Chapter 41
Psychiatric Complications

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Introduction

Patients are generally counseled extensively regarding the medical impact of hematopoietic cell transplantation (HCT). They attend educational visits with providers and transplant staff, supplemented by information available on the Internet, from special interest groups such as the American Cancer Society, the Leukemia & Lymphoma Society, the BMT InfoNet, and BetheMatch™, and from their referring providers. A great deal of attention is focused on determining performance status and the potential risk of the procedure based upon the patient's preexisting comorbid medical conditions. However, less attention is paid to the potential psychological and psychiatric complications of the HCT procedure.

A wide variety of psychiatric concerns can develop in the HCT patient, ranging from delirium and psychosis to depression, insomnia, and anxiety. This chapter will discuss the diagnosis of and intervention for the most commonly encountered psychiatric complications in this patient population.

Delirium and Altered Mental Status

While HCT patients undergo daily laboratory and physical evaluations, close attention must also be paid to mental status changes. Delirium, one manifestation of altered mental status or encephalopathy, is common in the hospital setting. It is estimated that up to 50% of patients undergoing HCT will develop delirium in the month following transplantation, with the first 2 weeks being the time of highest

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risk [1]. Delirium confers risk of prolonged hospital stay, functional and cognitive decline, and mortality [2–4]. While delirium is increasingly recognized as a serious complication of hospitalization in the medically ill, *the great majority of patients with delirium are underrecognized*. Presentation may be subtle, necessitating careful and thorough examination of the patient. Changes in level of arousal, slowed cognition, abrupt mood, or behavioral changes, as well as agitation or new-onset hallucinations, should trigger an immediate mental status evaluation. If delirium is identified, workup for the underlying medical etiologies should promptly ensue.

1. Evaluation and diagnosis
    a. Delirium is defined by the new onset of fluctuating disorientation, disturbance of memory, language, perception, visuospatial abilities, attention, and level of awareness over the course of hours to days.
    b. There are three subtypes: hypoactive, hyperactive, and mixed.
        i. Patients with hypoactive delirium are commonly undiagnosed because they present as primarily withdrawn and they are assumed to be depressed.
        ii. Hyperactive and mixed delirium cases present with agitation or obvious fluctuations in mental status and are easier to detect because of the disruptive nature of symptoms.
    c. At a minimum, mental status evaluation should include explicit testing of orientation and attention as well as short-term and long-term memory.
    d. Collateral information from nursing staff and family is recommended to discern the patient's baseline and to detect fluctuations.
    e. Consider the use of structured delirium assessment tools such as the Confusion Assessment Method (CAM) or Delirium Rating Scale-98.
2. Risk factors and underlying etiologies
    a. Pretransplant executive dysfunction, which could arise from a history of neurologic injury or neurocognitive disorder, is predictive of development of posttransplant delirium [1].
    b. Alcohol or benzodiazepine withdrawal can cause delirium in patients with physiologic dependence and is suggested by autonomic instability, tremulousness, and diaphoresis.
    c. Sleep-wake cycle disruptions, electrolyte and metabolic disturbances, hypoxia, dehydration, nutritional deficiencies, and infection are common causes.
    d. The medication list should be an area of focus. Deliriogenic medications often precipitate or contribute to delirium, especially when there is polypharmacy.
        i. Opioids for pain control, including patient controlled analgesia (PCA) in patients with mucositis
        ii. Anticholinergic or antihistamine agents used for vertigo and chemotherapy-induced nausea and vomiting (CINV).

iii. High-dose steroids for nausea or as part of a chemotherapy regimen.
iv. Use of benzodiazepines for nausea, anxiety, or sleep.
v. Impairment of hepatic or renal clearance results in accumulation of medications and can precipitate delirium.

e. It is important to rapidly exclude life-threatening etiologies.

i. Imaging for neurologic insults, such as infarct, hemorrhage, or posterior reversible encephalopathy syndrome (PRES).
ii. Lumbar puncture and cerebrospinal fluid testing to evaluate for central nervous system (CNS) infection.
iii. Complete blood cell count (CBC) and blood culture to evaluate for sepsis.
iv. Electroencephalogram (EEG) to evaluate for seizures.
v. Vital signs and Clinical Instrument for Withdrawal Assessment (CIWA) to evaluate for alcohol or benzodiazepine withdrawal.

f. Once immediately life-threatening etiologies of delirium are ruled out, other serious conditions, such as graft-versus-host disease, should be systematically investigated.
g. Transplant pharmacy specialists can provide critical insights in identifying pharmacologic causes of delirium.

3. Management

a. Identify and address the underlying causes.
b. Nonpharmacologic management:

i. Eliminate any noncritical deliriogenic medications and dose adjust necessary medications for renal and hepatic function.
ii. Frequent reorientation with clock, calendar, and familiar objects at the bedside.
iii. Mobilize and ambulate as soon and as much as safely possible.
iv. Address any sensory limitations by providing patient with glasses or hearing aids.
v. Behavioral interventions to promote normal sleep-wake cycle.

c. Pharmacologic management of delirium with antipsychotics are standard of care but not Food and Drug Administration (FDA) approved

i. Haloperidol (Haldol®)

- The gold standard of treatment, not highly sedating. Available PO (oral), IV (intravenous), and IM (intramuscular).
- Recommended dosing: 0.25–1 mg IV every 4 hours PRN (as needed).
  - Can give as often as every 30 minutes IV in cases of severe agitation.
  - Convert to PO as soon as possible.
  - Maximum daily dose 20 mg, but consider lower maximums in the frail or elderly.

- Cardiac monitoring is required while haloperidol is administered IV due to association with prolonged QTc and torsades de pointes; do not administer if QTc is >500 ms.

ii. Olanzapine (Zyprexa®)

- Antiemetic, anxiolytic, and sedating properties. Available PO and IM.
- Recommended dosing: 2.5–5 mg PO every 4 hours PRN.
  - Maximum daily dose 10 mg.
  - Do not combine with parenteral benzodiazepines due to risk of respiratory compromise.

iii. Quetiapine (Seroquel®)

- Sedating and anxiolytic. Only available PO.
- Recommended dosing: 12.5–25 mg PO every 4 hours PRN.
  - Maximum daily dose of 150 mg.

iv. Risperidone (Risperdal®)

- Modest sedation. Only available PO.
- Recommended dosing: 0.25–0.5 mg PO every 4 hours PRN.
  - Maximum daily dose of 2 mg.

v. Benzodiazepines are not recommended as monotherapy for delirium unless etiology is due to seizures, alcohol withdrawal, or benzodiazepine withdrawal.

- Lorazepam (Ativan®)
  - Renally excreted, available PO, IM, or IV.
  - Recommended dosing: 0.25–1 mg every 1–2 hours.
  - Maximum daily dose of 10 mg.

Depression

Major depression is a psychiatric disorder characterized by a sustained period of low mood or anhedonia, feelings of guilt or hopelessness, anorexia, lack of energy, difficulty concentrating, slowed thought or movement, and, sometimes, recurrent thoughts of death or suicide. Prevalence of depression is estimated to be as high as 30% in the 5 years following HCT in certain populations [5]. Depression is a complex disorder caused by biological, psychological, and social factors. It impacts quality of life (QOL) and worsens treatment outcomes. There is some evidence that pretransplant depression is associated with slower recovery of posttransplant white blood cell count [6, 7]. It is important to distinguish major depression from

adjustment disorder, grief, and hypoactive delirium since the treatment of each of these entities is distinct.

1. Diagnosis
    a. Depression does not impact orientation or attention; hypoactive delirium should be considered for any abrupt mood changes with fluctuating sensorium.
    b. To meet criteria for major depression, a patient must experience at least five depressive symptoms for a period of at least 2 weeks [8].
    c. At least one of the symptoms must be depressed mood or loss of interest for the majority of the day most days of the week.
    d. Other symptoms include poor appetite, insomnia or hypersomnia, changes or slowing in psychomotor activity, fatigue, feelings of worthlessness or inappropriate guilt, indecisiveness or impaired concentration, and thoughts of death or suicide.
    e. Other signs of depression may include low volume speech, social withdrawal, poor eye contact, and increased touching of the face but are not included in the formal diagnostic criteria.
    f. Severe depression may include mood-congruent auditory hallucinations or delusions of guilt, ruin, or poverty. Visual hallucinations are atypical and should prompt a medical workup, especially if disorientation is also present.
    g. Grief reactions may resemble major depression, but sadness tends to come and go, centers around the loss, and patients have intact self-esteem, presence of positive emotions, or capacity for joy.
    h. An adjustment disorder may have some symptoms of depression but has a trigger and does not meet full criteria for major depression.
    i. Screening for a history of mania or hypomania is important to exclude a diagnosis of bipolar disorder. Treatment of bipolar depression is different from unipolar depression.
2. Treatment
    a. For mild depression, counseling is often sufficient [9]. For patients with moderate to severe depression, antidepressant medication should be prescribed in addition to therapy.
    b. Selective serotonin reuptake inhibitors (SSRIs) are first-line due to the tolerability and relatively benign side effect profile.
    c. Medications may take up to 4 or more weeks for effect. Milder cases may respond as early as 2 weeks [10].
        i. Side effects of antidepressant medications commonly include nausea, diarrhea, headaches, weight gain, and sexual dysfunction.
        ii. Syndrome of inappropriate antidiuretic hormone (SIADH), platelet dysfunction, and gastrointestinal (GI) bleeds, though less common, are also potential risks.

Table 41.1 Selection of antidepressants for medical comorbidities [18–23]

Patient condition	Suggested antidepressant drug of choice
Depression with anxious distress	SSRI
Depression with lethargy and amotivation	Fluoxetine (Prozac®), bupropion (Wellbutrin®), or venlafaxine (Effexor®)
Preexisting cardiac disease	
Congestive heart failure/coronary artery disease	SSRI, bupropion (Wellbutrin®)
Heart block	SSRI, bupropion (Wellbutrin®)
Hypertension	SSRI
Hypotension	Venlafaxine (Effexor®), SSRI, bupropion (Wellbutrin®)
Neurologic disease	
Parkinson's disease	SSRI
Cerebrovascular accident (stroke)	SSRI
Migraine headaches	Amitriptyline (Elavil®), venlafaxine (Effexor®)
Miscellaneous	
Prostatic hyperplasia	Bupropion (Wellbutrin®), SSRI [excluding paroxetine (Paxil®)]
Irritable bowel syndrome	Amitriptyline (Elavil®), desipramine (Norpramin®)
Diabetes	SSRI
HIV	Mirtazapine (Remeron®)
Thrombocytopenia and leukopenia	Bupropion (Wellbutrin®)
Sexual dysfunction	Bupropion (Wellbutrin®)

SSRI selective serotonin reuptake inhibitors, *HIV* human immunodeficiency virus

iii. Selection of the agent is based upon side effect profile, drug-drug interactions, history of positive response, cost, and concurrent medical conditions (see Tables 41.1 and 41.2).
iv. Geriatric and HCT patients with complicated medical histories should begin at 50% dose with slower increases, no more often than every 3–7 days.
v. Patients with psychomotor retardation and neurovegetative symptoms such as anorexia, profound fatigue, and excess sleep may respond earlier.
vi. Partial response may indicate a need for dose escalation, while no response suggests the need to augment or change medications.
vii. If switching antidepressants, a 1- to 2-week washout is recommended for most agents, and up to 5 weeks for fluoxetine. Consider a cross-taper if the patient requires more aggressive treatment.
viii. When treatment response is achieved, medication should be continued for a minimum of 6 months. If the patient has experienced a depressive episode before, discontinuing medications may result in recurrence of depression in the future.

Table 41.2 Select antidepressants and dosing (consider starting at 50% dose if elderly or debilitated) [24]

Drug	Starting dose (daily)	Dosing range (daily)	Comments
Selective serotonin reuptake inhibitors (SSRI)			
Citalopram (Celexa®)	10–20 mg	20–40 mg	QTc prolongation increased with doses > 40 mg/day with a minimal increase in benefit
Escitalopram (Lexapro®)	10 mg	10–20 mg	Doses above 20 mg may confer little additional benefit
Fluoxetine (Prozac®)	10–20 mg	10–80 mg	More activating than other SSRIs
Paroxetine (Paxil®)	10–20 mg	20–50 mg	Possibly more anxiolytic than other SSRIs but more anticholinergic
Sertraline (Zoloft®)	25–50 mg	50–200 mg	High incidence of GI side effects
Serotonin norepinephrine reuptake inhibitors (SNRI)			
Duloxetine (Cymbalta®)	40–60 mg	60–120 mg	Dosed twice daily, best evidence for diminishing neuropathic pain as collateral benefit
Venlafaxine (Effexor®)	37.5–75 mg	150–225 mg	High risk of discontinuation syndrome, associated with hypertension at higher doses
Desvenlafaxine (Pristiq®)	25–50 mg	50–100 mg	Associated with hypertension
Levomilnacipran (Fetzima®)	20–40 mg	40–120 mg	May cause tachycardia
Other antidepressant agents			
Amitriptyline (Elavil®)	25–50 mg		Anticholinergic, sedating TCA
Bupropion (Wellbutrin®)	150 mg	300 mg	Many formulations, no sexual side effects, activating, helps with tobacco cessation
Methylphenidate (Ritalin®)	5 mg	15–30 mg	Divided TID dosing. Stimulant, off-label use
Mirtazapine (Remeron®)	15 mg	15–45 mg	May diminish nausea and increase appetite
Nortriptyline (Pamelor®)	50–75 mg	75–150 mg	Least anticholinergic TCA
Vilazodone (Viibryd®)	10 mg	20–40 mg	Take with food
Vortioxetine (Trintellix®)	5–10 mg	10–20 mg	Serotonin modulator

TCA tricyclic antidepressant

- If discontinuing an antidepressant, gradual taper should occur to avoid antidepressant discontinuation syndrome.
- Abrupt cessation results in flu-like symptoms, gastrointestinal distress, emotional lability, anxiety, agitation, as well as sensory and sleep disturbances, which can last 1–2 weeks [11].

- If discontinuation symptoms are significant, the agent can be reinstituted with a more gradual taper or changed to an agent with a longer half-life, such as fluoxetine, prior to tapering [12].

d. Grief and adjustment disorders are not typically treated with medication. Referral to grief counseling or psychotherapy is recommended.

Anxiety

Stress, in small amounts, may serve an adaptive purpose in motivating patients to adhere to treatment and follow-up. However, distress or excessive anxiety can be functionally impairing and may drastically impact QOL.

1. Anxiety disorders are among the most common mental health diagnoses in the general population.
2. Patients may present with generalized anxiety or panic attacks, episodes of intense physical and/or cognitive discomfort that typically subside within 30 minutes.
3. Anxiety may manifest as a stand-alone diagnosis or as part of a depressive illness. It may also be seen as hyperarousal in posttraumatic stress disorder.
4. Fortunately, psychotherapy, SSRIs, and serotonin norepinephrine reuptake inhibitors (SNRIs) provide relief of anxiety due to a broad spectrum of causes.

   a. Pharmacologic treatment is initiated in a similar manner as for a depressive illness.
   b. If anxiety is only intermittent, as can be the case with panic attacks, judicious use of a benzodiazepine with rapid onset can be considered for as-needed use only.
   c. Refer to Tables 41.2 and 41.3 for additional information on SSRIs, SNRIs, and select anxiolytic medications.

Sleep Disorders

Sleep disturbances are common in the HCT population. About 26% of patients meet clinical diagnostic criteria for insomnia in the first 100 days and many patients still report sleep difficulties at 1 year posttransplant [13–15]. In the oncologic setting, sleep difficulties may be secondary to the routines of the hospital setting or medication effects, such as urinary frequency due to diuretics or activation from steroids. These disorders can also result from untreated psychiatric conditions, such as depression or anxiety. The majority of oncology patients with insomnia are not asked about and do not discuss the problem with their healthcare providers. The consequences of insomnia can include impaired cognitive functioning, decreased

Table 41.3 Characteristics of selected anxiolytics and hypnotics [24]

Drug	Mechanism of action	Common dose	Half-life (hours)	Notes
Diphenhydramine (Benadryl®)	Antihistamine	25–50 mg HS	2–8 Elderly: 13.5	Potentially deliriogenic
Hydroxyzine (Atarax®)	Antihistamine	10–50 mg TID PRN	14–20	Anxiolytic; potentially deliriogenic
Eszopiclone (Lunesta®)	Non-BZD; interacts with $GABA_A$ receptor	Adult: 1–3 mg HS Elderly: 1–2 mg HS	6	High-fat meal delays absorption
Ramelteon (Rozerem®)	Melatonin receptor (MT1 and MT2) agonist	8 mg HS	1–5	High-fat meal delays absorption
Temazepam (Restoril®)	BZD, acting on benzodiazepine receptor	7.5–30 mg HS	8.8	Serum level may be increased by grapefruit juice
Zolpidem (Ambien®)	Non-BZD; interacting with $GABA_A$ receptor	10 mg HS, 12.5 mg ER Elderly and Women: 5–10 mg HS, 6.25 mg ER	2–3	Food may delay absorption
Alprazolam (Xanax®)	BZD	0.25–1 mg TID PRN	6–12	Fast onset, deliriogenic
Lorazepam (Ativan®)	BZD	0.5–2 mg TID PRN	12–18	Deliriogenic
Clonazepam (Klonopin®)	BZD	0.25–1 mg BID PRN	30–40	Deliriogenic
Buspirone (Buspar®)	Non-BDZ; $5\text{-}HT_{1A}$ agonist	10–60 mg divided BID to TID	2–3	Takes 1–2 weeks to have effects

HS at bedtime, *TID* three times daily, *PRN* as needed, *BZD* benzodiazepine, *GABA* γ-aminobutyric acid, *ER* extended release, *BID* two times daily

adherence to treatment, increased accidents and falls, fatigue, increased perception of physical pain, increased risk of developing depression, and overall decline in QOL [16]. For these reasons, patients should be screened for insomnia and offered appropriate treatment.

1. Diagnosis
    a. The International Classification of Sleep Disorders-3 (ICSD-3) characterizes insomnia as follows:
        i. A disruption of sleep lasting 30 minutes or more when falling asleep, awakening during the night, or awakening earlier in the morning than intended.

ii. The disturbance must occur at least three times per week and result in compromise of daytime functioning such as fatigue, anergia, excessive daytime sleepiness, social or vocational impairment, accidents, poor concentration, or behavioral changes.
iii. Short-term insomnia lasts less than 3 months. Chronic insomnia lasts for 3 or more months.

2. Treatment

a. Nonpharmacologic management includes stimulus control, relaxation training, sleep restriction, biofeedback, and/or referral to cognitive-behavioral therapy for insomnia (CBTI)
b. Pharmacologic interventions should be undertaken if insomnia persists despite nonpharmacologic interventions.
c. Untreated insomnia may contribute to delirium, but aggressive treatment with sedative/hypnotics can also result in delirium.
d. Medication often does not restore normal sleep architecture and most result in diminished levels of deep sleep and increased periods of REM sleep.
e. Of the available agents, ramelteon (Rozerem®) has the greatest likelihood of providing a sleep cycle more near to that which occurs without medication assistance.
f. See Table 41.3 for treatment options and dosing recommendations.

Mania, Psychosis, and Substance Abuse

1. While less common, HCT patients may develop mania and/or psychosis.
2. Symptoms of mania include euphoria or irritability, sleeplessness, rapid speech, distractibility, grandiosity, increased goal-directed activity, impulsivity, and, sometimes, hypersexuality.
3. Psychosis often includes paranoia, hallucinations, and disorganization of thought.
4. Delirium, which can overlap, would have a fluctuating course and should first be excluded.
5. If delirium is not felt to account for symptoms, medications should be examined next.

a. Steroids, stimulants, and antidepressant medications can precipitate mania or psychosis, especially in patients with an underlying bipolar spectrum disorder or primary psychotic illness.
b. Consider psychiatric consultation for additional assistance in management.

6. In patients with a history of steroid-induced mania or psychosis requiring a course of high-dose steroids, consider initiation of a prophylactic agent, such as olanzapine (Zyprexa®) 5–10 mg PO nightly.

7. If treatment-emergent mania occurs, decrease or discontinue the offending agent if possible.
8. Even if there is a history of depression, when a patient demonstrates manic symptoms, antidepressants should be discontinued and a mood-stabilizing medication started in exchange.
    a. Antipsychotic medications are fairly well-tolerated, effective mood stabilizing agents.
    b. Valproic acid (Depakote®) and lithium are also standard mood-stabilizing medications but can become toxic if not closely monitored.
        i. With close monitoring, these medications can also be safe if a patient has a history of robust response and/or intolerability of other agents.
9. If a patient exhibits unexpected behavioral changes not attributable to delirium, an underlying psychiatric diagnosis or medication effect, substance abuse should be considered on the differential and a urine drug screen should be obtained.
    a. Patients may use illicit substances to cope with disease symptoms, medication side effects, or emotional distress.
    b. Identifying and treating anxiety or depression, if present, may aid in achieving sobriety.
    c. Abrupt discontinuation of prescribed benzodiazepines or opioids is not recommended as an initial step due to risks of withdrawal.
    d. Referral to community sobriety support resources and collaboration with an addiction specialist is recommended in more complicated cases.

Drug Interactions and Dose Adjustments

1. Many psychotropic medications have drug interactions, the most relevant of which involve the CYP450 family of hepatic enzymes.
    a. The inhibition or induction of these enzymes can result in adverse drug reactions, toxicities, or reduced medication efficacy.
    b. Select agents' potential for interacting with specific enzymes is listed in Table 41.4. Weak (W) interactions are not clinically relevant, while moderate (M) and strong (S) interactions should be discussed with a pharmacist for potential dose adjustments.
2. The intent in medication dosing in patients with potential drug interactions or organ dysfunction is to adjust the dose to one that achieves a comparable whole body or receptor targeted dose as that seen in individuals with normal organ function.
    a. Once the agent is initiated, dose titration should occur at slower intervals (approximately 1.5–2 times longer) to allow the patient to reach a steady state blood concentration and allow both clinical effects and side effects to be assessed prior to further dose titration (see Table 41.5).

Table 41.4 Drug interactions involving the CYP450 families of enzymes [25–28]

Drug	1A2	2A6	2B6	2C8	2C9	2C19	2D6	2E1	3A4
Bupropion (Wellbutrin®)	–	–	–	–	–	–	W	–	–
Citalopram (Celexa®)	W	–	W	–	–	W	W	–	–
Desipramine (Norpramin®)	–	M	M	–	–	–	M	W	M
Diphenhydramine (Benadryl®)	–	–	–	–	–	–	M	–	–
Duloxetine (Cymbalta®)	–	–	–	–	–	–	M	–	–
Escitalopram (Lexapro®)	–	–	–	–	–	–	W	–	–
Eszopiclone (Lunesta®)	–	–	–	–	–	–	–	–	–
Fluoxetine (Prozac®)	M	–	W	–	W	M	S	–	W
Haloperidol (Haldol®)	–	–	–	–	–	–	M	–	M
Mirtazapine (Remeron®)	W	–	–	–	–	–	–	–	W
Olanzapine (Zyprexa®)	W	–	–	–	W	W	W	–	W
Paroxetine (Paxil®)	W	–	M	–	W	W	S	–	W
Quetiapine (Seroquel®)	–	–	–	–	–	–	–	–	–
Ramelteon (Rozerem®)	–	–	–	–	–	–	–	–	–
Risperidone (Risperdal®)	–	–	–	–	–	–	W	–	W
Sertraline (Zoloft®)	W	–	M	W	W	M	M	–	M
Temazepam (Restoril®)	–	–	–	–	–	–	–	–	–
Venlafaxine (Effexor®)	–	–	W	–	–	–	W	–	W
Zolpidem (Ambien®)	–	–	–	–	–	–	–	–	–

W = weak, M = moderate, S = strong

Table 41.5 Suggested dose adjustments for estimated renal function (mL/min) and degree of hepatic dysfunction [24]

	Renal dysfunction (estimated creatinine clearance in mL/min)			Hepatic dysfunction		
Drug	*30–50*	*10–30*	*< 10 and dialysis*	*Mild*	*Moderate*	*Severe*
Bupropion (Wellbutrin®)	None	None	50%	None	Consider ↓ 25%	75 mg maximum
Citalopram (Celexa®)	None	None	None	None	↓ 25%	↓ 50%
Diphenhydramine (Benadryl®)	None	↓ 25%	↓ 50%	None	↓ 25 %	↓ 50%
Duloxetine (Cymbalta®)	60 mg maximum	Do not use	Do not use	None	Do not use	Do not use
Escitalopram (Lexapro®)	None	None	None	None	↓ 25%	50%
Eszopiclone (Lunesta®)	None	None	None	None	None	1 mg, max dose 2 mg
Fluoxetine (Prozac®)	None	None	None	None	↓ 25%	↓ 50%
Haloperidol (Haldol®)	None	None	None	None	None	↓ 50%
Mirtazapine (Remeron®)	None	↓ 30%	↓ 50%	None	None	↓ 30%

Table 41.5 (continued)

	Renal dysfunction (estimated creatinine clearance in mL/min)			Hepatic dysfunction		
Olanzapine (Zyprexa®)	None	None	None	None	None	None
Paroxetine (Paxil®)	None	None	None	None	↓ 25%	↓ 50%
Quetiapine (Seroquel®)	None	None	None	None	↓ 30%	↓ 50%
Ramelteon (Rozerem®)	None	None	None	None	None	Do not use
Risperidone (Risperdal®)	None	↓ 25%	↓ 50%	None	None	↓ 40%
Sertraline (Zoloft®)	None	None	None	None	↓ 25%	↓ 50%
Temazepam (Restoril®)	↓ 25%	↓ 50%	↓ 90%	None	None	None
Venlafaxine (Effexor®)	↓ 25%	↓ 50%	↓ 75%	None	↓ 30%	↓ 90%
Zolpidem (Ambien®)	None	None	↓ 50%	None	None	↓ 50%

↓ = decrease dose by

Capacity

1. Legal capacity is not a gray area – a patient is either lawfully entitled or not entitled to make a given decision about his or her health care.
2. In order to demonstrate capacity, a patient must meet specific criteria. The criteria set forth by Appelbaum and Grisso [17] are commonly utilized. A patient must:
   a. Express a clear, consistent choice.
   b. Understand the relevant information provided.
   c. Reason and weigh the risks/benefits.
   d. Recognize the consequences of the current circumstances.
3. Any physician is empowered to complete a decision-making capacity evaluation.
   a. Multiple formalized tools are available.
4. The level of reasoning and understanding demonstrated by a patient should be commensurate to the risk entailed in the decision.
5. It should be noted that an inability to demonstrate capacity for one decision does not necessarily imply global incapacity; a patient may be able to designate a surrogate decision maker to assist.
6. Ideally, if a patient is determined to be incapacitated, the underlying etiology should be identified and, if possible, rectified in order to restore patient autonomy.
7. Sometimes, circumstances demand that capacity assessments are completed by a psychiatrist or obtained in conjunction with institutional ethics committees.

Psychiatric Consultation

Psychiatric consultation should be considered throughout the continuum of care of the HCT patient. Pre- and posttransplant consultation offers the possibility of optimizing a patient's medication to allow maximal stability throughout the transplant process and should be considered in any patient with a complicated psychotropic regimen, risk of serious medication interactions, or history of serious psychiatric illness. Consultation in the hospital should be considered at any time there is a psychiatric diagnostic or management question.

Collaborating with specialists, inpatient or outpatient, can both improve outcomes and help provide crucial psychosocial care for the HCT patient.

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