, 139–41, 143, 144, 146, 329, 341–2
 blood islands, 15–16
 blood loss. *See also* bleeding disorders
 anemia of prematurity and, 120–1
 anemia testing, 115, 116–17
 fetomaternal unit disorders causing, 117, 401–7
 blood pH, blood viscosity and, 188
 blood sampling
 delivery and, 452–3
 percutaneous umbilical, 142
 site of, 114, 450–1, 453, 459–60
 blood viscosity. *See* hyperviscosity; viscosity
 blood volume, in polycythemia, 192
 bone marrow. *See also* inherited bone marrow failure syndromes
 biopsy, 272, 463–5
 hematopoiesis in, 16–17, 19, 28–9
 reference intervals, 463–5
 “born again spleen,” viii
 brain
 hemodynamics of, 190
 tumors of, 387–8
 BSS. *See* Bernard–Soulier syndrome
 cancer. *See also* leukemia; tumor
 inherited bone marrow failure syndrome disposition to, 43–4, 51–3, 55, 56
 maternal, 412–13
 placental metastases, 412–13
 placental tumors, 407
 capillaries, blood viscosity and, 188
 CAPS. *See* cryopyrin-associated periodic syndromes
 carbamazepam, 413
 carbon monoxide, elevated levels of, 117–18, 157
 carcass blood flow, polycythemia disturbances in, 190
 CARD9 deficiency, 282
 cardiac failure, hemolytic disease of fetus and newborn and, 144–5
 cardiac output, in polycythemia, 188–9
 cardiopulmonary blood flow, polycythemia disturbances in, 188–9
 cardiopulmonary disorders, polycythemia and, 192–3
 carrier testing, 106
 cartilage hair hypoplasia (CHH), 68–70, 73
 catheter related thromboembolism
 arterial, 315–16, 317–18
 venous, 316, 318
 CBC. *See* complete blood count
 CBF. *See* cerebral blood-flow
 CCSK. *See* clear cell sarcoma of kidney
 CD. *See* cluster of differentiation
 CDA. *See* congenital dyserythropoietic anemia

Index

- cell-mediated immunodeficiency disorders, 66–74
 - management of, 83–4
 - screening for, 79–80, 81, 95, 96–7, 105–6
 - central nervous system (CNS) tumors, 387–8
 - central venous catheter (CVC), 316, 318
 - cerebral blood-flow (CBF), 190
 - cerebral sinovenous thrombosis (CSVT), 317, 318
 - cesarean section, for hemolytic disease of fetus and newborn, 144–5
 - CFU-C. *See* colony-forming unit in culture
 - CFU-E. *See* colony-forming unit-erythroid cells
 - CFU-GM. *See* granulocyte-macrophage colony-forming unit
 - CFU-Mix. *See* colony forming unit-mix
 - CFU-S. *See* colony-forming unit in spleen cell
 - CGD. *See* chronic granulomatous disease
 - Chédiak–Higashi syndrome (CHS), 68–70, 76, 282–5
 - chemokines, 34–5
 - chemotaxis, neutrophil, 280–1
 - chemotherapy
 - for leukemia, 370
 - maternal, 412–13
 - pharmacokinetic considerations of, 393
 - CHH. *See* cartilage hair hypoplasia
 - chorioangioma, 407
 - choriocarcinoma, 386, 407
 - choroid plexus tumors, 388
 - chronic granulomatous disease (CGD), 68–70, 77–8, 82, 285
 - chronic hyporegenerative neutropenias, 268–70
 - chronic infantile neurologic cutaneous and articular (CINCA) syndrome, 63, 68–70, 78
 - chronic intrauterine hypoxia, 212–13
 - CHS. *See* Chédiak–Higashi syndrome
 - CID. *See* combined immunodeficiency
 - CINCA syndrome. *See* chronic infantile neurologic cutaneous and articular syndrome
 - circulation, embryonic
 - development of, 15–19
 - circulatory overload, transfusion-associated, 348
 - clear cell sarcoma of kidney (CCSK), 389
 - CLP. *See* common lymphoid progenitors
 - cluster of differentiation (CD) antigens, 18–19, 32–3, 34, 80–1
 - CMN. *See* congenital mesoblastic nephroma
 - CMV. *See* cytomegalovirus (CMV)
 - CNS tumors. *See* central nervous system tumors
 - coagulation disorders. *See* bleeding disorders
 - coagulation factors, 295
 - deficiencies of, 343
 - congenital, 296–301
 - familial multiple, 300
 - laboratory investigations of, 294–5
 - development of, 293, 312
 - properties of, 296
 - screening tests of, 294, 295
 - Coats plus, 56
 - cobalamin deficiency, maternal, 416–17
 - Cohen syndrome, 49–50, 54
 - colony forming unit-mix (CFU-Mix), 11, 15
 - colony-forming unit in culture (CFU-C), 11, 18
 - colony-forming unit in spleen cell (CFU-S), 10–11
 - colony-forming unit-erythroid cells (CFU-E), 11, 18–19
 - colony-stimulating activity (CSA), 11
 - combined immunodeficiency (CID), 71–4
 - common lymphoid progenitors (CLP), 28
 - complement system
 - deficiencies of, 67, 78–9
 - development of, 31
 - complete blood count (CBC), 440. *See also* reference intervals
 - hereditary spherocytosis
 - diagnosis with, 161
 - historical attitudes toward, 453
 - Cone, Thomas, viii
 - congenital aleukocytosis, 270
 - congenital amegakaryocytic thrombocytopenia, 49–50, 248
 - congenital anemias
 - congenital dyserythropoietic anemia, 48–51
 - deficiency of adenosine deaminase 2, 48, 49–50
 - Diamond–Blackfan anemia, viii, 43, 45–8, 49–50
 - genetic variants in, 49–50
 - Pearson marrow-pancreas syndrome, 48, 49–50
 - congenital anomalies, in inherited bone marrow failure syndromes, 43, 45–55
 - congenital dyserythropoietic anemia (CDA), 48–51
 - congenital heart disease, thromboembolism in, 316
 - congenital hemangiomas, 391
 - congenital mesoblastic nephroma (CMN), 389
 - congenital neutropenias, 264–5, 290–2,
 - Cohen syndrome, 49–50, 54
 - cyclic neutropenia, 52, 268–9
 - genetic variants in, 49–50, 51, 53–4
 - glycogen storage disease type IB, 49–50, 54, 285
 - severe congenital neutropenia, 51–2, 268–9
 - Shwachman–Diamond syndrome, 43, 45–50, 52–3, 269–70, 288
 - WHIM syndrome, 49–50, 54
- congenital phagocytic defects, 67, 68–70, 77–8
 - congenital thrombocytopenias, 54
 - Bernard–Soulier syndrome, 249–50
 - congenital amegakaryocytic thrombocytopenia, 49–50, 248
 - genetic testing for, 253–4
 - genetic variants in, 49–50
 - gray platelet syndrome, 250
 - MYH9-related disease, 250
 - thrombocytopenia with
 - absent radii, 43, 45–50, 248–9
 - thrombocytopenia with increased risk of leukemia, 249
 - thrombocytopenia with radioulnar synostosis, 49–50, 249
 - Wiskott–Aldrich syndrome, 49–50, 68–70, 71–2, 76, 245–8, 288–9
 - congenital viral infections, 417–18, cytomegalovirus (CMV), 420–2
 - enterovirus, 424
 - herpes simplex virus, 423–4
 - human immunodeficiency virus, 426–7
 - human parvovirus B19, 425–6
 - neonatal hemolysis in, 158
 - rubella, 422–3
 - syphilis, 419–20
 - toxoplasmosis, 417–19

- corticosteroid therapy, for leukemia, 368–9
 corticosteroids, for alloimmune thrombocytopenia, 232–3
 cryoprecipitate, 342–4
 cryopyrin-associated periodic syndromes (CAPS), 78
 CSA. *See* colony-stimulating activity
 CSVT. *See* cerebral sinovenous thrombosis
 culture, of hematopoietic cells, 11, 13
 CVC. *See* central venous catheter
 cyanosis, in methemoglobinemia, 176–7
 cyclic neutropenia, 52, 268–9
 cytarabine, 370, 376–7
 cytochrome-b₅ reductase deficiency, 176, 177
 cytokines
 development of, 34–5
 neonatal, 30, 33
 cytomegalovirus (CMV), 83–4,
 diagnosis of, 421
 in granulocyte transfusions, 344
 hematologic manifestations of, 421–2
 intrauterine, 420–2
 thrombocytopenia and, 215–16
 transfusion transmitted, 332, 352, 353
 cytopenia. *See also* anemia;
 neutropenia;
 thrombocytopenia
 fetomaternal unit disorder causes of, 401
 in inherited bone marrow failure syndromes, 43, 44
 D antigen (RHD), 133, 134–5, 137, 139–41, 143, 144, 146, 341–2
 DADA2. *See* deficiency of adenosine deaminase 2
 Dam, H., 6
 dapsone, 158
 Darrow, Ruth, 4
 DAT. *See* direct antiglobulin test
 DBA. *See* Diamond–Blackfan anemia
 DC. *See* dendritic cells; dyskeratosis congenita
 deficiency of adenosine deaminase 2 (DADA2), 48, 49–50
 definitive erythrocytes, 27
 DEHP. *See* 2-(diethylhexyl) phthalate
 delayed hemolytic transfusion reactions (DHTRs), 346–7
 deletional hemoglobin H, newborn screening for, 96
 delivery
 blood sampling and, 452–3
 hemolytic disease of fetus and newborn management at, 143, 144–5
 dendritic cells (DC), 33
 developmental hemostasis, 293, 312
 Dewees, W.P., 2
 dexamethasone, 414
 DGS. *See* DiGeorge syndrome
 DHTRs. *See* delayed hemolytic transfusion reactions
 diabetes, maternal, 408
 immunologic changes in, 409
 polycythemia in infants of, 408
 thrombocytopenia in infants of, 409
 thrombosis in infants of, 408–9
 Diamond, Louis K., viii, 4–5, 133
 Diamond–Blackfan anemia (DBA), viii, 43, 45–8, 49–50
 DIC. *See* disseminated intravascular coagulation
 2-(diethylhexyl)phthalate (DEHP), 351
 DiGeorge syndrome (DGS), 68–70, 72–3, 252
 direct antiglobulin test (DAT), 157
 direct Coombs test, 157
 direct thrombin inhibitors, 413
 directed donor transfusions, 335
 disseminated intravascular coagulation (DIC)
 as acquired hemorrhagic disorder, 303–4
 in congenital herpes simplex virus infection, 423–4
 in enteroviral infections, 424
 in gestational hypertension, 410–11
 schistocytic hemolytic anemia in, 158
 thrombocytopenia and, 217
 DNA repair, Fanconi anemia defect in, 55
 DNA sequencing. *See* genetic testing
 DOCK8 deficiency, 68–70, 71
 donor exposure, 334–5
 donor leukocyte effects, in transfusion therapy, 347
 Down syndrome, 264
 acute myeloid leukemia of, 371–2, 374, 375–7
 transient myeloproliferative disorder of, 371
 clinical features of, 372–3
 diagnosis and definition of, 374–5
 differential diagnosis of, 374–5
 hematologic features of, 373–4
 management of, 376–7
 natural history and evolution of, 375–6
 pathogenesis and epidemiology of, 371–2
 Duffy antigen system (FY), 138
 dyskeratosis congenita (DC), 49–50, 56–7, 68–70, 73, 251
 early anemia of prematurity. *See* anemia of prematurity
 eclampsia, 409
 ECMO. *See* extracorporeal membrane oxygenation
 Ehrlich, Paul, 1–2, 10
 ELBW infants. *See* extremely low birth weight infants
 elliptocytes, 160, 162–3
 EMA. *See* eosin-5-maleimide
 embryonal tumors, 388
 embryonic hematopoiesis, 10
 human studies of, 14, 15–19
 murine studies of, 13–15
 sites of, 28–9
 embryonic immune system
 development, 25, 35, 36
 adaptive system, 25, 26, 31–5
 cells and organs, 28–9
 evolution of immunity and, 25–6
 innate system, 25, 26, 29–31
 origin of fetal hematopoietic stem cells in, 26–8
 end tidal carbon monoxide concentration (ETCOc), 117–18
 enoxaparin, 319–20
 enteral iron supplementation, 125
 enterovirus infection, 424
 diagnosis of, 424
 hematologic manifestations of, 424
 thrombocytopenia and, 215–16
 treatment of, 424
 enzyme replacement therapy, for adenosine deaminase deficiency, 83, 105–6
 eosin-5-maleimide (EMA), 162
 eosinopenia, 261–3
 eosinophilia, 261–3, 455–9,
 consistent approaches to, 270–1, 272
 eosinophilia of prematurity, 262, 455–9
 eosinophils
 production of, 261
 reference intervals, 261–2, 455–9
 epigenetic changes, in hematopoietic stem cell determination, 27–8
 EPO. *See* erythropoietin
 erythroblastosis fetalis, 4–5, 133.
 See also hemolytic disease of fetus and newborn
 erythroblasts
 in embryonic hematopoiesis, 16–17, 18
 primitive, 16–17

Index

- erythrocyte adenosine deaminase, 47
- erythrocyte transfusions
 - for anemia of prematurity, 121, 329–30
 - donor exposure and, 334–5
 - dose and administration of, 332–3
 - indications for, 329–31
 - red blood cell preparations for, 331–2
 - risks of, 330
 - thresholds for restrictive versus liberal, 331
- erythrocytes. *See also* anemia; polycythemia
 - antigen systems, 135–6, ABO, 134–5, 136–7, 143–4, 161, 329, 341–2
 - Duffy, 138
 - Kell, 137–8, 140
 - Kidd, 138–9
 - maternal antibodies to, 133–5, 136, 139–41, 142–3, 144, 157
 - MNS blood group, 139
 - Rhesus, 4, 133, 134–5, 137, 139–41, 143, 144, 146, 329, 341–2
 - blood viscosity and
 - concentration effects, 187
 - deformity effects, 187
 - daily production of, 10
 - definitive, 27
 - early investigators of, 10
 - glucose-6-phosphate dehydrogenase-deficient, 96
 - hematopoiesis, 16–17, 18, 28–9
 - hereditary enzymopathies of glucose-6-phosphate dehydrogenase deficiency, 96, 104–5, 165, 163, 164–7, 413
 - other enzyme deficiencies, 168–9
 - pyruvate kinase deficiency, 163, 164, 167–9
 - hereditary membrane disorders of
 - classification of, 159
 - hereditary elliptocytosis, 159, 160, 162–3
 - hereditary spherocytosis, 159–62, 445, 446
 - historical description of, 1–2
 - increased destruction of, 3, 156–7
 - increased production of, 156
 - indices
 - history of, 2
 - reference intervals, 444–5
 - maternal medication effects on, 413
 - morphology, 156, 450
 - neonatal lifespan of, 155
 - primitive, 15, 26–7
 - reference intervals
 - blood sampling relative to delivery, 452–3
 - blood sampling site effects on, 114, 450–1
 - erythrocyte count, 443
 - erythrocyte indices, 444–5
 - erythrocyte morphology, 450
 - fragmented red cells, 451
 - hematocrit, 113–15, 442–3, 444, 445, 450
 - hemoglobin concentration, 113–15, 441, 442, 450
 - immature reticulocyte fraction and reticulocyte hemoglobin content, 449, 450
 - monocytes, 458–60
 - nucleated red blood cells, 449
 - red blood cell distribution width, 446–8
 - reticulocyte count, 448–9
 - sickle, 95
 - transfusion preparations of, 331–2
- erythroid burst-forming unit (BFU-E), 11
- in embryonic hematopoiesis, 15, 18–19
- kinetics of, 18
- erythroids, culture of progenitor cells of, 11
- erythropoiesis, iron demand for, 124
- erythropoietin (EPO)
 - anemia of prematurity therapy with, 121–4
 - cost of therapy with, 123
 - historical review of, 6–7
 - iron status and, 122, 124–6
 - neuroprotection by, 123
 - physiological functions of, 120
 - reference intervals after
 - administration of, 448, 449
 - side effects of, 123
 - supplemental oxygen effects on, 118
 - transfusion therapy and, 335–6
- ETCOc. *See* end tidal carbon monoxide concentration
- evolution
 - of hematopoietic cells, 25–6
 - of immunity, 25–6
 - of lymphocytes, 26
- exchange transfusion, 337
 - administration of, 338
 - complications of, 338
 - component preparation for, 337–8
 - glucose-6-phosphate dehydrogenase deficiency and, 167
 - for hemolytic disease of fetus and newborn, 4–5, 144–6, 337
 - indications for, 337
 - partial, 195, 338–9
- extracorporeal membrane oxygenation (ECMO), 345
- extremely low birth weight (ELBW) infants
 - erythrocyte transfusions for, 329–30, 331
 - transfusion practices for, 335–6
- FA. *See* Fanconi anemia
- factor IX deficiency, 296, 297
- factor V deficiency, 296, 298
- factor V Leiden (FVL), 313–14
- factor VII deficiency, 296, 298
- factor VIIa, recombinant, 298, 302, 303, 305
- factor VIII deficiency, 296–7
- factor X deficiency, 296, 299
- factor XI deficiency, 296, 300
- factor XIII deficiency, 296, 300
- familial hemophagocytic lymphohistiocytosis (F-HLH), 68–70, 76, 392
- familial platelet disorder with associated myeloid malignancy, 49–50
- Fanconi anemia (FA), 54–6, congenital anomalies in, 43, 45–55
 - genetic variants in, 43–4, 49–50, 55
 - thrombocytopenia associated with, 251
- favism, 165, 166
- febrile nonhemolytic transfusion reactions (FNHTRs), 346
- ferritin, plasma levels of, 124
- ferritin index, 124
- fetal blood flow, polycythemia disturbances in, 190
- fetal development
 - infection during, 25
 - origin of hematopoietic stem cells in, 26–8
- fetal growth restriction (FGR), fetomaternal unit disorders causing, 407
- fetal hemoglobin (HbF), 3, 95, 98–102, 169
- fetal hydrops. *See* hydrops fetalis
- fetal hypoxia, polycythemia and, 191, 195
- fetal transfusions, 5, 141–2, 232, 339–40
- fetomaternal hemorrhage (FMH), 117, 401–2, 403

- diagnosis of, 403
 management of, 403
 maternal anti-erythrocyte
 antibody development via,
 134
 outcomes of, 403
 fetomaternal unit disorders, 401
 abruptio placentae and placenta
 previa, 402–3
 anemia causes in, 117, 401–7
 autoimmune syndromes, 157,
 411–12
 fetal growth restriction in, 407
 gestational hypertension, 265–6,
 409–11
 intrauterine infection, 158,
 417–27
 maternal diabetes, 408–9
 maternal malignancy, 412–13
 maternal medications, 158,
 217–18, 413–14
 maternal nutritional deficiencies,
 414–17
 neutropenia causes in, 402
 thrombocytopenia causes in, 401
 twin–twin transfusion syndrome,
 265–6, 402, 404–7
 FFP. *See* fresh frozen plasma
 FGR. *See* fetal growth restriction
 F-HLH. *See* familial
 hemophagocytic
 lymphohistiocytosis
 fibrinogen, 188
 fibrinogen deficiency, 296, 297
 fibrinolytic system, development of,
 293, 312
 fibroblastic-myofibroblastic
 tumors, 386–7
 fibromatosis, 386–7
 flow cytometry, lymphocyte
 enumeration using, 80–1
 FMH. *See* fetomaternal hemorrhage
 FNHTRs. *See* febrile nonhemolytic
 transfusion reactions
 folate deficiency, maternal, 415–16
 folic acid, for hereditary
 spherocytosis, 162
 fragmented red cells (FRC), 451
 fresh frozen plasma (FFP), 342–4
 functional asplenia, viii
 FVL. *See* factor V Leiden
 FY. *See* Duffy antigen system

 G6PD deficiency. *See* glucose-
 6-phosphate dehydrogenase
 deficiency
 Galen, 1
 gamma-beta-delta thalassemia, 173
 gammaglobulin
 for antibody deficiency, 84–5
 for enteroviral infections, 424

 gastrointestinal barrier defense,
 62–3
 gastrointestinal blood flow, 189
 gastrointestinal disorders, 193
 GATA1 gene, 371–2, 374
 G-CSF. *See* granulocyte colony
 stimulating factor
 GCT. *See* germ cell tumors
 gemtuzumab ozogamicin, for
 leukemia, 370
 gene therapy, for severe combined
 immunodeficiency disease,
 83, 105–6
 genetic counseling
 for homozygous alpha
 thalassemia, 171–2
 for inherited bone marrow failure
 syndromes, 44–7
 genetic screening. *See* newborn
 screening
 genetic testing
 for alloimmune
 thrombocytopenia, 230
 for congenital
 thrombocytopenias, 253–4
 in Diamond–Blackfan anemia, 47
 for immunodeficiency disorders,
 82–3
 for juvenile myelomonocytic
 leukemia, 371
 germ cell tumors (GCT), 385–6
 gestational diabetes, 408
 gestational hypertension (GH), 402,
 409
 neutropenia in infants of, 409–10
 polycythemia in infants of, 411
 thrombocytopenia in infants of,
 410–11
 transient hyporegenerative
 neutropenia and, 265–6
 GFR. *See* glomerular filtration rate
 GH. *See* gestational hypertension
 Gilbert syndrome, 96, 162, 167
 Glanzmann thrombasthenia (GT),
 253
 gliomas, 388
 glomerular filtration rate (GFR),
 polycythemia and, 189–90,
 193
 glucocorticoids, for Diamond–
 Blackfan anemia, 47–8
 glucose-6-phosphatase deficiency.
 See glycogen storage disease
 type IB
 glucose-6-phosphate
 dehydrogenase (G6PD)
 deficiency, 413
 hemolysis due to, 163,
 164–7
 historical studies of, 3
 newborn screening for, 96, 104–5,
 166

 glucose phosphate isomerase (GPI)
 deficiency, 168
 glutathione (GSH), 164
 glycogen storage disease type IB
 (GSD1B), 49–50, 54, 285
 GM-CSF. *See* granulocyte-
 macrophage colony-
 stimulating factor
 GPI deficiency. *See* glucose
 phosphate isomerase
 deficiency
 graft versus host disease (GVHD),
 83, 335, 348
 granule deficiency, neutrophil-
 specific, 288
 granulocyte colony stimulating
 factor (G-CSF), 36, 279
 for cyclic neutropenia, 52
 for functional phagocyte
 disorders, 281–2
 neutropenia management with,
 266, 267, 270
 consistent approach to, 271
 in gestational hypertension, 410
 for sepsis, 344
 for severe congenital
 neutropenia, 51–2
 granulocyte transfusions, 272–3,
 344–5
 granulocyte-macrophage colony-
 forming unit (CFU-GM), 11,
 279
 in embryonic hematopoiesis, 15,
 18
 kinetics of, 18
 granulocyte-macrophage colony-
 stimulating factor (GM-
 CSF), 36, 279
 for functional phagocyte
 disorders, 281–2
 for sepsis, 344
 granulocytes. *See also* neutrophils
 culture of, 11
 defects in, 67, 68–70, 77–8
 in embryonic hematopoiesis, 15,
 16–17
 granulopoiesis, 279
 gray platelet syndrome, 250
 Gricelli syndrome type 2 (GS2),
 68–70, 76
 growth factors, hematopoietic,
 34–5, 36
 GS2. *See* Gricelli syndrome type 2
 GSD1B. *See* glycogen storage
 disease type IB
 GSH. *See* glutathione
 GT. *See* Glanzmann
 thrombasthenia
 gut-associated lymphatic
 tissue, 29
 GVHD. *See* graft versus host
 disease

Index

- haptoglobin, 157
Hb. *See* hemoglobin
Hb Bart. *See* hemoglobin Bart
Hb CS. *See* hemoglobin Constant Spring
Hb E. *See* hemoglobin E
HbF. *See* fetal hemoglobin
HbH. *See* hemoglobin H
HbS. *See* sickle hemoglobin
HBV. *See* hepatitis B
HCV. *See* hepatitis C
HDFN. *See* hemolytic disease of fetus and newborn
HDW. *See* hemoglobin distribution width
HE. *See* hereditary elliptocytosis
heart disease, congenital, thromboembolism in, 316
HELLP syndrome, 409
helper T-cells, 34–5
hemangioblast, 13–14
hemangioma thrombocytopenia syndrome, 217
hemangiomas, 391
hemangiopericytoma (HPC), 387
hematocrit
 blood viscosity relationship with, 187
 history of, 2, 442
 perinatal factors influencing, 186
 polycythemia and hyperviscosity values, 185–6
 reference intervals, 113–15, 442–3, 444, 445, 450
hematology, historical review of, 1–4, 7
 erythroblastosis fetalis, 4–5
 hemorrhagic disease of newborn, 5–6
 physiologic anemia of infancy and anemia of prematurity, 6–7
hematopoiesis, 10
 early blood cell investigators of, 10
 embryonic, 14, 10, 13–19
 fetal sites of, 28–9
 fetal waves of, 26–8
 hematopoietic stem cell and progenitor cell identification methods for, 10–12
 stem cell model of, 12–13
hematopoietic cells. *See also specific cells*
 culture of, 11, 13
 evolution of, 25–6
 historical descriptions of, 1–2
 historical quantification of, 2
 progenitors of, 10–13
hematopoietic stem cell transplantation (HSCT) for leukemia, 368–9, 370, 371
 for severe combined immunodeficiency disease, 67–70, 105–6
hematopoietic stem cells (HSCs)
 development of, 29
 in embryonic hematopoiesis, 14, 10, 13–19
 fetal sites of, 28–9
 human embryonic stem cells, 19
 identification methods for, 10–12
 origin of fetal, 26–8
 site of origin of, 14
hemocytoblasts, 16–17
hemodynamics, 188
 brain, 190
 carcass, 190
 cardiopulmonary, 188–9
 fetal, 190
 gastrointestinal, 189
 renal, 189–90
hemoglobin (Hb)
 concentration
 changes after birth, 6–7, 98–102, 113, 114–15, 156, 442
 erythrocyte transfusions and, 329–30
 reference intervals, 113–15, 441, 442, 450
 developmental changes in, 169
 fetal, 3, 95, 98–102, 169
 historical quantification of, 2
 historical studies of, 3
 in reticulocytes, 449, 450
hemoglobin Bart (Hb Bart), 95–6, 98–102, 169, 169–2
hemoglobin Constant Spring (Hb CS), 170–1, 172
hemoglobin distribution width (HDW), 446–8
hemoglobin E (Hb E), beta thalassemia with, 173
hemoglobin F, in Diamond–Blackfan anemia, 47
hemoglobin F-Poole, 175
hemoglobin H (HbH), 95–6, 99–101, 169, 169
hemoglobin H (HbH) disease, 170–1
hemoglobin Hasharon, 175
hemoglobin M disorders, 176, 177
hemoglobin Portland, 171
hemoglobin SC disease, 174
hemoglobinopathies
 hemolysis due to, 169
 sickle cell disease, 174–5
 thalassemia syndromes, 169–73
 unstable hemoglobinopathies, 175
 historical studies of, 3
 methemoglobinemia, 175–7
newborn screening for, 174
 follow-up strategies for non-sickling hemoglobinopathies, 102–4
 follow-up strategies for sickling hemoglobinopathies, 102, 103
 limitations of non-genetic, 98–102
 methods for, 97–8
 results interpretation for, 98, 99–101
 sickle cell disease, 93–5, 98, 99–101, 102, 103
 thalassemia, 95–6, 98–102
hemolysis. *See also* hemolytic disease of fetus and newborn
 acquired hemolytic anemias
 alloimmune hemolysis, 157
 congenital infections, 158
 due to maternal autoimmune disease, 157
 due to maternal drugs, 158
 infantile pyknocytosis, 158–9
 intravenous immunoglobulin administration for, 274
 microangiopathic (schistocytic), 158
 vitamin E deficiency, 158
 adverse transfusion reactions, 346–7
 anemia testing, 117–18
 causes of, 155
 in cytomegalovirus, 422
 hemoglobin abnormalities, 169
 sickle cell disease, 174–5
 thalassemia syndromes, 169–73
 unstable hemoglobinopathies, 175
 hereditary enzyme abnormalities
 glucose-6-phosphate dehydrogenase deficiency, 163, 164–7
 pyruvate kinase deficiency, 163, 164, 167–9
 hereditary red blood cell membrane disorders
 classification of, 159
 hereditary elliptocytosis, 159, 160, 162–3
 hereditary spherocytosis, 159–62, 445, 446
 historical studies of, 3
 hyperbilirubinemia and, 118, 156–7
 laboratory features of, 156–6, anemia and increased red blood cell production, 156
 increased red blood cell destruction, 156–7

- normal neonatal erythrocyte lifespan and, 155
- hemolytic disease of fetus and newborn (HDFN)
- ABO mismatch causing, 134–5, 136–7, 143–4, 161, 329, 341–2
- clinical management of, 139
- delayed anemia, 146
- future direction of, 146
- in utero* therapy, 5, 141–2, 339–40
- interpretation of positive maternal antibody screen at delivery, 143, 144
- neonate diagnosis, 143–4
- perinatal communication, 142–3
- postnatal, 4–5, 144–6, 337
- prenatal prevention, 139–41
- worldwide practices, 146
- Duffy mismatch causing, 138
- historical review of, 4–5
- Kell mismatch causing, 137–8, 140
- Kidd mismatch causing, 138–9
- maternal anti-erythrocyte antibodies in, 133, 134–5, 157
- development of, 134–5, 136
- perinatal communication of, 142–3
- screening of, 139–40, 141, 143, 144
- surveillance of, 140–1
- maternal risk factors associated with, 136
- MNS blood group mismatch causing, 139
- Rhesus mismatch causing, 4, 133, 134–5, 137, 139–41, 143, 144, 146, 329, 341–2
- transient hyporegenerative neutropenia and, 265–6
- hemophagocytic lymphohistiocytosis (HLH), 68–70, 75–7, 83, 392
- hemorrhage
- adrenal, 385
- anemia testing, 115, 116–17
- fetomaternal unit disorders causing, 117, 401–7
- intracranial, 340–1
- maternal anti-erythrocyte antibody development after, 134
- hemorrhagic disease of newborn, historical review of, 5–6
- hemorrhagic disorders. *See* bleeding disorders
- hemostasis
- developmental, 293, 312
- maternal medication effects on, 413
- hemostatic proteins, 295, 296. *See also* coagulation factors
- heparin
- for disseminated intravascular coagulation, 304
- thromboembolism management with, 318–21
- heparin-induced thrombocytopenia (HIT), 217–18, 413
- hepatic tumors, 390–1
- hepatitis B (HBV), 352
- hepatitis C (HCV), 352–3
- hepatoblastomas, 390–1
- hepatomegaly, in transient myeloproliferative disorder, 372–3, 374–5
- hereditary elliptocytosis (HE), 159, 160, 162–3
- hereditary persistence of fetal hemoglobin (HPFH), 98–102
- hereditary pyropoikilocytosis (HPP), 160, 162–3
- hereditary spherocytosis (HS), 159–62, 445, 446
- herpes simplex virus (HSV), 423–4
- hES cells. *See* human embryonic stem cells
- Hewson, William, 1–2
- hexokinase deficiency, 168
- hexosemonophosphate (HMP) shunt, 163, 164
- HHS. *See* Hoyeraal–Hreidarsson syndrome
- high proliferative potential-colony-forming cells (HPP-CFCs), 11–12
- HIGM. *See* hyper-IgM syndrome
- Hippocrates, 1
- histiocytic disorders, 391–2
- HIT. *See* heparin-induced thrombocytopenia
- HIV. *See* human immunodeficiency virus
- HLH. *See* hemophagocytic lymphohistiocytosis
- HMP shunt. *See* hexosemonophosphate shunt
- Hole in the Wall Gang Camp, The, viii
- Holt, L. Emmett, 2
- Hoyeraal–Hreidarsson syndrome (HHS), 56, 57
- HPA. *See* human platelet antigens
- HPC. *See* hemangiopericytoma
- HPFH. *See* hereditary persistence of fetal hemoglobin
- HPP. *See* hereditary pyropoikilocytosis
- HPP-CFCs. *See* high proliferative potential-colony-forming cells
- HS. *See* hereditary spherocytosis
- HSCs. *See* hematopoietic stem cells
- HSCT. *See* hematopoietic stem cell transplantation
- HSV. *See* herpes simplex virus
- human embryonic stem (hES) cells, 19
- human immunodeficiency virus (HIV)
- hematologic manifestations of, 426
- intrauterine infection with, 426–7
- management of, 426–7
- perinatal infection with, 68–70, 79
- thrombocytopenia and, 215–16
- transfusion-acquired, 351, 352
- human parvovirus B19, 425
- diagnosis of, 425
- hematologic manifestations of, 425–6
- thrombocytopenia and, 215–16
- treatment of, 426
- human platelet antigens (HPA), 223–4, 225, 226, 230
- humors, historical concept of, 1
- Hurler’s syndrome, viii
- hydrops fetalis, 142, 144–5, 339–40, historical review of, 4–5
- homozygous alpha thalassemia, 3, 170, 171–2
- newborn screening for, 96, 99–101
- in parvovirus B19 infection, 425–6
- thrombocytopenia and, 212–13
- hyperbilirubinemia
- in glucose-6-phosphate dehydrogenase deficiency, 96, 104–5, 165–6, 167
- hemolysis and, 118, 156–7
- in hemolytic disease of fetus and newborn, 133, 136–7, 141, 142–6, 337
- in hereditary spherocytosis, 160–1, 162
- in infantile poikilocytosis, 163
- in pyruvate kinase deficiency, 167
- hyperglycemia, 349
- hyper-IgM syndrome (HIGM), 68–70, 75
- hyperimmunoglobulin E syndrome, 286
- hyperkalemia, transfusion therapy and, 350
- hyperleukocytosis
- in leukemia, 367–8, 369–70
- in transient myeloproliferative disorder, 373–5

Index

- hypertension. *See* gestational hypertension
- hyperviscosity, 185, 195, *See also* polycythemia
 definition of, 185–6
 etiologies of, 191
- hypocalcemia, 193–4, 350
- hypofibrinogenemia, 296, 297
- hypogammaglobulinemia. *See* antibody deficiency
- hypoglycemia, 193, 349
- hypoproliferative anemia, 118
- hypothermia, 266
- hypoxia. *See* fetal hypoxia
- hypoxic ischemic encephalopathy, 266
- IAT. *See* indirect antiglobulin test
- IBMFS. *See* inherited bone marrow failure syndromes
- ICH. *See* intracranial hemorrhage
- idiopathic neonatal neutropenia, 270
- IDM. *See* infants of diabetic mothers
- IFN- γ , 30–1
- IFS. *See* infantile fibrosarcoma
- IG%. *See* immature granulocyte percent
- IGH. *See* infants of gestational hypertension
- IG/ μ L blood. *See* immature granulocyte count
- IL. *See* interleukins
- ILC. *See* innate lymphoid cells
- immature granulocyte count (IG/ μ L blood), 454–5, 458
- immature granulocyte percent (IG%), 454–5, 458
- immature platelet count, 460–4
- immature platelet fraction (IPF)
 reference intervals, 460–4
 thrombocytopenia evaluation with, 205–6
- immature reticulocyte fraction (IRF), 449, 450
- immune dysregulation diseases, 67, 68–70, 75–7
- immune system. *See also* embryonic immune system
 development
 development of, 25, 35, 36
 adaptive system, 25, 26, 31–5
 cells and organs, 28–9
 evolution of immunity and, 25–6
 innate system, 25, 26, 29–31
 origin of fetal hematopoietic stem cells in, 26–8
 evolution of, 25–6
 neonatal
 development of, 25, 29, 30, 31, 32–3, 34, 35, 36
 immaturity of, 62–6
- immune thrombocytopenic purpura (ITP), 213–14, 341
- immune-mediated neutropenias, 267–8, 274
- immunity, 25–6, *See also* adaptive immunity; innate immunity
- immunodeficiency disorders, 62
 acquired, 68–70, 79
 antibody deficiencies, 67, 68–70, 74–5, 82, 84–5
 cell-mediated deficiencies, 66–74
 management of, 83–4
 screening for, 79–80, 81, 95, 96–7, 105–6
 classification of, 65–6, 67, 68–70
 complement deficiency, 67, 78–9
 congenital phagocytic defects, 67, 68–70, 77–8
 diagnostic approach to, 79–83
 immune dysregulation diseases, 67, 68–70, 75–7
 innate immunity defects, 67, 68–70, 78
 management of, 83–5
 newborn screening for
 severe combined
 immunodeficiency disease, 95, 96–7, 105–6
 T-cell deficiencies, 79–80, 81, 95, 96–7, 105–6
 single gene defects, 82–3
- immunoglobulin deficiency. *See* antibody deficiency
- immunoglobulins
 measurement of function of, 82
 neonatal, 34, 65–6
 normal plasma levels of, 65
 placental transport of, 136
- indirect antiglobulin test (IAT), for
 maternal anti-erythrocyte antibodies, 140–1
- INF. *See* interferons
- infantile fibrosarcoma (IFS), 387
- infantile hemangiomas, 390, 391
- infantile poikilocytosis, 163
- infantile pyknocytosis, 158–9
- infants of diabetic mothers (IDM), 408
 immunologic changes in, 409
 polycythemia in, 408
 thrombocytopenia in, 409
 thrombosis in, 408–9
- infants of gestational hypertension (IGH), 402, 409
 neutropenia in infants of, 409–10
 polycythemia in infants of, 411
 thrombocytopenia in infants of, 410–11
- infection. *See also* congenital viral infections; transfusion-transmitted infection
 glucose-6-phosphate dehydrogenase deficiency and, 165
 intravenous immunoglobulin administration for, 273–4
 neonatal, 25, 29, 30, 31, 32–3, 34, 35, 36, 62
 neutropenia in, 265, 266–7, 270
 neutrophilia in, 263
 in sickle cell disease, 174
 thrombocytopenia and, 215–16
- inherited bone marrow failure syndromes (IBMFS), 43, 57,
See also specific syndromes
- approach to evaluation of, 43, 44
 family history, 43–4
 laboratory evaluation, 44
 physical examination, 43, 45
 cancer risk in, 43–4, 51–3, 55, 56
 congenital anomalies in, 43, 45–55
 genetic counseling for, 44–7
 genetic variants in, 49–50
 neutropenia in, 270
 radiographic studies for, 44
- inherited thrombocytopenia syndromes. *See also* congenital thrombocytopenias
 approach to, 243–4
 exam findings, 245
 family history, 244–5
 peripheral smear, 244
 subsequent evaluations and care, 245, 246, 247
 genetic testing for, 253–4
 platelet function defects, 253
 thrombocytopenia associated with congenital syndromes, 250–2
 thrombocytopenia associated with von Willebrand factor abnormalities and increased platelet destruction, 252–3
- inherited thrombophilia (IT), 313–15
- innate immunity
 defects of, 67, 68–70, 78
 development of, 25, 26, 29–31
 evolution of, 26
 neonatal immaturity of, 62–3
- innate lymphoid cells (ILC),
 development of, 31
- INTERCEPT® system, 355
- interferons (INF), 34–5
- interleukins (IL)
 development of, 34–5
 eosinophil production regulation by, 261
 neonatal, 30

- International Society of Blood Transfusion (ISBT)
 human platelet-specific antigens, 223–4
 red blood cell antigen systems, 133, 134–6
- intracardiac thromboembolism, 316
- intracranial hemorrhage (ICH)
 alloimmune thrombocytopenia with, 228–9, 231, 232, 233–5
 bleeding disorders with, 293–4
 platelet transfusions and, 340–1
- intrauterine infections. *See* congenital viral infections
- intrauterine transfusion (IUT), 5, 141–2, 232, 339–40
- intravenous immunoglobulin (IVIG)
 for alloimmune thrombocytopenia, 232–5
 for antibody deficiency, 84–5
 consistent approach to administration of, 273–4
 for enteroviral infections, 424
 for functional phagocyte disorders, 282
 for hemolytic disease of fetus and newborn, 142, 145, 337
 for sepsis, 344
- intraventricular hemorrhage (IVH), 293–4
- IPEX syndrome, 68–70, 76–7
- IPF. *See* immature platelet fraction
- IRAK4 deficiency, 286
- IRF. *See* immature reticulocyte fraction
- iron deficiency anemia, 118, 124, 414–15
- iron status
 maternal effects on neonatal, 415
 of preterm infants, 120
 enteral iron supplementation, 125
 erythropoietin therapy and, 122, 124–6
 long-term, 125–6
 measurement of, 124–5
 parenteral iron supplementation, 125
 perinatal iron acquisition, 124
 postnatal iron sources, 125
- ISBT. *See* International Society of Blood Transfusion
- isoimmune neonatal neutropenia, 267
- isoniazid, 413
- IT. *See* inherited thrombophilia
- ITP. *See* immune thrombocytopenic purpura
- IUT. *See* intrauterine transfusion
- IVH. *See* intraventricular hemorrhage
- IVIG. *See* intravenous immunoglobulin
- jaundice
 in Down syndrome, 372
 in glucose-6-phosphate dehydrogenase deficiency, 165–6, 167
 in hereditary spherocytosis, 160–1, 162
 in pyruvate kinase deficiency, 167
- JK. *See* Kidd antigen system
- juvenile myelomonocytic leukemia (JMML), 370–1
- juvenile xanthogranuloma (JXG), 392
- kaposiform hemangioendothelioma (KHE), 391
- Kasabach–Merritt syndrome, 217
- Kell antigen system (KEL), 137–8, 140
- kernicterus
 in glucose-6-phosphate dehydrogenase deficiency, 96, 104–5, 165–6, 167
 in hemolytic anemia, 118
 in hemolytic disease of fetus and newborn, 133, 145–6
- KHE. *See* kaposiform hemangioendothelioma
- Kidd antigen system (JK), 138–9
- kidney tumors, 388–9
- KMT2A* gene, 367, 369
- Korber, E., 3
- lactic dehydrogenase (LDH), 157
- LAD. *See* leukocyte adhesion deficiency
- Landsteiner, Karl, 4
- Langerhans cell histiocytosis (LCH), 392
- large for gestational age (LGA)
 infants of diabetic mothers, 408
 polycythemia and, 191
- LCH. *See* Langerhans cell histiocytosis
- LDH. *See* lactic dehydrogenase
- leiomyosarcoma, 387
- leukemia, 367. *See also* transient myeloproliferative disorder
 acute lymphoblastic, 367–9
 acute myeloid, 52–3, 368, 369–70
 of Down syndrome, 371–2, 374, 375–7
 evaluation of suspected, 368, 370
 juvenile myelomonocytic, 370–1
 severe congenital neutropenia risk for, 51–2
 thrombocytopenia with increased risk of, 249
- leukemoid reactions, 263–4, 414
- leukocyte adhesion deficiency (LAD), 68–70, 77, 82, 264, 286–7
- leukocyte alloimmunization, in transfusion therapy, 347
- leukocytes. *See also* eosinophilia; neutropenia; neutrophilia; *specific leukocytes*
 blood viscosity and, 188
 daily production of, 10
 early investigators of, 10
 historical description of, 1–2
 in leukemia, 367–8, 369–70
 maternal medication effects on, 414
 reference intervals
 blood sampling site effects on, 453
 counts in preterm infants, 454–5, 458
 counts in term infants, 453–4
 eosinophils, 261–2, 455–9
 historical attitudes toward, 453
 in transient myeloproliferative disorder, 373–5
- leukoreduction
 cytomegalovirus prevention and, 353
 erythrocyte transfusion preparations, 332
- Levine, Philip, 4
- LGA. *See* large for gestational age
- Liley, A.W., 5
- lineage-committed hematopoietic cells, 11–13
- lipoprotein a, 315
- Lippman, H.S., 2
- liver
 acquired hemorrhagic disorders with disease of, 304–5
 hematopoiesis in, 16–17, 18–19, 28–9
 thrombocytopenia in failure of, 218
 tumors of, 390–1
- LMWH. *See* low molecular weight heparin
- long-term culture-initiating cells (LTC-IC), 12
- low molecular weight heparin (LMWH), 319–20, 321
- LTC-IC. *See* long-term culture-initiating cells
- Lucas, W.P., 2, 5–6
- lung disease, leukemoid reactions and, 263–4
- lung injury, transfusion-related, 347–8
- lupus erythematosus, 157, 411
- lymph nodes, development of, 29

Index

- lymphocytes. *See also* B-cells; T-cells
 evolution of, 26
 flow cytometry enumeration of, 80–1
 hematopoiesis, 16–17, 27, 28–9
 measurement of function of, 81–2
 newborn screening of, 79–80, 81, 95, 96–7, 105–6
 severe combined immunodeficiency disease subsets, 67–71
- macrophages
 culture of, 11
 development of, 29–30
 hematopoiesis, 15, 16–17, 18, 26–7, 28–9
- macrothrombocytopenia, 252
- major histocompatibility complex (MHC), 26, 31–2
 deficiencies of, 68–70, 71
 T-cell recognition of, 32–3
- malaria, 354
- malignancy. *See* cancer
- maternal antibodies
 in alloimmune thrombocytopenia, 223, 227–8, 230
 to blood group antigens, 133, 134–5, 157
 mechanisms for development of, 134–5, 136
 perinatal communication of, 142–3
 screening of, 139–40, 141, 143, 144
 surveillance of, 140–1
 in directed donor transfusions, 335
 neutropenia associated with, 267
- maternal disorders. *See also* fetomaternal unit disorders
 antibody deficiencies, 84–5
 immune thrombocytopenic purpura, autoimmune neonatal thrombocytopenia secondary to, 213–14
- MCA PSV. *See* middle cerebral artery peak systolic velocity
- MCH. *See* mean corpuscular hemoglobin
- MCHC. *See* mean corpuscular hemoglobin concentration
- MCV. *See* mean corpuscular volume
- MDS. *See* myelodysplastic syndrome
- mean corpuscular hemoglobin (MCH), 444–5
- mean corpuscular hemoglobin concentration (MCHC), 444–5
- mean corpuscular volume (MCV)
 changes after birth, 156
 in inherited bone marrow failure syndromes, 44
 reference intervals, 443, 445
 mean platelet volume (MPV), 460, 462
- medulloblastoma, 388
- megakaryocytes (MKs)
 hematopoiesis, 15, 16–17, 26–7
 in platelet production, 210–11
- menadione, 302
- Mendelian susceptibility to mycobacterial disease (MSMD), 287
- mesenchymal hamartoma, 390
- mesoderm cells, blood cell differentiation of, 13–15
- methemoglobinemia, 175–7
- methylene blue, 175, 177
- MHC. *See* major histocompatibility complex
- microangiopathic anemias, 158
- microscope, in history of hematology, 1–2
- middle cerebral artery peak systolic velocity (MCA PSV), 140–1
- Mirasol® system, 355
- MKs. *See* megakaryocytes
- ML-DS. *See* acute myeloid leukemia of Down syndrome
- MNS antigen system, 139
- molecular genetics. *See* genetic testing
- monocytes
 development of, 29–30
 neonatal, 30
 reference intervals, 458–60
- MPO deficiency. *See* myeloperoxidase deficiency
- MPV. *See* mean platelet volume
- MSMD. *See* Mendelian susceptibility to mycobacterial disease
- mucosa, barrier function of, 62–3
- multipotent hematopoietic cells, 11–13
- murine studies
 of embryonic hematopoiesis, 13–15
 origin of fetal hematopoietic stem cells in, 26–8
- MyD88 deficiency, 286
- myeloblasts, in leukemia, 369–70
- myelodysplastic syndrome (MDS), Shwachman–Diamond syndrome risk for, 52–3
- myeloperoxidase (MPO) deficiency, 287
- myeloproliferative disorder of Noonan syndrome (NS/MPD), 370–1
- MYH9-related disease, 250
- myofibroma, 387
- NADH-methemoglobin reductase deficiency, 176, 177
- Naiman, Laurie, 4
- NAIT. *See* alloimmune thrombocytopenia
- natalizumab, 413
- natural killer (NK) cells
 development of, 30–1
 disorders of, severe combined immunodeficiency disease, 67–71, 80, 81, 83–4, 95, 96–7, 105–6
 evolution of, 26
 flow cytometry enumeration of, 80–1
 normal ranges of, 64
- NBS. *See* newborn screening
- necrotizing enterocolitis (NEC)
 neutropenia in, 270
 polycythemia and, 193
 thrombocytopenia and, 216
 transfusion therapy and, 348–9
- Nelson, Waldo, viii
- NEMO deficiency, 68–70, 73–4, 287–8
- neonatal alloimmune thrombocytopenia. *See* alloimmune thrombocytopenia
- neonatal immune system
 development of, 25, 29, 30, 31, 32–3, 34, 35, 36
 immaturity of, 62–6
- neonatal lupus erythematosus (NLE), 411
- neonatal-onset multisystem inflammatory disorder (NOMID), 63, 68–70, 78
- Netherton syndrome, 68–70, 73
- NETs. *See* neutrophil extracellular traps
- neuroblastoma, 383–5
- neurologic disorders, polycythemia and, 194–5
- neuroprotection, erythropoietin therapy for, 123
- neutropenia, 264–5. *See also* congenital neutropenias
 with accelerated neutrophil destruction, 266–8, 270
 chronic hyporegenerative, 268–70
 consistent approach to bone marrow biopsy, 272
 granulocyte transfusion, 272–3
 intravenous immunoglobulin administration, 273–4
 consistent approaches to, 270–1
 evaluation, 270, 271
 granulocyte colony stimulating factor administration, 271

- definition of, 264
- fetomaternal unit disorders
 - causing, 402
- in infants of gestational hypertension, 409–10
- late-onset, 270
- phagocytic disorders with, 277
- transient hyporegenerative, 265–6, 270
- neutrophil extracellular traps (NETs), 281
- neutrophilia, 263–4
- neutrophils, 279
 - accelerated destruction of, 266–8
 - concentration
 - blood sampling site effects on, 453
 - counts in preterm infants, 454–5, 458
 - counts in term infants, 453–4
 - historical attitudes toward, 453
 - development of, 30, 279
 - function of, 289–90
 - chemotaxis, 280–1
 - diapedesis and basement membrane passage, 280
 - migration and adherence, 280
 - neutrophil extracellular trap creation, 281
 - phagocytosis, 281
 - respiratory burst, 281
 - therapies for deficiencies in, 281–2
 - functional disorders of, 290–2
 - CARD9 deficiency, 282
 - Chédiak–Higashi syndrome, 68–70, 76, 282–5
 - chronic granulomatous disease, 68–70, 77–8, 82, 285
 - glycogen storage disease type IB, 49–50, 54, 285
 - hyperimmunoglobulin E syndrome, 286
 - IRAK4 deficiency/MyD88 deficiency, 286
 - leukocyte adhesion deficiency, 68–70, 77, 82, 264, 286–7
 - Mendelian susceptibility to mycobacterial disease, 287
 - myeloperoxidase deficiency, 287
 - NEMO deficiency, 68–70, 73–4, 287–8
 - Shwachman–Diamond syndrome, 43, 45–50, 52–3, 269–70, 288
 - specific granule defect, 288
 - therapies for, 281–2
 - Wiskott–Aldrich syndrome, 49–50, 68–70, 71–2, 76, 245–8, 288–9
 - hematopoiesis, 28–9
 - neonatal, 30
 - neutrophil-specific granule deficiency, 288
 - newborn screening (NBS), 93
 - blood disorders screened via, 95–6
 - carrier testing, 106
 - future directions in, 106–7
 - for glucose-6-phosphate dehydrogenase deficiency, 96, 104–5, 166
 - for hemoglobinopathies, 174
 - follow-up strategies for non-sickling hemoglobinopathies, 102–4
 - follow-up strategies for sickling hemoglobinopathies, 102, 103
 - limitations of non-genetic, 98–102
 - methods for, 97–8
 - results interpretation for, 98, 99–101
 - sickle cell disease, 93–5, 98, 99–101, 102, 103
 - thalassemia, 95–6, 98–102
 - immunologic disorders with hematologic abnormalities screened via severe combined immunodeficiency disease, 95, 96–7, 105–6
 - T-cell deficiencies, 79–80, 81, 95, 96–7, 105–6
 - United States implementation of, 93–5
 - Newman, Paul, viii–ix
 - NIPT. *See* non-invasive prenatal testing
 - nitrites, 175
 - nitrous oxide, 175
 - NK cells. *See* natural killer cells
 - NLE. *See* neonatal lupus
 - erythematosis
 - NOD-like receptors (NLRs), 63
 - NOD/SCID murine model, 12
 - NOMID. *See* neonatal-onset multisystem inflammatory disorder
 - non-deletional hemoglobin H, newborn screening for, 96
 - non-invasive prenatal testing (NIPT), for homozygous alpha thalassemia, 171–2
 - Noonan syndrome, 252, 370–1
 - NRBC. *See* nucleated red blood cells
 - NS/MPD. *See* myeloproliferative disorder of Noonan syndrome
 - nucleated red blood cells (NRBC), 449
 - anemia tests, 115, 116–17
 - changes after birth, 156
 - nutritional deficiencies, maternal, 414–17
 - nutritional supplementation, erythropoietin therapy and, 122
 - Octaplas™, 343
 - OF. *See* osmotic fragility
 - Oski, Frank, 4
 - Osler, William, 1–2
 - osmotic fragility (OF), 161
 - oxygenation, polycythemia disturbances in
 - brain, 190
 - carcass, 190
 - cardiopulmonary, 188–9
 - fetal, 190
 - gastrointestinal, 189
 - renal, 189–90
 - P5'N deficiency. *See* pyrimidine 5'nucleotidase deficiency
 - PAIS. *See* perinatal arterial ischemic stroke
 - PALs. *See* peripheral arterial catheters
 - para-aortic splanchnopleura (PS), differentiated blood cells in, 13–15
 - parental donor transfusions, 335
 - parenteral iron supplementation, 125
 - Paris-Trousseau syndrome (PTS), 251–2
 - partial exchange transfusion (PET), 195, 338–9
 - parvovirus B19. *See* human parvovirus B19
 - pathogen recognition, neonatal immaturity of, 63
 - pathogen reduction/pathogen inactivation (PR/PI), 354–5
 - pattern recognition receptors (PRRs), neonatal immaturity of, 63
 - Pearson, Howard Allen, vii, ix
 - Pearson marrow-pancreas syndrome, 48, 49–50
 - Pediatric History Center (American Academy of Pediatrics), ix
 - penicillin prophylaxis, for sickle cell disease, 94
 - percutaneous umbilical blood sampling (PUBS), 142
 - perinatal arterial ischemic stroke (PAIS), 315, 317–18
 - perinatal asphyxia
 - polycythemia and, 191, 195
 - thrombocytopenia and, 214–15
 - peripheral arterial catheters (PALs), 315–16, 317–18

Index

- peripheral blood smear, 1–2
peripheral nerve tumors, 383–5
PET. *See* partial exchange
transfusion
Peyer’s patches, 29
PFA-100 closure time. *See* platelet
function analyzer-100
closure time
PGK deficiency. *See*
phosphoglycerate kinase
deficiency
pH, blood viscosity and, 188
phagocytes, 26, 279. *See also*
macrophages; monocytes;
neutrophils
congenital defects in, 67, 68–70,
77–8
development of, 29–30, 279
function of, 289–90
chemotaxis, 280–1
diapedesis and basement
membrane passage, 280
migration and adherence, 280
neutrophil extracellular trap
creation, 281
phagocytosis, 281
respiratory burst, 281
functional disorders of, 290–2
CARD9 deficiency, 282
Chédiak–Higashi syndrome,
68–70, 76, 282–5
chronic granulomatous
disease, 68–70, 77–8, 82, 285
glycogen storage disease type
IB, 49–50, 54, 285
hyperimmunoglobulin
E syndrome, 286
IRAK4 deficiency/MyD88
deficiency, 286
leukocyte adhesion deficiency,
68–70, 77, 82, 264, 286–7
Mendelian susceptibility to
mycobacterial disease, 287
myeloperoxidase deficiency,
287
NEMO deficiency, 68–70,
73–4, 287–8
Shwachman–Diamond
syndrome, 43, 45–50, 52–3,
269–70, 288
specific granule defect, 288
therapies for, 281–2
Wiskott–Aldrich syndrome,
49–50, 68–70, 71–2, 76,
245–8, 288–9
measurement of function
of, 82
phagocytosis, neutrophil, 281
phenobarbital, 413
phenytoin, 413
phlebotomy, anemia of prematurity
and, 120–1
phosphoglycerate kinase (PGK)
deficiency, 168
photochemical activation, 354–5
phototherapy
in glucose-6-phosphate
dehydrogenase deficiency,
165–6, 167
for hemolytic disease of fetus and
newborn, 145
for hereditary spherocytosis, 162
physiologic anemia of infancy, 156,
329–30
historical review of, 6–7
PIDDs. *See* primary immune
deficiency diseases
PKD. *See* pyruvate kinase deficiency
placenta. *See also* fetomaternal unit
disorders
anemia in disorders of, 401–7
blood sampling of, 452–3
fetal growth restriction in
disorders of, 407
hematopoiesis in, 28–9
immunoglobulin transport
across, 136
perinatal arterial ischemic stroke
and, 315, 317–18
placenta previa, 402–3
placental insufficiency,
thrombocytopenia and,
212–13
placental metastases, 412–13
placental tumors, 407
plasma
ferritin levels, 124
proteins in, 187
plasma transfusions, 342–4
plasmapheresis, for hemolytic
disease of fetus and
newborn, 142
plasticizers, 351
platelet distribution width, 462
platelet function analyzer (PFA)-
100 closure time, 462, 464
platelet transfusions, 340
for alloimmune
thrombocytopenia, 232, 235
dose and administration of, 342
indications and transfusion
thresholds for, 206–7, 340–1
intrauterine, 339–40
preparations for, 341–2
platelets. *See also* thrombocytopenia
antigens, 223–4, 225, 226, 230
blood viscosity and, 188
early investigators of, 10
function of, 211–12
historical description of, 1–2
increased destruction of, 252–3
inherited function defects
of, 253
production of, 210–11
daily, 10
reference intervals
blood sampling site effects on,
459–60
platelet count and mean
platelet volume, 460, 462
platelet function analyzer-100
closure time, 462, 464
reticulated platelets, immature
platelet fraction, and
immature platelet count,
460–4
template bleeding time, 461–2
thrombocytopenia evaluation
measurements of, 205–6
in transient myeloproliferative
disorder, 373–4, 377
pluripotent stem cells, 19
poikilocytes, 162–3
poikilocytosis, 160, 162–3
polycythemia, 185, 195
in asymptomatic newborns, 195
blood viscosity and, 186
definition of, 186–7
factors affecting, 187–8
definition of, 185–6
etiologies of, 191
hemodynamics in, 188
brain, 190
carcass, 190
cardiopulmonary, 188–9
fetal, 190
gastrointestinal, 189
renal, 189–90
historical studies of, 2
incidence of, 186
in infants of diabetic mothers, 408
in infants of gestational
hypertension, 411
management of, 195, 338–9
symptoms of, 191–2
blood volume abnormalities,
192
cardiopulmonary, 192–3
gastrointestinal, 193
hematologic, 193
hypocalcemia, 193–4
hypoglycemia, 193
neurologic, 194–5
renal, 193
portal circulation, development of,
15–16
portal vein thrombosis (PVT), 317,
318, 319
preeclampsia, 402, 409
pregnancy
anemia during, 414–17
chemotherapy and radiation
therapy during, 412–13
diabetes during, 408–9
hypertension in, 265–6, 409–11
infection during, 158, 417–27

- medication effects during, 158, 217–18, 413–14
 - nutritional deficiencies during, 414–17
 - preterm infants
 - anemia of prematurity in, 120, 126
 - historical review of, 6–7
 - physiology of, 120
 - therapy for, 120–4, 329–30
 - eosinophilia of, 262, 455–9
 - erythrocytes in, 445
 - erythropoietin levels in, 120
 - exchange transfusion with
 - glucose-6-phosphate dehydrogenase-deficient blood in, 167
 - hematocrit in, 443, 445
 - intravenous immunoglobulin use in, 84–5
 - iron deficiency anemia in, 124
 - iron status of, 120
 - enteral iron supplementation, 125
 - erythropoietin therapy and, 122, 124–6
 - long-term, 125–6
 - measurement of, 124–5
 - parenteral iron
 - supplementation, 125
 - perinatal iron acquisition, 124
 - postnatal iron sources, 125
 - leukocyte counts in, 454–5, 458
 - reticulocyte count in, 448–9
 - template bleeding time in, 461–2
 - vitamin E deficiency in, 158
 - pretransfusion testing, 329
 - prilocaine, 176
 - primary immune deficiency diseases (PIDDs), 65–6, 67, 68–70,
See also specific diseases
 - primitive erythroblasts, 16–17, 18
 - primitive erythrocytes, 15, 26–7
 - primitive hematopoiesis, 26–7
 - progenitor cells. *See also specific cells*
 - B-cell, 33–4
 - commitment of, 12–13
 - in embryonic hematopoiesis, 14, 10, 13–19
 - fetal sites of, 28–9
 - identification methods for, 10–12
 - origin of fetal, 26–8
 - site of origin of, 14
 - T-cell, 32
 - protein C deficiency, 314
 - protein S deficiency, 314–15
 - prothrombin deficiency, 296, 297–8
 - prothrombin gene mutations, 314
 - PR/PI. *See* pathogen reduction/pathogen inactivation
 - PRRs. *See* pattern recognition receptors
 - PS. *See* para-aortic splanchnopleura
 - PTS. *See* Paris-Trousseau syndrome
 - PUBS. *See* percutaneous umbilical blood sampling
 - pulmonary hypertension, 264
 - pulmonary resistance, in
 - polycythemia, 188–9
 - PVT. *See* portal vein thrombosis
 - pyknocytosis, 158–9
 - pyrimidine 5′nucleotidase (P5′N) deficiency, 168–9
 - pyruvate kinase deficiency (PKD), hemolysis due to, 163, 164, 167–9
 - Quick, Armand, 5
 - radiation, studies of hematopoietic effects of, 10–11
 - radiation therapy
 - maternal, 412–13
 - neonatal, 393
 - radioulnar synostosis with
 - amegakaryocytic thrombocytopenia (RUSAT), 49–50, 249
 - rasburicase, for leukemia, 368–9
 - RDW. *See* red blood cell distribution width
 - recombinant erythropoietin. *See* erythropoietin
 - recombinant FVIIa, 298, 302, 303, 305
 - recombinant tissue plasminogen activator (rTPA), 321–2
 - recommended universal newborn screening panel (RUSP), 93, 94
 - red blood cell distribution width (RDW), 446–8
 - red blood cell transfusions. *See* erythrocyte transfusions
 - red blood cells. *See* erythrocytes
 - reference intervals, 440
 - blood sampling for
 - delivery and, 452–3
 - site effects on, 114, 450–1, 453, 459–60
 - bone marrow, 463–5
 - end tidal carbon monoxide concentration, 117
 - erythrocytes
 - blood sampling relative to
 - delivery, 452–3
 - blood sampling site effects on, 114, 450–1
 - erythrocyte count, 443
 - erythrocyte indices, 444–5
 - erythrocyte morphology, 450
 - fragmented red cells, 451
 - hematocrit, 113–15, 442–3, 444, 445, 450
 - hemoglobin concentration, 113–15, 441, 442, 450
 - immature reticulocyte fraction and reticulocyte hemoglobin content, 449, 450
 - monocytes, 458–60
 - nucleated red blood cells, 449
 - red blood cell distribution width, 446–8
 - reticulocyte count, 448–9
- leukocytes
- blood sampling site effects on, 453
 - counts in preterm infants, 454–5, 458
 - counts in term infants, 453–4
 - eosinophils, 261–2, 455–9
 - historical attitudes toward, 453
- platelets
- blood sampling site effects on, 459–60
 - platelet count and mean platelet volume, 460, 462
 - platelet function analyzer-100 closure time, 462, 464
 - reticulated platelets, immature platelet fraction, and immature platelet count, 460–4
 - template bleeding time, 461–2
- regulatory T-cells, 33
- renal blood flow, polycythemia disturbances in, 189–90
- renal function, polycythemia and, 193
- renal tumors, 388–9
- renal vein thrombosis (RVT), 316–17, 318, 319
- reproductive technology, hemolytic disease of fetus and newborn risk and, 135
- respiratory barrier defense, 62–3
- respiratory burst, 281
- respiratory distress
 - hemolytic disease of fetus and newborn and, 144–5
 - transfusion therapy and, 348
- RET-He. *See* reticulocyte hemoglobin content
- reticular dysgenesis, 270
- reticulated platelets, 460–4
- reticulocyte count
 - anemia tests, 115, 116–17
 - changes after birth, 156
 - reference intervals, 448–9
- reticulocyte hemoglobin content (RET-He), 449, 450
- reticulocytosis, hemolysis and, 156–6
- retinoblastoma, 389–90
- Revesz syndrome (RS), 56, 57
- RH. *See* Rhesus antigen system

Index

- rhabdoid tumor of kidney (RTK), 389
 rhabdomyosarcoma (RMS), 386
 RHD. *See* D antigen
 Rhesus (Rh) antigen system (RH), 4, 133, 134–5, 137, 139–41, 143, 144, 146, 329, 341–2
 riboflavin, 355
 rifampicin, 413
 RMS. *See* rhabdomyosarcoma
 RS. *See* Revesz syndrome
 RTK. *See* rhabdoid tumor of kidney
 rTPA. *See* recombinant tissue plasminogen activator
 rubella, 422–3
 RUSAT. *See* radioulnar synostosis with amegakaryocytic thrombocytopenia
 RUSP. *See* recommended universal newborn screening panel
 RVT. *See* renal vein thrombosis
- sacroccygeal teratoma (SCT), 385
 sarcomas, 386–7
 SCD. *See* sickle cell disease
 schistocytic anemias, 158
 SCID. *See* severe combined immunodeficiency disease
 SCN. *See* severe congenital neutropenia
 Scott, Roland, 3
 screening. *See also* newborn screening
 for alloimmune thrombocytopenia, 231
 coagulation tests, 294, 295
 maternal anti-erythrocyte antibodies, 139–40, 141, 143, 144
 pretransfusion, 329
 SCT. *See* sacroccygeal teratoma
 SDPs. *See* single-donor platelets
 SDS. *See* Shwachman–Diamond syndrome
 secondary hemophagocytic lymphohistiocytosis, 76
 SEGA. *See* subependymal giant cell astrocytoma
 self-recognition, immune system, 26, 32–3
 SEPS. *See* subdiaphragmatic extralobar pulmonary sequestration
 sepsis
 granulocyte transfusions for, 344–5
 neonatal hemolysis in, 158
 neutropenia of, 265, 266–7, 270
 in sickle cell disease, 174
 thrombocytopenia and, 215–16
 severe combined immunodeficiency disease (SCID)
 diagnostic approach to, 80, 81
 lymphocyte subsets, 67–71
 management of, 83–4, 105–6
 newborn screening for, 95, 96–7, 105–6
 severe congenital neutropenia (SCN), 51–2, 268–9
 SGA. *See* small for gestational age
 SHM. *See* somatic hypermutation
 Shwachman–Diamond syndrome (SDS), 43, 45–50, 52–3, 269–70, 288
 sickle beta thalassemia, 174
 sickle cell disease (SCD)
 hemolysis due to, 174–5
 historical studies of, 3
 newborn screening for, 93–5, 98, 99–101, 102, 103
 sickle hemoglobin (HbS), 95, 98–102, 174
 Sidbury, J.B., 6
 silent carrier state, alpha thalassemia, 170
 silent transient myeloproliferative disorder, 374
 single-donor platelets (SDPs), 341–2
 sitosterolemia, 252
 skin, barrier function of, 62–3
 small for gestational age (SGA)
 infants of diabetic mothers, 408
 polycythemia and, 191–2
 Smith, Carl, 3
 Smith, Job Lewis, 2
 Sn-mesoporphyrin, 167
 soft tissue tumors, 386–7
 soluble transferrin receptor (sTfR), 124
 solvent/detergent-treated plasma, 343
 somatic hypermutation (SHM), 31–2
 spherocytes, 159–62
 spleen, hematopoiesis in, 17, 29
 splenectomy, for hereditary spherocytosis, 162
 splenic sequestration crisis, 174
 splenomegaly, in hereditary spherocytosis, 160–1
 stains, 1–2, 10
 stem cell model, of hematopoiesis, 12–13
 stem cells. *See* hematopoietic stem cells
 sTfR. *See* soluble transferrin receptor
 stroke, perinatal arterial ischemic, 315, 317–18
 subdiaphragmatic extralobar pulmonary sequestration (SEPS), 385
 subependymal giant cell astrocytoma (SEGA), 388
 supplemental oxygen, anemia with, 118
 syphilis, 419
 clinical manifestations of, 419
 diagnosis of, 419–20
 hematologic manifestations of, 420
 systemic resistance, in polycythemia, 188–9
- T helper cells, 34–5
 TACO. *See* transfusion-associated circulatory overload
 T-activation, 347
 TAGVHD. *See* transfusion-associated graft versus host disease
 TAPS. *See* twin anemia polycythemia syndrome
 TAR. *See* thrombocytopenia with absent radii
 TBD. *See* telomere biology disorder
 T-cell receptor (TcR), 32, 63
 T-cells, 31–2
 deficiencies of, 66–7, 72–3
 management of, 83–4
 screening for, 79–80, 81, 95, 96–7, 105–6
 severe combined immunodeficiency disease, 67–71, 80, 81, 83–4, 95, 96–7, 105–6
 development of, 29, 32–3
 evolution of, 26
 flow cytometry enumeration of, 80–1
 helper activity of, 34
 measurement of function of, 81–2
 neonatal immaturity of, 63, 64
 normal ranges of, 64
 TcR. *See* T-cell receptor
 TE. *See* thromboembolism
 telomere biology disorder (TBD), 43, 45–57
 template bleeding time, 461–2
 teratoma, 385, 387
 term infants, leukocyte counts in, 453–4
 TfR. *See* transferrin receptor
 TGF. *See* transforming growth factor
 thalassemia
 hemoglobin E with, 173
 hemoglobin S with, 174
 hemolysis due to, 169–73
 historical studies of, 3
 newborn screening for, 95–6, 98–102
 therapeutic hypothermia, 266

- THI. *See* transient hypogammaglobulinemia of infancy
- thrombocytopenia, 201, 207. *See also* alloimmune thrombocytopenia; inherited thrombocytopenia syndromes
- acquired, 210, 218
- asphyxia, 214–15
- autoimmune neonatal thrombocytopenia
- secondary to maternal immune thrombocytopenic purpura, 213–14
- disseminated intravascular coagulation/malformations, 217
- drug-induced, 217–18
- infection, 215–16
- liver failure, 218
- necrotizing enterocolitis, 216
- placental insufficiency and chronic intrauterine hypoxia, 212–13
- thromboses, 216–17
- classification and evaluation of, 203
- early-onset, 203–4
- late-onset, 204, 205
- platelet production measurements, 205–6
- definition and incidence of, 201–3
- in Down syndrome, 373–4
- fetomaternal unit disorders causing, 401
- heparin-induced, 413
- in infants of diabetic mothers, 409
- in infants of gestational hypertension, 410–11
- intravenous immunoglobulin administration for, 274
- platelet transfusions for, 206–7, 340–1
- polycythemia and, 193
- thrombocytopenia with absent radii (TAR), 43, 45–50, 248–9
- thrombocytopenia with increased risk of leukemia, 249
- thrombocytopenia with radiolunar synostosis, 49–50, 249
- thromboembolism (TE), 312, 322
- clinical presentations and locations of, 315
- arterial, 315–16
- venous, 316–17
- in infants of diabetic mothers, 408–9
- management of, 317
- arterial, 317–18
- heparin anticoagulation therapy, 318–21
- thrombolysis, 319, 321–2
- venous, 318, 319
- risk factors for
- clinical, 312–13
- developmental hemostasis and, 312
- inherited thrombophilia, 313–15
- thrombocytopenia and, 216–17
- thrombolytic therapy, 319, 321–2
- thrombophilia, 313–15
- thrombopoietin (Tpo), 210–11
- thrombotic thrombocytopenic purpura (TTP), 252–3
- thymus
- aplasia or hypoplasia of, 72–3
- development of, 29, 32
- T-cell differentiation in, 32–3
- transplant of, 83
- tissue plasminogen activator, 321–2
- TLR. *See* toll-like receptor
- TMD. *See* transient myeloproliferative disorder
- TNF. *See* tumor necrosis factor
- toll-like receptor (TLR), 30, 63, 286
- toll-like receptor (TLR) 3 deficiency, 68–70, 78
- Townsend, C.W., 5
- toxemia of pregnancy, 171
- toxoplasmosis, 417–19
- TPI deficiency. *See* triose phosphate isomerase deficiency
- Tpo. *See* thrombopoietin
- TRALI. *See* transfusion-related acute lung injury
- transferrin receptor (TfR), 124
- transforming growth factor (TGF), 34–5
- transfusion therapy, 329, 356. *See also* erythrocyte transfusions; exchange transfusion; platelet transfusions
- adverse reactions to, 346
- acute lung injury, 347–8
- allergic, 346
- circulatory overload, 348
- donor leukocyte effects, 347
- febrile nonhemolytic, 346
- graft versus host disease, 335, 348
- hemolytic, 346–7
- metabolic, 349–50
- necrotizing enterocolitis, 348–9
- plasticizer effects, 351
- transfusion-transmitted infection, 332, 351–5
- autologous transfusion, 336–7
- directed donor transfusions, 335
- donor exposure and, 334–5
- extracorporeal membrane oxygenation and, 345
- future directions in, 356
- granulocyte transfusions, 272–3, 344–5
- for hemolytic disease of fetus and newborn, 4–5, 141–2, 144–6, 337, 339–40
- intrauterine, 5, 141–2, 232, 339–40
- irradiated blood components, 341, 348
- maternal anti-erythrocyte antibody development after, 134–5
- plasma and cryoprecipitate transfusions, 342–4
- pretransfusion testing, 329
- recombinant erythropoietin and, 335–6
- whole blood, 333–4
- transfusion transmitted
- cytomegalovirus (TT-CMV), 332, 352, 353
- transfusion-associated circulatory overload (TACO), 348
- transfusion-associated graft versus host disease (TAGVHD), 335, 348
- transfusion-related acute lung injury (TRALI), 347–8
- transfusion-related
- immunomodulation (TRIM), 347
- transfusion-transmitted infection, 351–5
- cytomegalovirus, 332, 352, 353
- emerging pathogens, 354
- hepatitis B, 352
- hepatitis C, 352–3
- human immunodeficiency virus, 351, 352
- pathogen reduction/inactivation for prevention of, 354–5
- risks for, 351, 352
- West Nile virus, 352, 353
- Zika virus, 352, 353–4
- transient hypogammaglobulinemia of infancy (THI), 74
- transient hyporegenerative neutropenias, 265–6, 270
- transient myeloproliferative disorder (TMD), of Down syndrome, 371
- clinical features of, 372–3
- diagnosis and definition of, 374
- differential diagnosis of, 374–5
- hematologic features of, 373–4
- management of, 376–7
- natural history and evolution of, 375–6

Index

- transient myeloproliferative (cont.)
 pathogenesis and epidemiology
 of, 371–2
- transplantable stem cells, sources of,
 19
- Treponema pallidum*, 419–20
- TRIM. *See* transfusion-related
 immunomodulation
- triose phosphate isomerase (TPI)
 deficiency, 168
- trisomy 21. *See* Down syndrome
- TT-CMV. *See* transfusion
 transmitted
 cytomegalovirus
- TTP. *See* thrombotic
 thrombocytopenic purpura
- TTTS. *See* twin–twin transfusion
 syndrome
- tufted angioma, 391
- tumor, 382, 383, 393
 central nervous system, 387–8
 epidemiology of, 382, 384
 germ cell, 385–6
 hepatic, 390–1
 histiocytic disorders, 391–2
 peripheral nerve tumors and
 adrenal masses, 383–5
 placental, 407
 renal, 388–9
 retinoblastoma, 389–90
 soft tissue, 386–7
 treatment of, 393
 vascular, 391
- tumor necrosis factor (TNF), 34–5
- Turner syndrome, 75
- 22q11 deletion syndrome. *See*
 DiGeorge syndrome
- twin anemia polycythemia
 syndrome (TAPS), 402, 405
- twin–twin transfusion syndrome
 (TTTS), 402, 404–5
 acute intertwin transfusion, 402,
 405
 clinical manifestations of, 405–6
 hematologic outcomes in, 402
 neonatal management of, 406–7
 transient hyporegenerative
 neutropenia and, 265–6
 twin anemia polycythemia
 syndrome, 402, 405
- UACs. *See* umbilical arterial
 catheters
- UFH. *See* unfractionated heparin
- umbilical arterial catheters (UACs),
 315–16, 317–18
- umbilical blood sampling, 142
- umbilical cord, blood loss through,
 402–3
- umbilical cord clamping, delayed
- anemia of prematurity and, 121
- autologous transfusion by, 336–7
- hematocrit impact of, 186
- polycythemia and, 191
- unfractionated heparin (UFH), 320–1
- United States
 hemolytic disease of fetus and
 newborn in, 139
 newborn screening in, 93–5
- vaccination, severe combined
 immunodeficiency disease
 and, 83–4
- van Leeuwenhoek, Antonie, 1–2, 10
- vasa previa, 402–3
- vascular tumors, 391
- venous thromboembolism (VTE),
 312
 catheter related, 316, 318
 cerebral sinovenous thrombosis,
 317, 318
 intracardiac, 316
 management of, 318, 319
 portal vein thrombosis, 317, 318,
 319
 renal vein thrombosis, 316–17,
 318, 319
- very low birth weight (VLBW)
 infants
 erythrocyte transfusions for,
 329–30, 331
 leukocyte counts in, 454–5, 458
 platelet transfusions for, 340–1
 transfusion practices for, 334–7
- vessel size, blood viscosity and, 188
- viral infection. *See* infection
- viscosity, 186
 cerebral blood-flow and, 190
 definition of, 186–7
 factors affecting, 187–8
- vitamin B12 deficiency, maternal,
 416–17
- vitamin E deficiency, 158
- vitamin K
 deficiency of, 413
 as acquired hemorrhagic
 disorder, 301–3
 clinical presentation of, 301
 historical review of, 6
 in intraventricular
 hemorrhage, 293–4
 laboratory evaluation of, 301–2
 treatment of, 302
 mechanism of action of, 301
 prophylactic administration of,
 302–3
 sources of, 301
- VLBW infants. *See* very low birth
 weight infants
- volume, blood, 192
- volume of packed red blood cells.
See hematocrit
- von Gierke disease. *See* glycogen
 storage disease type IB
- von Willebrand factor (vWF)
 deficiency, 252–3, 296,
 298–9
- VTE. *See* venous thromboembolism
- vWF deficiency. *See* von Willebrand
 factor deficiency
- Waddell, W.W., 6
- Wallerstein, Harry, 4–5
- warfarin, 413
- WAS. *See* Wiskott–Aldrich
 syndrome
- WB transfusions. *See* whole blood
 transfusions
- Weiner, Alexander, 4–5
- West Nile virus (WNV), 352,
 353
- WHIM syndrome, 49–50, 54
- Whipple, G.H., 5–6
- white blood cells. *See* leukocytes
- whole blood (WB) transfusions,
 333–4
- Wilms tumor, 389
- Wintrobe, Maxwell, 1, 2, 3,
 442, 444
- Wiskott–Aldrich syndrome (WAS),
 49–50, 68–70, 71–2, 76,
 245–8, 288–9
- WNV. *See* West Nile virus
- worldwide newborn screening,
 94–5
- Wright, James Homer, 1–2
- xenotransplantation models, 12
- XIAP deficiency. *See* x-linked
 inhibitor of apoptosis
 deficiency
- X-linked agammaglobulinemia
 (XLA), 68–70, 74
- X-linked chronic granulomatous
 disease, 26
- x-linked inhibitor of
 apoptosis (XIAP)
 deficiency, 68–70, 76
- yolk sac, hematopoiesis in, 13–19,
 26–7, 28–9
- yolk sac tumor (YST), 386
- ZAP70 deficiency, 68–70, 71
- zidovudine (AZT), 426
- Zika virus (ZIKV), transfusion-
 acquired, 352, 353–4
- zinc protoporphyrin/heme (ZnPP/
 H) ratios, 125