$\hbox{@ Cambridge University Press}$

Cambridge University Press 978-0-521-88423-5 - Chronic Graft Versus Host Disease: Interdisciplinary Management Edited by Georgia B. Vogelsang and Steven Z. Pavletic Index More information

INDEX

Acquired Immune Deficiency Syndrome	patient education, 399-402	angiotensin II receptor blockers
(AIDS), 399	peer support, 402–403	(ARBs), 295
activities of daily living (ADL)	public policy, 403–404	angiotensin-converting enzyme inhibitors
assessments, 253	Aeromonas, 277	(ACEIs), 295
acute graft vs. host disease (aGVHD)	age considerations, 17	angular cheilitis, 191
with apoptosis, 94	alemtuzumab, 223, 362	animal models of cGVHD. See also mouse
in B6 animal model, 32	alendronate, 162, 163, 256-257	models
cGVHD vs., 31, 71, 89-91.	allogenic hematopoietic stem cell	B10.D2 (or B6.C)gBALB/c model,
(See also overlap syndrome)	transplantation (allo-HSCT), 31,	34-36
DLI associations with, 31, 56	33, 71	effector phase, 35
effector phase, 12	and Scl-cGVHD, 37	induction phase, 34–35
induction by mature αβ T cells (in	allo-HSCT. See allogenic hematopoietic	initial description, 34
donor allograft), 37	stem cell transplantation	mast cells, 35
pathophysiology of	alpha-1 antichymotrypsin, 79	reasons for choosing, 35-36
cGVHD vs., 31	alpha-1 antitrypsin (AAT), 79	cGVHD autoimmunity determination,
three-step model	American Academy of Oral Medicine	37–40
effects of HCT conditioning, 8, 9	(website), 189	DBA/2gBALB/c with sublethal
donor T-cell activation/cytokine	American College of Rheumatology Ad	irradiation/no BM rescue, 37
secretion, 8–11	Hoc Committee, 256–257	parentgF1 models, 32-34
cellular and inflammatory	American College of Sports	common features, 32
effectors, 8, 11–13	Medicine, 258	Scl-GVHD model, 37
pediatric patients, 369	American Nurses Association, 404	antibacterial drugs. See metronidazole;
peripheral blood elevations, 12	American Society for Blood and Marrow	norfloxacin
phototherapy treatment, 140–141, 176	Transplantation, 400	anti-cardiolipin antibody, 20
risk factors, 71	American Society of Clinical Oncology	anti-CD20 chimeric monoclonal
staging for, 147	(ASCO), 400, 404	antibodies, 33, 48. See also rituximab
as Th1 disease, 80	amikacin for Nocardia infection, 273	anti-cytokine therapy
acute leukemia, 361	ancillary and supportive care	minimal usage of, 142
acute lymphoblastic leukemia (ALL), 369	case histories	for pediatric cGVHD, 379
acute respiratory distress syndrome, 243	CY/12 GyTBI conditioning/PBT for	anti-dsDNA antibody, 20, 22
acyclovir, 129, 162, 163, 164, 223, 276	AML, 163–164	anti-epileptic agents, 107, 127
adenovirus, 221, 273, 277, 308	myeloablative conditioning/PBT for	antigen presenting cells (APCs), 8. See also
adrenal insufficiency, 292-293	CML, 164–165	dendritic cells (DCs)
adult-thymectomized BALB/c	myeloablative conditioning/PBT for	allogenic donor T cell activation, 8, 34
recipients, 18	MDS/RA, 159–162	BALB/c antigens, 34
advocacy for patients	PBT from HLA-matched sister,	donor APCs (plasmacytoid DC2 cells),
chronic lymphocytic leukemia (case	162–163	75, 177
study), 396-397	defined, 157	elimination by natural killer (NK) cells,
cross-community relationships, 399	evidence-based rating system, 158-157	10, 34
impact of cGVHD, 397-398	organ system monitoring, 157, 158-161	importance of, in cGVHD
Institute of Medicine (IOM) Report, 398	prevention focus, 157-160	development, 19
nonprofit (NPO) organizations,	Ancillary Therapy and Supportive Care	MHCII+, 35
398-399	Working Group (of NIH), 157	study approach, 34

409

410 INDEX

antimicrobial drugs, 127, 270, 272, 376	stimulatory, to PDGF, 37, 179	basal cell carcinoma (BCC), 330
anti-mitochondrial antibody, 20, 22	T-1 helper cells production of, 6	B-cell activating factor (BAFF), 19, 81
anti-neutrophil antibody, 20	autoimmune hemolytic anemia (AIHA),	soluble BAFF (sBAFF), 22
anti-nuclear antibody (ANA), 20, 22	240–241	B-cells
anti-smooth muscle antibody, 20	autoimmunity and cGVHD, 6	acquisition of miHAs, 37
antithymocyte globulin (ATG), 17, 48,	avascular necrosis, 127, 257	function assessment, 81
362, 377	definition/incidence, 291	recipient, interacting with CD4 cells,
APCs. See antigen presenting cells	pathophysiology/risk factors, 291	32–33
aplasia-associated complications, 3	as secondary/late effect, 328	role in GVHD pathophysiology, 19, 48 triggering of apoptosis, 19
aplastic anemia from HLA identical sibling donors,	treatment, 291–292 azathioprine, 125, 128, 135	beclomethasone dipropionate (BDP),
46, 71	for retroperitoneal fibrosis, 311	222, 224
HSCT for, 6	for squamous cell carcinoma, 330	biliary and gallbladder problems,
MG development and, 245	topical, for oral mucosal cGVHD, 191	224–225
apoptosis, 31	for vasculitis, 304	BIllingham, R. E., 4
aGVHD with, 94	azithromycin, 235, 279	biomarkers in cGVHD, 21–22
B cell receptor triggering, 19	for COP/BOS, 235	defined, 79
CTL induction, 11	azole drug class. See fluconazole;	for prediction/monitoring
epithelial, induction by TNF-α, 8	itraconazole; ketoconazole;	B cell function assessment, 81
Fas-mediated, of activated donor	posaconazole; voriconazole	genetic markers, 80
T-cells, 11		serum/cellular cytokine production
of target cells, 8	B6 (H-2b)gB6xDBAF1 (B6D2F1) strain	and Th1/Th2 paradigm, 79–80
Aquaphor® petroleum-based emollient,	pairing, 32	T cell function assessment, 80–81
176	B6 ^{bm12} gB6xB6 ^{m12} strain pairing, 32	role of Tregs, 21
arcuate vaginal synechiae, 208	B6gB6D2F1 model, 32	Biomarkers Working Group, 21–22
arrhythmias, 307	B10.D2 (or B6.C)gBALB/c animal model,	bisphosphonates, 130, 162. See also
aspergillus, 109, 268, 271, 277 assessment (clinical) of cGVHD, 56–66.	34–36	alendronate; risedronate for AVN treatment, 291
See also evaluation of cGVHD;	effector phase, 35	for bone loss prevention, 256
monitoring of cGVHD	induction phase, 34–35 initial description, 34	for glucocorticoid-induced
eyes, 57, 64–65, 66–67	mast cells, 35	osteoporosis, 157
focused medical history, 57	reasons for choosing, 35–36	for pediatric patients, 328
KPS score, 73, 89, 125, 137, 147	B10.D2g BALB/c Scl-GVHD model	vs. inappropriate HRT, 290
Lee Symptom Scale, 152	vs. clinical cGVHD, 37	blepharitis, 92, 201–202
lungs, 66	bacterial infections in cGVHD, 46, 129,	Blood and Marrow Transplant Clinical
mouth, 61	271, 272–273	Trials Network, 51
mouth evaluation, 57, 61	antibiotic prophylaxis, 129	BMT InfoNet, 399, 403
musculoskeletal/joints, 57, 66	commonness of, 268	BMT-Talk (list-serv), 403
skin/dermal appendages, 57–61	increased risks in, 268	bone marrow aplasia, 3, 238
Association of Cancer Online	MMF for, 109	Bone Marrow Survivor Study (BMT-SS)
Resources, 403	1970–1980 data, 46	questionnaire, 253
Association of Community Cancer	prevention of, 278–280	bone marrow transplants (BMTs)
Centers, 404	antifungal prophylaxis, 280–281	CNS/PNS dysfunction risks, 257–258 1980–1990 data, 46–48
astrovirus, 277 athymic BALB/c (nu/nu) recipients, 18	antiviral prophylaxis, 281–282	peripheral blood transplants vs.,
atomic bomb radiation exposure, 3	community-acquired respiratory	52–53, 120
atovaquone suspension for <i>Pneumocystis</i>	viruses (with antiviral agents), 282	bone metabolism
jiroveci, 276	IV immunoglobulin, 278–279	osteopenia and osteoporosis
autoantibodies, 17, 20, 32, 48	pneumocystis jiroveci	definitions/incidence, 289
ANA, 22, 32	prophylaxis, 281	pathophysiology/risk factors, 289
arthralgia/arthritis association, 92	prophylactic antibiotics, 279–280	treatment, 289–291
in B6gB6 ^{bm12} /B6 ^{bm12} gB6 model, 32	VZV/HSV prophylaxis, 282	bone mineral density (BMD)
B-cell dysfunction association, 379	of the skin, 276	DEXA measurements, 289
H-Y antigen, 20	treatment of, 277	hormone replacement therapy and, 290
myasthenia gravis association,	BALB/c (H-2d) recipients. See also adult-	BOOP. See bronchiolitis obliterans
245, 302	thymectomized BALB/c recipients;,	organizing pneumonia (BOOP)
PDGFR-α autoantibodies, 20	athymic BALB/c (nu/nu) recipients;,	BOS. See bronchiolitis obliterans syndrome
in PgF1 models, 33	cgBALB/c recipients	(BOS)
platelet bound, in persistent	nedocromil sodium stabilization of	bowel GVHD, 34, 35
thrombocytopenia, 240	mast cells, 35	bradyarrhythmias, 307, 308
serum test for CYP1A2, 223	second transplants, 34	breast cancer, 318, 328, 399

INDEX ■ 411

bronchiolitis obliterans organizing	CD4+CD25+ regulatory T cells, 11, 20	as late altered immunity, 6
pneumonia (BOOP), 216, 229	sCD13 antigen, 20	limited/extensive, 72-73, 88
bronchiolitis obliterans syndrome (BOS),	CD20 antagonists (rituximab), 141	monitoring of, 66-68
31, 37, 56, 67	CD28-mediated down-regulation of	morbidity/mortality burden, 341-342
clinical manifestations, 234	ΙκΒα, 110	onset after HSCT, 56
diagnostic criteria, 91, 234	CD31 antigen, 20	photographic evaluation, 67-68
risk factors/epidemiology, 233	CD80 costimulatory molecule, 10	phototherapy treatment, 140–141, 176
therapy/outcome, 234–235	CD86 costimulatory molecule, 10	political effects (in late 1970s), 4
w/wo organizing pneumonia, 31	ceftriaxone for Nocardia infection, 273	predictive models for prognosis of,
budesonide, enteric-coated, 222	cellular and inflammatory effectors, 11-13	72–74
bulbar conjunctival hyperemia	cellular effectors, 11–12	risk factors. (See risk factors for
("red eye"), 201	inflammatory effectors, 12	cGVHD development)
busulfan/cyclophosphamide myeloablative	TLRS and innate immunity, 12–13	symptoms mislabeled as, 57
regimens, 52	traffic of cellular effectors, 13	as Th2 disease, 80
1031110113, 32	central nervous system (CNS)	chronic GVHD antigens, 20
C. difficile, 277	manifestations of cGVHD, 277–278	chronic inflammatory demyelinating
	demyelinative disease, 247–249	neuropathy (CIDN), 245–246, 257
cachexia, 12, 108	· · · · · · · · · · · · · · · · · · ·	
calcineurin inhibitors, 104–108, 127, 135.	determination of cGVHD reality,	chronic lymphocytic leukemia (CLL) case
See also cyclosporine; tacrolimus	246–248	study, 396–397
drug interactions, 107–108	immune-mediated encephalitis,	chronic myeloid leukemia, 6, 72, 229, 361
pharmacokinetics	249–250	chronic obstructive lung disease, 327
absorption, 106	proposed diagnostic criteria, 247–249	chronic obstructive pulmonary disorder
distribution, 106–107	stroke from vasculitis/angiitis, 249	(COP), 229, 230
metabolism, 107	cerebral vasculitis, 304	cicatricial ectropion (of eyelids), 201–202
pharmacology	cevimeline, 129	CIDN. See chronic inflammatory
clinical pharmacology, 106	cgBALB/c recipients, 34	demyelinating neuropathy (CIDN)
mechanism of action, 105-106	cgBALB/c (H-2d) recipients, 34	cirrhosis, primary biliary, 56
posterior leukoencephalopathy	cGVHD. See chronic graft vs. host disease	cisplatinum vs. thalidomide, 246
from, 247	(cGVHD)	City of Hope National Medical Center
with prednisone, 101	cheilitis, angular, 191	study, 377
toxicity, 108	Childhood Cancer Survivor Study, 253	clarithromycin, 104
calcium channel blockers, 107, 127, 295	children. See pediatric cGVHD	Class II invariant chain peptide (CLIP), 40
calcium supplementation, 162, 163, 164, 165	Children's Oncology Group study, 18	classification system, 74
Campath-1H antibody prophylaxis, 17,	chloroquine, 19–20. See also	historical background, 87–89
48, 117	hydroxychloroquine (HCQ)	ideal system characteristics, 87
Campylobacter, 277	chronic graft vs. host disease (cGVHD).	Seattle group, 89
cancer-related issues	See also cutaneous cGVHD;	clindamycin for <i>Pneumocystis</i>
basal cell carcinoma (BCC), 330	gastrointestinal GVHD; genital	jiroveci, 276
cancer-related fatigue (CRF), 259	cGVHD; hepatic cGVHD;	clinical cGVHD vs. B10.D2g BALB/c
Childhood Cancer Survivor	pathophysiology of chronic graft	Scl-GVHD model, 31
Study, 253	vs. host disease; sclerodermatous	clinical trials for treatment testing
<i>1</i> .	GVHD; steroid-resistant cGVHD;	biostatistical considerations
early onset vs. secondary cancer, 330	syngeneic GVHD	missing data, handling of, 357
Functional Assessment of Cancer	aGVHD vs., 31, 71, 89–91. (See also	prevention trials, 356–357
Therapy-Bone Marrow	overlap syndrome)	treatment trials, 350
Transplant scale, 253	= -	
mucosal carcinoma, 330–331	assessment. (See assessment (clinical) of	data collection
radiation related cancers, 330	cGVHD)	adverse (AE)/serious adverse events
secondary cancer surveillance, 194	autoimmunity and, 6	(SAE), 354
skin/mucosal carcinoma, 330-331	determination of, 37–40	case reports forms, 353–354
squamous cell carcinoma, 330	as barrier to allo-HSCT, 31	multi-institutional study
thyroid carcinoma, 331	clinical, vs. B10.D2g BALB/c Scl-	considerations, 354
candidiasis, oral, 183, 191	GVHD model, 37	patient-reported outcomes, 354
cardiac involvement, in cGVHD	defined/described, 5-4, 17, 56	timing, 353
diagnosis, 308	diagnosis. (See diagnostic criteria for	drug development considerations, 352
future directions, 308-309	establishment of cGVHD)	FDA review of studies, 357–358
incidence, 306	DLI associations with, 31, 56	future challenges, 358
presentation, 307-308	dynamics of, 94-95	participant selection
prognosis/clinical course, 308	effector phase, of skin GVHD, 35	exclusion criteria, 352
cataracts, 126–127, 326–327	evolution of, 31	general considerations, 351-352
CD4 cells, interacting with recipient B	and graft vs. leukaemia effects, 6	primary and secondary endpoints
cells, 32–33	impact of HRQOL on, 56, 68, 341-343	disease activity vs. damage, 355

412 INDEX

clinical trials for treatment testing (cont.)	pulmonary, 80, 125. (See also	diagnostic criteria, 231-233
physician/patients, supporting	bronchiolitis obliterans)	risk factors/epidemiology, 231
information, 355–356	fibrosing, 179	therapy and outcome, 231–233
response as an endpoint, 355	non-infectious, 270, 271, 272	Cryptosporidium, 277
selection of, 354–355	of rehabilitation	CTLs. See cytotoxic T lymphocytes
treatment methods	contractures, 258–259	Cushing's syndrome (iatrogenic)/adrenal
ancillary therapy/supportive	edema, 260–262	insufficiency, 292–293
care, 353	fatigue, 259–260	definition/incidence, 292–293
cGVHD evaluation/management, 352	of steroid treatments, 125	treatment, 293
glucocorticoid administration, 353	conjunctivitis	cutaneous cGVHD. See also skin fibrosis
interventions/medication	pseudomembranous conjunctivitis, 199	diagnosis, 171–175
administration, 353	pseudomembranous conjunctivitis, 199	· ·
clinimetrics, 148	keratoconjunctivitis, 202	diagnostic criteria/features, 169–171
		distinctive criteria, 91–92
clobetasol 0.05% cream/ointment	superior limbic keratoconjunctivitis,	effector phase, 35
for cutaneous cGVHD, 176	201	future research directions, 178–179
for genital cGVHD, 212	connective tissue tumors, 330	histologic studies, 96–97
clobetasol 0.05% cream/ointment (for	Consensus Development Project on	manifestations of, 169–19
cutaneous cGVHD), 176	Criteria for Clinical Trials in	in pediatric patients, 373–374
clofazimine, 141	cGVHD (of NIH)	prevention of, 178
clotting factors in cGVHD, 238, 240	ancillary/supportive care guidelines,	prognosis/clinical course, 171
coagulation system abnormalities in	157	resembling dermatological
cGVHD, 238	on cGVHD biomarkers, 21	conditions, 172
cobweb vaginal synechiae, 208	COP/BOS recommendations, 229	skin/dermal appendage assessment,
cognitive effects of cGVHD treatment,	criteria development procedures, 94	57–61
316–317	cutaneous cGVHD proposed	treatment, 175–178
concentration, 316-317	criteria, 169	cyclooxygenase-2 (COX-2), 101
memory, 316	drug development recommendations,	cyclophosphamide myeloablative regimens
mood, 317	351	for aplastic anemia, 71
Cognitive Neuroscience (COG) study,	ocular GVHD scoring system, 202	with busulfan, 52
23–24	oral cGVHD standardized criteria, 187	for dysphagia/right hemiparesis, 249
colon disorders. See stomach, small	on predictive categories, 125	with fludarabine, 52
intestine, colon disorders	standardization attempts, 53	for retroperitoneal fibrosis, 311
Common Terminology Criteria for	constitutional syndrome, 273	for vasculitis, 304
Adverse Events, ver. 3.0 (CTC	coronary artery disease, 307	cyclosporine (CSA), 48, 135. See also
AE v3.0), 202	coronary hearty disease (CHD), 328	Gengraf [®] ; Neoral [®] ; Sandimmune [®]
complications	corticosteroids, 101–104	for bile issues, 225
aplasia-associated, 3	drug interactions, 104	cGVHD induced by, 72
endothelial, 12	for dysphagia/right hemiparesis, 249	for chronic myelogenous leukemia,
esophageal (of gastrointestinal cGVHD)	for oral cGVHD, 188–189	229
diagnosis, 217–218	pharmacokinetics	clinical pharmacology, 106
future advances, 219	absorption, 103	contraindications to usage, 128
incidence, 216	distribution, 103	drug interactions, 107–108, 109
presentation, 216	metabolism, 103–104	evaluative studies, 120
prevention, 218–219	pharmacology	HLA-identical siblings, 75, 88–89
	genomic mechanisms, 101	
significance for prognosis, 216		with hydroxychloroquine (pediatric
therapy, site-specific, 218	immunosuppression mediation,	patients), 75
fascitis, contractures, serositis, 125	101–103	intravaginal, for genital cGVHD, 213
of glucocorticoid treatment, 129	nongenomic mechanisms, 103	mechanism of action, 105–106
hematologic	pulse corticosteroid therapy, 103	methotrexate vs., 47
clotting factors, 240	rituximab with, 240	pharmacokinetics
coagulation system abnormalities, 238	survival rate improvement from, 146	absorption, 106
cytopenia, patient evaluation, 238	topical	distribution, 106–107
red blood cell abnormalities,	for cutaneous cGVHD, 176	metabolism, 107
240–241	for oral mucosal cGVHD, 190–191	with prednisone, 127
thrombocytopenia, 238-240	for vaginal restenosis, 211	for retroperitoneal fibrosis, 311
venous thromboembolism, 240	toxicity, 104	sGVHD induced by, 39, 40
white blood cell abnormalities, 241	CpG ODNs	topical
infections, 80, 117	aggravation of GVHD severity, 19	for vaginal restenosis, 211
of methylprednisolone/CsA, 120	critical illness polyneuropathy (CIPN), 246	topical, for oGVHD cal, 204
ophthalmological, 66-67	cryptogenic organizing pneumonia	topical, for oral mucosal cGVHD, 191
of prednisone (high-dose) 126-127	clinical manifestation 231-232	toxicity 108

INDEX ■ 413

CYP 3A4 inhibitors, 104. See also	lungs, 92	Transplantation (EBMT) registry,
clarithromycin; ketoconazole	mouth, 92	331, 361
cysteinyl leukotriene receptor-1 (cysLT1R)	musculoskeletal system, 92	European Organization of Research and
antagonists, 21	nails, 92	Treatment of Cancer Quality of
cytokines	skin, 91-92	Life Questionnaire (EORTC
polymorphisms, 80	DLCO (single-breath carbon monoxide	QLQ-C30), 253
secretion by donor T cells, 10-11	testing method), 230	evaluation of cGVHD. See also assessment
cytolytic T cells (CTLs), 32	DLI. See donor leukocyte infusions	(clinical) of cGVHD; Karnofsky
cytomegalovirus (CMV), 273–274	donor leukocyte infusions (DLI), 362	performance status (KPS) score;
cardiac association, 308	aGVHD/cGVHD association with, 31,	patient-reported outcomes (PROs)
as co-factor in GVHD development, 20	56, 360	measurement
monitoring for, 129	for relapsed disease, and Scl-GVHD, 37	mouth evaluation, 57, 61
prophylaxis of, 281-282	donor T-cell activation (in acute GVHD),	musculoskeletal/joints evaluation, 57,
secondary, in oral cGVHD, 183	8-10	66, 91
serositis association with, 305	activation by APCs, 8	diagnostic criteria, 91
in viral pneumonia, 273-274	TNF-α involvement, 12	distinctive criteria, 92
cytomegalovirus (CMV) gastrointestinal	dry eye syndrome (DES), 64, 66-67, 87,	ophthalmological evaluations, 66-67
disease, 277	95, 158, 159-162. See also ocular	photographic evaluation, 67-68
cytopenia (single-/multilineage), patient	GVHD	evaluation of therapeutic response (in
evaluation, 238	dual energy x-ray absorptiometry	cGVHD). See also clinimetrics
cytotoxic T lymphocytes (CTLs)	(DEXA), 289	measurement
induction of apoptosis, 11	dyspareunia, 209	approach limitations, 149-151
use of, by granule exocytosis	dysphagia, 124–125, 216	characteristics, 147-146, 148-149
pathways, 11	dyspnea, 66, 91, 163, 230, 273, 305	scale definitions, 148-149
		response criteria
daclizumab, 282, 379	eczema vs. cutaneous cGVHD, 169	challenges, 150
dapsone for Pneumocystis jiroveci, 281	edema/edema management, 260-262	and diagnosis/staging, 147
DBA anti-B6 cytolytic T cells (CTLs), 32	effector phase of GVHD, 11, 12	importance of, 146
DBA (H-2 ^d) strain pairing, 32	of skin GVHD, 35	measurement selection indicators,
DBY antigen, 20	EIF1AYantigen, 20	147–148
demyelinative disease (of CNS), 245–246, 247–249	eIF-4E (eukaryotic initiation factor 4E) binding protein phosphorylation, 110	of NIH, 151–154. (<i>See also</i> National Institutes of Health)
dendritic cells (DCs), 10, 17, 22, 134,	8-methoxypsoralen (8-MOP), 379	future directions, 154–155
308, 361	Elidel® (pimecrolimus cream), 176	therapeutic outcomes, 149
dermal appendage assessment, 57–61	engraftment syndrome, 18	Exserohilum, 276
dermal sclerosis, 61, 66, 98, 169, 171	enterovirus, 308	extracorporeal photopheresis (ECP), 18,
dermatomyositis, 149	EORTC QLQ-C30. See European	136–137, 162, 177, 235, 296, 379
diabetes mellitus, 295	Organization of Research and	eyes. See ophthalmological issues
diagnostic criteria for establishment	Treatment of Cancer Quality of Life	-/
of cGVHD	Questionnaire (EORTC QLQ-C30)	FACT-BMT. See Functional Assessment
bronchiolitis obliterans syndrome	eosinophilia, 31, 48, 57, 80, 81	of Cancer Therapy-Bone Marrow
(BOS), 91, 234	eosinophilic fascitis, 96–97, 117	Transplant scale (FACT-BMT)
cardiac involvement, 308	episcleritis, 201	factor VIII glycoprotein, 240
central nervous system (CNS), 247–249	epithelial apoptosis, 8	famciclovir for Varicella-Zoster virus
gastrointestinal tract, 91, 217–218	erythema nodosum leprosum (ENL), 111	(VZV), 276
genitalia, 91	erythematous papular lesions	Fas TNF-receptor family, 11–12
hepatic cGVHD, 223–224	(of cGVHD), 172	activation of donor T-cells, 11
lungs, 91	esophageal complications (of	fascitis, 31, 169, 171
mouth, 91	gastrointestinal cGVHD)	Fialkow, P. J., 6
musculoskeletal/joints, 91	diagnosis, 217–218	fibroblastic periductal/periacinar stroma, 9
renal involvement, 310	future advances, 219	fibrosis
skin, 91–8	incidence, 216	multiple organs, 37
diarrhea, 73, 74, 89, 90, 125	presentation, 216	of skin, 31
disability, defined, 252	prevention, 218–219	effector phase of skin GVHD, 35
distinctive criteria seen in cGVHD.	significance for prognosis, 216	halofuginone blocking of, 35
See also individual topic listings	therapy, site-specific, 218	processes implicated in, 20
eyes, 92	esophageal mucositis, 46	filamentary keratitis, 201
gastrointestinal tract, 92	estrogen replacement therapy, 162, 208,	fluconazole (azole drug class), 108, 129,
hair, 92	211, 213, 290	281
hematopoietic/immunologic systems, 92	etanercept, 379	fludarabine, 52, 269, 362
liver. 92	European Group for Blood and Marrow	fluticasone, 272

414 INDEX

Food and Drug Administration (FDA)	absorption, 103	cytopenia, patient evaluation, 238
interest in PROs, 335	distribution, 103	red blood cell abnormalities, 240-241
Ford, C. E., 3, 6	metabolism, 103-104	thrombocytopenia, 238-240
4-aminoquinolines, 19–20	risks of, 129, 257	venous thromboembolism, 240
FOXP3 antibody	glucose intolerance, 126-127	white blood cell abnormalities, 241
activated T cell expression, 20, 121	steroid-induced, 246	hematopoietic cell transplantation (HCT).
mutations, 11	graft composition factors, 17	See also allogenic hematopoietic stem
fractures (of osteoporosis), management of, 256	graft vs. leukemia (GVL) activity, 6, 9–10, 79	cell transplantation (allo-HSCT) cGVHD as barrier to success, 146
Functional Assessment of Cancer Therapy-	granule exocytosis pathways, 11	effects of conditioning with, 8, 9
Bone Marrow Transplant scale (FACT-BMT), 253, 339	granulocyte colony stimulating factor (G-CSF)	HLA-identical HCT, 9 pediatric patients, 75
Functional Assessment of Chronic Illness	causative for cGVHD, 71, 72	in pediatric patients, 376
Therapy (FACIT) portfolio, 339 fungal disease, 274–275	HCT donor pretreatment with, 11 PBSC association with, 360 peripheral blood mobilization, 17, 22	pretreatment of donors with G-CSF, 11 hematopoietic stem cell transplant (HSCT), 3–4
callbladdon and biliams muchlanes 224, 225	granulomatous angiitis, 249	for aplastic anemia, 6
gallbladder and biliary problems, 224–225	Grover's transient acantholytic	effects of conditioning, 8
gastrointestinal GVHD, 124–125, 277 esophageal complications	dermatosis, 95	exogenous stimulus from, 6
diagnosis, 217–218	Guillain-Barre syndrome, 245	onset of cGVHD after, 56
future advances, 219	gynecological manifestations of cGVHD.	Hemophilus influenzae, 273
incidence, 216	See genital cGVHD	hepatic cGVHD, 31
presentation, 216	8	diagnosis, 223–224
prevention, 218–219	HA-1 antigen, 20	future advances, 224
significance for prognosis, 216	halofuginone, 35	incidence, 222
therapy, site-specific, 218	haptoglobulin, 79	in pediatric patients, 375
in pediatric patients, 375	HCT. See hematopoietic cell	presentation, 222
stomach, small intestine, colon	transplantation (HCT)	prevention, 224
disorders	Health Consensus Development Project on	significance for prognosis, 222
diagnosis, 221-222	Criteria for Clinical Trials in Chronic	therapy, site-specific, 224
future advances, 222	Graft vs. Host Disease, 21–22	hepatic veno-occlusive disease. See
incidence, 219–221	health-related quality of life (HRQOL)	sinusoidal obstructive syndrome
presentation, 221	biomarker availability and, 79	(SOS)
prevention, 222	cGVHD's impact on, 56, 68, 341–343	herpes simplex virus (HSV), 183, 277
significance for prognosis, 221	as clinical research endpoints, 253	histocompatibility (minor) antigens, 20
therapy, site-specific, 222	conceptual model for long-term	histologic studies
G-CSF. See granulocyte colony stimulating factor (G-CSF)	transplant survivors, 337 ECP and, 137	assessment utility of, 99 biopsies, results reporting, 98–99
gender consideration, 17	functional status/symptoms vs.,	liver, 97–98
genetic biomarkers for cGVHD, 80	336–337	oral, 97
Gengraf®, 106	future research directions, 344	overview, 94–95
genital cGVHD	genital cGVHD and, 214	skin, 96–97
clinical features of, 208	health status vs. preference-based	histopathological aspects of cGVHD, 93–13
evaluation (clinical) of, 211–212	assessment, 343	historical background
grading system, clinical, 208–209 histology of, 210–211	interpretation issues, 343 measure selection criteria, 149, 151,	Chronic Graft Versus Host Disease, 5–4
incidence of, 207	337–340, 343	classification/prognostic factors, 87–89
risk factors for, 208	health status vs. preference-based	Graft Versus Host Disease, 4
symptoms/signs, 209–210	assessment, 343	hematopoietic stem cell transplant, 3–4
treatment/response, 211–213	minimally important clinical	HLA histocompatibility antigen. See
Giardia, 277 global scoring system, 56, 92–93	differences, 343 response shift, 343	human leukocyte antigen (HLA) system
glucocorticoid receptors (GR), 101, 102	timing of outcome assessment, 343	Hodgkin's disease, 246
inhibition of T cell proliferation, 102	morbidity/mortality burden of cGVHD,	hormone replacement therapy (HRT), 208,
glucocorticoid-induced osteoporosis	341–342	290. <i>See also</i> estrogen replacement
(GIO), 130, 157, 255, 289	outcome evaluation, 344	therapy; testosterone replacement
management of, 256–257	QOL defined, 335–336	therapy
glucocorticoids. See budesonide,	heat-shock proteins (HSP), 101	human leukocyte antigen (HLA) system, 4
enteric-coated	hematologic complications of cGVHD	anti-HLA antibodies, 23
evaluative studies, 120	clotting factors, 240	as biomarker in cGVHD, 21
pharmacolzinatics	congulation exetom abnormalities 238	class I differences 10

INDEX ■ 415

donor-recipient disparity, 71	nonmyeloablative/reduced intensity	Karnofsky performance status (KPS) score,
HLA-identical HCT, 9	conditioning transplants, 52	73, 88, 89, 125, 137, 147
identical sibling donors, 46, 71, 75,	peripheral blood vs. bone marrow	keratoconjunctivitis sicca, 57, 92, 134, 158.
88-89	grafts, 49–51	See also ocular GVHD
chronic myelogenous leukemia	infections in cGVHD	ketoconazole (azole drug class), 104, 107
case, 229	bacterial infections. (See bacterial	Klebsiella pneumoniae, 273
mismatched transplants, 51–52	infections in cGVHD)	kyphoplasty (vertebroplasty), 256
human papilloma virus (HPV) disease,	central nervous system, 277–278	nyphophacty (verteerophacty), 200
214–207, 330	complications from, 80, 117	laboratory markers for prognosis of
H-Y antigens, 20	gastrointestinal, 277	cGVHD
hydrocortisone, 103	general concepts, 268	
		donor APCs, 75
for Cushing's syndrome, 293	prevention of, during cGVHD	minor histocompatibility antigens, 75
intravaginal, for genital cGVHD, 213	treatment, 129–130	OX40 expression, 74–75
hydroxychloroquine (HCQ), 19–20, 75,	prophylaxis recommendations (See	regulatory T cells, 75
128, 142, 272, 378	under bacterial infections in	soluble biomarkers, 75
hyperkeratosis, 201–202	cGVHD)	lacrimal gland involvement, 31, 34,
hyperlipidemia, 294	related to immunosuppression, 282–283	202–203
hypertension, 126–127, 295	respiratory infections. (See respiratory	laser (CO2, low-lever), for oral mucosal
hypoxemia, 273	tract infections in cGVHD)	cGVHD, 191
	skin/soft tissue, 276-277	Lee cGVHD Symptom Scale (HRQOL
ichthyosis, 171	syndromic approach to patients,	measure), 339
imipenem for <i>Nocardia</i> infection, 273	268-270	Lee Symptom Scale, 152
immune cytopenias, 56	viral, 72	leukemia
immune globulin, intravascular	Infectious Disease Society of America, 274	acute leukemia, 361
evaluative studies, 120	inflammatory cytokines, 8, 21, 101–102	acute lymphoblastic leukemia (ALL), 369
for vasculitis, 304	inflammatory effectors, 12	chronic lymphocytic leukemia study,
immune-mediated encephalitis, 249–250	inflammatory gene polymorphisms, 80	396–397
immunizations for infections	infliximab, 235, 282, 308, 379	chronic myeloid leukemia, 6, 72, 229, 361
in cGVHD, 278	influenza, 129, 233, 273, 278, 282	from HLA identical sibling donors, 46
immunophilins, 101	Institute of Medicine (IOM) Committee	treatments for, 3
	Report on Psychosocial Services	
immunosuppressive therapies, 17, 31.	to Cancer Patients/Families	Leukemia and Lymphoma Society, 400
See also azathioprine; calcineurin		The Leukemia Society, 403
inhibitors; corticosteroids;	in a Community Setting	lichen planus eruption, 5, 210
cyclosporine; mycophenolate	recommendations, 398	characteristics of, 172–173
mofetil; sirolimus; tacrolimus	insulin resistance/diabetes mellitus, 295	cutaneous cGVHD, 169, 171
approach to treatment, 125-126	Intercultural Cancer Council, 404	genitals, 91
bile duct dropout (ductopenia)	interferon-gamma (IFN-γ)	oral, 91, 139, 182, 190
and, 98	acute GVHD association, 10	PUVA treatment, 177
for BOS, 234–235	predictive role in post-transplant	of skin, 91, 172–173
combination regimens, 120	GVHD, 79–80	vulva, 210
discontinuation of, 124	interleukin-2 (IL-2), 22	lichen sclerosus, 61
for gastrointestinal cGVHD, 218	response role in Graft vs. Host Disease	lichen-planus-like sclerosus, 61, 91,
GVHD associated, 10, 12	induction, 10	169, 182
infections related to, 282-283	interleukin-4 (IL-4), 10	lidocaine (viscous), 190, 191
local/low-dose systemic, 56	interleukin-10 (IL-10), 10	limited/extensive chronic graft vs. host
low-dose radiation/chemotherapy, 52	predictive role in post-transplant	disease (cGVHD), 72–73, 88
and new tumor development, 330	GVHD, 79–80	linezolid for Nocardia infection, 273
prophylaxis combined with, 118–120	International Bone Marrow Transplant	Listeria monocytogenes, 277
recurrent malignancy risks, 128–129	Registry (IBMTR), 3, 88–89, 118,	liver. See hepatic cGVHD
Seattle group revisions, 89	361, 369	Lorenz, E., 3
sirolimus. (See sirolimus)	International Classification of Functioning,	lungs and cGVHD, 17, 34
	Disability and Health (ICF), 252	bronchiolitis obliterans syndrome.
topical medications, 57, 93	invasive aspergillosis, 275	•
2000-present trends, 49		(See bronchiolitis obliterans
withdrawal of, 130	invasive fungal infection (IFI), 274	syndrome)
incidence and trends of cGVHD	IPEX syndrome (humans), 11	chronic myelogenous leukemia
1970–1980 data, 46	itraconazole (azole drug class), 107, 129, 281	(case study), 229
1980–1990 data, 46–48		cryptogenic organizing pneumonia
1990-2000 data, 48-49	Jacobsen, L. O., 3	clinical manifestation, 231-232
2000-present data, 49	Japanese Marrow Donor Program (JMDP)	diagnostic criteria, 231–233
future challenges, 52-53	Registry, 70	risk factors/epidemiology, 231
HLA-mismatched transplants, 51-52	Johns Hopkins Center, 377	therapy and outcome, 231-233

416 INDEX

lungs and cGVHD (cont.)	medical evaluations, 66	National Cancer Institute, 400
diagnostic approach	medical photographs, 67-68	National Institutes of Health, 5, 21-22.
chest imaging, 230-231	ophthalmology evaluations, 66-67	See also Consensus Development
clinical assessment, 229-230	pulmonary function testing (PFT), 67	Project on Criteria for Clinical Trials
procedures, 231	monoclonal antibodies (MoAb) for	in cGVHD
pulmonary function testing, 230	pediatric cGVHD, 379	Ancillary Therapy and Supportive Care
Lymphoma Research Foundation, 403	mononeuritis multiplex, 246	Working Group, 157
Lymphoma Society, 403	montelukast (cysLT1R antagonist), 21	categorization criteria, 56, 70, 151
7 1	mortality (non-relapse) from cGVHD, 56	consensus on cGVHD, 31, 74
mast cells, 35	MOS-SF-36 HRQOL measure, 339	grading/staging of GVHD, 11, 89-91
Mathé, G., 6	mouse models	retrospective validation, 99–100
MD Anderson Symptom Inventory, 339	bone marrow transplant experiments, 3	histologic criteria, 94
Medical Outcomes Study (Short	CpG ODNs response, 19	National Marrow Donor Program
Form-12), 341	inflammatory cytokines/receptors	(NMDP), 70, 73, 89, 399, 403
meibomian gland dysfunction, 199,	investigations, 13	HLA matching study, 51
201, 203	Th1/Tc1 vs. Th2/Tc2 responses, 18	on PBSC grafts, 51
memory (CD62L+) T cells, 9	mouth evaluation, 57, 61	natural killer (NK) cells
meropenem for <i>Nocardia</i> infection, 273	moxifloxacin for Nocardia infection, 273	elimination of host APCs, 10, 34
metabolic effects of cGVHD	mucosal carcinoma, 330-331	role of, 21
bone metabolism	mucositis, oral/esophageal, 46	use of, by granule exocytosis
avascular necrosis (AVN), 291–292	murine studies	pathways, 10
osteopenia/osteoporosis, 289	CNS complications post-allo-HSCT, 304	natural killer T (NKT) cells, 21
case presentations	of GVHD/MHC, 8–9, 17	role of, 21
multi-focal AVN, 296	Th2 approximation, 18	nedocromil sodium, 35
sclerodermatous cGVHD, 297–298	Murphy, J. B., 4	Neoral [®] , 106
steroid refractory aGVHD, 296–297	musculoskeletal/joints evaluation, 57,	neuraminidase inhibitors for respiratory
Cushing's syndrome/adrenal	66, 91	virus, 274
insufficiency, 292–293	diagnostic criteria, 91	neurological manifestations from cGVHD
disturbed growth/development, 296	distinctive criteria, 92	central nervous system (CNS)
thyroid function, abnormal, 295	in pediatric patients, 373–374	demyelinative disease, 247–249
metabolic syndrome (MS), and	myasthenia gravis (MG), 20, 216, 245,	determination of cGVHD reality,
components	262–263	246–248
components	clinical course, 302	immune-mediated encephalitis,
hyperlipidemia, 294	diagnosis, 303	249–250
hypertension, 295	future directions, 303	proposed diagnostic criteria,
insulin resistance/diabetes	incidence, 302	247–249
mellitus, 295	site-specific therapy, 303	stroke from vasculitis/angiitis, 249
obesity, 295	mycophenolate mofetil (MMF), 108–109,	peripheral nervous system (PNS),
definition and incidence, 293	139–140	243–246
risk factors, 294	drug interactions, 108–109	myasthenia gravis, 20, 216, 245
	for myasthenia gravis, 303	polymyositis, 98, 244–245
metapneumovirus, 273 methicillin-resistant S. aureus (MRSA), 273	for pediatric cGVHD, 377	post-transplant peripheral
methotrexate	pharmacology/pharmacokinetics, 108	neuropathy, 245–246
for chronic myeloid leukemia, 229	for retroperitoneal fibrosis, 311	neutropenia, 6, 127, 139, 241, 273,
cyclosporine vs., 47	for steroid-resistant cGVHD, 128	281, 379
100-day post-transplant data, 46	toxicity, 109	nitric oxide synthase (NOS2), 101
leukoencephalopathy from, 247	mycophenolic acid (MPA). See	Nocardia infections, 273
	mycophenolate mofetil (MMF)	NOD2/CARD15 variants, 20, 24, 80
pediatric patients, 75	myeloablative preparative regimens,	nongenomic mechanisms, 103
methylprednisolone, 103, 104, 120, 128,	18, 46	
234, 250, 304	cyclophosphamide	nonmyeloablative preparative regimens, 18, 38, 52, 295
metronidazole (antibacterial), 109	with busulfan, 52	non-tuberculosis mycobacteria, 273
MHCII+ antigen presenting cells	with fludarabine, 52	norfloxacin (antibacterial), 109
(APCs), 35	HLA-identical siblings, 75	norovirus, 221, 277
microangiopathic hemolysis, 241		11010VII us, 221, 277
mineralocorticoid receptors (MR), 101	myocarditis, 307	abority 224 252 202 205
minocycline for <i>Nocardia</i> infection, 273	mairra (CDC2L) T asll- 0	obesity, 224, 253, 293, 295
minor histocompatibility antigens (mHA),	naive (CD62L+) T cells, 9	ocular chronic graft vs. host disease
9, 19	National Bone Marrow Transplant	(oGVHD)
mislabeling of symptoms as cGVHD, 57	Link, 403	clinical manifestations, 199–202
monitoring of cGVHD, 66–68. See also	National Bone Marrow Transplant Link	diagnosis/staging, 202–26
assessment (clinical) of cGVHD	(nbmtLINK), 399	management, 203-204

INDEX ■ 417

bandage contact lens (BCTL), 203	dry mouth, 87	T-cells, role of, 18
cyclosporine, topical, 204	evaluation, 57, 61, 91	Th1/Tc1 vs. Th2/Tc2 responses, 18
drainage, decrease of, 203-204	health care, 190	thymic regulation, 18–19
evaporation control, 203	histologic studies, 97	patient advocacy. See advocacy for patients
flaxseed oil supplementation, 204	oral sicca, 129	Patient-Reported Outcomes Measurement
lubrication, 203	in pediatric patients, 374	Information System (PROMIS), 147
ocular surface inflammation,	treatments, 129	335, 344, 354, 357
decrease of, 204	xerostomia, 92, 185, 191	PBT. See peripheral blood transplantation
steroids, topical, 204	oral mucosal cGVHD, 46	(PBT)
pathophysiology, 202–203	management, 190	PDGF-BB (platelet-derived growth
in pediatric patients, 374	symptoms, 182–20	factor-BB) biomarker, 22
ocular issues	treatment, 24–193	PDGFR-α autoantibodies, 20
blepharitis, 201–202	organ system monitoring, 157, 158–161	pediatric cGVHD
bulbar conjunctival hyperemia	orofacial sclerosis, 187	clinical manifestations
("red eye"), 201	oropharyngeal cGVHD, 216	cutaneous, 373–374
cataracts, 126–127, 326–327	osteogenic sarcoma, 330	eyes, 374
cicatricial ectropion (of eyelids),	osteonecrosis of the jaw (ONJ), 256	gastrointestinal tract, 375
201–202	osteopenia, 162, 165, 289, 296, 328	hematopoietic system, 376
distinctive criteria, 92	osteoporosis, 126–127, 255–257	immune system, 376–377
dry eyes. (See dry eye syndrome)	clinical manifestations, 255–256	liver, 375
episcleritis, 201	glucocorticoid-induced, 130, 157, 255,	mouth, 374
evaluations, 57, 64–65, 66–67	256–257	musculoskeletal, 373–374
filamentary keratitis, 201		
hyperkeratosis, 201–202	management of, 256	respiratory tract, 375–376 incidence, 369–370
• •	fractures, 256 and osteopenia	issues in cGVHD
lacrimal gland involvement, 31, 34,	*	
202–203	definitions/incidence, 289	cognitive development, 319–321
meibomian gland dysfunction, 201	pathophysiology/risk factors, 289	dependency/overprotection, 319
ocular sicca, 129	treatment, 289–291	manifestations, 373
pseudomembranous conjunctivitis, 199	risk factors, non-disease specific, 255	MMF for steroid-resistant cGVHD, 128
pseudomembranous	as secondary/late effect, 328	oral cGVHD, incidence of, 182
keratoconjunctivitis, 202	overlap syndrome, 57, 90, 117, 352	pathobiology, 372–373
superior limbic keratoconjunctivitis, 201		predictive models of cGVHD, 75
trichiasis, 201–202	p27 ^{kip1} (p27 kinase inhibitory protein 1), 110	prednisone effects, 126–127
odynophagia, 124–125, 158, 160, 164	p70 ^{s6} (70-kD ribosomal S6) kinase	preparative regimen, 372
Oncology Nursing Society, 404	phosphorylation, 109	prevention, 377
opioids, 191, 259	pamidronate, 256, 290, 296, 328	relapsed disease procedures, 70
oral chronic graft vs. host disease	pancreatic diseases	risk of cGVHD, 71
Consensus Development Project	cancer, 399	salvage regimens
criteria, 187	diagnosis, 225	anti-cytokine therapy, 379
diagnosis, 187–24	incidence, 225	extracorporeal photopheresis.
biopsy, 188	presentation, 225	(See extracorporeal
histopathological/molecular features,	prevention, 226–216	photopheresis (ECP))
183–21	significance for prognosis, 225	hydroxychloroquine (HCQ), 378
incidence, 182, 182–21	therapy, site-specific, 225	monoclonal antibodies (MoAb),
management of, 189-190	papular/papulosquamous rash, 61	379
oral mucosal cGVHD. (See oral	parenchymal disorders, 230	mycophenolate mofetil, 377
mucosal cGVHD)	parentgF1 cGVHD animal models, 32-34	pentostatin, 377–378
in pediatric patients, 182	parentgF1 models, 32	sirolimus, 377
presentation, 182	parent-into-F1 SLE-cGVHD model, 33-34	thalidomide, 379
salivary gland cGVHD, 31, 34, 183-187	pathophysiology of chronic graft vs. host	severe combined immune deficiency, 240
management, 191-194	disease	sirolimus usage, 110
treatment, 192	B-cells, role of, 19	soluble biomarkers, 75
sclerotic oral cGVHD, 187-23	chronic GVHD antigens, 20	Spanish (Pediatric) Transplant group, 75
management, 194	classification evolution, 23-24	stem cell source
secondary cancer surveillance, 194	defined, 17	peripheral blood stem cells, 370-37
significance, for prognosis/clinical	complications, 31	umbilical cord blood, 371–372
course, 188	factors affecting, 17–18	unrelated donors, 370
oral issues	histopathological aspects of cGVHD,	supportive care, 380
destruction of lacrimal/salivary	93–13	therapeutic trial study, 22
glands, 95	pathogens, role in GVHD development,	toxicity/late effects, 379–380
distinctive criteria, 92	19–20	treatment, 377

418 INDEX

pentamidine (IV) for Pneumocystis	photographic evaluation of cGVHD. See	prednisolone, 102, 103, 256, 306
jiroveci, 276	extracorporeal photopheresis (ECP)	prednisone, 103, 272
pentostatin, 142, 269, 283, 377-378	picornavirus, 273	case studies, 160, 162
periacinar stroma, 97	pilocarpine, 129	combined with
pericardiocentesis for serositis, 306	pimecrolimus cream (Elidel®), 176	azathioprine, 125
peripheral blood stem cells (PBSCs)	plasmacytoid DC2 cells, 75, 177	calcineurin inhibitors, 101
bone marrow transplants vs., 52–53,	platelet antibodies, 20	cyclosporine, 127
360–362	platelet-derived growth factor (PDGF), 20	hydroxychloroquine (pediatric
donor association with cGVHD, 21	platelets/clotting factors in cGVHD, 238	patients), 75
elevations, in aGVHD, 12	Pneumocystis jiroveci (PCP), 271, 276	thalidomide, 125
G-CSF association, 360	Pneumocystis pneumonia, 129, 157	morbidity risks (long-term usage),
G-CSF mobilization, 17, 22, 71	pneumonia. See bronchiolitis obliterans	126–127
impact on cGVHD, 360–362	organizing pneumonia; cryptogenic	for myasthenia gravis, 302
and incidence of aGVHD/cGVHD,	organizing pneumonia;	onset, tapering, discontinuation of,
71–72	pseudomonas pneumonia	125–126
prevention of GVHD, 11	pneumonitis, 305	pediatric patients, 75
as source in pediatric cGVHD, 370–371	political effects of Chronic Graft Versus	for polymyositis, 245
as stem cell source, 37, 71 Treg cell measurement, 20	Host Disease, 4 polyarteritis nodosa, 246, 304	for primary adrenal insufficiency, 293 short-/long-term, 48
women and, 207	polymorphisms, cytokine gene/	prevention focus
peripheral blood transplantation (PBT), 22,	inflammatory gene, 80	ancillary and supportive care,
71, 72, 120, 158	polymyositis, 98, 244–245, 262	157–160
peripheral nervous system (PNS)	posaconazole (azole drug class), 108, 129	bacterial infections in cGVHD,
manifestations of cGVHD, 243–246	posterior leukoencephalopathy, 247	278–280, 280–281
myasthenia gravis, 20, 216, 245	post-transplant acute limbic encephalitis	community-acquired respiratory
polymyositis, 98, 244–245	(PALE), 278	viruses (with antiviral
post-transplant peripheral neuropathy,	predictive models for prognosis of	agents), 282
245–246	cGVHD, 72–74	IV immunoglobulin, 278–279
peripheral neuropathy, post-transplant,	biomarkers	pneumocystis jiroveci
245–246	B cell function assessment, 81	prophylaxis, 281
pharmacokinetics. See also individual	genetic markers, 80	prophylactic antibiotics, 279–280
drugs	serum/cellular cytokine production	VZV/HSV prophylaxis, 282
calcineurin inhibitors	and Th1/Th2 paradigm, 79–80	cutaneous cGVHD, 178
absorption, 106	T cell function assessment, 80–81	esophageal (of gastrointestinal
distribution, 106–107	clinical/research needs, 74	cGVHD), 218–219
metabolism, 107	extensive skin involvement,	hepatic cGVHD, 224
glucocorticoids	thrombocytopenia, progressive	pancreatic diseases, 226-216
absorption, 103	onset (John Hopkins-II), 73	pediatric cGVHD, 377
distribution, 103	historical background, 87-89	peripheral blood stem cells
metabolism, 103-104	Karnofsky performance status score,	(PBSCs), 11
mycophenolate mofetil (MMF), 108	88, 89	stomach, small intestine, colon
sirolimus	KBS, diarrhea, weight loss, cutaneous/	disorders, 222
absorption, 110	oral chronic GVHD	primaquine for Pneumocystis jiroveci,
distribution, 110	(CIBMTR), 74	276
metabolism/elimination, 110	laboratory markers	primary biliary cirrhosis, 56, 98, 117
thalidomide	donor APCs, 75	pro-opiomelanocortin, 101
absorption, 113	minor histocompatibility antigens, 75	prophylaxis methods (of cGVHD). See also
distribution, 113	OX40 expression, 74–75	immunosuppressive therapies
metabolism/elimination, 114	regulatory T cells, 75	agnostic autoantibodies to PDFG
pharmacology of cGVHD. See also	soluble biomarkers, 75	receptor, 121
individual drugs	limited/extensive, 72–73, 88	of bacterial infections, 278–280
calcineurin inhibitors. (See calcineurin	model summary, 74	antifungal prophylaxis, 280–281
inhibitors)	NIH consensus classifications, 74	antiviral prophylaxis, 281–282
corticosteroids. (See corticosteroids)	onset type, 73	community-acquired respiratory
glucocorticoids. (See glucocorticoids)	pediatric cGVHD, 75	viruses (with antiviral
mycophenolate mofetil.	progressive-type onset, elevated	agents), 282
(See mycophenolate mofetil)	bilirubin/lichenoid histology	IV immunoglobulin, 278–279
sirolimus. (See sirolimus)	(John Hopkins-I), 73	pneumocystis jiroveci prophylaxis,
tacrolimus. (See tacrolimus)	testing John Hopkins II in other data	281
thalidomide. (See thalidomide) pharyngeal candidiasis, 183	sets, 73–74 thrombocytopenia (Seattle), 73	prophylactic antibiotics, 279–280 VZV/HSV prophylaxis, 282
priar yrigear caricilliasis, 100	unomoocytopema (seattle), 13	v 2 v / 113 v propilylaxis, 202

INDEX ■ 419

Campath-1H antibody, 17, 48, 117	genital/gonadal effects, 319	activities of daily living, 253
combined immunosuppression,	lack of libido, 319	Bone Marrow Survivor Study
118–120	social effects of treatment, 318	questionnaire, 253
corticosteroids. (See corticosteroids)	altered physical appearance, 318	EORTC QLQ-C30, 253
cyclosporine. (See cyclosporine (CSA))	disruption of social networks, 318	FACT-BMT, 253
immunomagnetic devices, 117	extended caregivers demands, 318	joint range of motion/muscle
methotrexate. (See methotrexate)	pulmonary function testing (PFT), 230	strength, 253
prednisone. (See prednisone)	pulmonary issues	quality of life measures, 253
regulatory T cells, 120-121	bronchiolitis obliterans organizing	impact of organ system involvement
removing/inactivating donor T cells	pneumonia. (See bronchiolitis	arthritis/arthralgia, 254
T cell depletion ex vivo, 117-118	obliterans organizing	avascular necrosis, 257
T cell depletion in vivo, 118	pneumonia)	fascitis, 254–255
T cell depletion vs. unmanipulated	bronchiolitis obliterans syndrome.	musculoskeletal problems, 253-254
transplants, 118	(See bronchiolitis obliterans	osteoporosis, 255-257
stem cell source, 120	syndrome)	myasthenia gravis, 262-263
tacrolimus. (See tacrolimus)	diagnostic criteria, 91	neurological abnormalities, 257–258
T-cell depletion of donor marrow, 47	distinctive criteria, 92	polymyositis, 262
Th2 cytokines (experimental), 11	morbidity/mortality in cGVHD, 80	pulmonary rehabilitation, 258
thalidomide. (See thalidomide)	pulmonary function testing (PFT), 66	steroid myopathy (SM), 263
thymus tissue implants, 120	pulmonary insufficiency, 46, 87	weakness of patients, 262
timing of cGVHD, 117	secondary/late effects	renal involvement in cGVHD
prostate cancer, 399	chronic obstructive lung	clinical course, 309–310
Protopic® ointment, 176	disease, 327	diagnosis, 310
pseudomembranous conjunctivitis, 199	restrictive lung disease, 327	future directions, 310
pseudomembranous	pulse corticosteroid therapy, 103	incidence, 309
keratoconjunctivitis, 202	pure red blood cell dyscrasia, 245	renal transplantation, 4
Pseudomonas, 273, 277 pseudomonas pneumonia, 229	pure red cell aplasia (PRA), 240	respiratory syncytial virus (RSV), 273, 282 respiratory tract infections in cGVHD,
psoralen and ultraviolet A therapy	quadrivalent HDV vaccine	270–276
(PUVA), 128	quadrivalent HPV-vaccine (GARDASIL®), 214	bacterial pneumonia, 272–273
psoriasis vs. cutaneous cGVHD, 169	quality of life (QOL). See health-related	blood and urine tests, 271–272
psychiatric effects of cGVHD treatment, 317	quality of life (QOL). See Health-Telated	bronchioalveolar lavage tests, 271–272
agitation, 317	quality of file (TIRQOL)	diagnostic work-up, 271
depression, 317	radiation exposure (from atomic bomb),3	in pediatric patients, 375–376
mania, 317	radiation related cancers, 330	respiratory syncytial virus (RSV),
psychosocial issues in cGVHD	rapamycin (mTOR). See sirolimus	273, 282
caregiver needs, 322	reactive emotions to cGVHD	sinusitis, 276
cognitive effects of treatment, 316-317	anxiety, 315	viral pneumonia
concentration, 316-317	helplessness, 315–316	cytomegalovirus (CMV), 273-274
memory, 316	uncertainty, 316	fungal diseases, 274–275
mood, 317	worry, 315	pneumocystis jiroveci (PCP), 276
demands of treatment/side effects	red blood cell abnormalities in cGVHD,	restrictive lung disease, 5-4, 327
activity limitations/work change,	240-241	retinitis, 281, 305
314–315	reduced intensity conditioning (RIC), 33,	retinoids, 141–142
family burden, 315	49, 52, 70, 182, 329, 362	retroperitoneal fibrosis
needs based treatment response, 322	regulatory immune populations	clinical course, 310–311
overview, 314	antigen presenting cells, 21	diagnosis, 311
pediatric issues, 319–321	biomarkers, 21–22	incidence, 310
cognitive development, 319–321 dependency/overprotection, 319	immune reconstitution impact, 22–23	site-specific therapy, 311 rheumatoid arthritis, 19, 117, 128, 149, 246
psychiatric effects of treatment, 317	inflammatory responses, 21	ribavirin, inhaled, 274
agitation, 317	macrophages, neutrophils, eosinophils, 21	risedronate, 256–257, 290
depression, 317	NK/NKT cells, 21	risk factors for cGVHD development, 18,
mania, 317	Tregs, 20–21	47. See also acute chronic graft vs.
reactive emotions, 315–316	regulatory T cells, 11	host disease (aGVHD); aplastic
anxiety, 315	rehabilitation of cGVHD patients	anemia; chronic myeloid leukemia;
helplessness, 315–316	background information, 252 complications/treatments	peripheral blood stem cells (PBSCs)
uncertainty, 316	contractures, 258–259	age of donor/recipient, 71
worry, 315	edema, 260–262	conditioning regimen, 72
sexuality	fatigue, 259–260	cyclosporine A prophylaxis duration, 72
body image, 319	evaluation assessments	HLA donor-recipient disparity, 71

420 INDEX

risk factors for cGVHD development (cont.)	sclerosing cholangitis, 34	therapeutic monitoring, 110–111
peripheral blood stem cell	sclerosis	toxicity, 111
transplantation, 71–72	cGVHD-associated, 21	site-specific therapy
previous aGVHD, 71	deep sclerosis, 67, 68, 91	for esophageal complications, 218
skin/oral biopsy positive screening	frank sclerosis, 32	for hepatic cGVHD, 224
(post-HCT), 72	lichen sclerosis, 97, 151	for myasthenia gravis, 303
stratification system (Johns Hopkins	pulmonary restriction from, 66, 92	for pancreatic diseases, 225
Center), 89	skin sclerosis, 46, 61, 99	for stomach, small intestine, colon
tacrolimus prophylaxis, 72	systemic, 37, 98, 149	disorders, 222
viral infections, 72	sclerotic oral cGVHD, 187–23	for vasculitis, 304
rituximab, 141	management, 194	Sjögren's disease, 5–4, 6, 31, 56, 149, 303
with corticosteroids, 240	•	· -
	scoring system	skin and soft tissues infections, 277–278
for myasthenia gravis, 303	global, 56, 92–93	dermal appendage assessment, 57–61
risks of, 223	individual organ systems, 92	skin carcinoma, 330–331
for steroid-resistant cGVHD, 48	secondary and late effects	skin fibrosis, 31
suppression of cGVHD progression,	bones/joint complications	effector phase of skin GVHD, 35
19, 33	avascular necrosis (AVN), 328	halofuginone blocking of, 35
rotavirus, 221, 277	osteoporosis, 328	processes implicated in, 20
RPS4Y antigen, 20	malignancies, 328-331	sleep issues, 259-260
	lymphomas, 329	prednisone, high-dose, 126-127
salivary gland cGVHD, 31, 34, 183-187	post allogeneic SCT leukemia, 329	small intestine disorders. See stomach,
management, 191–194	solid tumors	small intestine, colon disorders
treatment, 192	pathogenesis, 330	social effects of cGVHD treatment, 318
salmeterol inhalers, 272	skin/mucosal carcinoma,	altered physical appearance, 318
Salmonella, 277	330–331	disruption of social networks, 318
	thyroid carcinoma, 331	extended caregivers demands, 318
salvage therapy in cGVHD		soluble CD13 biomarker, 20
anti-cytokine therapy, 142	treatment/prevention, 331	
autologous transplantation, 142	ocular (non-malignant late effects),	Spanish (Pediatric) Transplant
azathioprine, 135. (See also	326–327	group, 75
azathioprine)	pulmonary effects, 327	spirometric pulmonary testing, 230
background information, 134	serositis, 125, 302	spleen derived products, 3
calcineurin inhibitors, 135. (See also	clinical course, 305–306	staging for aGVHD, 147
cyclosporine; tacrolimus)	diagnosis, 306	Staphylococcus pyogenes, 276
CD20 antagonists (rituximab), 141	future directions, 306	statins, 291, 294
clofazimine, 141	incidence, 305	Stem Cell Trialists Group, 49
extracorporeal photopheresis.	site-specific therapy, 306	stem cells
(See extracorporeal	serum amyloid (SAA), 79	bone-marrow derived, 33
photopheresis (ECP))	severe combined immune deficiency	donor, engraftment of, 9
hydroxychloroquine, 19–20, 75,	(SCID), 246	epithelial, 12
128, 142	sexuality and cGVHD	hematopoietic, 6
mycophenolate mofetil, 139–140.	body image, 319	memory stem cells, 9
(See also mycophenolate mofetil)	genital/gonadal effects, 319	peripheral. (See peripheral blood stem
pentostatin, 142	lack of libido, 319	cells (PBSCs))
retinoids, 141–142	Shigella, 277	unrelated, and nonmyeloablative HCT
sirolimus, 135–136. (See also sirolimus)	sialogogue therapy, 129	regimens, 117
	for salivary cGVHD, 191	steroid-resistant cGVHD, 48, 128
thalidomide, 137–139. (See also	sicca syndrome, 5–4, 23, 46, 117, 129,	stomach, small intestine, colon disorders
thalidomide)	201, 217	diagnosis, 221–222
topical phototherapy, 140–141		•
total lymphoid irradiation (TLI), 140	Sickness Impact Profile (HRQOL	future advances, 222
Sandimmune [®] , 106	measure), 339	incidence, 219–221
sB-cell activating factor (sBAFF), 22	Simonson, M., 4	presentation, 221
Scedosporium, 276	sinusoidal obstructive syndrome	prevention, 222
Schirmer's test (tear test), 5–4, 57, 64–65,	(SOS), 12	significance for prognosis, 221
66, 202	sirolimus, 109–111	therapy, site-specific, 222
sclerodermatous GVHD (Scl-cGVHD),	drug interactions, 111	Streptococcus aureus, 273, 276, 277
17, 20, 56, 87, 117. See also B10.D2	for pediatric cGVHD, 377	Streptococcus pneumoniae, 272, 277
(or B6.C)gBALB/c animal model	pharmacokinetics	stroke (from vasculitis/angiitis), 249
correlation with clinical cGVHD, 37	absorption, 110	superior limbic keratoconjunctivitis, 201
manifestation data (1969-1976), 46	distribution, 110	supportive care for cGVHD. See ancillary
neuropathic association (possible), 246	metabolism/elimination, 110	and supportive care
survivors of, and allo-HSCT, 37	pharmacology, 109-110	syngeneic GVHD (sGVHD), 39

trial (1995), 151

Cambridge University Press 978-0-521-88423-5 - Chronic Graft Versus Host Disease: Interdisciplinary Management Edited by Georgia B. Vogelsang and Steven Z. Pavletic Index More information

INDEX ■ 421

systemic lupus erythematous (SLE), 19, 32,	T-helper type 1 subset (Th1)(secreting	treatment testing, treatment
33–34, 117, 128, 303, 318	IL-1/IFN-γ), 10, 11	methods; individual drugs
systemic sclerosis, 37, 98, 149	T-helper type 2 subset (Th2)(secreting	of cGVHD, 125, 128.
systemic vasculitis, 149	IL-4, IL-5, IL-10, IL-13), 10, 11	(See also cyclosporine;
	thoracoabdominal irradiation (TAI), 140	immunosuppressive therapies)
T cells. See also Tregs (regulatory T cells)	three-step model (in sequence), acute	azathioprine, 125, 128
depletion of donor marrow	Chronic Graft Versus Host Disease	calcineurin inhibitors.
prophylaxis, 47	(aGVHD)	(See calcineurin inhibitors)
function assessment	effects of HCT conditioning, 8	goal of, 125
functional T cell assays, 80	donor T-cell activation/cytokine	hydroxychloroquine, 19-20, 75, 128
immunological/molecular	secretion, 8–11	immunosuppressive treatment
characterization, 80-81	cytokine secretion by donor T-cells,	approach, 126
prophylaxis involvement	10–11	infection prevention, 129-130
regulatory T cells, 120–121	donor T-cell activation, 8–10	methylprednisolone, 103, 128
T cell depletion ex vivo (TCD),	regulatory T-cells, 11	mycophenolate mofetil (MMF).
117–118	cellular and inflammatory effectors,	(See mycophenolate mofetil)
T cell depletion in vivo (TCD), 118	11–13	outcomes, post-initial treatment,
T cell depletion vs. unmanipulated	cellular effectors, 11–12	130–132
transplants, 118	inflammatory effectors, 12	prednisone (onset, tapering,
role of	TLRs and innate immunity, 12-13	discontinuation), 125-126
direct anti-antigen allogenic	traffic of cellular effectors, 13	psoralen/ultraviolet A therapy
response, 18	thrombocytopenia in cGVHD,	(PUVA), 128
Th1/Tc1 vs. Th2/Tc2 responses, 18	238–240, 377	randomized treatment summaries,
TH2 self (recipient)-reactive, 56	thymic regulation, 18–19	125–126
T helper cells, 6, 72, 241	thyroid carcinoma, 331	secondary treatment indications, 13
tacrolimus (TAC), 48, 72, 135	TMP/SMX for Pneumocystis jiroveci, 276	systemic treatment indications,
case studies, 160, 162	TNF-α (tumor necrosis factor-alpha). See	124–125
for chronic myelogenous leukemia, 229	also TRAIL:DR4,5 ligand; TWEAK:	of cutaneous cGVHD, 175–178
clinical pharmacology, 106	DR3 ligand	extracorporeal photopheresis
contraindications to usage, 128	cardiac association, 308	(ECP). (See extracorporeal
drug interactions, 107-108	induction of epithelial apoptosis, 8	photopheresis (ECP))
mechanism of action, 105-106	predictive role in post-transplant	phototherapy, 176
pharmacokinetics	GVHD, 79-80	systemic retinoids, 178
absorption, 106	prednisolone and, 102	topical corticosteroids/
distribution, 106–107	role in acute GVHD pathophysiology, 12	immunomodulators, 176
metabolism, 107	toll-like receptors (TLRs), 10	of oral mucosal cGVHD, 24-193
topical, for oral mucosal cGVHD, 191	and innate immunity, 12–13	of salivary cGVHD, 192
toxicity, 108	Tlr4 gene, 12	TRECs. See T-cell receptor excision circles
for vasculitis, 304	TLR9, 19	(TRECs)
tacrolimus (TAC) ointment, 176	topical corticosteroids	Tregs (regulatory T cells), 23-24, 56
target cell apoptosis, 8	for cutaneous cGVHD, 176	as cGVHD prophylaxis, 120-121
T-cell receptor excision circles (TRECs), 19	for ocular GVHD, 204	deficiency of, 11
telangiectasia, 169	for oral mucosal cGVHD, 190–191	measurement in peripheral blood, 20
testosterone replacement therapy, 290	for vaginal restenosis, 211	trends of cGVHD
TGF-β1, 35	topical phototherapy, 137, 140–141	1970–1980, 46
Th1/Th2 cytokines, 11, 79–80	total body irradiation (TBI), 75, 245, 362	1980–1990, 46–48
TH2 self (recipient)-reactive T cells, 56	in aplastic anemia/leukemia	1990–2000, 48–49
thalidomide, 48, 111–114	transplantation, 46	2000-present, 49
City of Hope/Stanford evaluation,	bone loss, 289	future challenges, 52–53
118–120	cGVHD vs., 326	HLA-mismatched transplants, 51–52
drug interactions, 114	in HCT conditioning, 8	nonmyeloablative/reduced intensity
neuropathy as side effect, 246	in mice experiments, 3	conditioning transplants, 52
for pediatric cGVHD, 379	pediatric risk factor, 320	peripheral blood vs. bone marrow
pharmacokinetics	renal impairment, 309	grafts, 49–51
absorption, 113	Schirmer's test results, 201	triamcinolone 0.1% for cutaneous
distribution, 113	TB risk factor, 273	cGVHD, 176
metabolism/elimination, 114	vs, conventional regimens, 52	trichiasis, 201–202
pharmacology, 112-113	total lymphoid irradiation (TLI), 140	trimethoprim for Pneumocystis jiroveci,
with prednisone, 125	toxoplasma, 277	276, 279
toxicity, 114	TRAIL:DR4,5 ligand, 11	trimethoprim/sulfamethoxazole (TMP/
trial (1995), 151	treatment. See also clinical trials for	SMX), 279

 $\hbox{@ Cambridge University Press}$ www.cambridge.org



422 INDEX

tuberculosis (TB), 273
tumor necrosis factor-alpha. See TNF-α
(tumor necrosis factor-alpha)
tumors as secondary/late effect
pathogenesis, 330
skin/mucosal carcinoma, 330–331
thyroid carcinoma, 331
treatment/prevention, 331
TWEAK: DR3 ligand, 11

ulcers (in deep sclerosus), 61 umbilical cord blood transplantation, 17, 72, 364–366 ursodeoxycholate, 129 UTY antigen, 20

vaccinations against infections, 129 vaginal cGVHD. *See* genital cGVHD vaginal restenosis, 211 vaginal stenosis, 207 valacyclovir, 129, 272, 276, 282 Varicella-Zoster virus (VZV), 276, 277 vasculitic neuropathies with mononeuritis multiplex, 246 vasculitis clinical course, 303-304 diagnosis, 304 future directions, 304-305 incidence, 303 oral vasculitis, 5-4 sensory multiple mononeuropathy from, 257 site-specific therapy, 304 stroke from, 249 systemic vasculitis, 149 venous thromboembolism in cGVHD, 240, 328 vertebroplasty (kyphoplasty), 256 Vibrio, 277 viral infections as cGVHD risk factor, 72 viral pneumonia cytomegalovirus (CMV), 273-274 respiratory viruses, 273

vitamin D supplementation, 130, 162, 163, 164, 165
voriconazole (azole drug class), 108, 129, 275, 281
vulvar burning, 209
vulvar vestibulitis syndrome, 209
vulvovaginal cGVHD. See genital cGVHD
wasting syndrome, 56, 87

wasting syndrome, 56, 87
weakness in patients with cGVHD, 262
Weiden, P. L., 6
weight loss, 34, 57, 73, 74, 89, 92, 124–125
white blood cell abnormalities
in cGVHD, 241
Women's Health Initiative (WHI) study, 328

xerosis, 171 xerostomia, 92, 185, 191

ZFY antigen, 20 zoledronate (IV), 256, 290 zoledronic acid, 165, 290