Index

AAV8-FVIIa (gene therapy), 103
abatacept, 105
abciximab, 229–230
acidocalcisomes, 237
acquired hemophilia, 93–111, 267
clinical manifestations, 95
investigational agents, 102–103
laboratory tests, 95–97
relapse, 101–102
treatment, 97–101
activated coagulation factors
factor V
binding, 24
complex with factor Xa, 7
factor VII see recombinant activated factor VII
factor VIII
binding, 24
complex with factor IXa, 6
factor X, 5, 6–7, 24, see also anti-Xa test
complex with factor Va, 7
factor XI (factor XIa), 72–73
activated partial thromboplastin time (aPTT), 8–9, 32–33
acquired hemophilia, 96
circulating anticoagulants, 34–35
hemophilia B, 61
hemophilia C, 76
liver disease, 273
lupus anticoagulant, 35
sample storage, 31
activated protein C
concentrates, 163
resistance (APC-R), 39–40
screening tests, 39–40
activated prothrombin complex concentrates, 53
acquired hemophilia, 98
activities of daily living, 260
acute promyelocytic leukemia, 153, 177
ADAMTS-13 deficiency, 247, 248, 250, 273
adenovirus-associated virus
FVIIa vector, 103
hemophilia B gene therapy, 67–68
adenosine monophosphate see cAMP
adherence of platelets, 4–5, see also Bernard–Soulier syndrome
adhesion molecules, endothelial dysfunction, 27
ADP (adenosine diphosphate), 23
ecto-ADPase on, 19
platelet aggregometry, 216
platelets, 216
adult respiratory distress syndrome, 161
Advate (factor VIII concentrate), 51
afibrinogenemia (congenital), Glanzmann’s thrombasthenia vs, 220
aggregation of platelets, 24, 211–213
defects see Glanzmann’s thrombasthenia with ristocetin, 201
testing, 38–39
aggregometry, platelets, 39, 215, 216, 218, 219, 220, 221
aging
definition, 259–260
hemostasis, 259–270
LMW heparins and, 306
AIDS
hemophilia A and, 49, 266
Aimafix (factor IX concentrate), 63
AktS epsilon phosphorylation, 115
albumin, factor IX fusion protein, 66
alemtuzumab, 105
algorithms
acquired hemophilia, 96
immune thrombocytopenia, 141
TTP (thrombotic thrombocytopenic purpura), 251
alkaline phosphatase, 242
alloantibodies see factor IX inhibitors; factor VIII inhibitors
alloimmunization, platelet transfusions, 227
allostatic load, 263
all-trans-retinoic acid, 153
α₂-antiplasmin (α₂-plasmin inhibitor), 42, 170, 174
α₂-macroglobulin, 174
α-FXIIa, 112, 113, 116, 117
α-granules, platelets, 211, 213
Alphanate (factor VIII concentrate), 51
AlphaNine SD (factor IX concentrate), 63
alteplase, 181
amniocentesis, hemophilia B, 61
anamnestic increase, factor VIII inhibitors, 88
anaphylaxis
factor IX products, 86
von Willebrand factor, 205
anemia
aging, 260, 261
of chronic disease, platelet dysfunction, 230
liver disease, 276
microangiopathic hemolytic, 159, 248, 249
anervysms
DIC (disseminated intravascular coagulation), 152–153, 158
angiogenesis, factor XII and, 113, 115
animals, factor XI deficiency, 76
anistreplase, 181
annexin II, 177
anti-Xa test, see also anti-FXa assay
liver disease, 279
anti-angiogenic agents, venous thromboembolism, 285, 290
antibiotics
liver disease, 278
platelet dysfunction, 230
antibodies, see also autoantibodies; factor IX inhibitors; factor VIII inhibitors from FFP (fresh frozen plasma) therapy, 132
monoclonal, CD20, 105
non-neutralizing, 83
to platelets, 138, 227
anticoagulant factors, 19–21
anticoagulants (circulating)
aging, 266
liver disease, 276
screening tests, 34–35
anticoagulants (therapeutic), see also heparin;
vitamin K antagonists; specific drugs
liver disease, 279
post-thrombotic syndrome prevention, 192
risk, 189
anti-D immunoglobulin, immune thrombocytopenia, 142
antifibrinolytic therapy
acquired hemophilia, 98, 99
DIC, 164
hemophilia C, 77, 78
hyperfibrinolysis, 179
immune thrombocytopenia, 146
platelet disorders, 226
von Willebrand disease, 203
anti-FXa assay, 307–308, see also anti-Xa test
anti-idiotypic antibodies, 105
antiplatelet agents, 228
liver disease, 279
antiplatelet factors, 16–19
antisense oligonucleotides, factor XI, 79
antithrombin, 5
DIC, 159
therapy, 163–164
factor XII inhibition, 118
measurement, 34
antithrombin III, 21
aortic aneurysm, 152–153
myeloproliferative disorders, 231
resistance, 229
before tests, 31
assays, 8–9, 41–42, see also specific assays
factor VIII, 37–38
von Willebrand factor, 37, 198–199
ATP (adenosine triphosphate), platelets, 216
atrial fibrillation, 267
@RISTOS project, 289
autoactivation see contact activation
autoantibodies, acquired hemophilia, 94
elimination, 104–105
immunoadsorption, 99
autoimmune diseases, with immune thrombocytopenia, 137–138
Awareness of Neutropenia in Chemotherapy (ANC) Study Group Registry, thrombosis, 287, 288
azathioprine, immune thrombocytopenia, pregnancy, 146
B1 and B2 receptors, bradykinin, 121
B7 (T-cell costimulatory molecule), blockade, 104
back-activation of factor IX, 240–241
Baltimore Longitudinal Study, D-dimers, 264
BARI 2D study, D-dimers, 264
BAX499 (TFPI blocker), 104
B cells, factor VIII on, 104–105
Bebulin (factor IX concentrate), 64
hemiparin, 297, 298, 302
BeneFIX (factor IX concentrate), 64
Beriate (factor VIII concentrate), 51
Berinin P (factor IX concentrate), 63
Beriplex P/N (factor IX concentrate), 64
Bernard–Soulier syndrome, 217–219
platelet aggregation, 38
β2-glycoprotein I, aging, 266
β-FXIIa, 112–113, 117
BETAFACT (factor IX concentrate), 63
β-lactam antibiotics, platelet dysfunction, 230
β-thromboglobulin, liver disease, 273
Bethesda assay, 83, 96–97
biological agents (protein therapies), hemophilia B, 65–68
Biostate (factor VIII concentrate), 51
bleeding, see also menstrual bleeding aspirin, 229
gastrointestinal aspirin and NSAIDs, 229
liver disease, 230–231
von Willebrand disease, 200
hemophilia C, 75–76
history-taking, 214
iliopsoas muscle, 47
intracranial, 47, 60
disease, 230–231, 275–277
local measures, 225–226
mucocutaneous, von Willebrand disease, 200
bleeding score, von Willebrand disease, 201
bleeding time, 35, 198, 214–215
blood-borne viruses, hemophilia A and, 49, 266–267
blood component transfusions, liver disease, 276–277
blood count, platelet disorders, 214
blood flow, control of clotting, 7–8
blood groups, on test results, 31
blood sampling, 30–32
bone marrow biopsy, immune thrombocytopenia, 139
bradykinin (BK), 114, 115, 121, 241
Budapest protocol, immune tolerance induction, 99–100
bypassing agents, 53, 65, 87
acquired hemophilia, 98
thrombosis, 88
C1 esterase inhibitor, 118
C46T polymorphism, 120
calcium, 3, 18
calibrated automated thrombinography, 41
calibration, prothrombin time, 33
calmodulin, 18
cAMP (cyclic AMP), 16, 213
cancer see malignant disease
cancer procoagulant, 157
carbohydrate deficient glycoprotein syndrome, 75
carboxyl glutamic acid, 57
cardiopulmonary bypass fibrinolysis, 177
platelets, 231
Cardiovascular Health Study, on frailty, 263
Carriers
hemophilia A, 47
hemophilia B, 60–61, see also Victoria (Queen)
catalytic domains
factor XI, 72
factor XII, 117–118
catheter-directed thrombolytic therapy, post-thrombotic syndrome prevention, 192
cationic PAMAM dendrimers, 242
CaVenT study, 192–193
CD11c-positive dendritic cells, 105
CD20 monoclonal antibodies, 105
CD80/86, synapse with CTLA4, 104
CEAP scale, post-thrombotic syndrome, 187
cell surface binding, 3
cell surface receptors, fibrinolysis, 174–175
centenarian paradox, 265, 267
central nervous system, DIC, 161–162
central venous pressure, liver disease, 276–277
cephalosporins, platelet dysfunction, 230
certoparin, 297
cesarean section
factor VIII-von Willebrand factor concentrates, 204, 205
immune thrombocytopenia, 146
Charlson’s index, 260
Chediak–Higashi syndrome, 222
chemotherapeutic agents, 3
chemotherapy (cytotoxic), venous thromboembolism, 284–285
risk factors, 287, 288
childbirth
factor VIII-von Willebrand factor concentrates, 204, 205–206
hemophilia C, 76, 78
von Willebrand disease, 200
children
acquired hemophilia, 94
hemophilia A, inhibitor development, 84
immune thrombocytopenia, 137, 145–146
LMW heparins, 305
Wiskott–Aldrich syndrome, 225
cholestatic liver disease, 272
chondroitin sulfate, as adulterant, 303–304
chorionic villus sampling, hemophilia B, 61
Christmas disease see hemophilia B
chromogenic anti-FXa assay, 307
chromogenic substrates, 40
chronic disseminated intravascular coagulation, 159
chronic immune thrombocytopenia, 137
chronic kidney disease, see also renal failure
LMW heparins, 305–306
platelet dysfunction, 230
circulating anticoagulants
  aging, 266
  liver disease, 276
screening tests, 34–35
cirrhosis, fibrinolysis, 176–177
citrine, 3
Clauss assay, fibrinogen, 33–34
clopidogrel, 31, 229
closure time see Platelet Function Analyzer
clot lysability, 173
collagen binding site on factor XII, 115
collagen binding assay, von Willebrand disease, 37, see also vWF-CB
combined deficiency of vitamin K-dependent clotting factors, 59, 61, see also vitamin K-dependent clotting factor deficiency
combined inherited factor V and factor VIII deficiency, 127–132
combined single-factor deficiencies, inheritance, 133–134
comorbidities, 260–261, 262
cancer patients, 289, 290, 291–292
c名片, 297, 298, 300
complement regulatory proteins, endothelial dysfunction, 27
cyclophosphamide acquired hemophilia, 100
  immune thrombocytopenia, 145
  TTP, 252–253
cyclosporine, TTP, 253
cytokines DIC, 157
  endothelial dysfunction, 27
  factor VIII immune response, 85
  on T-regulatory cells, acquired hemophilia, 104
cytoskeletons of platelets, 211
defects, 223–225
dabigatran, 164–165, 292, 308, 309
dalteparin, 297, 298, 300
cancer patients, 289, 290, 291–292
danaparoid, 303
danazol
  immune thrombocytopenia, 144
  TTP, 254
DDAVP see desmopressin
d-dimers aging, 262, 264
  DIC, 159, 179
  liver disease, 273
congenital amegakaryocytic
  thrombocytopenia, 210
congenital combined deficiency of vitamin K-dependent clotting factors, 59, 61, see also vitamin K-dependent clotting factor deficiency
congenital thrombotic thrombocytopenic purpura, 248
CONKO-004 trial, 290
contact activation (autoactivation), 73, 112, 113, 117–118, 119
  polyphosphates and, 238–239
contamination, LMW heparins, 121, 303–304
continuous infusions, factor VIII products, 86
contraceptives, on test results, 31
coronary artery bypass grafts, shear stress, 25
corticosteroids acquired hemophilia, 100
  immune thrombocytopenia, 140
  children, 145
  TTP, 252–253
costs, post-thrombotic syndrome, 190
CRASH2 trial, 164
cross-reactive material negative deficiency, factor XI, 74
cryoprecipitate, DIC, 162
CTLA4 blockade of B7, 104
  fusion protein (abatacept), 105
  synapse with CD80/86, 104
Cumulative Index Rating Scale–Geriatric, 260
cyclic AMP (cAMP), 16, 213
cyclooxygenase, 17
cyclophosphamide acquired hemophilia, 100
  immune thrombocytopenia, 144–145
cyclosporine, TTP, 253
dabigatran, 297, 298, 300
cancer patients, 289, 290, 291–292
danaparoid, 303
danazol
  immune thrombocytopenia, 144
  TTP, 254
DDAVP see desmopressin
D-dimers aging, 262, 264
  DIC, 159, 179
  liver disease, 273
deep vein thrombosis
  aging, 265–266
costs, 190
  endothelium and, 25
post-thrombotic syndrome incidence, 187
pregnancy, 304
prevention, 190–191
degranulation, platelets, 5, 231
delivery see childbirth
delta (δ)-granules, platelets, 211
disorders, 222–223
δ-storage pool diseases, 221
dendrimers, polyphosphate inhibitors, 242
dendritic cells, CD11c-positive, 105
dense granules, platelets, 211
disorders, 221
polyphosphates, 237
dense tubular system, platelets, 210–211
dental procedures
  factor VIII-von Willebrand factor concentrates, 204
  hemophilia C, 78
dermatan sulfate, 21
desmopressin, 48–49
  acquired hemophilia, 99
  combined inherited factor V and factor VIII deficiency, 131
  hemophilia A, 88
  hemophilia C, 78–79
  liver disease, 278
  platelet disorders, 226
  von Willebrand disease
diagnosis, 201
  management, 23, 202–203
  pregnancy, 205
desmoteplase, 181
dexamethasone, immune thrombocytopenia, 140
  children, 145
  rituximab with, 143
diacylglycerol (DAG), 213
diarrheal hemolytic uremic syndrome, 247, 250
  disseminated intravascular coagulation (DIC), 151–168
  hyperfibrinolysis, 178, 179
  hypofibrinolysis, 180
  leukemia, 153, 177
  scoring system, 159–161
  TFPI decrease, 21
diurnal variation, 31
dog breeds, factor XI deficiency, 76
  Döhle-like bodies, 224
drotrecogin alpha, DIC, 163
drug-induced DIC, 155
drug-induced immune thrombocytopenia, 138
drug-induced platelet disorders, 228–230
drug-induced thrombotic thrombocytopenic purpura, 249b
duteplase, 181
economic burden, post-thrombotic syndrome, 190
ecto-ADPase, 19
eculizumab, hemolytic uremic syndrome, 254
EGF-like domains, factor XII, 116
elastic compression stockings, 191–192, 193
elasticity, assays, 41, 179
elderly patients see aging
electrical impedance aggregometry, 39, 215
electron microscopy, platelets, 216–217
electrophoretic vWF multimer analysis, 199
elotrombopag, 143–144
emergencies, immune thrombocytopenia, 146
Emoclot (factor VIII concentrate), 51
endogenous thrombin potential, 41
  liver disease, 273
endomitosis, megakaryocytes, 209
endopolyphosphatases, 236
endothelial protein C receptor, 8
endothelins, 22
endothelium, 8, 14–29
  activation, aging, 265
  dysfunction, 26–27
  factor XII interaction, 115
  polyphosphates and, 241
  endothelium-dependent relaxing factor, 18
  endotoxins, DIC, 157
enoxaparin, 297, 298, 299, 300, 309–310
  cancer patients, 288–289, 290
  generic versions, 301
  liver disease, 306
ENOXICAN II study, 288–289
enzyme-linked immunosorbent assay, acquired hemophilia, 96, 97
enzymes, 3
epidermal growth factor, 116
epidural anesthesia
  factor VIII-von Willebrand factor concentrates, 204
  hemophilia C, 78
  immune thrombocytopenia, 146
  epinephrine, platelet aggregation, 38, 216
  epsilon (ε)-aminocaproic acid
  hemophilia C, 78
  von Willebrand disease, 203
  epftibatide, 229–230
ERK1/2
  factor XII on, 119
  phosphorylation, 115
Escherichia coli
  exopolyphosphatase, polyP-binding domain, 241–242
hemolytic uremic syndrome, 247
estrogens
  on factor XII expression, 118
  platelet disorders, 226
  on test results, 31
  von Willebrand disease, 203
ethnicity
  Ashkenazi Jews, hemophilia C, 73
  factor VIII inhibitors, 84
  euglobulin lysis time, 179
  exercise training, post-thrombotic syndrome, 193
exopolyphosphatases, 236
recombinant, 241–242
exposure days (ED), factor VIII inhibitor development, 84, 85
ex vivo gene therapy, hemophilia B, 67, 68
FVIII gene, 46, 83–84
FIX gene, 58, 84
FXII gene, 120
factor V, 6
deficiency, 36
combined with factor VIII deficiency, 127–132
inhibitors, 132
polyphosphates on activation, 239
pregnancy, 132
factor Va
binding, 24
complex with factor Xa, 7
factor V Leiden mutation, 8, 39
aging, 266
factor V Quebec, 223
factor VII, 5
factor VIIa see recombinant activated factor VII
factor VIII, 6, 46, see also immune tolerance induction
aging, 265
on B cells, 104–105
deficiency, see also hemophilia A combined with factor V deficiency, 127–132
desmopressin postinfusion levels, 48
factors affecting levels, 31
gene, 46, 83–84
liver disease, 271
porcine, 88, 99
recombinant B-domain-deleted (OBI-1), 102–103
pregnancy, 132
replacement therapy, 49–52
acquired hemophilia, 99
dosages, 52
F5F8D, 131
type of von Willebrand factor, 203–204
role of von Willebrand factor, 94, 198
von Willebrand disease, target levels, 202
factor VIIIa
binding, 24
complex with factor IXa, 6
Factor Eight Inhibitor Bypassing Activity (FEIBA), 53, 87–88
acquired hemophilia, 98
factor VIII inhibitors, 52–54, see also acquired hemophilia
A2 and C2 domains, 84
hemophilia, 82–92
management, 87–89
types, 83
factor IX, 57–58, see also immune tolerance induction
back-activation, 240–241
concentrates, 62–65
deficiency see hemophilia B
endothelium and, 26
extended-half-life preparations, 65–66
gene, 58, 84
low levels, 61–62
factor IX, 6, 58
endothelium and, 26
Factor IX Grifols (factor IX concentrate), 63
factor IX inhibitors, 62, 65, 86
hemophilia, 82–92
management, 87–89
factor Xa, 5, 6–7, 24, see also anti-Xa test complex with factor Va, 7
factor XI, 7, 71–73
activation, 112
concentrates, 78
deficiency, see also hemophilia C
cross-reactive material negative, 74
dog breeds, 76
factor XII binding site, 114
replacement therapy, 77–78
secretion defect, 75
thrombosis, 79
factor Xlla, 72–73
factor XI inhibitors, 75, 77
factor XII, 9, 73, 112–118
deficiency, 36, 112–126
functions, 119–120
gene, 120
polyphosphates and, 241
regulation, 118–119
factor XIII assays, 37–38
deficiency, 36, 37
family history, factor VIII inhibitor development, 85
Fanhdi (factor VIII concentrate), 51
fasting, for tests, 31
Fc-fusion proteins, factor IX, 65–66
FEIBA see Factor Eight Inhibitor Bypassing Activity fetoscopy, factor IX, 61
fever, splenectomy, 142
fibrin, 4, see also D-dimers DIC, 156–157
lysability, 173
polyphosphates on, 239–240
thrombin binding, 7
t-PA binding, 172
fibrinogen
aging, 265
binding by glycoprotein IIb-IIIa, 211–213
concentrate, DIC, 162
congenital absence, Glanzmann’s thrombasthenia vs, 220
degradation products, 178
DIC, 159
measurement, 33–34
normal range, 34
sample storage, 31–32
fibrinolysis, 169–185
modulators, 173–174
pathologic, 175–180
test panel, 179
fibrinolytic factors, endothelial, 22
fibrinolytic inhibitors, 42–43, see also
thrombin-activatable fibrinolysis inhibitor
depthelial, 22
fibronectin type I region, factor XII, 116
fibronectin type II region, factor XII, 114–116
“finger” domain, factor XII, 116
flow cytometry, platelets, 216
fradicaparine, 297, 298
free oscillation rheometry, 41
fresh frozen plasma
combined inherited factor V and factor VIII
deficiency, 131, 132
DIC, 162
hemophilia C, 77–78
liver disease, 278
freshness, plasma samples, 31–32
fusion proteins, recombinant, factor IX, 65–66
gamma carboxyl glutamic acid residues, factor IX, 57
gamma (γ)-glutamyl carboxylase
defect, 59
gene, 133
gastrointestinal bleeding
aspirin and NSAIDs, 229
liver disease, 230–231
von Willebrand disease, 200
generic low-molecular-weight heparins, 300–301
gene therapy
AAV8-FVIIa, 103
hemophilia B, 54, 66–68
platelet disorders, 228
genetic counseling, hemophilia B carriers, 61
Geriatric Depression Scale, 261
geriatrics see aging
GGCX gene see γ-glutamyl carboxylase
giant hemangiomas, DIC, 158
giant platelets see macrothrombocytes
Glanzmann’s thrombasthenia (GT), 219–220
antibodies, 227
platelet aggregation, 38
global assays, coagulation factors, 41–42
Glu117Stop mutation, hemophilia C, 73–74
Glu-Plg (human plasminogen), 171
glycopegalation see polyethylene glycol
moieties
glycoprotein(s), see also beta2-glycoprotein I
platelets, 211
von Willebrand factor binding, 23
glycoprotein lb, 4, 5, 6
von Willebrand factor, interaction, 197
glycoprotein lb/V complex, 211
deficiency, see Bernard–Soulier syndrome
glycoprotein lbA, von Willebrand factor, assay, 37
glycoprotein lbo, in von Willebrand factor assay, 198
glycoprotein Ib-IIIa, 211–213
antagonists, 229–230
defects, see Glanzmann’s thrombasthenia
von Willebrand factor binding, 198
glycoprotein VI, 5
glycosaminoglycans, as adulterants, 304
G-proteins, disorders, 223
growth factors
endothelial, 22
epidermal growth factor, 116
platelet-derived growth factor (PDGF), gray
platelet syndrome, 222
transforming growth factor-β1 (TGF-β1), on
factor XII expression, 119
guanidinosuccinic acid, 230
Gulf State Hemophilia and Thrombophilia
Center, register, 266–267
Haemate P (factor VIII concentrate), 51
Haemocetin (factor VIII concentrate), 51
Haemonine (factor IX concentrate), 63
Haemosolvex Factor IX, 64
Hageman factor see factor XII
half-lives, factor VIII products, 54
haplotypes, factor VIII inhibitor
development, 84
Helicobacter pylori, testing in immune
thrombocytopenia, 139
HELLP syndrome, TTP vs, 255
hemangiomas, DIC, 158
hemarthroses
hemophilia A, 47
hemophilia B, 60
hematopoietic stem cell transplantation, 228
hematuria, hemophilia A, 47
Hemo-B-RAAS (factor IX concentrate), 63
Hemofil M (factor VIII concentrate), 51
Hemoleven®, 78
hemolysis see HELLP syndrome
hemolytic anemia, microangiopathic, 159, 248,
249
hemolytic uremic syndrome, 247–248,
250
differential diagnosis, 250
treatment, 251, 254
hemophilia, 2, see also acquired hemophilia
aging, 266–267, 268
aPTT, 9
factor VIII inhibitors, 82–92
factor IX inhibitors, 82–92
Index 321
hemophilia A, 36, 45–56
    aging, 267
    blood-borne viruses and, 49, 266–267
    children, factor VIII inhibitor
devlopment, 84
    clinical manifestations, 46–47
    clotting, 4
    desmopressin, 88
    hemophilia B vs, 61
    management, 48–54
hemophilia B, 45–46, 57–70, see also under
carriers
    clinical manifestations, 59–60
    clotting, 4
    differential diagnosis, 61–62
    factor IX inhibitors, 86
    gene therapy, 54, 66–68
    laboratory tests, 61
    treatment, 62–68
hemophilia B<sub> cynos</sub>, 58–59, 60
hemophilia B<sub>M</sub>, 59, 60
hemophilia C (factor XI deficiency), 36, 71–81
    bleeding, 75–76
    inheritance, 73–75
    treatment, 77–79
    variability, 7, 9
hemostasis
    aging, 259–270
    endothelium and, 22–23
    rebalanced, 274–275, 280
hemostatic envelopes, 5
heparan sulfate, 15, 20–21
heparin, 21, see also low-molecular-weight
heparins; unfractionated heparin
cancer patients, 287–289
liver disease, 279
monitoring, 307–308
porcine mucosal, 299
synthetic derivatives, 302, see also
fondaparinux
on test results, 32
heparin cofactor II, 21
heparin-like substances, see also circulating
anticoagulants
liver disease, 276
hepatic artery thrombosis, liver transplantation,
prevention, 279
hepatitis C virus, hemophilia A and, 49
hepatocyte nuclear factor-4, on factor XII
expression, 118, 120
herbal remedies, platelet dysfunction, 230
hereditary angioedema, 118
Hermansky–Pudlak syndrome, 222
high-molecular-weight kininogen (HK), 71,
72, 112–114, 115
high-responding inhibitors, 82–83
histones, polyphosphates and, 241
historical aspects, 1–4, 14
    factor IX, 57
    hemolytic uremic syndrome, 247
    hemophilia A, 45
    TTP, 246–247
history-taking
    platelet disorders, 214
    von Willebrand disease, 200–201
HIV, hemophilia A and, 49, 266
Holstein Mini Mental Status, 261–262
hospitalization, DVT risk, 190–191, 289
HT DEFIX (factor IX concentrate), 64
human immunodeficiency virus, hemophilia A
and, 49, 266
hyperfibrinolysis, 176–180
liver disease, 276
hypofibrinolysis, 180
hyponatremia, desmopressin, 203, 226
ibuprofen, on platelets, 229
idiopathic thrombocytopenic purpura, 137–150
IgG, Fc-fusion proteins, factor IX, 65–66
iliopsoas muscle, bleeding, 47
Immunate (factor VIII concentrate), 51
immune modulation, 89
immune response, see also alloimmunization
factor VIII, 85
immune thrombocytopenia, 137–150
immune tolerance induction, 53–54, 62, 88–89
    acquired hemophilia, 99–100, 104–105
Immune (factor IX concentrate), 63
immunoadsorption, factor VIII
autoantibodies, 99
immunodeficiency, from monoclonal
antibodies, 105
immunological assays, von Willebrand
disease, 37
immunosuppression, acquired
hemophilia, 100–101
impedance aggregometry, 39, 215
independent activities of daily living
(IADL), 260
inducible PGHS-2, 17
infections
    DIC, 152, 154
    on test results, 31
inflammation
    aging, 260
    endothelial dysfunction, 27
    factor XII in, 113, 114, 120–121
    polyphosphates in, 241
    post-thrombotic syndrome, 189
    on test results, 31
inflammatory bowel disease, LMW
heparins, 306–307
inflammatory markers, aging, 262
infusions, factor VIII products, 86
initiation, clotting, 4–5
inositol triphosphate, 213
interleukins on T-regulatory cells, acquired
hemophilia, 104
International Immune Tolerance Induction
Study, 53
international normalized ratio (INR), 33
International Society on Thrombosis and
Haemostasis, scoring system for
DIC, 159–161
intracranial bleeding
hemophilia A, 47
hemophilia B, 60
intrahepatic microthrombosis, 279, 280
intranasal desmopressin, 202
intravenous immunoglobulin
acquired hemophilia, 101
immune thrombocytopenia, 140–142
children, 145
investigations see laboratory tests
Iran, combined inherited factor V and factor VIII deficiency, 128
“Ivy bleeding time”, 35
joints see hemarthroses
kallikrein, 112, 113, 117, 121
KASKADIL (factor IX concentrate), 64
Khorana score, 287, 288
kinetics, factor VIII inhibitor, 83
Koate-DVI (factor VIII concentrate), 51
Kogenate FS (factor VIII concentrate), 51
kringle domains
factor XII, 117
plasminogen, 171
KyberSept trial, 163
laboratory tests
acquired hemophilia, 95–97
of coagulation, 30–44
hemophilia B, 61
heparin monitoring, 307–308
TTP, 249–250
lanoteplase, 181
laparoscopy, splenectomy, 142
lectin mannose binding protein gene (LMAN1 gene), 128–129
Leiden mutation see factor V Leiden mutation
lepirudin, DIC, 164
leukemia, DIC, 153, 177
leukocytes
endothelial dysfunction, 27
factor XII on, 116, 121
telomere length, 262
lipoprotein (a), 170, 174
lipoprotein (low density), 24–25
liver disease, 271–283, see also intrahepatic microthrombosis
bleeding, 230–231, 275–277
DIC, 161
fibrinolysis, 176–177
LMW heparins, 279, 306
liver transplantation, 274–275
aprotinin, 180
fibrinolysis, 177
hepatic artery thrombosis, prevention, 279
LMAN1 gene (lectin mannose binding protein gene), 128–129
localization of clotting, 7–8
low density lipoprotein, 24–25
low-molecular-weight heparins (LMWH), 296–310
cancer patients, 287–288, 290, 291, 292
contamination, 121, 303–304
DIC, 162
liver disease, 279, 306
monitoring and dosages, 307–308
neutralization, 303
post-thrombotic syndrome prevention, 192
low-responding inhibitors, 82–83
lupus anticoagulant
acquired hemophilia, 96
tests for, 35
lysophosphatidylcholine, NOS-III gene and, 19
lysosomal trafficking regulator gene, 222
Lys-Plg (truncated plasminogen), 171
macroph thrombocytes, 218, 224
malignant disease
DIC, 152, 153, 154, 157, 177
LMW heparins, 305
thrombosis, 284–295
malnutrition, 262
manufacture, LMW heparins, 297–298
mast cells, polyphosphates, 243
MCFD2 gene (multiple coagulation factor deficiency 2 gene), 128–129
megakaryocytes, 209
menstrual bleeding
combined inherited factor V and factor VIII deficiency, 131
hyperfibrinolysis, 177
treatment, 226
methylprednisolone
Budapest protocol, 100
immune thrombocytopenia, 145
TTP, 252, 253
microangiopathic hemolytic anemia, 159, 248, 249
microangiopathy, thrombotic, 25–26, 246–258
microparticles
circulating tissue factor, 7
platelet-derived, 40
microplasmin, 182
microthrombocytopenia, 225
microthrombosis, intrahepatic, 279, 280
Million Women study, 289
Mini Mental Status (Holstein), 261–262
Mini Nutritional Assessment, 262
monitoring, see also laboratory tests
LMW heparins, 307–308, 310
monoclonal antibodies, CD20, 105
monocytes, factor XII on, 116
Mononine (factor IX concentrate), 63
monteplase, 181
mortality
acquired hemophilia, 94
immune thrombocytopenia, 138
mucocutaneous bleeding, von Willebrand disease, 200
multimeric analysis, von Willebrand factor, 37, 38, 199, 201
Multiplate aggregometer, 39
multiple coagulation factor deficiency 2 gene (MCFD2 gene), 128–129
multiple myeloma, thromboprophylaxis, 290
multiple single-factor deficiencies, inheritance, 133–134
muscles, hematomas, 47, 60
myeloproliferative disorders, platelet dysfunction, 231
MYH9-related disorders, 223–224
nadroparin, 297
cancer patients, 290
Nanotiv (factor IX concentrate), 63
nasopharynx, hemophilia C, 75
neonates
acquired hemophilia, 94
combined inherited factor V and factor VIII deficiency, 131
LMW heparins, 308
nephrotic syndrome, factor IX inhibitors, 86
neutrophils
Chediak–Higashi syndrome, 222
factor XII binding, 115, 121
Nijmegen modification, Bethesda assay, 83
nitric oxide, 18–19
basal production, 19
on platelets, 230
shear stress and, 24
nitric oxide synthase, 18
NN1731 (rFVIIa analog), 88, 103
Nonafact (factor IX concentrate), 63
non-alcoholic fatty liver disease (NAFLD), 272, 279
non-diarrheal hemolytic uremic syndrome, 248
treatment, 254
non-muscle myosin II-A heavy chain, 224
non-neutralizing antibodies, 83
non-overt disseminated intravascular coagulation, 160–161
non-steroidal anti-inflammatory drugs, 228–229
Noonan syndrome, factor XI deficiency, 75
NOS-III gene, 18–19
NovoSeven® see recombinant activated factor VII
nucleotide assays, platelets, 216
OBI-1 (recombinant B-domain-deleted porcine factor VIII), 102–103
obstetrics
DIC, 154, 157–158
TPP, 255
Octanex F (factor IX concentrate), 63
Octaplex (factor IX concentrate), 64
organ dysfunction, DIC, 161–162
oscillation rheometry, 41
overall hemostatic potential, 41–42
overt disseminated intravascular coagulation, 159, 160
Owen assay, prothrombin time, 33
ox-brain thromboplastin, hemophilia B, 59
P2Y12 receptor defect, 223
drugs causing, 229
PAMAM dendrimers, 242
paraproteinemias, platelet dysfunction, 231
partial thromboplastin time see activated partial thromboplastin time
PEG moieties see polyethylene glycol moieties
penicillins, platelet dysfunction, 230
pentasaccharides, 302
persistent immune thrombocytopenia, 137
PGHS-1 gene, 17
Phe283Leu mutation, hemophilia C, 74
phosphatidic acid, 3
phosphatidylinositol bisphosphate, 213
phosphatidylinerine, 3, 4, 210, 213
Scott syndrome, 225
phosphodiesterase inhibitors, 230
phospholipase, endothelial cell cytosolic (PLA-2), 17
phospholipase C, 213
phospholipids, 3, 4
plasma-derived factor VIII concentrates, 49, 51
plasma-derived factor IX, 62
plasma exchange, TTP, 247, 251–252
plasmapheresis, acquired hemophilia, 99
plasma sampling, 30–32
plasma thromboplastin antecedent see factor XI
plasmin, 169, 171, 182
plasminogen, 42, 169, 171
plasminogen activator inhibitor-1 (PAI-1), 16, 22, 42–43, 169–170, 173
aging, 264–265
DIC, 178
diurnal variation, 31
plasminogen activator inhibitor-2 (PAI-2), 173
plasminogen activators, 171–173, see also tissue plasminogen activator; urokinase-type plasminogen activator
plasminogen receptors (Plg receptors), 175
platelet-derived growth factor (PDGF), gray platelet syndrome, 222
platelet-derived microparticles, 40
platelet factor 4
grey platelet syndrome, 222
liver disease, 273
Platelet Function Analyzer (PFA-100), 39, 198, 215
platelet-poor plasma samples, 38
platelet-rich plasma samples, 38
platelets, 1–2, 4–5, 209–213
acquired disorders, 228–231
activation, 5–6, 210, 211
control of clotting, 8
secondary defects, 220–223
adherence defects see Bernard–Soulier syndrome
aggregometry, 39, 215, 216, 218, 219, 220, 221
antibodies, 138, 227
collagen receptor, 115
counts, 35, 214
immune thrombocytopenia, 138, 140
liver disease, 272–273
cytoskeletal defects, 223–225
giant see macrothrombocytes
inhibition (antiplatelet factors), 16–19
polyphosphates, 236–245
protection of thrombin, 5
qualitative disorders, 209–235
receptor defects, 223
secretion disorders, 220–222
signal transduction defects, 223
structural, 8
transfusions, 227
combined inherited factor V and factor VIII deficiency, 131
DIC, 162
liver disease, 278
TTP, 254
von Willebrand disease, 205
von Willebrand factor and, 23, 197–198
polyethylene glycol moieties, 65, 103
polymyxin B, 242
polypharmacy, 262
polyphosphates
bacterial, 9, 237, 238
inhibitors, 241–242
platelets, 236–245
porcine factor VIII, 88, 99
recombinant B-domain-deleted (OBI-1), 102–103
porcine mucosal heparin, 299
portal vein thrombosis, 279
post-thrombotic syndrome, 186–196
management, 190–194
PPXbd (anti-polyphosphate), 242
Prader–Willi syndrome, factor XI deficiency, 75
prednisone
immune thrombocytopenia, 140
children, 145
TTP, 252, 253
pregnancy
acquired hemophilia, 94
on coagulation test results, 31
combined inherited factor V and factor VIII deficiency, 132
desmopressin, 48–49
DIC, 154, 157–158
enoxaparin, 300
immune thrombocytopenia, 146
LMW heparins, 304
TTP, 255
diagnostic evaluation, 250
von Willebrand disease, 205–206
prekallikrein, 112, 113, 114, 117
prenatal diagnosis
combined inherited factor V and factor VIII deficiency, 130
hemophilia B, 60–61
vitamin K-dependent clotting factor deficiency, 133
primary fibrinolysis, 176–177
primary prophylaxis
hemophilia A, 49, 50–52
hemophilia B, 64–65
Proflin line SD (factor IX concentrate), 64
proline-rich region, factor XII, 117
prolylcarboxypeptidase, 113, 117
propagation (phase), 6–7
proplatelets, 209
prostacyclin, 16–18
nitric oxide and, 18
shear stress and, 24
prostacyclin synthase, 17
prostaglandin H$_2$, 17
prostaglandin H synthase (PGHS), 17
prostaglandin I$_2$, 17–18, 24–25
basal production, 19
prostate, transurethral resection, fibrinolysis, 177
protamine sulfate, 303
protease-activated receptor-1, 5
PROTECHT study, 290
protein C, 8, 19–20, see also activated protein C
DIC, 159
screening tests, 39–40
protein S, 8, 20
DIC, 159
screening tests, 39
protein therapies
hemophilia B, 65–68
proteoglycans, 20–21
prothrombin, 1
aging, 266
prothrombinase, 24, 26
prothrombin complex concentrates, see also activated prothrombin complex concentrates
recombinant, 104
for vitamin K-dependent clotting factor deficiency, 133
Prothrombinex VF (factor IX concentrate), 64
prothrombin fragment 1 + 2
liver disease, 273
prothrombin time, 8–9, 33
coaulation factor deficiencies see factor XII
hemophilia B$_{m}$, 59
liver disease, 273
Prothromplex T (factor IX concentrate), 64
Prothrombinex (factor IX concentrate), 64
PROWESS study, 163
purification
factor VIII concentrates, 49
factor IX concentrates, 62
purpura fulminans, 157
pyrexia, splenectomy, 142

qualitative defect, von Willebrand
disease, 199–200
qualitative disorders, platelets, 209–235
quality of life, post-thrombotic syndrome, 189
quantitative defect, von Willebrand
disease, 199
Quebec platelet syndrome, 223
Quick assay, prothrombin time, 33

rebalanced hemostasis, liver disease, 274–275, 280
recombinant activated factor VII, 53, 87–88
acquired hemophilia, 98, 103
DIC, 162–163
hemophilia C, 79
liver disease, 278
recombinant factor VIII, 50, 51
B-domain-deleted porcine (OBI-1), 102–103
recombinant factor IX, 62
recombinant fusion proteins
factor IX, 65–66
recombinant human factor VII see recombinant
activated factor VII
recombinant prothrombin complex
concentrate, 104
recombinant tissue factor pathway inhibitor
(TFPI), DIC, 164
Recombinant (factor VIII concentrate), 51
red cell concentrate, liver disease, 278
Refacto (factor VIII concentrate), 51
renal failure, see also chronic kidney disease
DIC, 161
platelet dysfunction, 230
ReoRox oscillation, 41
Replenine-VF (factor IX concentrate), 63
Rescue Immune Tolerance Study
(RESIST), 53–54
respiratory failure, DIC, 161
reteplase, 181
reviparin, 297, 298
ristocetin, 197–198
platelet aggregometry, 216
Bernard–Soulier syndrome, 219
ristocetin cofactor assay (vWF:RCo), 37, 198,
199, 201, 202
rituximab, 89
acquired hemophilia, 101, 105
immune thrombocytopenia, 143
children, 145
TTP, 233
rivaroxaban, 165, 292, 308, 309
romiplostim, 143–144
Rosenthal syndrome see hemophilia C
ROTEM (thromboelastometry), 41
saruplase, 181
SAVE-ONCO trial, venous
thromboembolism, 287, 288, 290
schistocytes, microangiopathic hemolytic
anemia, 248, 249
Schwartzman phenomenon, 27
Scott syndrome, 225
screening tests
bleeding disorders, 32–35
factor VIII inhibitors, 83
hemophilia B carriers, 60–61
thrombotic disorders, 39–40
secondary fibrinolysis, 177–178
secondary prophylaxis
hemophilia A, 52
von Willebrand disease, 205
selective serotonin reuptake inhibitors, platelet
dysfunction, 230
semuloparin, 290, 302, 305
sepsis
DIC, 153, 157
endothelial dysfunction and, 27
factor XII autoactivation, 118
hypofibrinolysis, 180
serpins, 173
shear stress, 24
coronary artery bypass grafts, 25
NOS-III gene and, 19
von Willebrand factor and, 23, 197
Shiga toxin-producing organisms, hemolytic
uremic syndrome, 247
signal transduction defects, platelets, 223
single-chain t-PA, 171–172
sinovitis, hemophilia A, 47
skin surgery, hemophilia C, 78
smoking, on test results, 31
snake venoms, DIC, 158
socioeconomic impact, post-thrombotic
syndrome, 189–190
spleen, immune thrombocytopenia, 138
splenectomy
immune thrombocytopenia, 142, 146
TTP, 254
stabilization of clots, 7
staphylokinase, 171, 172–173, 182
storage, plasma samples, 31–32
storage pool diseases, platelets, 221–223
streptokinase, 171, 172, 181
stress, 31
stroke
C46T polymorphism, 120
factor XI, 79
subdural bleeding, 47, 60
surface binding (cells), 3
surgery
factor VIII-von Willebrand factor
concentrates, 204
hemophilia C, 78
postoperative thromboprophylaxis,
287–289
for post-thrombotic syndrome, 194
s-VCAM (endothelial activation marker), 265
Index 327

T46 alleles, 120
tachyphylaxis, desmopressin, 48
TBSF FIX (factor IX concentrate), 63
TEG (thromboelastography), 41, 179
telomere length, leukocytes, 262
temperature, aPTT, acquired hemophilia, 96
template bleeding time, 35
tenase complex, 58, 94
tenecteplase, 181
tests of coagulation, 30–44
thienopyridines, 229
thrombasthenia see Glanzmann’s
thrombasthenia
thrombin, 1, 5, 6, 7, 20, 24, 213, see also
  endogenous thrombin potential
  antithrombin measurement, 34
  back-activation of factor IX, 240–241
  curve measurement, 41
  deficiency, 34
  DIC, 156, 178
  negative feedback, 8
  polyphosphates on generation, 239
thrombin-activatable fibrinolysis inhibitor, 43, 173
  polyphosphates and, 240
thrombocytopения
Bernard–Soulier syndrome, 218
congenital amegakaryocytic, 210
desmopressin for von Willebrand
disease, 202
immune, 137–150
liver disease, 273, 276
TTP, 248
X-linked, 225
thromboelastography, 41, 179
thromboembolism, see also deep vein
  thrombosis; venous thromboembolism
  aging, 265–266
  DIC, 153
  factor XII, 120
  before tests, 31
thrombolytic therapy, 181–182
  post-thrombotic syndrome
  prevention, 192–193
thrombomodulin, 8, 19–20
  endogenous thrombin potential test, 273
  soluble, 20
thromboplastin, 1, 5
  ox-brain, hemophilia B, 59
  prothrombin time, 9
thrombopoiesis, 209–210
thrombopoietin, 210
  agents mimicking, 143–144, 145–146
  liver disease, 278
  deficiency, immune thrombocytopenia, 138
thrombosis, see also deep vein thrombosis;
  venous thromboembolism
  bypassing agents, 88
  endothelium and, 23–26
  factor XI and, 79
  factor XII and, 120
  liver disease, 277–280
  malignant disease, 284–295
  polyphosphates on, 241
  pregnancy, 304
thrombotic microangiopathy, 25–26,
  246–258
thrombotic thrombocytopenic purpura
  (TTP), 25, 246–247
  clinical manifestations, 248–249
  congenital, 248
  differential diagnosis, 250
  laboratory tests, 249–250
  pregnancy, 255
  differential diagnosis, 250
  relapse, 252–254
  secondary causes, 249b
  treatment, 251–254
thromboxane A₂, 23, 213
  aspirin on, 229
  deficiency, 223
ticagrelor, 229
ticlodipine, 229
tifacogin, DIC, 164
tinzaparin, 297, 298, 300
tirofiban, 229–230
tissue factor pathway inhibitor (TFPI), 5, 6–7,
  8, 21, 40
  blockade, 103, 104
  polyphosphates on, 239
  recombinant, DIC, 164
  release by LMWHs, 296
tissue factors, 5
  circulating, 7
  endothelial dysfunction, 27
tissue plasminogen activator (t-PA), 16, 22, 42,
  171–172
  DIC, 178
  receptors, 175
  stimulators, 182
  tissue plasminogen activator inhibitor-1 see
  plasminogen activator inhibitor-1
tooth extraction, hemophilia C, 78
tPA see tissue plasminogen activator
tranexamic acid
  DIC, 164
  hemophilia C, 78
  von Willebrand disease, 203
transforming growth factor-β (TGF-β), on
  factor XII expression, 119
transfusion-related acute lung injury, liver
disease, 277
transmission electron microscopy,
  platelets, 216–217
transurethral resection of prostate,
  fibrinolysis, 177
trauma
  DIC, 158
  fibrinolysis, 177
  LMW heparins, children, 305
  T-regulatory cells, acquired hemophilia,
  104
  turbidometric aggregometry, 215
  two-chain t-PA, 171–172
ulcerative colitis, LMW heparins, 306–307
ulcers (venous), incidence, 187
ultra-low-molecular-weight heparins, 302
Uman Complex D.I. (factor IX concentrate), 64
umbilical vein endothelial cells, factor XII and, 115
unfractionated heparin cancer patients, 287–288, 291
DIC, 162
LMW heparin vs, 299
Upshaw–Schulman syndrome, 248
urinary tract, hemophilia C, 75, 77, 78
urokinase, 22, 181
urokinase plasminogen activator receptor (u-PA receptor), 115, 175
urokinase-type plasminogen activator (u-PA), 172, 177
valvular reflux, venous, 188
VCAM see s-VCAM
venoactive drugs, 193–194
venoms, DIC, 158
venous thromboembolism, 190–191
aging, 265–266
factor XI, 79
liver disease, 277–278, 279
malignant disease, 284–295
pregnancy, 304
venous ulcer, incidence, 187
venous valvular reflux, 188
Victoria (Queen), 46, 58
Vienna CAT registry, venous thromboembolism, 287, 288
Villalta scale, post-thrombotic syndrome, 186–187
vinca alkaloids
immune thrombocytopenia, 144
TTP, 253–254
viruses
hemophilia A and, 49, 266–267
hemophilia B gene therapy, 67–68
vitamin K antagonists (VKA), see also warfarin
cancer patients, 291–292
liver disease, 279
post-thrombotic syndrome prevention, 192
vitamin K-dependent clotting factor deficiency, 133, see also congenital combined deficiency of vitamin K-dependent clotting factors
vitamin K-dependent epoxide reductase, 59
vitronectin, 22
volume overload, desmopressin, 203
von Willebrand disease, 23, 36, 197–208
classification, 199–200
diagnosis, 200–201
management, 202–206
tests, 36–37, 198–199
von Willebrand factor, 4, 6, 22–23, 197–199
aging, 265
anaphylaxis, 205
assays, 37
binding to factor VIII, 94
in factor VIII products, 53
immune tolerance induction, 89
inhibitor development, 85
factors affecting levels, 31
liver disease, 273
multimers
analysis, 37, 38, 199, 201
TTP, 247
polyphosphate binding, 243
transfusional therapy, 203–204
vulnerability, 263
vWF antigen, measurement, 37, 198–199, 201
vWF:CB, 198–199, see also collagen binding assay
vWF:RCo see ristocetin cofactor assay
warfarin, see also vitamin K antagonists
cancer patients, 290
hemophilia C, 79
WAS protein, 224–225
Weibel–Palade bodies, 198
Wilate (factor VIII concentrate), 51
Wiskott–Aldrich syndrome, 224–225
Xigris, DIC, 163
X-linked thrombocytopenia, 225
Xyntha/Refacto AF (factor VIII concentrate), 51
zinc, factor XII on endothelium, 115