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Table 1

Summary recommendations for screening and prevention of late complications in long-term HCT survivors

Tissues/organs	Late Complications	General Risk Factors	Monitoring Tests	Monitoring Tests and Preventive Measures In All HCT Recipients	Monitoring Tests and Preventive Measures In Special Populations
Immune system	<ul style="list-style-type: none"> - Infections 	<ul style="list-style-type: none"> - Donor source - HLA disparity - T-cell depletion - GVHD - Prolonged immunosuppression - Venous access devices 	<ul style="list-style-type: none"> - CMV antigen or PCR in patients at high risk for CMV reactivation 	<ul style="list-style-type: none"> - PCP prophylaxis for initial 6 months after HCT - Immunizations post-transplant according to published guidelines - Administration of antibiotics for endocarditis prophylaxis according to American Heart Association guidelines 	<ul style="list-style-type: none"> - Patients with cGVHD: Antimicrobial prophylaxis targeting encapsulated organisms and PCP for the duration of immunosuppressive therapy - Patients with cGVHD: Screening for CMV reactivation should be based on risk factors, including intensity of immunosuppression.
Ocular	<ul style="list-style-type: none"> - Cataracts - Sicca syndrome - Microvascular retinopathy 	<ul style="list-style-type: none"> - TBI/radiation exposure to head and neck - Corticosteroids - GVHD 	<ul style="list-style-type: none"> - Ophthalmologic exam 	<ul style="list-style-type: none"> - Routine clinical evaluation at 6 months and 1 year after HCT and at least yearly thereafter - Ophthalmologic examination with measurement of visual acuity and fundus examination at 1 year after HCT, subsequent evaluation based on findings and risk-factors - Prompt ophthalmologic examination in patients with visual symptoms 	<ul style="list-style-type: none"> - Patients with cGVHD: Routine clinical evaluation, and if indicated, ophthalmologic examination more frequently
Oral	<ul style="list-style-type: none"> - Sicca syndrome - Caries 	<ul style="list-style-type: none"> - GVHD - TBI/radiation exposure to head and neck 	<ul style="list-style-type: none"> - Dental assessment 	<ul style="list-style-type: none"> - Education about preventive oral health practices - Clinical oral assessment at 6 months and 1 year after HCT and at least yearly thereafter with particular attention to intra-oral malignancy evaluation - Dental assessment at 1 year after HCT and then at least yearly thereafter 	<ul style="list-style-type: none"> - Pediatric recipients: Yearly assessment of teeth development - Patients with cGVHD: Consider more frequent oral and dental assessments with particular attention to intra-oral malignancy evaluation
Respiratory	<ul style="list-style-type: none"> - Idiopathic pneumonia syndrome - Bronchiolitis obliterans syndrome - Cryptogenic organizing pneumonia 	<ul style="list-style-type: none"> - TBI/radiation exposure to chest - GVHD - Infectious agents - Allogeneic HCT - Busulfan exposure 	<ul style="list-style-type: none"> - PFT's - Radiologic studies (e.g. chest X-ray, CT scan) 	<ul style="list-style-type: none"> - Routine clinical evaluation at 6 months and 1 year after HCT and at least yearly thereafter - Assessment of tobacco use and counselling against smoking - PFT's and focused radiologic assessment for allogeneic HCT 	<ul style="list-style-type: none"> - Patients with cGVHD: Some experts recommend earlier and more frequent clinical evaluation and PFT's

Tissues/organs	Late Complications	General Risk Factors	Monitoring Tests	Monitoring Tests and Preventive Measures In All HCT Recipients	Monitoring Tests and Preventive Measures In Special Populations
	<ul style="list-style-type: none"> - Sino-pulmonary infections 			<ul style="list-style-type: none"> - recipients with symptoms or signs of lung compromise 	
Cardiac and vascular	<ul style="list-style-type: none"> - Cardiomyopathy - Congestive heart failure - Arrhythmias - Valvular anomaly - Coronary artery disease - Cerebrovascular disease - Peripheral arterial disease 	<ul style="list-style-type: none"> - Anthracycline exposure - TBI/radiation exposure to neck or chest - Older age at HCT - Allogeneic HCT - Cardiovascular risk-factors before/after HCT - Chronic kidney disease - Metabolic syndrome 	<ul style="list-style-type: none"> - Cumulative dose of anthracyclines - Echocardiogram with ventricular function, ECG in patients at risk and in symptomatic patients - Fasting lipid profile (including HDL-C, LDL-C and triglycerides) - Fasting blood sugar 	<ul style="list-style-type: none"> - Routine clinical assessment of cardiovascular risk factors as per general health maintenance at 1 year and at least yearly thereafter - Education and counseling on "heart" healthy lifestyle (regular exercise, healthy weight, no smoking, dietary counseling) - Early treatment of cardiovascular risk factors such as diabetes, hypertension and dyslipidemia - Administration of antibiotics for endocarditis prophylaxis according to American Heart Association guidelines 	
Liver	<ul style="list-style-type: none"> - GVHD - Hepatitis B - Hepatitis C - Iron overload 	<ul style="list-style-type: none"> - Cumulative transfusion exposure - Risk factors for viral hepatitis transmission 	<ul style="list-style-type: none"> - LFT's - Liver biopsy - Serum ferritin - Imaging for iron overload (MRI or SQUID) 	<ul style="list-style-type: none"> - LFT's every 3-6 months in the first year, then individualized, but at least yearly thereafter - Monitor viral load by PCR for patients with known hepatitis B or C, with liver and infectious disease specialist consultation - Consider liver biopsy at 8-10 years after HCT to assess cirrhosis in patients with chronic HCV infection - Serum ferritin at 1 year after HCT in patients who have received RBC transfusions; consider liver biopsy or imaging study for abnormal results based on magnitude of elevation and clinical context; subsequent monitoring is suggested for patients with elevated LFT's, continued RBC transfusions, or presence of HCV infection 	
Renal and genitourinary	<ul style="list-style-type: none"> - Chronic kidney disease - Bladder dysfunction - Urinary tract infections 	<ul style="list-style-type: none"> - TBI - Drug exposure (e.g. calcineurin inhibitors, amphotericin, aminoglycosides) - CMV - Hemorrhagic cystitis 	<ul style="list-style-type: none"> - Urine protein - Serum creatinine - BUN 	<ul style="list-style-type: none"> - Blood pressure assessment at every clinic visit, with aggressive hypertension management - Assess renal function with BUN, creatinine and urine protein at 6 months, 1 year and at least yearly thereafter 	

Tissues/organs	Late Complications	General Risk Factors	Monitoring Tests	Monitoring Tests and Preventive Measures In All HCT Recipients	Monitoring Tests and Preventive Measures In Special Populations
				<ul style="list-style-type: none"> - Consider further workup (kidney biopsy or renal ultrasound) for further workup of renal dysfunction as clinically indicated 	
Muscle and connective tissue	<ul style="list-style-type: none"> - Myopathy - Fasciitis/scleroderma - Polymyositis 	<ul style="list-style-type: none"> - Corticosteroids - GVHD 	<ul style="list-style-type: none"> - Evaluate ability to stand from a sitting position - Clinical evaluation of joint range of motion 	<ul style="list-style-type: none"> - Follow general population guidelines for physical activity - Frequent clinical evaluation for myopathy in patients on corticosteroids 	<ul style="list-style-type: none"> - Patients with cGVHD: Physical therapy consultation in patients with prolonged corticosteroid exposure, fasciitis or scleroderma - Patients with cGVHD: Frequent clinical evaluation by manual muscle tests or by assessing ability to go from sitting to standing position for patients on prolonged corticosteroids
Skeletal	<ul style="list-style-type: none"> - Osteopenia/osteoporosis - Avascular necrosis 	<ul style="list-style-type: none"> - Inactivity - TBI - Corticosteroids - GVHD - Hypogonadism - Allogeneic HCT 	<ul style="list-style-type: none"> - Dual photon densitometry - MRI to evaluate patients with joint symptoms 	<ul style="list-style-type: none"> - Dual photon densitometry at 1 year for adult women, all allogeneic HCT recipients and patients who are at high risk for bone loss; subsequent testing determined by defects or to assess response to therapy - Physical activity, vitamin D and calcium supplementation to prevent loss of bone density 	<ul style="list-style-type: none"> - Patients with cGVHD: Consider dual photon densitometry at an earlier date in patients with prolonged corticosteroid or calcineurin inhibitor exposure.
Nervous system	<ul style="list-style-type: none"> - Leukoencephalopathy - Late infections - Neuropsychological and cognitive deficits - Calcineurin neurotoxicity - Peripheral neuropathy 	<ul style="list-style-type: none"> - TBI/radiation exposure to head - GVHD - Exposure to fludarabine - Intrathecal chemotherapy 		<ul style="list-style-type: none"> - Clinical evaluation for symptoms and signs of neurologic dysfunction at 1 year and yearly thereafter - Diagnostic testing (e.g., radiographs, nerve conduction studies) for those with symptoms or signs 	<ul style="list-style-type: none"> - Pediatric recipients: Annual assessment for cognitive development milestones
Endocrine	<ul style="list-style-type: none"> - Hypothyroidism - Hypoadrenalism - Hypogonadism - Growth retardation 	<ul style="list-style-type: none"> - TBI/radiation exposure (e.g. head and neck, CNS) - Corticosteroids - Young age at HCT - Chemotherapy exposure 	<ul style="list-style-type: none"> - Thyroid function tests - FSH, LH, testosterone - Growth velocity in children 	<ul style="list-style-type: none"> - Thyroid function testing yearly post-HCT, or if relevant symptoms develop - Clinical and endocrinologic gonadal assessment for post-pubertal women at 1 year, subsequent followup based on menopausal status - Gonadal function in men, including FSH, LH and testosterone, should be assessed as warranted by symptoms 	<ul style="list-style-type: none"> - Pediatric recipients: Clinical and endocrinologic gonadal assessment for pre-pubertal boys and girls within 1 year of transplant, with further followup as determined in consultation with a pediatric endocrinologist - Pediatric recipients: Monitor growth velocity in children

Tissues/organs	Late Complications	General Risk Factors	Monitoring Tests	Monitoring Tests and Preventive Measures In All HCT Recipients	Monitoring Tests and Preventive Measures In Special Populations
					annually; assessment of thyroid, and growth hormone function if clinically indicated - Patients with cGVHD: Slow terminal tapering of corticosteroids for those with prolonged exposure - Patients with cGVHD: Consider stress doses of corticosteroids during acute illness for patients who have received chronic corticosteroids
Mucocutaneous	<ul style="list-style-type: none"> - Cutaneous sclerosis - Genital GVHD 	<ul style="list-style-type: none"> - GVHD - TBI/radiation exposure to pelvis 	<ul style="list-style-type: none"> - Pelvic exam 	<ul style="list-style-type: none"> - Counsel patients to perform routine self exam of skin and avoid excessive exposure to sunlight without adequate protection - Annual gynecologic exam in women to detect early involvement of vaginal mucosa by GVHD 	<ul style="list-style-type: none"> - Patients with cGVHD and TBI recipients: Consider more frequent gynecologic evaluation based on clinical symptoms
Second cancers	<ul style="list-style-type: none"> - Solid tumors - Hematologic malignancies - PTLD 	<ul style="list-style-type: none"> - GVHD - TBI/radiation exposure - T-cell depletion - Exposure to alkylating agents or etoposide 	<ul style="list-style-type: none"> - Mammogram - Screening for colon cancer (e.g. colonoscopy, sigmoidoscopy, fecal occult blood testing) - Pap smear 	<ul style="list-style-type: none"> - Counsel patients about risks of secondary malignancies annually and encourage them to perform self exam (e.g. skin, testicles/genitalia) - Counsel patients to avoid high risk behaviors (e.g. smoking) - Follow general population recommendations for cancer screening 	<ul style="list-style-type: none"> - Patients with cGVHD: Clinical and dental evaluation with particular attention towards oral and pharyngeal cancer - TBI and chest irradiation recipients: Screening mammography in women starting at age 25 or 8 years after radiation exposure, whichever occurs later but no later than age 40
Psychosocial and sexual	<ul style="list-style-type: none"> - Depression - Anxiety - Fatigue - Sexual dysfunction 	<ul style="list-style-type: none"> - Prior psychiatric morbidity - Hypogonadism 	<ul style="list-style-type: none"> - Psychological evaluation 	<ul style="list-style-type: none"> - Clinical assessment throughout recovery period, at 6 months, 1 year and annually thereafter, with mental health professional counseling recommended for those with recognized deficits - Encouragement of robust support networks - Regularly assess level of spousal/caregiver psychological adjustment and family functioning 	

Tissues/organs	Late Complications	General Risk Factors	Monitoring Tests	Monitoring Tests and Preventive Measures In All HCT Recipients	Monitoring Tests and Preventive Measures In Special Populations
				<ul style="list-style-type: none"> - Query adults about sexual function at 6 months, 1 year and at least annually thereafter 	
Fertility	<ul style="list-style-type: none"> - Infertility 	<ul style="list-style-type: none"> - TBI/radiation exposure - Chemotherapy exposure 	<ul style="list-style-type: none"> - FSH, LH levels 	<ul style="list-style-type: none"> - Consider referral to appropriate specialists for patients who are contemplating a pregnancy or are having difficulty conceiving - Counsel sexually active patients in the reproductive age group about birth control post-HCT 	
General health				<ul style="list-style-type: none"> - Recommended screening as per general population (see text) 	

HCT indicates hematopoietic cell transplantation; cGVHD, chronic graft-versus-host disease; CMV, cytomegalovirus; PCR, polymerase chain reaction; PCP, Pneumocystis pneumonia; TBI, total body irradiation; PFT's, pulmonary function tests; CT, computed tomography; ECG, electrocardiogram; LFT's, liver function tests; MRI; magnetic resonance imaging; SQUID, superconducting quantum interference device; HCV, hepatitis C; RBC, red blood cell; BUN, blood urea nitrogen; CNS, central nervous system; FSH, follicle stimulating hormone; LH, luteinizing hormone; PTLN, post-transplant lymphoproliferative disorder;

Table 2

Abbreviated summary recommendations for screening and prevention of late complications in long-term HCT survivors organized by time after transplantation

Recommended Screening/Prevention	6 mo	1yr	Annually
Immunity			
Encapsulated organism prophylaxis	2	2	2
PCP prophylaxis	2	2	
CMV testing	2	2	2
Immunizations	1	1	1
Ocular			
Ocular clinical symptom evaluation	1	1	1
Ocular fundus exam	+	1	+
Oral Complications			
Clinical assessment	1	1	1
Dental assessment	+	1	1
Respiratory			
Clinical pulmonary assessment	1	1	1
Smoking tobacco avoidance	1	1	1
Pulmonary function testing	+	+	+
Chest radiography	+	+	+
Cardiac and vascular			
Cardiovascular risk-factor assessment	+	1	1
Liver			
Liver function testing	1	1	+
Serum ferritin testing		1	+
Kidney			
Blood pressure screening	1	1	1
Urine protein screening	1	1	1
BUN/creatinine testing	1	1	1
Muscle and connective tissue			
Evaluation for muscle weakness	2	2	2
Physical activity counseling	1	1	1
Skeletal			
Bone density testing (adult women, all allogeneic transplant recipients and patients at high risk for bone loss)		1	+
Nervous system			
Neurologic clinical evaluation	+	1	1
Evaluate for cognitive development		1	1
Endocrine			
Thyroid function testing		1	1
Growth velocity in children		1	1
Gonadal function assessment (prepubertal men and women)	1	1	1
Gonadal function assessment (postpubertal women)		1	+

Recommended Screening/Prevention	6 mo	1yr	Annually
Gonadal function assessment (postpubertal men)		+	+
Muco-cutaneous			
Skin self-exam and sun exposure counseling	1	1	1
Gynecologic exam in women	+	1	1
Second cancers			
Second cancer vigilance counseling		1	1
Screening for second cancers		1	1
Psychosocial			
Psychosocial/QOL clinical assessment	1	1	1
Sexual function assessment	1	1	1

1 = recommended for all transplant recipients

2 = recommended for any patient with ongoing chronic GVHD or immunosuppression

+ = reassessment recommended for abnormal testing in a previous time period or for new signs/symptoms