

From *CJON*, 21(5, Suppl.), 7–18:

Distress, Fatigue, and Sexuality

Understanding and treating concerns and symptoms in patients with multiple myeloma

Catamero et al.

FIGURE 1.

PATIENT EDUCATION TIP SHEET: ANXIETY AND DISTRESS

Many patients experience a variety of difficult emotions. Anxiety and distress are often observed at various times during cancer screenings, diagnosis, treatment, or recurrence.

- Anxiety is fear, dread, and uneasiness caused by stress.
- Distress is emotional, mental, social, or spiritual suffering. Patients may have feelings of vulnerability, sadness, depression, panic, and isolation.

For patients, anxiety may increase pain, affect sleep, and cause nausea and vomiting. Anxiety and distress may affect a patient's ability to cope with the diagnosis or treatment, which may lead to delays in treatment. Anxiety can substantially interfere with the quality of life of patients and their families.

SYMPTOMS OF ANXIETY AND DISTRESS

Uncontrolled worry, fear, or sorrow; trouble focusing or problem solving; muscle tension; trembling or shaking; restlessness; dry mouth; and irritability or anger

MANAGING THE SYMPTOMS

Do

- Remember that you are not alone.
- Take a time out—doing yoga, relaxing, and stepping back from the issue help to clear thoughts.
- Share feelings and fears.
- Caregivers should listen carefully and offer support. Do not deny or discount feelings. Encourage talking.
- It is okay to feel sad and frustrated.
- Get help through counseling and/or support groups.
- Use meditation, prayer, or other types of spiritual support if it helps.
- Exercise and walking can help, as well as yoga.
- Talk with your healthcare provider about using antidepressant medicines.
- Medications to treat myeloma, such as steroids, can make anxiety worse. Discuss your feelings with your treatment team.

Do not

- Keep feelings inside.
- Force someone to talk if they are not ready to.
- Blame yourself or another person for feeling fearful or anxious.
- Try to reason with a person whose fears and anxieties are severe; talk with the doctor about medicines and other kinds of help.

Note. Based on information from Holland & Alici, 2010; Jacobsen et al., 2006; Lamers et al., 2013; Pirl, 2004; Williams & Dale, 2006.

FIGURE 3.

PATIENT EDUCATION TIP SHEET: PREVENTING AND MANAGING FATIGUE

Cancer-related fatigue is characterized by a distressing, persistent, subjective sense of tiredness or exhaustion related to cancer or cancer treatment that is not proportional to recent activity and interferes with usual functioning. The symptoms affect physical, psychological, and social functioning, and can cause significant distress for patients and caregivers. Fatigue can become chronic, leading to isolation, loneliness, and deconditioning of the body.

SYMPTOMS OF FATIGUE

- Physical: An unrelenting feeling of tiredness or exhaustion that is not relieved by sleep
- Psychological: Absentmindedness, forgetfulness, difficulty communicating, unpleasant emotions, mental exhaustion, and impaired concentration and memory
- Social: Fatigue that limits ability to socialize, impairs relationships, and leads to feeling isolated or lonely

Always report your symptoms to your healthcare team.

MANAGING THE SYMPTOMS

The following suggestions may help with symptoms of fatigue. Always check with your healthcare provider before taking new medications or starting an exercise program.

- Nonpharmacologic: Exercise, cognitive behavioral interventions, sleep interventions, ginseng, management of other symptoms, massage/aromatherapy, mindfulness-based stress reduction, multicomponent rehabilitative intervention, psychoeducational interventions, and yoga
- Pharmacologic: Corticosteroids (low doses) and erythropoiesis-stimulating agents
- Other: Blood transfusions

Note. Based on information from Oncology Nursing Society, 2017.

FIGURE 2.
HEALTHCARE PROVIDER TIP SHEET: PREVENTING AND MANAGING FATIGUE

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ASSESSMENT

Check vital signs, testosterone levels, thyroid levels, complete blood count with differential, electrolytes, and liver and kidney function; check for hyponatremia and other signs of dehydration (skin turgor); assess for depression, general appearance, and affect; check for cognitive impairments and infection; assess for muscle weakness; and involve caregivers and/or family members with assessments and interventions.

MANAGING THE SYMPTOMS

The following nonpharmacologic suggestions may help with symptoms of fatigue: Exercise, cognitive behavioral interventions, sleep interventions, ginseng, management of other symptoms, massage/aromatherapy, mindfulness-based stress reduction, multicomponent rehabilitative intervention, psychoeducational interventions, and yoga.

Note. Based on information from Oncology Nursing Society, 2017.

FIGURE 5.
PATIENT EDUCATION TIP SHEET: DISCUSSIONS ABOUT CONTINUING TREATMENT AFTER CORTICOSTEROID SIDE EFFECTS

Steroids commonly prescribed for multiple myeloma treatment include dexamethasone, prednisone, prednisolone, and methylprednisolone.

STRATEGIES FOR CONTINUING TREATMENT

- Steroids are commonly taken on a highly regular schedule (e.g., once per week). Side effects commonly follow a predictable pattern, particularly those affecting mood and energy.
- Maintain a symptom journal to help identify the pattern of any side effects and aid recall of side effects to discuss with your healthcare provider. Learning the pattern of side effects allows you to adapt your lifestyle to accommodate mood and energy levels.
- Patients may find that exercise or simple activities can help “burn off” the hyperactivity or jitters that steroids may cause. Relaxation, meditation, or mindfulness techniques can also help.
- Caregivers may identify mood and behavior changes in patients with multiple myeloma on steroids in advance of the patient. Caregivers should talk with the healthcare provider if they are concerned at the degree of these changes.
- Steroids should be taken with food.
- Patients should take an over-the-counter or prescription medication to prevent gastrointestinal issues.

- Steroids can cause sleeplessness and should be taken early in the morning. In some cases, the increased energy caused by taking steroids has a delayed effect. As such, taking steroids in the evening may allow improved sleep patterns.
- Be aware of symptoms of infection: a fever of more than 100.5°F (38°C), shaking chills even without fever, dizziness, shortness of breath, and low blood pressure. Contact your healthcare provider if these symptoms occur.
- Medications to prevent infection, shingles (small blister-like rash anywhere on the body; usually painful with or without rash), and thrush (white coating on tongue, bad taste, and painful swallowing) may also be prescribed.
- Know the signs and symptoms of high and low blood sugar (e.g., aggressiveness, confusion, difficulty waking, increased thirst, frequent urination). If you have diabetes, consult with your endocrinologist or diabetes educator before starting treatment with steroids.
- Always report any concerning symptoms to your healthcare team as soon as they occur.

Note. From “Steroid-Associated Side Effects: A Symptom Management Update on Multiple Myeloma Treatment,” by T. King & B. Faiman, 2017, *Clinical Journal of Oncology Nursing*, 21, pp. 242–243. Copyright 2017 by Oncology Nursing Society. Adapted with permission.

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FIGURE 4.**PATIENT EDUCATION TIP SHEET: COMMON SIDE EFFECTS OF CORTICOSTEROIDS RELATED TO DISTRESS, FATIGUE, AND SEXUALITY****NEUROPSYCHIATRIC**

Cognitive, behavioral, and mood changes

- Risk factors include higher doses and a history of neuropsychiatric effects from steroids and older age.
- Mania-like symptoms are more commonly associated with short-term use and depressive symptoms with long-term use.
- Hyperactivity and jitters are more closely associated with days taking steroids, and they abate on nonsteroid days.
- Steroid psychosis is rare, but patients with overt mood changes are at risk for suicide and should be monitored.
- Early recognition, diagnosis, and treatment of neuropsychiatric complications in patients receiving steroids are key to management.
- Educate patient and family to possible neuropsychiatric effects.
- Monitor patients for changes in mood, cognition, or behavior using an appropriate screening tool, such as the Hospital Anxiety and Depression Scale.
- Dose reduction or discontinuation in the presence of neuropsychiatric effects is the most effective management.
- Tapering doses can be useful to minimize the severity of mood changes (steroid "highs and lows").
- The use of antipsychotic or mood stabilizers may be indicated.
- Avoid concomitant clarithromycin, which can increase circulating levels of corticosteroids and increase risk of neuropsychiatric effects.
- Consider referral to support groups and psychosocial services to aid coping.
- Relaxation, mindfulness techniques, and exercise may aid coping.

CONSTITUTIONAL

"Let-down effect"

- More commonly associated with days immediately after taking steroids
- Characterized by weakness and fatigue
- Tapering steroid doses may help.
- Educate patient to adapt lifestyle and activities around energy levels.

Flushing or sweating

- Assess for other causes, such as infection or cardiovascular abnormalities, and manage appropriately.
- Educate on appropriate clothing and maintaining hydration.

Insomnia

- More common on nights after taking steroids
- Educate to take dose in the morning.
- Educate patients about sleep hygiene practices (e.g., avoiding caffeine, alcohol, and electronic screens before bedtime). Establish an appropriate sleep environment, and suggest meditation or relaxation techniques.
- Consider pharmacologic interventions if insomnia is severe or ongoing.

SEXUAL DYSFUNCTION

Lowered libido

- Initiate assessments or conversations around sexual function and intimacy to help identify potential issues.
- May require dose reduction or hormone therapy

Note. From "Steroid-Associated Side Effects: A Symptom Management Update on Multiple Myeloma Treatment," by T. King & B. Faiman, 2017, *Clinical Journal of Oncology Nursing*, 21, pp. 242–243. Copyright 2017 by Oncology Nursing Society. Adapted with permission.

FIGURE 6.
PATIENT EDUCATION TIP SHEET: TALKING ABOUT SEXUALITY AND INTIMACY

Sexual dysfunction is not the result of normal aging. Rather, it occurs because of physical illness, medications, psychological factors, or some combination of these conditions. After discussing these topics and questions with your healthcare provider, be sure to seek appropriate referrals.

TOPICS TO DISCUSS WITH YOUR HEALTHCARE PROVIDER

It is important to discuss sexual concerns with your healthcare provider. The following are several topics to discuss if you are having difficulties engaging in sexual activity:

- I am not interested in having sexual intercourse but would like to be.
- Vaginal dryness
- Fearful of being touched by your partner
- Inability to obtain or maintain an erection during sexual intercourse
- Inability to achieve an orgasm
- Pain associated with intercourse

QUESTIONS TO DISCUSS WITH YOUR HEALTHCARE PROVIDER

- How will my treatment affect my sexual activity?
- Are these changes in my sexual function normal?
- What precautions do I need to take while I am on treatment for multiple myeloma or after stem cell transplantation?
- Is oral sex safe while on therapy? What precautions should I take?

Note. Based on information from Clayton & Ramamurthy, 2008.

FIGURE 8.
SPECIALIST REFERRAL NETWORK FOR SEXUAL DYSFUNCTION

The oncologist and healthcare team should build a referral network of specialists for the treatment of sexual dysfunction. The type of referral will depend on the problem with which the patient presents. A comprehensive referral network should include the following:

- A mental health professional who provides sex therapy and sexual counseling
- A gynecologist who has expertise in assessing and treating pain with sexual activity or one who can help women make decisions about hormone replacement therapy after cancer
- An urologist who has specialized knowledge and skill regarding problems of the male and female urinary tract and the male reproductive organs, and who provides medical treatment for loss of sexual desire and erectile dysfunction
- An endocrinologist who treats the deficiency or excess production of hormones causing diseases such as diabetes, thyroid diseases, and menopause
- A sperm bank that can store semen samples for men about to begin cancer treatment that could potentially damage fertility
- An infertility clinic offering in vitro fertilization and donor gamete programs that has a good success rate and staff who are familiar with cancer-related infertility in men and women
- A genetics clinic that can counsel cancer survivors regarding their concerns about birth defects or cancer risks in their offspring

Note. From "Sexual Dysfunction in Multiple Myeloma: Survivorship Care Plan of the International Myeloma Foundation Nurse Leadership Board," by T.A. Richards, P.A. Bertolotti, D. Doss, & E.J. McCullagh, 2011, *Clinical Journal of Oncology Nursing*, 15, p. 62. Copyright 2011 by Oncology Nursing Society. Adapted with permission.

TABLE 1.
MULTIPLE MYELOMA FATIGUE ASSESSMENT

LABORATORY TEST/CONSIDERATION	EXPECTED RESULT IF CAUSE OF FATIGUE
Perform complete blood count.	Assess for low hemoglobin (anemia) and low white blood cell count (leukopenia).
Perform complete metabolic panel.	Assess for electrolyte abnormalities (hypokalemia, elevated creatinine, hypercalcemia), liver function (elevated transaminases), uncontrolled hyperglycemia, and dehydration.
Assess level of thyroid stimulating hormone.	Thyroid stimulating hormone can be high with hypothyroidism.
Assess sleep quality and duration.	Does the patient get adequate rest/sleep? Does the patient snore, have morning headaches, or have signs of sleep apnea? Does the patient experience frequent nighttime urination (nighttime diuretic use, enlarged prostate in men)?
Assess exercise patterns.	Does the patient exercise? Is exercise timed to be not too close to bedtime?
Assess for signs of infection.	Assess bladder and bowel habits, fever, and night sweats.
Evaluate disease markers.	Assess for multiple myeloma markers (SPEP, UPEP, serum free light chain assay) to rule out disease progression as a cause of fatigue.

Note. Based on information from National Comprehensive Cancer Network, 2017a.

FIGURE 7.**HEALTHCARE PROVIDER TIP SHEET: DISCUSSING SEXUAL DYSFUNCTION**

When discussing sexual dysfunction, it is important to remember that it is only a problem if the individual defines it as one. In addition, sexual activity is not required for a person or relationship to be normal.

USE OPEN-ENDED QUESTIONS

When discussing a patient's sexual function, a relaxed, nonjudgmental, and professional conversation can make an awkward topic easier to approach.

- "Patients with cancer may have problems with intercourse. Have you experienced sexual problems?"
- "Are you having any difficulties participating in sexual intercourse?"
- "Are you concerned about your sexual response?"
- "Has your level of sexual activity decreased or changed?"
- "Has your cancer diagnosis or treatment affected how you feel about yourself?"
- "Have you discussed your feelings with your partner?"
- "Do you have any questions or concerns about your sexual function?"

MANAGEMENT STRATEGIES

When managing sexual dysfunction, it is important to address other conditions, such as thyroid dysfunction, renal dysfunction, diabetes, cardiovascular disease, or depression, that may affect sexual function. In addition, the underlying causes of sexual dysfunction must be thoroughly assessed, including nerve root compression, peripheral neuropathy, opioid therapy, treatment effects, and medication side effects.

PHYSIOLOGIC INTERVENTIONS

- Vaginal dryness and dyspareunia: For first-line treatment, use nonhormonal vaginal moisturizers and lubricants. For second-line treatment, use vaginal estrogen replacement (low-dose estradiol rings or creams).
- Testosterone replacement (remains controversial)
- Erectile dysfunction: Use oral PDE-5 inhibitors (e.g., sildenafil), vacuum erection devices, and penile prosthesis.
- Avoid sexual intercourse if neutropenic (absolute neutrophil count less than

1,000) or thrombocytopenic (platelet count less than 50,000) to minimize risk of infection or bleeding.

PSYCHOLOGICAL INTERVENTIONS

- Cognitive behavioral stress management, relaxation training, sexual education, or sexual counseling
- Partner participation in therapy may improve intimacy and body image.
- To improve intimacy between partners, one technique is to redefine sexual activity as a continuum between no intercourse and intercourse. The purpose is to allow partners to become familiar with one another's sexual changes.

REFERRALS

Several areas of the health profession are concerned with sexuality and sexual function, including mental health professionals, sex therapists and counselors, gynecologists, urologists, endocrinologists, sperm banks, infertility clinics, and genetic counselors.

ADDITIONAL RESOURCES

CancerCare

- www.cancercares.org

Cancer Survival Palace

- www.cancersurvivorsplace.org

Livestrong Fertility

- www.livestrong.org/we-can-help/livestrong-fertility

National Cancer Institute Office of Cancer Survivorship

- <http://dccps.nci.nih.gov/ocs>

National Coalition for Cancer Survivorship

- www.canceradvocacy.org

Oncolink: OncoLife survivorship care plan

- www.oncolink.org/oncolife

Note. Based on information from Goncalves & Groninger, 2015; Richards et al., 2011; Tomlinson, 1998.

From *CJON*, 21(5, Suppl.), 19–36:

Renal, GI, and Peripheral Nerves

Evidence-based recommendations for the management of symptoms and care for patients with multiple myeloma

Faiman et al.

FIGURE 2.

HEALTH CONDITIONS OR DRUGS THAT LEAD TO ACUTE RENAL INSUFFICIENCY IN MULTIPLE MYELOMA

HEALTH CONDITIONS

- Diabetes
- Hypertension
- Advanced age
- Rhabdomyolysis (muscle injury or death leads to release of muscle contents, including creatinine, into the blood)
- Dehydration (from decreased fluid intake, fluid losses, or loop diuretics)
- Hypercalcemia
- Progressive disease or cast nephropathy (particularly light chains)

DRUGS

- Nonsteroidal anti-inflammatory agents, including cyclooxygenase-2 inhibitors
- Aminoglycoside antibiotics
- Radio-contrast dyes or IV contrast agents (e.g., for computed tomography scans)

OTHER FACTORS

- Increased intake of creatinine (high-protein meal)
- Sepsis, infection

Note. Based on information from Faiman et al., 2011; Thomas et al., 2015.

FIGURE 1.

CLASSIFICATION OF ACUTE RENAL FAILURE

RIFLE SYSTEM

- Risk: 1.5 times or greater baseline serum creatinine level or greater than 25% decrease in GFR
 - Urine output: Less than 0.5 ml/kg per hour for greater than 6 hours
- Injury: 2 times or greater baseline serum creatinine level or greater than 50% decrease in GFR
 - Urine output: Less than 0.5 ml/kg per hour for greater than 12 hours
- Failure: 3 times or greater baseline serum creatinine level or greater than 75% decrease in GFR, or serum creatinine level greater than 4 mg/dl with a rapid increase of 0.5 mg/dl within 48 hours
 - Urine output: Less than 0.3 ml/kg per hour for greater than 24 hours or anuria for greater than 12 hours
- Loss: Dialysis greater than 4 weeks
- End-stage renal disease: Dialysis greater than 3 months

ACUTE KIDNEY INJURY NETWORK CRITERIA

- Stage 1: 1.5–1.9 times baseline serum creatinine level or rise of 0.3 mg/dl or greater within 48 hours
 - Urine output: Less than 0.5 ml/kg per hour for greater than 6 hours
- Stage 2: 2–2.9 times baseline serum creatinine level
 - Urine output: Less than 0.5 ml/kg per hour for greater than 12 hours
- Stage 3: 3 times or greater baseline serum creatinine level or serum creatinine level 4 mg/dl or greater, with a rapid increase of 0.5 mg/dl within 48 hours, or need for renal replacement therapy
 - Urine output: Less than 0.3 ml/kg per hour for 24 hours or greater or anuria for more than 12 hours

KIDNEY DISEASE: IMPROVING GLOBAL OUTCOMES STAGING

- Stage 1: 1.5–1.99 times baseline serum creatinine level or 0.3 mg/dl or greater above baseline
 - Urine output: Less than 0.5 ml/kg per hour for greater than 6 hours
- Stage 2: 2–2.99 times baseline serum creatinine level
 - Urine output: Less than 0.5 ml/kg per hour for more than 12 hours
- Stage 3: 3 times or greater baseline serum creatinine level or serum creatinine level 4 mg/dl or greater, or need for renal replacement therapy
 - Urine output: Less than 0.3 ml/kg per hour for 24 hours or anuria for 12 hours or greater

GRADES 0–3 STAGING

- Grade 0: Decrease in GFR to less than 25% of baseline value
- Grade 1: Serum creatinine level increased by less than a factor of 2 with decrease in GFR from 25%–50%
- Grade 2: Serum creatinine level increased by more than a factor of 2 but no dialysis
- Grade 3: Serum creatinine level increased by more than a factor of 2 and dialysis

GFR—glomerular filtration rate

Note. To convert the values for creatinine to micromoles per liter, multiply by 88.4.

Note. Based on information from Dimopoulos, Sonneveld, et al., 2016; Hingorani, 2016; Khwaja, 2012; Thomas et al., 2015.

TABLE 1.
COMMON MEDICATIONS USED TO TREAT MM AND RENAL CONSIDERATIONS AS OF SEPTEMBER 2017

DRUG	INDICATION	RENAL CONSIDERATIONS	CLINICAL TRIAL DATA
Bortezomib	Newly diagnosed MM; relapsed, refractory MM	<ul style="list-style-type: none"> No dose reduction required Give after dialysis on dialysis days. 	Bridoux et al., 2016; Chanan-Khan et al., 2007; Dimopoulos, Roussou, et al., 2016; Palumbo et al., 2016; San Miguel et al., 2008; Zanetti et al., 2015; Ziogas et al., 2017
Carfilzomib	Newly diagnosed MM; relapsed MM	<ul style="list-style-type: none"> Increased creatinine may result. Hydration before and after treatment 	Badros et al., 2013; Kwon & Niesvizky, 2013; Mikhael et al., 2015; Shah, 2013; Stewart, 2015; Stewart et al., 2015
Daratumumab	Relapsed, refractory MM	<ul style="list-style-type: none"> No dose reduction required 	Laubach et al., 2017
Elotuzumab	Relapsed, refractory MM	<ul style="list-style-type: none"> No dose reduction required 	Jakubowiak et al., 2016; Lonial et al., 2015; Mateos et al., 2016
Ixazomib	Relapsed MM	<ul style="list-style-type: none"> Dose reduction for GFR less than 30 (3 mg on days 1, 8, and 15 every 28 days) Not dialyzable 	Richardson et al., 2015
Lenalidomide	Newly diagnosed MM; relapsed, refractory MM	<ul style="list-style-type: none"> Dose reduction according to the degree of renal insufficiency (days 1–21 of each 28-day cycle) CrCl greater than 60 ml/min, 25 mg/day CrCl 30–60 ml/min, 10 mg/day CrCl less than 30 ml/min (not requiring dialysis), 15 mg alternate days CrCl less than 30 ml/min (requiring dialysis), 5 mg/day after dialysis 	Dimopoulos, Cheung, et al., 2016; Weber et al., 2007
Melphalan	Newly diagnosed MM; relapsed, refractory MM	<ul style="list-style-type: none"> No dose reduction for conditioning treatment Dose reduction of as much as 50% for renal insufficiency (BUN 30 mg/dl or greater) for palliative treatment 	Palumbo et al., 2007, 2014; Roy et al., 2015
Panobinostat	Relapsed, refractory MM	<ul style="list-style-type: none"> Mild to severe renal impairment does not affect plasma concentration. Effect in patients with end-stage renal disease or on dialysis is not known. 	Libby et al., 2015; Richardson et al., 2016; San-Miguel et al., 2014
Pomalidomide	Relapsed, refractory MM	<ul style="list-style-type: none"> Dose reduction for renal insufficiency or dialysis: 3 mg daily for days 1–21 every 28 days Give after dialysis on dialysis days. 	Conticello et al., 2017; Richardson et al., 2014; Siegel et al., 2016
Thalidomide	Newly diagnosed MM; relapsed, refractory MM	<ul style="list-style-type: none"> No dose reductions required 	Palumbo et al., 2008; Rajkumar et al., 2006; Singhal et al., 1999
Valacyclovir, acyclovir	Herpes zoster or shingles prevention	<ul style="list-style-type: none"> Dose reduction for reduced CrCl 	Kim et al., 2011; Swaika et al., 2012

BUN—blood urea nitrogen; CrCl—creatinine clearance; GFR—glomerular filtration rate; MM—multiple myeloma
Note. Renal considerations were based on prescribing information for the agents.

FIGURE 3.
HEALTHCARE PROVIDER TIP SHEET: RENAL CARE PLAN FOR PATIENTS WITH STABLE MM

Comorbidities (e.g., diabetes, hypertension, increased age), dehydration, hypercalcemia, progressive disease, and cast nephropathy (particularly light chains) can all contribute to a decline in renal function. Acute renal failure because of disease progression or acute tubular necrosis is generally reversible if corrected early. Avoid drugs that can worsen preexisting kidney disease.

HISTORY AND PHYSICAL EXAMINATION

- Quarterly review of medications, changes in medical history, and physical examinations are recommended.

BLOOD TEST

- Perform CBC, CMP, SPEP, SIFE, 24-hour UPEP, UIFE, LDH, serum FLC assay, beta-2-microglobulin every three months if stable.
- Vitamin D deficiency (vitamin D 1-25, vitamin D 25 hydroxy), hyperparathyroidism (serum PTH-intact) should be assessed at baseline and periodically.

BONE SURVEYS

- Perform metastatic skeletal survey annually or earlier if new skeletal symptoms occur.

URINALYSIS

- Perform urinalysis quarterly if on bisphosphonates to assess for albuminuria.

NEPHROLOGIST FOLLOW-UP

- See nephrologist annually or as needed if decline in GFR is less than 30.

DIAGNOSTIC IMAGING

- Perform renal ultrasound to rule out hydronephrosis with new onset renal insufficiency. Avoid the use of IV dye or contrast with PET-CT or MRI scans if possible.

MEDICATIONS

- Avoid the use of NSAIDs, aminoglycosides, COX-2 inhibitors. Many over-the-counter supplements and medications can contribute to worsening renal dysfunction, but others can be given safely with dose reduction. Consult a trusted website, such as Medicines Complete, to evaluate safety.
- Bisphosphonates must be used with caution, and serum creatinine must be obtained prior to each dose.
- ESAs must be used with caution with recent safety concerns (e.g., stroke).

CALCULATION OF MEDICATION DOSE

- Many drugs to treat MM require a dose decrease for patients with renal insufficiency based on GFR or creatinine clearance.

- Many medications used to treat MM are safe to give after dialysis on a dialysis day.
- Drugs that require dose reduction based on GFR
 - Lenalidomide
 - Ixazomib
 - Carfilzomib
 - Melphalan
- Supportive care drugs that may require dose reduction based on GFR
 - Amoxicillin clavulante
 - Acyclovir
 - Low-molecular-weight heparins and factor inhibitors (e.g., rivaroxaban)
- Drugs that are potentially nephrotoxic
 - NSAIDs, including COX-2 inhibitors
 - Vancomycin, aminoglycoside antibiotics
 - Radio-contrast IV dye

GENERAL PREVENTIVE RULES TO PROTECT KIDNEY FUNCTION

- Be aware of the nephrotoxic potential of specific drugs.
- Be aware of the increased risk in the elderly.
- Assess the risk–benefit ratio for treatment with any drug.
- Avoid dehydration.
- Limit dose and duration of treatment, particularly if the drug is known to be nephrotoxic.
- Adjust dose based on GFR.
- Avoid combining potentially nephrotoxic drugs.

CBC—complete blood count; CMP—comprehensive metabolic panel; COX—cyclooxygenase; ESA—erythropoiesis-stimulating agent; FLC—free light chain; GFR—glomerular filtration rate; LDH—lactate dehydrogenase; MM—multiple myeloma; MRI—magnetic resonance imaging; NSAID—nonsteroidal anti-inflammatory drug; PET-CT—positron-emission tomography–computed tomography; PTH—parathyroid hormone; SIFE—serum immunofixation; SPEP—serum protein electrophoresis; UIFE—urine immunofixation; UPEP—urine protein electrophoresis

Note. From “Renal Complications in Multiple Myeloma and Related Disorders: Survivorship Care Plan of the International Myeloma Foundation Nurse Leadership Board,” by B.M. Faiman, P. Mangan, J. Spong, & J.D. Tariman, 2011, *Clinical Journal of Oncology Nursing*, 15, pp. 71–72. Copyright 2011 by Oncology Nursing Society. Adapted with permission.

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FIGURE 4.

PATIENT EDUCATION TIP SHEET: RENAL CARE PLAN FOR PATIENTS WITH MM

HISTORY AND PHYSICAL EXAMINATIONS

- Regular review of medications, changes in medical history, and physical examination
- Call your primary care provider for annual physical examination.
- Your hematology-oncology practitioner will review medications at each visit.

BLOOD TESTS

- Perform CBC, CMP, SPEP, SIFE, 24-hour UPEP, UIFE, LDH, serum FLC assay, and beta-2 microglobulin every three months. Special tests for bone loss may be ordered on an individual basis.
- Contact your treating hematology-oncology provider for monitoring.

BONE IMAGING

- Long-term or late effects of chronic kidney disease include osteoporosis.
- Talk with your primary care provider or hematology/oncology provider about bone density scans to monitor your bone health.

URINALYSIS

- Check annually if not on pamidronate or zoledronic acid. Check quarterly if you are receiving one of these drugs.
- Contact your treating hematology-oncology provider for monitoring.

NEPHROLOGIST OR KIDNEY SPECIALIST FOLLOW-UP

- See nephrologist annually or as needed if change in creatinine or GFR occurs.
- Call your nephrologist or kidney specialist.

DIAGNOSTIC IMAGING

- Avoid the use of IV dye or contrast with PET, CT, or MRI scans.
- Any provider may order one of these tests. You should alert whoever is ordering these tests that you have a diagnosis of MM and that IV dye may not be safe.

MEDICATIONS

- Avoid the use of NSAIDs, such as ibuprofen. Many medications and over-the-counter supplements (including Chinese herbs) can worsen renal impairment, but others can be given safely at lower doses.

- Bisphosphonates (zoledronic acid and pamidronate) are often used to prevent bone fractures and can be used with caution. Your provider should check your kidney function before each dose.
- ESAs, such as darbepoetin alfa and erythropoietin, are used to treat anemia. These must be used with caution, and a CBC must be obtained before each dose.
- All medications should be reviewed with your provider before starting, including herbal and over-the-counter medications.

DOSE ADJUSTMENTS

- Tell your providers if you have a decrease in kidney functioning. Certain medications to treat your cancer or other health conditions, such as antibiotics, will require a dose reduction or change in the way the medicines are given (e.g., days of the week).
- Contact your healthcare team for monitoring.

OTHER FACTORS

- Maintain adequate hydration; 2.5 liters of fluid per day is recommended. It is important to avoid dehydration, particularly during hot days or if you have a raised temperature.

CBC—complete blood count; CMP—comprehensive metabolic panel; CT—computed tomography; ESA—erythropoiesis-stimulating agent; FLC—free light chain; GFR—glomerular filtration rate; LDH—lactate dehydrogenase; MM—multiple myeloma; MRI—magnetic resonance imaging; NSAID—nonsteroidal anti-inflammatory drug; PET—positron-emission tomography; SIFE—serum immunofixation; SPEP—serum protein electrophoresis; UIFE—urine immunofixation; UPEP—urine protein electrophoresis

Note. From "Renal Complications in Multiple Myeloma and Related Disorders: Survivorship Care Plan of the International Myeloma Foundation Nurse Leadership Board," by B.M. Faïman, P. Mangan, J. Spong, & J.D. Tariman, 2011, *Clinical Journal of Oncology Nursing*, 15, pp. 71–72. Copyright 2011 by Oncology Nursing Society. Adapted with permission.

FIGURE 5.
HEALTHCARE PROVIDER TIP SHEET: ASSESSMENT AND DIFFERENTIAL DIAGNOSIS OF DIARRHEA

ASSESSMENT OF DIARRHEA

- Determine if a change in bowel habits is present.
- Determine the severity grade of diarrhea, and rule out contributing factors.
- Determine the duration of symptoms by calculating the number of stools over normal baseline, nocturnal diarrhea, stool consistency (watery or soft), urgency, and frequency with bowel movements.

GRADING OF DIARRHEA SEVERITY

- Grade 1: Increase of less than 4 stools per day over baseline; mild increase in ostomy output compared to baseline
- Grade 2: Increase of 4–6 stools per day over baseline; moderate increase in ostomy output compared to baseline
- Grade 3: Increase of 7 or greater stools per day over baseline; incontinence; hospitalization indicated; severe increase in ostomy output compared to baseline; limiting self-care activities of daily living
- Grade 4: Life-threatening consequences; urgent intervention indicated

DIFFERENTIAL DIAGNOSIS AND POTENTIAL CAUSES

- Careful analysis of causative agent(s) is essential to appropriate management and intervention.
- Infection: Diagnosed based on symptoms, history (such as travel or close contact with diarrheal illness), and stool culture to rule out viral or bacterial causes
- Inflammation: Intestinal inflammatory disorders, such as Crohn’s disease, ulcerative colitis, and irritable bowel syndrome, will predispose patients to develop diarrhea.
- Malignancy: Can occur in certain types of cancers, such as colon, endometrial, ovarian, and sarcoïd, as well as T-cell lymphoma

- Immunodeficiency: Immunoglobulin A deficiency
- Graft-versus-host disease: Immune-related diarrhea, which usually occurs after donor allogeneic hematopoietic cell transplantation in hematologic cancers and blood disorders
- Radiation therapy: Cancer treatment–induced diarrhea
- Identify any associated symptoms and potential complicating factors.
- Abdominal pain, gas, cramping, and signs and symptoms of dehydration
- Signs of fever, orthostatic symptoms, abdominal pain, weakness (denotes complicated diarrhea)
- Assess current medications (chemotherapy or targeted therapy) and diet (high fiber, lactose intolerance, and laxative use).
- Anxiety, malnutrition, and severe constipation might contribute to diarrhea.

PRELIMINARY INVESTIGATIONS

- Conduct a physical assessment to evaluate abdominal pain and localized abdominal tenderness and to rule out bowel obstruction.
- Consider abdominal x-ray to rule out obstruction or perforation.
- Evaluate complete blood count with differential to evaluate for neutropenia.
- Obtain a comprehensive metabolic panel to assess for electrolyte abnormalities (primarily magnesium and potassium).
- Order stool culture to rule out viral pathogens (e.g., *Clostridium difficile*, salmonella, shigella, giardia).
- Determine a severity grade of diarrhea.

Note. Based on information from Benson et al., 2004; Kinnebrew et al., 2014; Oncology Nursing Society, 2017; Smith et al., 2008; Tam et al., 2013.

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FIGURE 6.

PATIENT EDUCATION TIP SHEET: MANAGEMENT OF GASTROINTESTINAL SIDE EFFECTS IN MULTIPLE MYELOMA

KEY POINTS

Many of the drugs used to treat multiple myeloma may be associated with gastrointestinal side effects, including nausea, vomiting, diarrhea, and constipation. Managing side effects can reduce your discomfort and can allow you to receive the best treatment for your multiple myeloma. Your healthcare provider may change your dose or schedule of medication to help manage your symptoms. Do not stop or adjust medications without discussing it with your healthcare provider.

TYPES OF GASTROINTESTINAL SYMPTOMS

- Nausea: An unpleasant feeling in the throat and stomach
- Vomiting: A forceful emptying of the stomach contents
- Constipation: Decreased frequency of defecation accompanied by discomfort and difficulty
- Diarrhea: An abnormal increase in the frequency and the amount of fluid in the stool

Always report symptoms early to your healthcare team. Keep skin clean and dry with good hygiene to prevent skin breakdown.

MANAGEMENT OF NAUSEA

You may be asked about the circumstances surrounding episodes, upper abdominal pain, pain when swallowing, hiccups or heartburn, weight loss, dizziness upon standing, and your medication history.

- General dietary and lifestyle recommendations for nausea: Eat small, frequent meals; do not eat fatty or fried foods; avoid strong odors; do not exercise after eating; wear loose clothing; begin appropriate medications before chemotherapy; and use relaxation, acupuncture, biofeedback, and guided imagery.
- Loss of appetite, still able to eat normally: Adjust dosages of medications, drink enough water and other fluids, and keep track of effects of medications in a daily diary.
- Decreased ability to eat or drink: Consider asking for different medications, and see your physician for physical examination and evaluation should the medications be causing you to feel sick.
- Inability to eat or drink: You may need hospitalization or medications through a vein. Contact your healthcare provider immediately.
- Medications that may be ordered by your healthcare team include lorazepam, prochlorperazine, promethazine, metoclopramide, ranitidine, famotidine, and dexamethasone.

MANAGEMENT OF VOMITING

You will be asked about the appearance of the fluid (whether digested or undigested), whether a trigger was involved, and whether it was new or different from other times.

- 1 episode in 24 hours: This is usually self-limiting; continue medications for nausea.
- 2–5 episodes in 24 hours: New medications, oral or through a vein, may be needed. Contact a physician immediately.

- 6 or more episodes in 24 hours: This may require hospitalization to assess fluid status and rule out bowel blockage. Contact your healthcare provider immediately.
- Medications that may be ordered by your healthcare team include aprepitant, ondansetron, and granisetron.

MANAGEMENT OF CONSTIPATION

You will be asked about any abdominal pain, bloating, nausea, vomiting, inability to urinate, confusion, and diarrhea alternating with constipation.

- Mild: Increase fluid and fiber intake, increase physical activity, and start stool softeners.
- Moderate: You may need to speak with a dietitian about your food intake; consider laxatives and stimulants.
- Severe: Bowel obstruction should be assessed by a healthcare provider. Dehydration may require fluids through a vein. Treatment for a blocked colon may be discussed. Medication changes may be ordered by a physician. Referral to a gastrointestinal specialist may be arranged by a physician.
- Medications that may be ordered by your healthcare team include docusate, senna, magnesium sulfate, magnesium citrate, lactulose, and bisacodyl.

MANAGEMENT OF DIARRHEA

You will be asked about any history of irritable bowel syndrome, colitis, diverticulitis, and medications other than routine chemotherapy. Your healthcare provider will want to know whether you have gas and whether the diarrhea is a leakage or sudden occurrence.

- Fewer than 4 stools a day: Drink more liquids. Avoid caffeinated, carbonated, heavily sugared beverages. Dietary changes may be needed, such as a decrease in fiber, greasy, or fried food. Discontinue any medications, such as over-the-counter herbal medications, that cause diarrhea. Keep the rectal area clean. Loperamide, cholestyramine, or bismuth subsalicylate may be recommended to treat the diarrhea after each loose bowel movement.
- 4–6 stools per day: Medications should be recommended, and you may need fluids and salts. Your healthcare provider must be notified if you have more than 4–6 stools per day for more than 24 hours.
- 7–9 stools per day: Hospitalization may be considered for fluid replacement. A stool culture will be ordered to see whether the diarrhea is the result of an infection, and medications will be given to control frequency. You should take very good care of your skin and use disposable pads or diapers. Cancer therapy may be stopped for a period of time, or the dose of your cancer medication may need to be changed.
- Medications that may be ordered by your healthcare team include loperamide, diphenoxylate, cholestyramine, and octreotide.

Note. Based on information from Amgen, 2016; Fairman et al., 2013; Millennium Pharmaceuticals, 2017; National Comprehensive Cancer Network, 2016; Novartis, 2015; Smith et al., 2008; Takeda Pharmaceutical Company, 2015, 2016.

FIGURE 7.
HEALTHCARE PROVIDER TIP SHEET: MANAGEMENT OF DIARRHEA IN MULTIPLE MYELOMA

INITIAL MANAGEMENT OF MILD DIARRHEA

- Counseling on dietary modifications and ensuring adequate oral hydration
- Eat smaller, more frequent, lactose-free, low-fat meals.
- BRAT diet (bananas, rice, applesauce, and toast)
- Avoid caffeine and alcohol.
- Avoid greasy, fried, acidic, or spicy foods.
- Discontinue high osmolar food supplements.
- Consider adding probiotics if diarrhea persists.

PHARMACOLOGIC INTERVENTIONS WITH HIGHEST LEVELS

OF EVIDENCE

- For grade 1 diarrhea (an increase of less than 4 stools daily over baseline or mild increase in ostomy output as compared with baseline but not interfering with activities of daily living) and not responding to dietary intervention
 - Initiate loperamide 4 mg following first loose bowel movement and then 2 mg every 4 hours.
 - Alternatively, patients can be instructed to take 4 mg after initial loose bowel movement and then 2 mg after each subsequent loose bowel movement.
- For persistent grades 1–2 diarrhea (after 24 hours of loperamide)
 - Begin high-dose loperamide at an initial dose of 4 mg followed by 2 mg every 2 hours and 4 mg every 4 hours at night.
 - Consider atropine-diphenoxylate, 1–2 tablets every 6–8 hours.
 - If diarrhea persists for more than 24 hours, start oral antibiotics.
- For grade 2 diarrhea (increase of 4–6 stools daily over baseline, moderate increase in ostomy output compared with baseline) or if unresponsive to 48 hours of high-dose loperamide
 - Stop loperamide and start octreotide, 100–150 mcg subcutaneously three times daily or other second-line agents (tincture of opium).
 - Expert opinion considers tincture of opium 0.6 ml orally every 4–6 hours useful. Because of lack of randomized, controlled trials, it cannot be unequivocally recommended for practice.
 - Patient should be seen for further evaluation, including complete stool, blood work, and skin assessment.
 - IV hydration is recommended if unable to take adequate fluids orally.
- For complicated grade 2 diarrhea and grades 3–4 diarrhea (increase of 7 stools daily over baseline or a severe increase in ostomy output over baseline)
 - Consider hospital admission.
 - Administer octreotide 100–150 mcg subcutaneously every 8 hours or 25–50 mcg per hour via IV.
 - Initiate IV fluids as needed for at least 24 hours.
 - Initiate total parenteral nutrition as indicated.
 - Initiate antibiotics (if an infectious cause is suspected).
 - Perform stool workup (for pathogens), laboratory studies, and skin assessment.
- For patient experiencing significant diarrhea, hold chemotherapy until complete resolution of symptoms for at least 24 hours without antidiarrheal therapy.

EVIDENCE-BASED DOSE MODIFICATIONS FOR CANCER

- Many targeted agents can cause diarrhea. Dose modifications are at the discretion of the treating provider and are dependent upon the type of cancer, goals of cure versus control of the cancer, and diarrhea severity.

MANAGEMENT OF DIARRHEA IN TARGETED AGENTS OF INTEREST

Common causes of moderate to severe chemotherapy-induced diarrhea by class and incidence include the following:

- Histone deacetylase inhibitors: Panobinostat (overall incidence 68%, with grades 3 and 4 incidence of 25%)
 - At first sign of abdominal cramping, loose stools, or onset of diarrhea, begin antidiarrheal medication.
 - Grade 2 (moderate diarrhea, 4–6 stools per day): Interrupt panobinostat until resolved and then restart at the same dose.
 - Grade 3 (severe diarrhea, 7 or more stools per day, IV fluids, or hospitalization required): Interrupt panobinostat treatment until resolved and then restart at a reduced dose.
 - Grade 4 (life-threatening): Permanently discontinue panobinostat.
- Immunomodulatory drugs: Lenalidomide (29%) and pomalidomide (35%)
 - At onset, rule out other causes of infection and begin antidiarrheal medication.
 - For lenalidomide and pomalidomide, the manufacturer recommends holding the medication for moderate to severe diarrhea and resuming when the diarrhea returns to grade 2.
 - Symptomatic management with cholestyramine or loperamide is recommended.
 - Lenalidomide-induced diarrhea typically occurs after 17.7 months of therapy; diarrhea occurs in 46% of patients with continuous lenalidomide/dexamethasone.
- Proteasome inhibitors: bortezomib (52% with monotherapy; less common with combined therapy), carfilzomib (25%), ixazomib (42%, with 6% grade 3)
 - Administer antidiarrheal for grade 1 diarrhea associated with proteasome inhibitor use.
 - Management of proteasome inhibitor-associated diarrhea: Withhold therapy until symptoms of toxicity have resolved to grade 1 or baseline, and rule out other causes of diarrhea.
 - If bortezomib or carfilzomib: Resume with one dose level reduction at the discretion of the provider.
 - If ixazomib: Diarrhea rarely leads to treatment discontinuation; symptomatic management with loperamide is recommended.
- Selinexor (XPO1 inhibitor; 42% diarrhea overall and 3% grade 3): Administer antidiarrheal for mild grade 1 toxicity, and encourage dietary strategies.
 - Weight loss and anorexia are unique side effects of selinexor. Dose modification for severe grade 3 toxicities, such as weight loss and anorexia, should be considered.

Note. Based on information from Amgen, 2016; Fairman et al., 2013; Millennium Pharmaceuticals, 2017; National Comprehensive Cancer Network, 2016; Novartis, 2015; Smith et al., 2008; Takeda Pharmaceutical Company, 2015, 2016.

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FIGURE 8.

HEALTHCARE PROVIDER TIP SHEET: PERIPHERAL NEUROPATHY EVALUATION AND MANAGEMENT

PRIOR TO START OF THERAPY

- Baseline neurosensory examination of extremities (based on the use of neurotoxicity assessment)
 - For preexisting neuropathy, rule out other possible causes.
- Take B-complex vitamins, including B₁, B₆, B₁₂ (based on anecdotal evidence).
- Take folic acid.
- Provide patient education on signs and symptoms of peripheral neuropathy.

MILD SYMPTOMS OR GRADE 1

- Neurosensory examination of extremities (based on the use of neurotoxicity assessment)
- Continue therapy and educate patient to notify clinicians immediately if peripheral neuropathy worsens.

MODERATE SYMPTOMS OR GRADE 2

- Neurosensory examination of extremities based on the use of neurotoxicity assessment
- If symptoms are intermittent, continue therapy.
- If continuous, stop therapy and see if symptoms continue.
- If symptoms resolve, restart therapy at a reduced dose.
- Consider amitriptyline.
- Try using amino acids, such as acetyl-L-carnitine and alpha-lipoic acid, on an empty stomach (based on anecdotal evidence).
- For intermittent symptoms, try gently massaging areas with cocoa butter.

SEVERE SYMPTOMS OR GRADE 3

- Hold therapy until resolution to baseline.
- Perform nerve conduction studies.
- Make sure patient is on amino acids (based on anecdotal evidence).
- Consider using gabapentin or pregabalin.
- Try lidocaine patch on affected area every 12 hours.
- Provide education on decreased sensation in extremities and safety issues.
- Assess need for assistance with ADLs.

NEUROTOXICITY ASSESSMENT

Ask patients to rate the following items on a scale from 0 (not at all) to 4 (very much). Healthcare providers may find discussion of patients' responses helpful in determining the grade of neuropathy as defined by the National Cancer Institute CTCAE. However, there is no direct correlation between assessment scores and toxicity grades.

- I have numbness or tingling in my hands.
- I have numbness or tingling in my feet.
- I feel discomfort in my hands.
- I feel discomfort in my feet.
- I have joint pain or muscle cramps.
- I feel weak all over.
- I have trouble buttoning buttons.
- I have trouble feeling the shape of small objects when they are in my hand.
- I have trouble walking.

CTCAE GRADING

Peripheral sensory neuropathy

- 1: Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function
- 2: Sensory alteration or paresthesia (including tingling); interfering with function but not ADLs
- 3: Objective sensory alteration or paresthesia; interfering with ADLs
- 4: Disabling or life-threatening
- 5: Death

Neuropathic pain

- 1: Mild pain not interfering with function
- 2: Moderate pain; pain or analgesics interfering with function but not ADLs
- 3: Severe pain; pain or analgesics severely interfering with ADLs
- 4: Disabling; referral to neurology or pain management
- 5: Death

ADL—activity of daily living; CTCAE—Common Terminology Criteria for Adverse Events
Note. Based on information from Calhoun et al., 2003; Cella et al., 1993; National Cancer Institute, 2010.

From *CJON*, 21(5, Suppl.), 37–46:

Heart and Lung Complications

Assessment and prevention of venous thromboembolism and cardiovascular disease in patients with multiple myeloma

Noonan et al.

FIGURE 1. VENOUS THROMBOEMBOLISM RISK FACTORS

- Recent history of immobilization or bed rest
- Recent surgery
- Older age
- History of venous thromboembolism
- Obesity
- Male gender
- Trauma, particularly to the lower extremities
- Malignancy
- Medications: immunomodulatory drugs, oral contraceptives, erythropoietin
- Pregnancy or postpartum period
- History of stroke
- Presence of central venous line

Note. Based on information from Brown et al., 2016; Fahrni et al., 2015; Heit et al., 2016; Palumbo et al., 2008; Story, 2014.

FIGURE 2. MEDICAL AND FAMILY HISTORY RISK FACTORS FOR VENOUS THROMBOEMBOLISM

- Complete thrombosis history (Was thrombosis idiopathic or provoked by surgery, a long car or airplane ride, or immobility?)
- Pregnancy
- History of vascular disease, nephrotic syndrome, malignancy, polycythemia vera, heparin-induced thrombocytopenia, thyroid disease, systemic lupus erythematosus
- Antiphospholipid syndromes
- Sickle cell disease
- History of recent infection or inflammation
- Recent exposure to dehydration
- Recent prolonged travel by air or automobile
- Trauma or bone fracture
- Varicose veins
- Family history of venous thromboembolism or known inherited thrombophilia, such as Factor V Leiden, prothrombin gene *G20210A* mutation, and protein C or S

Note. Based on information from Fahrni et al., 2015; Heit et al., 2016; Kesieme et al., 2011.

FIGURE 3. SIGNS AND SYMPTOMS OF PULMONARY EMBOLISM AND DEEP VEIN THROMBOSIS

PULMONARY EMBOLISM

- Dyspnea or tachypnea
- Chest discomfort
- Tachycardia
- Low-grade fever
- Pleural rub

DEEP VEIN THROMBOSIS

- Unilateral swollen, erythematous, and warm extremity
- Dull ache, pain, or tight feeling over affected area
- Low-grade fever
- Distension of superficial venous collateral vessels
- Positive Homan's sign

Note. Based on information from Rome et al., 2008; Story, 2014.

FIGURE 4. LABORATORY TESTS FOR THROMBOPHILIA

DEFICIENCY OF COAGULATION FACTOR INHIBITORS

- Protein S deficiency
- Protein C deficiency
- Antithrombin III deficiency

INCREASED LEVEL OR FUNCTION OF THE COAGULATION FACTORS

- Activated protein C resistance
- Factor V Leiden
- Prothrombin gene mutation
- Increased levels of Factors VIII, IX, or XI
- Increased lupus anticoagulant
- Dysfibrinogenemias

Note. Based on information from Story, 2014.

TABLE 2.
ANTICOAGULATION MEDICATIONS USED TO TREAT OR PREVENT VENOUS THROMBOEMBOLISM

MEDICATION	CATEGORY	USE IN MALIGNANCIES	NURSING CONSIDERATIONS
Dabigatran	Direct oral anticoagulant IIa Inhibitors	Use in malignancy is under investigation.	<ul style="list-style-type: none"> ■ Major side effect is bleeding. ■ Bleeding cannot be reversed. ■ Long half-life ■ Renally excreted ■ Blood levels do not require monitoring.
Enoxaparin, dalteparin	Low-molecular-weight heparin	Commonly used in patients diagnosed with cancer	<ul style="list-style-type: none"> ■ Major side effect is bleeding. ■ Hold with thrombocytopenia. ■ Patient should be taught how to perform SC injections. ■ Patients should not take nonsteroidal anti-inflammatory drugs. ■ Monitor renal status with serum creatinine levels.
Fondaparinux	Pentasaccharide; selec- tive anti-Xa activity	Used in patients with cancer; used when patients develop heparin-induced thrombocytopenia	<ul style="list-style-type: none"> ■ Major side effect is bleeding. ■ Hold with thrombocytopenia. ■ Long half-life
Heparin	Unfractionated heparin	Used in the inpatient setting for all patients, including patients with cancer	<ul style="list-style-type: none"> ■ Major side effect is bleeding. ■ Monitor for heparin-induced thrombocytopenia. ■ Hold with thrombocytopenia. ■ Administered via IV or SC ■ Not commonly used in the homecare setting ■ Monitored by aPTT ■ Very short half-life
Rivaroxaban, apixaban	Direct oral anticoagulant Xa Inhibitors	Use in malignancy is under investigation.	<ul style="list-style-type: none"> ■ Major side effect is bleeding. ■ Long half-life ■ Does not require blood monitoring ■ Rivaroxaban is mostly renally excreted. ■ Apixaban has renal and hepatic excretion. ■ Monitor renal function. ■ Bleeding cannot be reversed; however, aPCC is under investigation.
Warfarin	Oral vitamin K agonists	Used in patients with cancer	<ul style="list-style-type: none"> ■ Major side effect is bleeding. ■ Numerous medication interactions ■ Hold with thrombocytopenia. ■ Requires INR/PT blood monitoring ■ Can be reversed with vitamin K ■ Dose is dependent on oral intake of food high in vitamin K. ■ Long half-life

aPCC—activated prothrombin complex concentrate; aPTT—activated partial thromboplastin time; INR—international normalized ratio; PT—prothrombin time; SC—subcutaneous
Note. Based on information from Awad & Cocchio, 2013; Piran & Schulman, 2016; Streiff et al., 2016.

FIGURE 5.
VENOUS THROMBOEMBOLISM PREVENTION

- Exercise regimen to increase mobility and prevent stasis
- Compression stockings and devices
- Weight control
- Dehydration prevention
- Cardiac management
- Aspirin/anticoagulation prophylaxis for long car rides or airplane flights, pregnancy, and surgery
- Aspirin/anticoagulation while taking immunomodulatory drugs
- Avoidance of medications that increase the risk of venous thromboembolism (oral contraceptives, erythropoietin)

Note. Based on information from Bates et al., 2012; Elias et al., 2016; Moheimani & Jackson, 2011; Rome et al., 2008.

TABLE 3.
CHEMOTHERAPY AND IMMUNOTHERAPY ASSOCIATED WITH MULTIPLE MYELOMA CARDIOVASCULAR TOXICITY

CHEMOTHERAPY CATEGORY	CHEMOTHERAPY DRUGS	CARDIAC TOXICITY	NURSING CONSIDERATIONS
Alkylating agents	Cyclophosphamide	HF, LVD, pericardial effusion, myopericarditis; venous thromboembolism	Baseline MUGA or echocardiogram
	Cisplatin		
Angiogenesis inhibitors	Lenalidomide, pomalidomide	Venous thromboembolism	Prophylaxis with aspirin or LMWH or warfarin is recommended for those with two or more multiple myeloma-related risk factors. Bradycardia is defined as heart rate less than 60 bpm.
	Thalidomide	Venous thromboembolism, bradycardia	
Anthracycline	Doxorubicin	LVD, dilated cardiomyopathy, HF	Baseline MUGA or echocardiogram
Antibody-based tyrosine kinase inhibitors	Bevacizumab, trastuzumab	HF, cardiomyopathy, arterial thrombotic event, HTN, LVD	Baseline MUGA or echocardiogram
Proteasome inhibitor	Bortezomib, carfilzomib	HF, LVD	Baseline MUGA or echocardiogram
Small molecule tyrosine inhibitor	Dasatinib, lapatinib, imatinib mesylate, sunitinib	HF, LVD, myocardial ischemia, HTN	Baseline MUGA or echocardiogram

HF—heart failure; HTN—hypertension; LMWH—low-molecular-weight heparin; LVD—left ventricular dysfunction; MUGA—multigated acquisition scan
Note. Based on information from Hamo & Bloom, 2015; Yeh & Bickford, 2009.

FIGURE 7.**PATIENT TIP SHEET: PREVENTING BLOOD CLOTS AND CARDIOVASCULAR EVENTS**

Patients with cancer, particularly MM, are at high risk of developing blood clots (thromboembolic events) and heart problems, or experiencing worsening of preexisting heart problems. If you have MM, you may be able to prevent blood clots or improve your outcomes if you get blood clots or have heart problems. You can learn how to recognize the symptoms of blood clots early enough to improve the likelihood of successful treatment and decrease the likelihood of complications. Since treatments for MM can increase the risk for blood clots and heart disease, your healthcare provider may change your treatment based on your symptoms.

TYPES OF THROMBOEMBOLIC EVENTS

- **DVT:** A small blood clot in the arm, leg, hand, or foot; DVT is the most common type of thromboembolic event. Signs of DVT include swelling, aching, pain, tightness, or a lump in the arm, leg, hand, or foot; fast heartbeat; and veins larger than usual (distended).
- **PE:** A blood clot that travels to the lungs. Signs of PE include anxiety, fast heartbeat and fast breathing, chest pain, new onset of shortness of breath, and coughing up blood.
- **Cerebral infarction (stroke):** The result of a blood clot that travels to the brain. Signs include change in emotional or mental behavior and confusion, severe headache, chest pain, loss of coordination, and sudden numbness or weakness.

TESTS THAT YOU MAY UNDERGO

To see if you may have a blood clot, your nurse or healthcare provider will perform tests, which may include:

- An ultrasound of your arms or legs if they are swollen or painful
- A test called a ventilation/perfusion scan, or VQ scan, that checks to see if there is a blockage in blood flow in your lungs
- A CT scan to look for a blood clot in your lungs. Tell your healthcare provider if you have kidney problems; the IV contrast dye may be hard on your kidneys.
- Electrocardiogram or echocardiogram

TREATMENT OF BLOOD CLOTS

- DVT, PE, and stroke are considered medical emergencies. Report any symptoms to your healthcare provider immediately.
- The treatments or medications you receive will be based on your individual risk factors.

- You may need to receive medications to prevent new blood clots from forming.
- Low-dose aspirin may be suggested if you have no risk factors for blood clots or only one risk factor.
- Pills or injectable anti-clotting drugs may be prescribed if you have more than one risk factor. Risk factors include lack of activity, obesity, smoking, personal or family history of blood clots, taking estrogen compounds (hormone replacement), taking drugs to increase the amount of red blood cells (e.g., erythropoietin, epoetin alfa, darbepoetin alfa), recent surgery, and prolonged air travel or sitting for long periods of time.

WAYS TO REDUCE YOUR BLOOD CLOT RISK

- Exercise, such as walking, ankle circles, and knee-to-chest lifts
- Weight loss
- Smoking cessation
- Take medications prescribed by your healthcare providers.
- Notify your healthcare providers if you have ever been diagnosed with a blood clot.
- Report concerning signs and symptoms immediately to your healthcare providers, including shortness of breath, chest pain or tightness, cough, or swelling of an extremity.

WAYS TO PREVENT HEART DISEASE

- The American Heart Association recommends regular activity or exercise to decrease your risk of blood clots and stroke and lower your blood pressure.
- Stop smoking if you already smoke, or do not start.
- Eat a healthy diet with more fruits and vegetables than oils, fats, and carbohydrates. People with a lower body mass index are less likely to have heart problems, diabetes, or high blood pressure.
- See a primary care provider for regular blood pressure, diabetes, and cholesterol monitoring.
- Remember that most patients with MM are living longer than ever. By staying as active as possible and leading a heart healthy lifestyle, you can reduce your risk of complications and stay as healthy as possible.

CT—computed tomography; DVT—deep vein thrombosis; MM—multiple myeloma; PE—pulmonary embolism

Note. Based on information from Elias et al., 2016; Rome et al., 2008; Story, 2015.

From *CJON*, 21(5, Suppl.), 47–59:

Bone Health, Pain, and Mobility

Evidence-based recommendations for patients with multiple myeloma

Rome et al.

FIGURE 1.

DIAGNOSTIC CRITERIA FOR ACTIVE MULTIPLE MYELOMA DISEASE: MYELOMA-DEFINING EVENTS

To meet the definition for a diagnosis of active multiple myeloma warranting treatment, a person must have at least 10% clonal bone marrow plasma cells, or biopsy-proven bone or soft tissue (extramedullary) plasmacytoma, and any one or more of the following features attributable to the disease process:

- Calcium elevation: Greater than 1 mg/dl above the upper limits of normal, or greater than 10.5 mg/dl
- Renal insufficiency: Creatinine greater than 2 mg/dl or creatinine clearance less than 40 ml per minute
- Anemia: Hemoglobin less than 10 g/dl or 2 g below baseline
- Bone disease: Diffuse osteoporosis; one or more osteolytic lesions on skeletal imaging

ADDITIONAL DIAGNOSTIC CRITERIA ADDED TO THE 2014 INTERNATIONAL MYELOMA WORKING GROUP CRITERIA

- Greater than 60% clonal bone marrow plasma cell
- Serum free light chain ratio (involved:uninvolved) of 100 or greater
- More than one focal lesion (5 mm or greater) detected by magnetic resonance imaging

Note. Based on information from Durie et al., 2003; Rajkumar et al., 2011a, 2014.

FIGURE 6.

PATIENT EDUCATION TIP SHEET: MOBILITY AND SAFETY IN MULTIPLE MYELOMA

KEY POINTS

Physical activity can help reduce side effects of multiple myeloma and your therapy, such as fatigue and weakness. By keeping active, you can also reduce your risk of injury from falls. Your healthcare provider can direct you in safe activities that will benefit you and that you can enjoy. The following are some general recommendations.

- Avoid inactivity or a sedentary lifestyle and return to daily activities as soon as possible, unless otherwise directed by your healthcare team.
- Engage in daily physical activity, including exercise, routine activities, and recreational activities.
- Discuss physical activity and weight control with your healthcare provider. This should be a part of your treatment plan. Consider an appropriate exercise program and possible referral to an exercise specialist who will work with your healthcare team.
- Consider nutrition consultation to optimize nutrition.
- Delay exercise if severely anemic and return to exercise when the anemia has improved.
- If you are fatigued, inform your healthcare team and employ energy conservation measures, such as structured daily routine and setting priorities.

- If you experience severe fatigue from your therapy, do 10 minutes of light exercises daily if approved by your healthcare team.
- If you have difficulty sleeping, speak to your healthcare team regarding strategies to promote adequate sleep.
- Avoid public gyms and pools if you have a compromised immune system.
- Avoid chlorine exposure (e.g., swimming pools) if undergoing radiation therapy.
- Avoid pools, lakes, or ocean water if you have an indwelling catheter or other tube coming out of your body. Also, avoid resistance training of muscles in the area of the catheter or tube to avoid it being pulled.
- Your exercise program may need to be modified if you have other medical problems that put you at risk for injury or harm.
- Your exercise programs can be modified for your safety if you have significant neuropathies, balance, or limb problems. For example, a stationary bike may be safer than a treadmill.
- Make sure to let your healthcare team know if you have changes in your ability to move or exercise safely.

Note. Based on information from Denlinger et al., 2014; National Comprehensive Cancer Network, 2017a, 2017b, 2017d; Rock et al., 2012; Schmitz et al., 2010.

FIGURE 2.

PATIENT EDUCATION TIP SHEET: MANAGING BONE HEALTH IN MULTIPLE MYELOMA

KEY POINTS

Most patients with multiple myeloma will develop bone lesions, leading to pain, possible fractures, and decreased mobility. Maintaining bone health is important for reducing pain and the risk for fractures, as well as for maximizing mobility. Side effects from treatment, like neuropathy or muscle weakness, can affect your ability to move safely. Your healthcare provider may change your medication dose or schedule to help manage your symptoms.

PREVENTION OF FRACTURES

Make sure you have tests done if they are recommended by your healthcare provider.

- Laboratory tests (e.g., complete blood count, creatinine)
- Bone health monitoring laboratory tests (e.g., vitamin D, alkaline phosphatase, calcium, specific hormones for men and women)
- Radiologic imaging (e.g., positron-emission tomography, computed tomography, magnetic resonance imaging, bone survey, bone density test)

Take medications and supplements if they are prescribed or recommended by your healthcare provider.

- Bisphosphonates (e.g., zoledronic acid, pamidronate)
- Supplements (e.g., calcium, vitamin D); your healthcare provider may check your kidney function while you are taking these.
- Pain medication for bone pain

Maximize your nutrition.

- Review a dietary plan with your healthcare provider.

- Meet with a nutritionist if recommended by your healthcare provider.
- Perform good daily oral hygiene and have a dental examination every six months. Be sure to inform your dentist if you are taking a bone-strengthening medication.

Maximize your functioning.

- Talk to your healthcare provider about a plan for daily physical activities, including activities that help with balance, strength, and fitness.
- If needed, use devices to help you with mobility, including a cane or walker.
- If needed, use pain medication to help decrease your pain and improve your mobility.
- Improve your sleep quality to promote your well-being and decrease your pain and fatigue.

Be aware of symptoms that require immediate attention.

- Sudden onset of pain (may indicate a new fracture)
- Back pain with sudden change in sensation in lower or upper extremities or loss of bowel or bladder control (may indicate spinal nerve damage)
- Noticeable changes in mental status, such as increased sleepiness, confusion, or irritability
- Severe constipation, nausea or vomiting, and excessive thirst and urination
- Falling, tripping, or loss of balance

Note. Based on information from Denlinger et al., 2014; National Comprehensive Cancer Network, 2017b, 2017d; Rock et al., 2012; Schmitz et al., 2010.

FIGURE 3.
 PATIENT EDUCATION TIP SHEET: PREVENTING AND MANAGING MULTIPLE MYELOMA PAIN

KEY POINTS

Most patients with multiple myeloma have pain at some time. The pain can be caused by bone disease, including fractures, or by neuropathic pain caused by nerve damage. In addition, you may experience pain during medical tests or treatments, including when you have your blood drawn or an IV placed.

To best treat pain, it is important to undergo a thorough assessment by your healthcare provider. Tell your healthcare team important information, such as where the pain is located and how it feels. Include descriptions of how intense it is, how long it lasts, when it started, and what makes it worse or better. Let them know what has been tried to relieve the pain—what has worked, what has not. As part of the assessment, you will need to undergo a physical examination and may need radiologic imaging (i.e., x-ray, magnetic resonance imaging, positron-emission tomography) if you have muscle or bone pain.

Medications may be prescribed to treat bone disease and decrease bone pain. Starting on anti-myeloma therapy and using bisphosphonate therapy can treat and prevent bone disease.

The use of IV bisphosphonates (pamidronate or zoledronic acid) can reduce pain and prevent skeletal events secondary to bone involvement. Procedures like vertebroplasty or kyphoplasty, local radiation, or even surgery may be used to treat pain and prevent further bone damage.

Treatment of neuropathic pain is difficult and, therefore, prevention is important. For patients receiving bortezomib therapy, subcutaneous administration is associated with lower rates of peripheral neuropathy than IV administration. Dosing and scheduling adjustments can also be made to prevent worsening of symptoms. You should also receive antiviral medication (e.g., acyclovir) to prevent activation of varicella-zoster virus, more commonly known

as shingles. Pain medications, such as narcotics and other classes of drugs, may be prescribed for acute and ongoing pain. Any medication should be taken as prescribed for best effect.

Procedural pain may be difficult to avoid because procedures and interventions are needed for assessment of disease response and activity. If you experience pain or anxiety related to procedures, be sure to ask your healthcare team if there are medications available to reduce the pain and relieve anxiety. Share laboratory test results with healthcare providers, such as your hematologist and your primary care provider, to avoid unnecessary repetition of blood draws.

TIPS AND REMINDERS

- Be sure to inform your healthcare team of new onset of pain or pain that is not helped by treatment.
- Keep a calendar to remember when you are due for your next bisphosphonate treatment.
- If you are taking narcotics to treat your pain, be sure to stay on a bowel regimen to prevent constipation.
- Take medications for pain as prescribed, adjusting doses only after discussion with your healthcare team.
- If proteasome inhibitors (such as bortezomib, carfilzomib, or ixazomib) are part of your treatment plan, be sure you are receiving antiviral medication to prevent shingles.
- Physical activity can help with pain management. Consider a physical therapy evaluation to promote safe activity and strengthening.

Note. Based on information from Denlinger et al., 2014; Moreau et al., 2011; National Comprehensive Cancer Network, 2017a, 2017b, 2017c, 2017d; Rock et al., 2012; Schmitz et al., 2010.

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FIGURE 4.
HEALTHCARE PROVIDER TIP SHEET: PAIN MANAGEMENT IN MULTIPLE MYELOMA

With improvements in supportive care and treatment, patients with MM are living longer. Because pain is a major symptom of MM, pain prevention and management are important for patient quality of life.

SOURCES OF PAIN

- Bone disease: Osteoporosis, osteolytic bone lesions, pathologic fractures, and/or vertebral compression fractures are common findings at MM diagnosis and throughout the course of the disease.
- Neuropathic pain: Neuropathic pain is not as common as pain caused by bone involvement; however, it can be difficult to treat and influence quality of life. Neuropathic pain can present as PN, which may be present at diagnosis or related to treatment. Postherpetic neuralgia, another cause of neuropathic pain, is a direct result of reactivation of VZV.
- Procedural pain: Throughout their illness, patients with MM undergo multiple procedures that can cause acute pain. Routine blood work and frequent bone marrow biopsies are sources of recurrent, acute pain.

ASSESSMENT, PREVENTION, AND MANAGEMENT

To best treat pain, it is important to perform thorough assessments at baseline and at each encounter. The healthcare team should collect information regarding pain location, intensity, and duration, as well as when it started and what makes it worse or better, including treatments. A physical examination should be performed, and radiologic imaging (i.e., x-ray, magnetic resonance imaging, positron-emission tomography) may be needed to evaluate new musculoskeletal pain.

Medications may be prescribed for bone disease. Anti-myeloma therapy and use of bisphosphonate therapy can treat and prevent bone disease. The use of IV bisphosphonates (pamidronate and zoledronic acid) can reduce pain and prevent skeletal events secondary to bone involvement. Analgesic medications, such as narcotics, may be prescribed to better manage pain and allow for improved mobility. Procedures like local radiation, vertebroplasty or kyphoplasty, or even surgical fixation may be used to treat pain and prevent additional bone damage.

Treatment of neuropathic pain is difficult and, therefore, prevention is important. For patients receiving bortezomib therapy, subcutaneous administration is associated with lower rates of PN than IV administration. Dosing and scheduling adjustments can also be made to prevent worsening of symptoms. Patients

receiving bortezomib or ixazomib therapy should also receive antiviral medication (e.g., acyclovir) to prevent activation of VZV. Pain medications, such as narcotics and other classes of drugs, may be prescribed for acute and chronic pain.

Procedural pain may be difficult to avoid because procedures and interventions are needed for assessment of disease response and activity. Patients may experience pain or anxiety related to procedures. Be sure to discuss the use of premedications to reduce procedural pain and anxiety. When possible, consolidate the collection of blood for different laboratory tests into as few blood draws as possible to minimize the number of painful venipunctures.

TIPS AND REMINDERS

- Remind patients to inform the healthcare team of new onset of pain or pain that is not well managed before they start any self-treatment with over-the-counter medications.
- Assess pain at each visit or encounter.
- Ensure that the primary provider prescribes medications for pain, adjusting doses based on the patient's response.
- If narcotics are prescribed to manage pain, make sure a bowel regimen is also prescribed to prevent constipation.
- If the patient is receiving bortezomib, carfilzomib, or ixazomib as part of the treatment plan, be sure an antiviral medication to prevent shingles is also prescribed.
- Bortezomib given by subcutaneous injection is associated with lower risk of PN than IV administration.
- Physical activity can help with pain management. Consider recommending that the provider prescribe a physical therapy evaluation to promote safe physical activity and strengthening.
- Make sure that the patient receives premedications for painful or anxiety-producing procedures, such as bone marrow biopsy or magnetic resonance imaging.

MM—multiple myeloma; PN—peripheral neuropathy; VZV—varicella-zoster virus
Note. Based on information from Denlinger et al., 2014; Moreau et al., 2011; National Comprehensive Cancer Network, 2017a, 2017b, 2017c, 2017d; Rock et al., 2012; Schmitz et al., 2010.

FIGURE 5.
HEALTHCARE PROVIDER TIP SHEET: MOBILITY AND SAFETY IN PATIENTS WITH MULTIPLE MYELOMA

Evidence suggests that exercise is an effective intervention for reducing side effects such as fatigue, cognitive impairment, sleep problems, depression, pain, anxiety, and physical dysfunction. An individual plan of care should be based on physical activity, the overall level of functioning, frailty, and fall risk. Perform focused clinical evaluation as appropriate.

- Weight/body mass index
- Vital signs
- Functional status and frailty status
- Barriers to physical activity and safety
 - Environment, including gym access, home, outdoor space, and home safety
 - Financial
 - Physical limitations
 - Time/competing demands and priorities
 - Knowledge/interests
 - Social support

Assess factors and comorbidities that can impede safe activity and exercise with the healthcare team at each patient encounter.

- Cardiovascular and pulmonary disease
- Arthritis and musculoskeletal issues, including steroid myopathy
- Pain, including neuropathy
- Bone health and/or presence of lytic lesions, including the need for assistive devices
- Hematologic problems, including anemia, neutropenia, and thrombocytopenia
- Fatigue and its contributing factors, including endocrine, electrolyte, sleep, and other dysfunctions
- Emotional distress, including depression, anxiety, and substance abuse
- Nutritional deficits
- Medications, including polypharmacy
- Prior and current participation in physical activity and other health behaviors

- Eating habits and patterns
- Alcohol and tobacco use
- Physical activity habits and patterns

Based on results of the mobility and safety assessment, make recommendations along with the healthcare team regarding the level of activity and exercise, including long- and short-term goals (light, moderate, and vigorous exercise). Make periodic reassessment and recommend modifications, if needed.

- All survivors should avoid inactivity or a sedentary lifestyle and should return to daily activities as soon as possible.
- Survivors who are able should engage in daily physical activity, including exercise, routine activities, and recreational activities.
- Physical activity and exercise recommendations should be tailored to the individual's abilities and preferences. Even light activity can improve physical functioning in survivors, and clinicians should advise survivors against inactivity.
- General recommendations
 - Overall volume of weekly activity should be at least 150 minutes of moderate-intensity activity or 75 minutes of vigorous-intensity activity, or an equivalent combination (light exercise: no noticeable change in breathing pattern; moderate exercise: can talk but not sing; vigorous exercise: can say a few words without stopping to catch breath).
 - Survivors should engage in two to three sessions per week of strength training and stretching that includes major muscle groups.
 - Stretch major muscle groups on a routine basis.
- Inactive survivors can begin with one to three light- or moderate-intensity sessions of 20 minutes or more per week, with progression based on how well they tolerate the activity.
- Walking and using a stationary bike are safe for virtually all survivors.

Note. Based on information from Denlinger et al., 2014; National Comprehensive Cancer Network, 2017a, 2017b, 2017d; Rock et al., 2012; Schmitz et al., 2010.

From *CJON*, 21(5, Suppl.), 60–76:

Myelosuppression, Bone Disease, and Acute Renal Failure

Evidence-based recommendations for oncologic emergencies

Brigle et al.

TABLE 1.
GRADING CRITERIA FOR HEMATOLOGIC TOXICITY ADVERSE EVENTS

ADVERSE EVENT	UNIT OF MEASURE	GRADE 1	GRADE 2	GRADE 3	GRADE 4
Anemia	Hemoglobin (g/dl)	Less than LLN to 10	8–10	Less than 8	Life threatening; urgent intervention indicated
Neutropenia	Absolute neutrophil count (x 10 ⁹)	Less than LLN to 1.5	1–1.5	0.5–1	Less than 0.5
Thrombocytopenia	Platelet count (x 10 ⁹)	Less than LLN to 75	50–75	25–50	Less than 25

LLN—lower limits of normal
Note. Based on information from National Cancer Institute, 2010.

TABLE 2.
ETIOLOGY OF AND CONTRIBUTING FACTORS FOR ANEMIA IN PATIENTS WITH CANCER

ETIOLOGY	CONTRIBUTING FACTORS
Relative loss of red blood cells	<ul style="list-style-type: none"> ■ Surgical blood loss ■ Acute or chronic gastrointestinal hemorrhage ■ Excessive diagnostic phlebotomy ■ Disseminated intravascular coagulation
Increased red blood cell destruction	<ul style="list-style-type: none"> ■ Hemolytic anemia ■ Cold agglutinin disease
Decreased red blood cell production	<ul style="list-style-type: none"> ■ Treatment-induced myelosuppression ■ Renal impairment ■ Nutritional deficiencies ■ Anemia of chronic disease ■ Tumor infiltration of the bone marrow ■ Inherited genetic disorder (i.e., thalassemia) ■ Myeloid malignancy

Note. Based on information from Miller, 2010; National Comprehensive Cancer Network, 2017a.

TABLE 3.
TESTING PROCEDURES FOR ANEMIA IN PATIENTS WITH MULTIPLE MYELOMA

DIFFERENTIAL DIAGNOSIS	TESTS TO PERFORM
Hemolysis	<ul style="list-style-type: none"> ■ Direct antiglobulin test ■ Disseminated intravascular coagulation panel ■ Haptoglobin ■ Indirect bilirubin ■ Lactate dehydrogenase
Hemorrhage	<ul style="list-style-type: none"> ■ Stool guaiac ■ Endoscopy
Inherited disorder	Obtain thorough family history.
Myelodysplastic syndrome	Bone marrow biopsy
Myeloid malignancy	Bone marrow biopsy
Nutritional deficiency	<ul style="list-style-type: none"> ■ Iron, total iron-binding capacity, ferritin ■ Vitamin B₁₂ ■ Folate
Radiation-induced myelosuppression	Obtain medical history.
Renal dysfunction	Glomerular filtration rate less than 60 ml/minute/1.73 m ²

Note. Based on information from National Comprehensive Cancer Network, 2017a.

FIGURE 1.
PREVENTIVE MANAGEMENT OF ANEMIA FOR PATIENTS WHO REFUSE BLOOD TRANSFUSION

PRIOR TO INITIATION OF MYELOSUPPRESSIVE CHEMOTHERAPY

- Regard risk of anemia during treatment decision making.
- Supplement with daily folic acid and vitamin B₁₂.
- Coagulation abnormalities should be evaluated and corrected.
- Provide IV iron for treatment of iron deficiency.
- If appropriate, initiate erythropoiesis-stimulating agents in applicable patients.
- Use antifibrinolytic drugs for management of oral bleeding.
- Manage mucositis effectively.
- Incorporate proton pump inhibitors and stool softeners to decrease the risk of gastrointestinal bleeding.
- Suppress menses in applicable patients.

Note. Based on information from National Comprehensive Cancer Network, 2017a.

FIGURE 4.
CORRECTED CALCIUM LEVEL CALCULATION

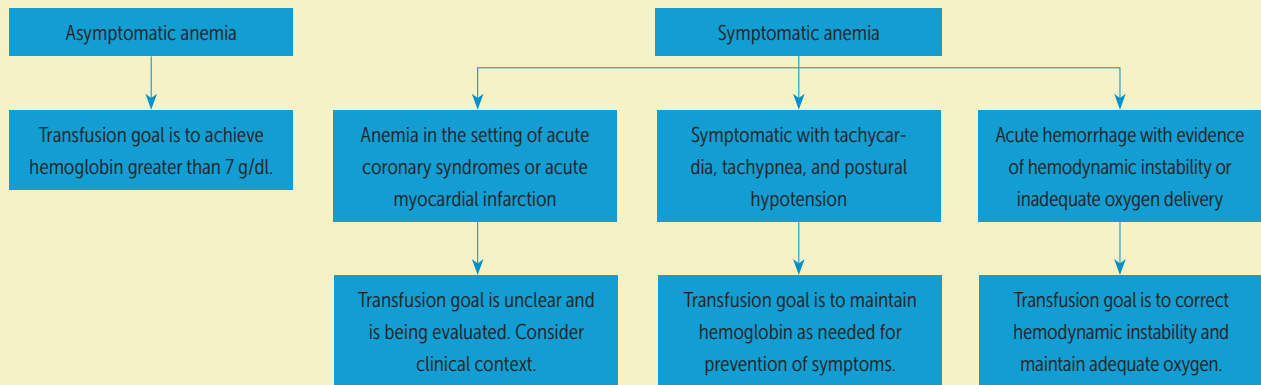
$$\text{Total calcium (mg/dl)} + 0.8 \times (4.0 - \text{serum albumin [g/dl]})$$

- Example: A person with a mildly elevated calcium level of 11 mg/dl and a normal albumin of 4.2 g/dl has a corrected ionized calcium level of 10.8 mg/dl.
- Example: A person with a mildly elevated calcium level of 11 mg/dl and a low serum albumin of 2.5 g/dl has a corrected ionized calcium level of 12.2 mg/dl.

Note. The formula will help determine the free or ionized calcium, will correct for low albumin, and give a more accurate assessment of the serum calcium level. The lower the albumin, the higher the corrected serum calcium.

Note. Based on information from Focus Information Technology, 2017; Kaplan, 2012a.

FIGURE 2.
INDICATIONS FOR RED BLOOD CELL TRANSFUSION IN PATIENTS WITH ANEMIA



Note. Based on information from National Comprehensive Cancer Network, 2017a.

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FIGURE 3.
PATIENT TIP SHEET: NEUTROPENIC
PRECAUTIONS, SIGNS, AND SYMPTOMS
OF INFECTION

PREVENTING INFECTION

- Clean your hands frequently and ask others to do the same.
- Shower or bathe daily.
- Use an unscented lotion to keep your skin moist.
- Avoid direct contact with pet waste.
- Wash your hands after touching animals.
- Use gloves when gardening.
- Brush your teeth and gums with a soft toothbrush.
- Avoid crowded places or people who are sick.
- Do not share food utensils and cups.
- Do not share personal items like toothbrushes.
- Keep household surfaces clean.
- Cook meat and eggs thoroughly.
- Wash raw fruits and vegetables.
- Get a seasonal flu vaccine.

SIGNS AND SYMPTOMS

- Fever of 100.4°F or higher for more than one hour or a one-time temperature of 101°F or higher
- Chills or sweats
- New cough or change in cough
- Shortness of breath
- Sore throat, new mouth sores, or nasal congestion
- Stiff neck
- Diarrhea or vomiting
- Burning, pain, or increased urination
- Unusual vaginal discharge
- New onset pain
- Redness, soreness, or swelling in any area, particularly around ports and surgical wounds
- Change in mental status

Note. Based on information from Centers for Disease Control and Prevention, 2017; Hughes et al., 2002.

FIGURE 5.
THREE-PRONGED APPROACH TO MEDICATION
MANAGEMENT OF SEVERE HYPERCALCEMIA
OF MALIGNANCY

CALCITONIN

- 4 IU/kg subcutaneous every 12 hours; dose may be increased to 6–8 IU/kg.
- Rapid but short acting
- Concomitant corticosteroid use can prolong effect.

HYDRATION

- 200–300 cc per hour infusion
- Goal is euvolemia to abrogate effects of nausea and renal dysfunction.
- Concomitant use of loop diuretic for renal and cardiac dysfunction

BISPHOSPHONATE THERAPY

- Zoledronic acid 4 mg or pamidronate 60–90 mg, via IV, every four weeks
- Denosumab 120 mg, subcutaneous, every four weeks. Not restricted by renal function.

Note. Based on information from Amgen Inc., 2016b; Faiman & Bilotti, 2014; National Comprehensive Cancer Network, 2017b; Pace, 2015; Thomas & Chung, 2016.

FIGURE 6.
HEALTH CONDITIONS, DRUGS, AND RISK
FACTORS FOR ACUTE KIDNEY FAILURE

HEALTH CONDITIONS

- Diabetes
- Hypertension
- Advanced age
- Rhabdomyolysis (muscle breakdown of creatinine, leading to increased blood creatinine)
- Dehydration (from decreased fluid intake, fluid losses, or loop diuretics)
- Hypercalcemia
- Progressive multiple myeloma disease or cast nephropathy (particularly light chains)
- Amyloid light chain amyloidosis or light chain deposition disease

DRUGS

- Nonsteroidal anti-inflammatory agents, including cyclooxygenase-2 inhibitors
- Aminoglycoside antibiotics
- Radio-contrast dyes or IV contrast agents
- Loop diuretics, other medications (such as ACE inhibitors)

OTHER FACTORS

- Increased intake of creatinine (high protein meal)
- Sepsis, infection

Note. Based on information from Faiman et al., 2011; Thomas et al., 2015.

TABLE 4. HEALTHCARE PROVIDER TIP SHEET: ASSESSMENT, INTERVENTION, AND PATIENT EDUCATION FOR HYPERCALCEMIA OF MALIGNANCY

METHOD	ASSESSMENT	INTERVENTION	PATIENT EDUCATION
Patient and caregiver interview	<ul style="list-style-type: none"> Has there been a change in mental status, physical function, or bathroom patterns? New onset of pain? Current medications including supplements? 	<ul style="list-style-type: none"> Interview the patient and the caregiver. If the patient is experiencing confusion, a caregiver may be able to provide more accurate answers. Discontinue vitamin D and calcium supplements. Review for thiazide or lithium use. 	<ul style="list-style-type: none"> Patient education should include the caregiver. Repeat patient education as the calcium level decreases and mental status improves.
Review of systems	<ul style="list-style-type: none"> General: increased fatigue, somnolence, lethargy Gastrointestinal/genitourinary: nausea, vomiting, constipation; increased urine output to no urine output Neurologic: restlessness, confusion, seizure activity Pain: acute onset or new pain indicating fracture 	<ul style="list-style-type: none"> Depending on degree of symptoms, patient may be at risk for falls, seizures, or aspiration. Reassurance and reorientation. Anti-emetics and stool softeners for gastrointestinal symptoms. Monitor for rectal bleeding and frequent assessment for acute abdominal pain indicating obstruction or ileus. Pain medication for comfort 	<ul style="list-style-type: none"> Explain symptoms related to increasing level of calcium; explain that acute pain may indicate new disease activity. Weight-bearing activity is important to reduce bone resorption. Provide rationale for instituting fall, seizure, or aspiration precautions.
Laboratory values	<ul style="list-style-type: none"> Ionized calcium greater than 12 mg/dl (correct for low albumin) Elevated creatinine from baseline Potassium Sodium Magnesium Complete blood count Echocardiogram changes Multiple myeloma disease workup 	<ul style="list-style-type: none"> Calcitonin with or without corticosteroids, hydration with or without loop diuretics, and bisphosphonates to reduce serum calcium Thiazide diuretics should be avoided. Hydrate to euvolemia to correct for dehydration and renal insufficiency Monitor for treatment-related sequelae, including first infusion reaction to bisphosphonates, fluid overload, hyperglycemia, and electrolyte imbalance. Hypercalcemia of malignancy is related to active disease; therefore, treat as indicated. 	<ul style="list-style-type: none"> Explain rationale for close monitoring, medication use, and the urgency of the medical situation. Educate regarding change in MM therapy as needed, including side effect monitoring and prevention.

Note. Based on information from Faiman & Bilotti, 2013; Kaplan, 2012a; Pace, 2015; Shane and Berenson, 2015.

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TABLE 5.
HEALTHCARE PROVIDER TIP SHEET: ASSESSMENT, INTERVENTION, AND PATIENT EDUCATION FOR SPINAL CORD COMPRESSION

METHOD	ASSESSMENT	INTERVENTION	PATIENT EDUCATION
Patient and caregiver interview	<ul style="list-style-type: none"> ■ Back pain: location, intensity, and duration ■ Sensory/motor changes ■ Weakness; paresthesia; changes in bowel, bladder, or sexual function ■ Review current medications and interventions already attempted. 	<ul style="list-style-type: none"> ■ Interview the patient and the caregiver. ■ Institute pain management and safety measures. 	<ul style="list-style-type: none"> ■ Patient education should include the caregiver.
Review of systems	<ul style="list-style-type: none"> ■ General: acute onset of back pain ■ Gastrointestinal/genitourinary: bladder or bowel incontinence or retention, sexual dysfunction ■ Neurologic: paresthesia, muscle weakness, progressive sensory/motor changes 	<ul style="list-style-type: none"> ■ Pain medication for comfort ■ Monitor and maintain bladder and bowel output. ■ Depending on degree of symptoms, patient may be at risk for falls. ■ Physical therapy and mobility, if no additional risk for further cord compromise 	<ul style="list-style-type: none"> ■ Explain symptoms related to spinal cord compression; explain that acute pain may indicate new disease activity. ■ Provide rationale for instituting fall precautions and mobility restrictions, if needed.
Diagnostic workup	<ul style="list-style-type: none"> ■ Magnetic resonance image of full spine ■ Multiple myeloma disease workup 	<ul style="list-style-type: none"> ■ Premedicate before magnetic resonance imaging for patients who are claustrophobic and for pain. ■ Spinal cord compression may be related to active disease; therefore, treat as indicated. ■ If radiation therapy, manage side effects related to field of radiation. ■ If surgery, postoperative care is needed. 	<ul style="list-style-type: none"> ■ Explain rationale for close monitoring and urgency of the medical situation. ■ Neurologic changes may improve with time. ■ Educate regarding change in multiple myeloma therapy as needed, including side effect monitoring and prevention.

Note. Based on information from Kaplan, 2012b.